Dear Colleagues,

With this last issue for 2007 we tried once again to gather recent news about Tinnitus and as one can notice there is a lot, even after selection. It is a good sign, more and more people get interested which will help us to find a cure. Our objective is to improve dissemination in order to assure that the information is easily available for everyone. The indicated chapters could help the reader to make his own preference choice.

An important achievement for our community is the edition, Progress in Brain Research, of Tinnitus: Pathophysiology and Treatment, by B.Langguth, G.Hajak, T.Kleinjung, A.Cacace and A.Moller. Following TRI’s annual meetings, it was decided to gather knowledge and dress a state of the art of the actual research in tinnitus. With the 50 chapters it covers different areas and demonstrates again that pluridisciplinarity is essential.

Finally we would like to take the opportunity to remind you that we appreciate your comments and suggestions in order to improve our work and we encourage all motivated persons to contact us.

Berthold Langguth       Benjamin Questier       Susanne Staudinger
American Tinnitus Association Grant Announcement

The American Tinnitus Association (ATA) invites you to submit a tinnitus-related grant - $300,000 maximum award.

Research Grant awards are for a maximum of $50,000 per year for up to 2 years, or a maximum of $100,000 per year for up to 3 years for exceptional projects.

ATA accepts proposals twice annually, by June 30th and December 31st.

ATA's Student Grant awards up to $10,000 for one year to PhD candidates and medical residents in the United States.

You can download an application from the ATA website at http://www.ata.org/research/apply.html

learn more about grants at http://www.ata.org/research/research_faq.html

Research Grant applicants may be from any country. Applications may be for tinnitus-related basic or clinical research. Grants applications will be peer-reviewed in a competitive process.

Please feel free to contact Amy Harris, Director of Research and Support, with any question: amy@ata.org or 800-634-8978 x218

Association for Research in Otolaryngology: TRC Request for Applications

The Tinnitus research Consortium invites applications for grants-in-aid on the following topics:

Behavioral Neurobiology of Tinnitus: Mechanisms of or Sites Associated with the Percept of or Reactions to Tinnitus

The Letter of Intent Receipt Date is December 15, 2007. Applications must be received by February 1, 2008. For more information, please visit the ARO website:

http://www.aro.org/announcements/announcements.html
Upcoming Meetings

Meetings exclusively dedicated to Tinnitus are marked red.

December 2007


When: December 1, 2007
Where: Poliklinik der Charité, Campus Charité Mitte, Berlin

Februar 2008

The Association for Research in Otolaryngology ARO

31st MidWinter Meeting:

When: February 16 - 21, 2008
Where: Phoenix Convention Center, Phoenix, Arizona, USA
Contact: Lisa Astorga, ARO Meeting Manager
E-Mail: lastorga@talley.com
Detailed information: [http://www.aro.org/mwm/mwm.html](http://www.aro.org/mwm/mwm.html)

April 2008

10th International Conference on Cochlear Implants and Other Implantable Auditory Technologies

When: April 10 - 12, 2008
Where: Manchester Grand Hyatt, San Diego, California, USA
E-Mail: ci@ci-2008.com

May 2008

Internationales Tinnitus-Symposium

10 Jahre Österreichische Tinnitus-Liga (ÖTL)

When: May 1 - 3, 2008
Where: Bildungszentrum Raiffeisenhof, Graz - Austria
Contact: Manfred Koller, President ÖTL
Phone: +43 (0)316/68 52 55 11 (Mrs Zettl, Mrs Haingartner)
Fax: +43 (0)316/68 52 55 99
E-Mail: koller-oetl@sime.com
Detailed information: [http://www.tinnitus.at/53409699a012fd601/index.html](http://www.tinnitus.at/53409699a012fd601/index.html)
May 2008

2nd International Symposium of the Politzer Society On Otosclerosis & Stapes Surgery
When: May 8 – 10, 2008
Where: Biarritz, France
Contact: Scientific secretariat Giesèle Bouissou, Service ORL - CHU Purpan TSA 40031, 31059 - Toulouse Cedex 9, France
Phone: +33 (0)561 77 77 04
Fax: +33 (0)561 49 36 44
E-Mail: bouissou.g@chu-toulouse.fr

June 2008

ICA 2008 XXIXth International Congress of Audiology
When: June 8 – 12, 2008
Where: Hong Kong
Contact: Ms Kate Kwan/ Ms Rachel Cheng, Room 2704, 27/F, C C Wu Building 302-308 Hennessy Road, Wanchai, Hong Kong
Phone: 852 2372 0090
Fax: 852 2372 0490
E-Mail: enquiry@ica2008.com

IXth International Tinnitus Seminars
When: June 15 - 18, 2008
Where: Göteborg, Sweden
Contact: Congrey Seden AB, Ref. Tinnitus 2008 P.O. Box 5078 402 22 Göteborg, Sweden
Phone: +46-31-708-6000
Fax: +46-31-708-6025
E-Mail: tinnitus2008@congrex.com
Detailed information: http://www.congrex.se/ITS2008

July 2008

CHHA-AMEC IFHOH Congress 2008 - A Global Community of Communication
When: July 2 – 6, 2008
Where: Sheraton Vancouver Wall Center
Contact: Congress Secretariat, 205-2415 Holly Lane, Ottawa, Ontario, CA, K1V 7P2
Phone: 1-800-263-8068 (in Canada) or 613-526-1584 (outside Canada)
Fax: 613-526-4718
E-Mail: congress2008@chha.ca
The 10th International Workshop on the Mechanism of Hearing

When:    July 27 – 31, 2008
Where:   Keele University, UK
Contact: Dr. N.P. Cooper
         School of Life Sciences
         Keele University
         Keele, Staffordshire
         ST5 5BG
         UK
Phone:   +44-1782-583056
Fax:     +44-1782-583055
E-Mail:  secretary@mechanicsofhearing.com
Detailed information:  http://www.mechanicsofhearing.com
Progress in Brain Research - Tinnitus: Pathophysiology and Treatment

On the idea and the effort of Aage Møller a considerably book about tinnitus could be published, which shows the wide and complex field of tinnitus treatment. It is also to the merit of Aage Møller that this book is published within the famous series Progress in Brain Research, which is a Series in Neuroscience, published by Elsevier, Amsterdam, that combines the advantages of both journals and books; it is available for purchase in a similar way as books in general, and Pub Med covers the contents of Progress in Brain Research in the same way as journals are covered, providing easy access to the contents of the different volumes.


The book, published November, 2007, consists of 50 chapters written mainly by the contributors to the first meeting of TRI, held in Regensburg 2005. A few other contributions were added to provide coverage of aspects that were not represented at the Regensburg meeting.

This volume of Progress in Brain Research covers a wide range of basic and clinical research together with clinical experience of treatment of tinnitus using various methods, many of which are new. Researchers and clinicians who have written the 50 chapters of the book are from many different disciplines of science and medicine, suggesting a new approach to the enormously difficult and multifaceted problems related to tinnitus and its treatment. These chapters also reflect discussions and the outcome of small group meetings at the Regensburg conference and which brought many new aspects on tinnitus and its treatment to light. The importance of interdisciplinary research was emphasized in the organization of the Regensburg meeting and one of its purposes was to promote such an interdisciplinary approach to tinnitus. This way of approaching tinnitus and its treatment is reflected in many of the chapters in the book.

Treatment with drugs is discussed in several chapters. Behavioral treatments and treatments using electrical stimulation of the skin, the ear or structures of the central nervous system are discussed. The efficacy of these different treatments is discussed in several chapters of the book.

Since most forms of tinnitus are disorders of the nervous system some of the chapters concerns the neuroscience of tinnitus. Other chapters concern how such knowledge can be used in treatment of tinnitus. The similarities between some forms of tinnitus and pain, especially central neuropathic pain, are discussed in other chapters. The last chapter is a “Consensus for tinnitus patient assessment”.

The content of the book has been organized and edited to provide a comprehensive coverage of tinnitus and its treatment aimed at a broad readership of both researchers in basic science and clinical disciplines as well as clinicians who treat patients with tinnitus.

Aage Møller

In the following you find the abstracts of the different chapters

CONTENTS

Tinnitus: Pathophysiology and Treatment

Edited by: Berthold Langguth, Göran Hajak, Tobias Kleinjung, Anthony Cacace and Aage Møller

Foreword
Berthold Langguth, Göran Hajak, Tobias Kleinjung, Anthony Cacace and Aage Møller

SECTION I

INTRODUCTION

1. Tinnitus: Presence and future
A R Møller

School of Behavioral and Brain Sciences, University of Texas at Dallas, GR41, P.O. Box 830688, Richardson, TX 75083-0688, USA.

Tinnitus has many forms; it can be caused by sounds generated in the body (objective tinnitus) that reaches the ear through conduction in body tissue, but much more common is the tinnitus that occurs
without any physical sound reaching the ear. Such tinnitus (subjective tinnitus) is a phantom sensation, where abnormal neural activity is generated in the ear, the auditory nerve, or the central nervous system. There are many forms of subjective tinnitus and it can occur with different severity. Subjective tinnitus often occurs in connection with hearing loss such as may occur after exposure to loud sounds (noise), or after administration of drugs such as certain antibiotics, but often no cause can be found. Tinnitus often occurs together with presbyscusis and it can occur in deafness. Tinnitus is a part of the symptoms of Ménière’s disease and individuals with vestibular Schwannoma almost always have tinnitus. Some individuals who have severe tinnitus hear sounds as distorted and some have hyperacusis (reduced tolerance to sounds) or phonophobia (fear of sounds). Tinnitus can be referred to one ear, or both ears, or to a location inside the head. The anatomical location of the physiological abnormality of chronic subjective tinnitus, however, is rarely in the ear but more often in the auditory nervous system. There are indications that the pathophysiology of unilateral and bilateral tinnitus is different. There is considerable evidence that expression of neural plasticity plays a central role in the development of the abnormalities that cause many forms of chronic subjective tinnitus. Expression of neural plasticity can change the balance between excitation and inhibition in the nervous system, promote hyperactivity, and it can cause reorganization of specific parts of the nervous system or redirection of information to parts of the nervous system not normally involved in processing of sounds (non-classical or extralemniscal pathways). Since there are many kinds of subjective tinnitus, search for a (single) cure for tinnitus is futile. Testing of new treatments is hampered by the fact that it is not possible to distinguish between different forms of tinnitus for which different treatments may be effective.

SECTION II
PATHOPHYSIOLOGY

2. Pathophysiology of tinnitus
J Eggermont
Departments of Physiology & Biophysics, and Psychology, University of Calgary, Calgary, AB, Canada.
Guided by findings from neural imaging and population responses in humans, where tinnitus is well characterized, several morphological and physiological substrates of tinnitus in animal studies are reviewed. These include changes in ion channels, receptor systems, single unit firing rate, and population responses. Most findings in humans can be interpreted as resulting from increased neural synchrony.

3. The role of neural plasticity in tinnitus
A R Møller
School of Behavioral and Brain Sciences, University of Texas at Dallas, GR41, PO Box 830688, Richardson, TX 75083-0688, USA.
There is considerable evidence that expression of neural plasticity plays a central role in the development of the abnormalities that cause many forms of tinnitus. Expression of neural plasticity can change the balance between excitation and inhibition, promote hyperactivity, and cause re-organization of specific parts of the nervous system or redirection of information to parts of the nervous system not normally involved in processing of sounds (such as the non-classical, or extralemniscal pathways). The strongest promoter of expression of neural plasticity is deprivation of input, which explains why tinnitus often occurs together with hearing loss or injury to the auditory nerve.

4. Tinnitus and Pain
A R Møller
School of Behavioral and Brain Sciences, University of Texas at Dallas, GR41, PO Box 830688, Richardson, TX 75083-0688, USA.
Tinnitus has many similarities with the symptoms of neurological disorders such as paresthesia and central neuropathic pain. There is considerable evidence that the symptoms and signs of some forms of tinnitus and central neuropathic pain are caused by functional changes in specific parts of the central nervous system and that these changes are caused by expression of neural plasticity.
The changes in the auditory nervous system that cause tinnitus and the changes in the somatosensory systems that cause central neuropathic pain may have been initiated from the periphery, i.e. the ear or the auditory nerve for tinnitus and receptors and peripheral nerves in the body for pain. In the chronic condition of tinnitus and pain, abnormalities in the periphery may no longer play a role in the pathology, but the tinnitus is still referred to the ear and central neuropathic pain is still referred to the location on the body of the original pathology. In this chapter we will discuss specific similarities between tinnitus and pain, and compare tinnitus with other phantom disorders. Since much more is known about pain than about tinnitus, it is valuable to take advantage of the knowledge about pain in efforts to understand the pathophysiology of tinnitus and find treatments for tinnitus.

5. The Darwinian plasticity hypothesis for tinnitus and pain
D De Ridder
Department of Neurosurgery, University Hospital Antwerp, Wilrijkstraat 10, 2650 Edegem, Belgium.

We present the hypothesis that expression of neural plasticity is a form of adaptation based on natural selection, where cells or cell groups deprived of sensory input actively go and look for information in order to survive. The Darwinian model of brain plasticity can explain the symptomatology induced by deprivation of input which was not well explained by classical plasticity without contradicting pertinent data from the neurophysiological, neuroanatomical, functional neuroimaging, and clinical literature. Applying the concept of Darwinian plasticity to sensory plasticity that causes symptoms and signs of disease might lead to the development of new treatments for deprivation of input induced symptomatology. We will use results from the application of electrical and magnetic stimulation of the auditory and the somatosensory cortices for treatment of tinnitus and for alleviating some forms of pain in support of the Darwinian hypothesis about neural plasticity. We will also review the literature regarding physiological and anatomical, as well as imaging data that support the existence of this hypothetical form of plasticity.

6. The relevance of spontaneous activity for the coding of the tinnitus sensation
N Weisz, K Dohrmann, T Elbert
INSERM U821, Brain Dynamics and Cognition, Lyon, France.

In this chapter we will present support for the hypothesis that synchronous neuronal activity of cell assemblies within the auditory cortex could be the underlying neural code of tinnitus. Such synchronous activity is reflected in the ongoing oscillatory activation pattern that can be recorded non-invasively using MEG and EEG techniques. We conclude that such an oscillatory model of tinnitus can explain many different observations regarding tinnitus.

7. Applications of magnetic resonance spectroscopy to tinnitus research: Current issues and future perspectives
A T Cacace
The Neurosciences Institute and Advanced Imaging Research Center, Department of Neurology, Albany Medical College, 47 New Scotland Avenue, Albany, NY, USA.

Conducting tinnitus research on humans poses challenges for investigators because of its subjective nature, the complexities involved in establishing underlying generator sites, the diversity of potential causes, and the inherent difficulties in dissociating reactive changes in the central nervous system (CNS), secondary to peripheral hearing loss, from those effects that may be due to tinnitus. One area of considerable interest concerns biomarker development, particularly in the areas of metabolism and biochemistry. Establishing a biomarker or a profile of metabolic and neurobiochemical constituents of tinnitus-related activity within the CNS could be of considerable importance for understanding the fundamental properties of this disorder. Therefore, in an effort to gain greater insight into mechanisms of tinnitus, magnetic resonance spectroscopy (MRS) is being proposed as one of the several tools that can address pertinent issues. Apart from its long-standing use in analytical chemistry and physics, MRS is also being applied with greater frequency in the neurosciences to gain insight into human brain
function under normal and pathological states. By considering the history of this method and advances made to date, MRS has the potential to: (1) identify unique in vivo metabolic and neurobiochemical biomarkers associated with tinnitus in specific regions of the CNS, (2) clarify and track disease pathogenesis, (3) monitor short and long-term treatment effects, and (4) serve as a tool in testing of drugs that may be used in treatment of tinnitus.

8. Functional imaging of chronic tinnitus: the use of positron emission tomography
P Eichhammer, G Hajak, T Kleinjung, M Landgrebe, P Sand, B Langguth
Department of Psychiatry, University of Regensburg, Universitaetsstrasse 84, 93053 Regensburg, Germany.
Recent advances in functional imaging have opened new possibilities for understanding tinnitus. Especially, positron emission tomography (PET) has been increasingly used in the last two decades to identify cortical networks, which are involved in the generation of various forms of chronic tinnitus. PET studies have confirmed that the anatomical location of the anomalies that cause many forms of tinnitus are regions of the brain that are normally involved in auditory processing as well as regions engaged in emotional processing. These findings have contributed to the development of new more causally oriented treatment strategies. In particular, identification of increased activity of the auditory cortex by PET has prompted the use of focal brain stimulation techniques such as electrical or transcranial magnetic stimulation in treatment of tinnitus. PET studies that map distinct neurochemical pathways and receptors by the use of specific ligands may in the future provide new possibilities for pharmacologically based treatment of some forms of tinnitus.

9. The role of the dorsal cochlear nucleus
J Kaltenbach
Department of Otolaryngology, Head and Neck Surgery, Wayne State University School of Medicine, Detroit, MI 48201, USA.
It has been hypothesized that tinnitus percepts may arise, in part, from increases in spontaneous neural activity in the central auditory system. The DCN is the lowest central auditory nucleus where this hyperactivity is observed, and it is most prominent following exposure to intense sound or ototoxic insult. Efforts to develop effective treatments for tinnitus will probably benefit from a better understanding of the mechanisms underlying the induction of hyperactivity in the DCN. This chapter will summarize the evidence linking tinnitus to altered activity in the DCN and review some of the likely mechanisms underlying the induction of hyperactivity following injury to the ear.

10. Neural mechanisms underlying somatic tinnitus
S Shore
Kresge Hearing Research Institute, Department of Otolaryngology, University of Michigan, 1301 E Ann St., Ann Arbor, MI 48109, USA; Department of Molecular and Integrative Physiology, University of Michigan, 1301 E Ann St., Ann Arbor, MI 48109, USA; Department of Biomedical Engineering, University of Michigan, 1301 E Ann St., Ann Arbor, MI 48109, USA.
Somatic tinnitus is clinically observed modulation of the pitch and loudness of tinnitus by somatic stimulation. This phenomenon and the association of tinnitus with somatic neural disorders indicate that neural connections between the somatosensory and auditory systems may play a role in tinnitus. Anatomical and physiological evidence supports these observations. The trigeminal and dorsal root ganglia relay afferent somatosensory information from the periphery to secondary sensory neurons in the brainstem, specifically, the spinal trigeminal nucleus and dorsal column nuclei, respectively. Each of these structures has been shown to send excitatory projections to the cochlear nucleus. Mossy fibers from the spinal trigeminal and dorsal column nuclei terminate in the granule cell domain while en passant boutons from the ganglia terminate in the granule cell domain and core region of the cochlear nucleus. Sources of these somatosensory-auditory projections are associated with proprioceptive and cutaneous, but not nociceptive, sensation. Single unit and evoked potential recordings in the dorsal cochlear nucleus indicate that these pathways are physiologically active.
Stimulation of the dorsal column and the cervical dorsal root ganglia elicits short- and long-latency inhibition separated by a transient excitatory peak in DCN single units. Similarly, activation of the trigeminal ganglion elicits excitation in some DCN units and inhibition in others. Bimodal integration in the DCN is demonstrated by comparing responses to somatosensory and auditory stimulation alone with responses to paired somatosensory and auditory stimulation. The modulation of firing rate and synchrony in DCN neurons by somatosensory input is physiological correlate of somatic tinnitus.

11. Neural Network Models of Tinnitus
F T Husain
Brain Imaging and Modeling Section, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bldg. 10, Rm 8S235D, MSC 1407, 9000 Rockville Pike, Bethesda, MD 20892, USA.

In this chapter we review the relatively recent effort on the part of neuroscientists to use computational neural network modeling to investigate the neural basis of subjective tinnitus. There are advantages and challenges in using a modeling framework to understand this complex auditory disorder. The foremost challenge to modeling a subjective condition such as tinnitus is the evaluation of the occurrence of tinnitus in the model. We propose comparing measures of the model’s activities (simulated neuronal activity, behavioral activity, or neuroimaging activity) with experimental data obtained from studies of tinnitus in humans and animals; strong agreement with experimental data will provide support for the validity of the simulation of tinnitus in a particular model. A major advantage of neural network modeling is that it allows experimentation not possible in animals. Models make it possible to evaluate the contribution of different neural mechanisms affecting tinnitus in a principled manner. A model makes predictions that can be tested by experiments thus leading to the designing of focused experiments. We review several neural models of tinnitus and discuss published findings from simulations using these models. We conclude with a proposed scheme for investigating tinnitus that combines neural network modeling with brain imaging experiments.

12. Salicylate-induced tinnitus: molecular mechanisms and modulation by anxiety
J-L Puel, M Guitton
Inserm U583 and University Montpellier 1, INM-Hôpital Saint Eloi, 80 rue Augustin Fliche, 34295 Montpellier cedex 5, France.

Tinnitus is a pathology, which severely impairs the quality of life, and for which no efficient therapy exists. One reason is the lack for clear understanding of the molecular mechanisms of this pathology. For example, the anatomical site and the molecular pathways responsible for the generation of tinnitus are still under debate. This is due, in part, to the difficulty to induce and measure tinnitus in animals. This paper summarizes the recent discoveries provided by the use of salicylate as a model of tinnitus. The first is the demonstration that salicylate acts at the periphery by activating on cochlear NMDA receptors that are not “normally” implicated in the transmission of auditory message to the brain. The second discovery is the clear demonstration that strong relationships exist between anxiety and perception of tinnitus. Interestingly, application of NMDA antagonists onto the round window membrane abolished tinnitus, even in animals receiving a treatment with the anxiogenic serotonergic agent meta-chlorophenylpiperazine (mCPP). In addition to classical psychotherapeutic treatments, targeting cochlear NMDA receptors, by local infusion of drugs into the middle ear to reach the cochlea, may represent a promising therapeutic strategy to cure incapacitating tinnitus, even in depressed or chronically anxious patients.

13. Behavioral tests for the detection of tinnitus in animals
J Turner
Department of Surgery/Otolaryngology Head and Neck Surgery, Southern Illinois University School of Medicine, Springfield, IL 62794-9629, USA; Department of Psychology, Illinois College, Jacksonville, IL 62650, USA.

The fact that so little is currently known about the pathophysiology of tinnitus is no doubt partly due to the relatively slow development of an animal model. Not until the work of Jastreboff et al. (1988a, b)
did tinnitus researchers have at their disposal a method of determining whether their animals experienced tinnitus. Since then, a variety of additional animal models have been developed. Each of these models will be summarized in this chapter. It is becoming increasingly clear that in order to study tinnitus effectively, researchers need some verification that a drug, noise exposure or other manipulation is causing tinnitus in their animals. As this review will highlight, researchers now have a variety of behavioral options available to them.

SECTION III
EPIDEMIOLOGY

14. Genetics of chronic tinnitus
P Sand, B Langguth, T Kleinjung, P Eichhammer
Department of Psychiatry, University of Regensburg, Regensburg, Germany.
Susceptibility to chronic tinnitus is highly variable and of particular interest when it comes to defining strategies for prevention and treatment. While several rare monogenic disorders have been described that are associated with tinnitus, the genetic underpinnings of the more common forms of the syndrome are still poorly understood. The present article incorporates recent advancements in the field, including the epidemiology of tinnitus in subjects with neuropsychiatric illness, and highlights pilot studies of candidate genes.

15. Hyperacusis, sound annoyance and loudness hypersensitivity in children
C Barros Coelho, T G Sanchez, R S Tyler
Department of Otolaryngology of the University of São Paulo Medical School, São Paulo, Brazil.
The objective of the present study was to estimate the prevalence of hyperacusis among school-aged children. We define hyperacusis as lowered loudness discomfort levels (LDL) associated with an abnormal annoyance to sounds. We used questionnaires, interviews, and estimates of LDL in a study of 506 children from 5 to 12 years of age from 15 different schools. Participants with LDL in the lowest 5th percentile were classified as having loudness hypersensitivity; an abnormal annoyance to sounds if they responded „yes“ to the question „Are you bothered by any kind of sounds or noise?“ could describe the sound, and were able to identify at least 10 sounds from a list of 20 as being annoying. Phonophobia was defined as a fear of sound. Children with LDL in the lowest 5th percentile typically had LDLs lower than 90dB HL; 42% of the participants in this group were bothered by sounds and 3.2% had hyperacusis. Fifty percent of the participants with hyperacusis had tinnitus and mild hearing loss in the left ear was an associated risk factor. Phonophobia was experienced by 9% of the children. It is concluded that hyperacusis in children is prevalent, and should be considered in clinical examinations.

16. Tinnitus in children and associated risk factors
C Barros Coelho, T G Sanchez, R S Tyler
Department of Otolaryngology of the University of São Paulo Medical School, São Paulo, Brazil.
The objective of the study was to estimate the prevalence of tinnitus and explore the risk factors in school-aged children age 5-12 years. For that we asked „Do you hear a noise inside your ears/head?“ and required children to be able to describe the sounds perceived and their location. We refer to this as tinnitus sensation. Additionally, we asked „Does it bother or annoy you?“ and „In what situations does it bother or annoy you?“ to determine if this experience was bothersome. We refer to this as tinnitus annoyance. Associations to demographic and audiological factors were studied. Approximately 37% of children reported tinnitus sensation and 17% reported tinnitus annoyance. Related factors were age, hearing loss, and history of noise exposure, motion sickness and hyperacusis. Estimates of the prevalence of tinnitus clearly depend on how tinnitus is defined. In the present study, participants were asked „Do you hear a noise inside your ears/head?“ but we did not make distinctions regarding the duration or character of their tinnitus. Our estimates of tinnitus annoyance were also broad, and did not attempt to quantify the degree of annoyance.
17. Can somatic testing identify subjects whose tinnitus can be suppressed by specific treatments?
R A Levine, E Nam, Y Oron, J R Melcher
Eaton-Peabody Laboratory, Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, MA 02114-3096, USA.

Studies have established that the somatosensory system of the upper cervical region and head can be intimately involved in tinnitus. Tinnitus can arise directly from a disorder of the head and upper neck through activation of the somatosensory system. "Somatic testing" (a series of strong muscle contractions of the head and neck) can (1) modulate the tinnitus percept of approximately 80% of people with ongoing tinnitus, and (2) elicit a sound percept in approximately 50% of people with no tinnitus. These somatic phenomena are equally prevalent among people with or without functioning cochlea. Likely neural pathways underlying both the induction and modulation of tinnitus have been revealed in animal studies. Because somatic influences are fundamental to the operation of the auditory system, in general, and to tinnitus, in particular, somatic testing should be incorporated into all evaluations of tinnitus (1) to improve understanding of the role of the somatosensory system in any individual and (2) to identify subgroups of tinnitus patients who may respond to a particular treatment modality (as has already been shown for the tinnitus associated with temporomandibular disorder). Our clinical experience and review of reports of treatment modalities directed toward the somatosensory system supports the hypothesis that these modalities can benefit individuals with symmetric hearing thresholds but asymmetric widely fluctuating tinnitus. Treatment modalities involving the somatosensory system should be re-assessed by targeting this tinnitus subgroup.

18. Myofascial trigger points: another way of modulating tinnitus
C A Rocha, T G Sanchez
Department of Otolaryngology of the University of São Paulo School of Medicine, Av. Padre Pereira de Andrade, 545/174-F, São Paulo, SP, Brazil 05469-000.

Tinnitus is a multifaceted symptom that may have many causes (otologic, neurological, metabolic, pharmacological, vascular, musculoskeletal and psychological) several of which often occur in the same patient. Tinnitus can often be modulated by different kinds of stimuli. In this chapter we describe the results of a study of modulation of tinnitus from stimulation of myofascial trigger points (MTPs). MTPs are small hypersensitive areas in palpable taut bands of skeletal muscles found in patients with the myofascial pain syndrome where stimulation of MTPs causes local and referred pain. We found a strong correlation between tinnitus and the presence of MTPs in head, neck and shoulder girdle (p<0.001). In 56% of patients with tinnitus and MTPs, the tinnitus could be modulated by applying digital compression of such points, mainly those of the masseter muscle. The worst tinnitus was referred to the side that had the most MTPs (p<0.001); Compression of the trigger point on the same side as the tinnitus was significantly more effective than the opposite side in six out of nine of the studied muscles. Compression of MTPs was most effective in patients who have had chronic pain earlier in the examined areas.

19. Assessment of temporomandibular and cervical spine disorders in tinnitus patients
A Bjorne
Vertigo, Tinnitus and Pain Unit, Ystad Hospital, Sturegatan 2A, SE-271 31 Ystad, Sweden.

In treating patients with temporomandibular joint (TMJ) dysfunction it was noticed that tinnitus and vertigo were common in such patients and there was also muscular tension in jaw and neck. During treatment of these patients it was also noted that injection of lidocaine in a jaw muscle (m. pt. lat.) reduced not only their muscular problems but also that the tinnitus was reduced while the local anesthetic was active.
Evaluation of 39 patients with disabling tinnitus, and all suffered from tinnitus, revealed that 10 of them had bilateral tinnitus and TMJ disorders revealed that pain in the face, temples or jaw occurred often among these patients. Many of such patients had also symptoms of cervical spine disorders, head, neck and shoulder pain, and limitations in side bending and rotation were also frequent complaints. One-third of these patients could influence tinnitus by jaw movements and 75% could trigger vertigo by head or neck movements. Treatment of jaw and neck disorders in 24 patients with Ménière's disease had a beneficial effect on not only their episodic vertigo but also on their tinnitus and aural fullness. At the 3-year follow-up, intensity of all symptoms were significantly reduced (p<0.001).

20. Tinnitus severity, depression and big five personality traits
B Langguth, P Eichhammer, G Hajak, T Kleinjung, P Sand
Department of Psychiatry, University of Regensburg, Regensburg, Germany.
A growing number of self-report measures for the evaluation of tinnitus severity has become available to research and clinical practice. This has led to an increased awareness of depression and personality as predictors of tinnitus severity in addition to loudness and other psychoacoustic measures. However, the net impact of personality dimensions on tinnitus ratings has not been investigated when the effect of depressed mood is controlled. In the present study, we demonstrate the role of the big five personality traits, ‘Neuroticism’, ‘Extraversion’, ‘Openness’, ‘Agreeableness’, and ‘Conscientiousness’, in affecting scores on two standard instruments for grading tinnitus-related complaints, the tinnitus handicap inventory (THI), and the tinnitus questionnaire (TQ). When 72 individuals with chronic tinnitus were examined, ‘Agreeableness’ negatively correlated with THI scores (p=.003), whereas the anxiety trait ‘Neuroticism’ correlated both with depressive symptomatology (p<.001) and TQ scores (p=.028), but not with THI ratings (n.s.). In addition to confirming the established roles of trait anxiety and depression, low ‘Agreeableness’ was thus identified as a novel predictor of tinnitus severity on the THI.

21. Insomnia in Tinnitus patients
T Crönlein, B Langguth, P Geisler, P Eichhammer, G Hajak
Sleep Disorders and Research Center, Department of Psychiatry and Psychotherapy, University of Regensburg, Universitätsstr. 84, 93053 Regensburg, Germany.
Sleep problems are common in individuals with tinnitus but it is not known if they can be seen as a reaction to the acoustic percept of tinnitus disturbing normal sleep, or if there are common causes. Sleep problems further impair the quality of life of individuals with tinnitus and the impairment correlates with the severity of the tinnitus. However the nature of the relationship between tinnitus and disturbed sleep in individuals with tinnitus is not clearly understood. Preliminary studies suggest that chronically disturbed sleep (insomnia) in individuals with tinnitus that is not caused by organic disorders exists unrelated to the tinnitus. We studied the relationship between tinnitus and insomnia in a retrospective sleep study of 13 hospitalized patients with insomnia and tinnitus. Patients with sleep apnea, periodic leg movements, or a severe psychiatric disorder were excluded. We collected physiologic sleep measures (EEG, EOG, EMG, and respiration) and subjective sleep information from a morning protocol during two nights. We also obtained information about performance in sustained attention tasks and the scores of self-rated depression scale and self-rated daytime-tiredness scale. Thirteen age- and sex-matched inpatients with primary insomnia who did not have tinnitus served as controls. There were no significant differences between the physiologic data obtained in patients with tinnitus and in the controls. Both groups had low sleep efficiency but the patients with both insomnia and tinnitus had longer subjective sleep latencies than insomnia patients without tinnitus (controls). No differences were found in sustained attention tasks, subjective daytime tiredness, and depression rating scores between the two groups. Similarities between the results from these two groups suggest that sleep specific psychotherapeutic methods, which are established for treating insomnia, should be further developed for the use in patients with insomnia and tinnitus.
SECTION IV
TREATMENT

22. Tinnitus treatment - State of the Art
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Clinical and scientific research has opened up a wide range of options for treating patients with tinnitus. Many of these options are sophisticated and are delivered through specialist tinnitus clinics. However tinnitus is a very common complaint. Most patients with tinnitus need to be satisfactorily cared for by front line clinicians. This chapter describes how one clinician who has looked after some thousands of patients with tinnitus looks after them now. It describes the model I use to explain tinnitus to the patient and develop a management plan. It describes how I assess patients with tinnitus. It lists the treatment options available. It describes the management provided at the first (and usually only) encounter. It stresses the value of a written report. It describes further management and onward referral. It describes my use of drugs in those patients for whom the tinnitus remains overwhelming.

A. Drug treatment

23. Drug treatment for tinnitus
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Many of the drug treatments that are presently in use for tinnitus are aimed at either the cochlea, e.g. using intratympanic injections of gentamicin, dexamethasone or lidocaine, or the CNS using systemic delivery. Earlier benzodiazepines and anticonvulsants have been used and more recently, antidepressants have been introduced, partly in an attempt to treat the emotional aspect of tinnitus. The fact that there are many different forms of tinnitus with different and often multiple causes and that the pathophysiology is poorly understood, are obstacles to finding effective treatments. This situation has been exacerbated by the lack of clinical trials to formally test even some of the most commonly used drugs, as well as a lack of preclinical studies to investigate novel agents. It is suggested that the animal models of tinnitus that have been developed could be used to screen potential anti-tinnitus drugs as a preliminary step before conducting clinical trials.

24. Antidepressants for treatment of tinnitus
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Antidepressants are commonly prescribed for tinnitus. Research thus far provides some support for that treatment, but the literature also raises concerns because tinnitus is a side effect of antidepressant medication. In this chapter, four published double blind placebo-controlled trials of antidepressants for tinnitus are reviewed. Explanations for the discrepant results are offered, including that antidepressants appear to work best for tinnitus patients who are depressed or anxious, who have more severe tinnitus or who are treated for a longer time with an adequate dose of medication. Possible mechanisms of action are reviewed, with serotonergic and antimuscarinic mechanisms appearing to be the most important. At this time there is no indication that one specific type of antidepressant is more likely to lead to tinnitus as a side effect, or have a beneficial effect on tinnitus. Given SSRIs are tolerated better, these antidepressants have advantages over tricyclic antidepressants and should be used as a first line of treatment.
25. Acamprosate
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Acamprosate, a drug used to treat alcohol dependence, was first reported as a potential treatment for tinnitus in 2005. The drug may improve tinnitus by a dual mechanism of action, acting both as a glutamate antagonist and as a GABA agonist. It is suggested that its action may be both on the ear and the nervous system.

26. Zinc as a possible treatment for tinnitus
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Zinc is an essential trace element present in all organs, tissues, fluids, and secretions of the body and it is widely distributed in the central nervous system, including the auditory pathway in synapses of the VIII nerve and in the cochlea. Zinc is an essential component of Cu/Zn superoxide dismutase (SOD) and in certain enzymes and it is important for proper function of the immune system. Three possible mechanisms have linked zinc to tinnitus; cochlear Cu/Zn SOD activity, synaptic transmission, and depression. Evidences in the literature suggest prevalence rates of zinc deficiency in individuals with tinnitus from 2 to 69%, affecting elderly individuals more frequently. Four among five small studies indicate that administration of zinc has a beneficial effect on tinnitus but these results still have to be confirmed in clinical trials with larger samples using a cross-over design, validated tinnitus handicap questionnaires, measurements of tinnitus magnitude, and accessing the coexistence of other symptoms such as depression, phonophobia, and hyperacusis.

27. Gabapentin
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Several lines of evidence suggest that loss of central inhibition after deprivation of input from the ear (peripheral deafferentation) may be one cause of chronic tinnitus. Aging and acoustic trauma, the two most common causes of peripheral damage to the auditory system, each decrease input to central auditory structures. Loss of input to tonic inhibitory systems would release excitatory structures from inhibition regulation. The increased activity resulting may be interpreted by more rostral structures in the auditory pathway as tinnitus. Down-regulation of gamma-amino butyric acid (GABA), a major inhibitory neurotransmitter of the central auditory pathway, is a potential mechanism for the loss of inhibition. Both animal studies and human clinical trials implicate loss of inhibition, and specifically loss of GABA function, in the development of acoustic trauma-induced tinnitus.

28. Lidocaine: neurobiological targets and effects on the auditory system
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Lidocaine, a local anesthetic and anti-arrhythmic agent, is also known both as a tinnitus- and as a pain-suppressing drug. The sites of action in tinnitus suppression are in the cochlea as well as in the central auditory nervous system. In the present study, audiological and brain imaging studies in humans were used to identify the anatomical structure where lidocaine has its action on tinnitus. Molecular studies were used to elucidate the action of lidocaine on the cellular level. Various ion channels and receptors (e.g. voltage-gated Na(+), K(+) and Ca(2+) channels, glutamate, GABA, glycine and vanilloid receptors), found in the auditory system and possibly connected to tinnitus, are affected by lidocaine. Identification of molecular structures involved in expression of neuroplasticity in the auditory system in tinnitus and modeling the binding sites of local anesthetics could lead to the design of subtype-specific inhibitors that could provide new pharmacological targets for treatment.
29. Antioxidants, metals, vitamins and herbal remedies in tinnitus therapy
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The use of complementary and alternative medicine (CAM) is very popular in western countries and several CAM products are often used by individuals with tinnitus with or without medical guidance. CAM pharmacological approach to tinnitus today is mainly based on vitamins and minerals (dietary supplements), antioxidants, and herbal medications. Despite the popularity of CAM products, the evidence regarding their efficacy against tinnitus is in general scarce and their potential toxic effects are often underestimated or even neglected. In this paper the available literature on the efficacy of dietary supplements, antioxidants, and herbal medications against tinnitus is reviewed, and some of the major potential toxic effects are discussed. It is concluded that the use of CAM products in tinnitus therapy in general lack substantial scientific support, and that these substances are probably not clinically effective either. However, it is difficult to draw clear-cut conclusions regarding CAM pharmacological approach to tinnitus. In fact, the subjective nature of tinnitus and the reported variability in patient’s response to therapy indicate that several non-pharmacological factors may be influencing drug effects, with the placebo effect playing a major role. Nevertheless, in view of the potential harm that may occur from inappropriate use of CAM products, physicians need to be aware of their principal characteristics with particular emphasis on toxicity and possibilities of interaction with prescription drugs.

30. Melatonin
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Melatonin is a neurohormone that is secreted by the pineal gland and known to impact the sleep-wake cycle. Melatonin is regarded to be a safe and natural sleep aid. Since many people with tinnitus suffer sleep disturbance, melatonin has been studied as a therapeutic agent for tinnitus. A review of the literature suggests that melatonin has a beneficial effect on tinnitus, especially for patients with sleep disturbance, but it does not seem to modify the strength or frequency of the tinnitus.

31. Botulinum toxin for the treatment of somatic tinnitus
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Subjective tinnitus is an auditory sensation experienced in the absence of external or internal acoustic stimuli. It causes significant morbidity and can progress to a chronic debilitating condition. Somatic tinnitus is tinnitus that can be modulated by stimulation of the somatic sensory system. It occurs because of interactions between the auditory and the somatosensory system that may occur at several levels of the central nervous system. In the present chapter, we discuss how botulinum toxin can improve tinnitus and discuss the mechanism of its action, and how it relates to its effects on chronic pain.

B. Hearing Devices

32. Hearing aids for the treatment of Tinnitus
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Clinical evidence shows that the use of hearing aids in tinnitus patients provides two benefits: it makes the patient less aware of the tinnitus and it improves communication by reducing the annoying sensation that sounds and voices are masked by the tinnitus. Hearing loss reduces stimulation from external sounds resulting in increased awareness of tinnitus and deprivation of input may change the function of structures of the auditory pathways. Tinnitus is often caused by expression of neural plasticity evoked by deprivation of auditory input. With hearing aid amplification, external sounds can provide sufficient activation of the auditory nervous system to reduce the tinnitus perception and it may elicit expression
of neural plasticity that can reprogram the auditory nervous system and thereby have a long-term beneficial effect on tinnitus by restoring neural function. To obtain the best results, hearing aids should be fitted to both ears, use an open ear aid with the widest amplification band, and disabled noise reducing controls. In some cases a combination device would be preferable. The conditions required in order to obtain good results include not only the use of devices, but above all, their adaptation to the needs of the single patient, by counseling and customization. Wearing the hearing aid must become second nature to the patient even though it is only one element of the therapy.

33. Cochlear Implants
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The clinical observation that multichannel intra-cochlear cochlear implants have a suppressive effect on tinnitus in profoundly deaf patients is supported by many published studies. Whilst there are problems with that literature, specifically in the way that tinnitus outcomes are reported, the finding of tinnitus benefit is consistent. New developments in this area include the use of functional imaging to investigate tinnitus suppression by cochlear implant stimulation and consideration of a reported worsening effect on tinnitus of binaural implantation. Following work on hearing aids, it is suggested that optimization of the benefit of monaural cochlear implantation on tinnitus in a tinnitus-specific electrode configuration might include the use of a low knee point compression algorithm and disabling directional microphone function: these strategies are potentially also of benefit in patients whose tinnitus results in sleep disturbance. Opportunities for stimulation strategies for tinnitus suppression that bypass speech processing are also identified.

C. Electrical and magnetic stimulation
34. Transcranial magnetic stimulation (TMS) for treatment of chronic tinnitus - clinical effects
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Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive method used to induce electrical current in the brain through impulses of strong magnetic fields applied externally. The technique can relieve tinnitus by modulating the excitability of neurons in the auditory cortex to decrease the hyperexcitability that is associated with generating the neural activity that causes some form of tinnitus. This chapter will review clinical studies using rTMS for the treatment of tinnitus.

35. TMS for treatment of chronic tinnitus – neurobiological effects
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Results of neurophysiological and neuroimaging studies suggest that some forms of chronic tinnitus can be regarded to be „hyperexcitability syndromes", caused by abnormal focal brain activity. Low frequency repetitive magnetic stimulation (rTMS) is an efficient method to selectively reduce the abnormally increased activity in distinct cortical areas. An increasing amount of clinical data suggest that low frequency rTMS might be an effective therapy that is directed at the cause of some forms of chronic tinnitus. To further explore the underlying neurobiological mechanisms we investigated the effect of rTMS on cortical excitability in healthy human subjects using the protocol, which has been successfully used for the treatment of tinnitus. We determined different parameters of motor cortex excitability (resting motor threshold, RMT; active motor threshold, AMT; short intracortical inhibition, ICI; short intracortical facilitation, ICF; and the duration of the cortical silent period, CSP) before and after 5 days of low frequency rTMS (2000 stimuli/day at 110% of RMT) over the left auditory cortex. Five sessions of low frequency rTMS resulted in a significant prolongation of the CSP. All other signs of cortical excitability that we studied remained unchanged. These findings suggest, that low frequency rTMS may evoke long-term depression (LTD)-like effects resulting in enhancement of subcortical inhibition.
36. Electrical Stimulation of Auditory and Somatosensory Cortices for Treatment of Tinnitus and Pain
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The efficacy of electrical stimulation of the auditory cortex using extradural implanted electrodes for treatment of tinnitus was studied in 12 patients suffering tinnitus. The effect of similar stimulation of the somatosensory cortex for treatment of neuropathic pain was studied in five patients. It was shown that patients with pure tone type of tinnitus experienced a significant 97% suppression on average while those who had noise type tinnitus only had non-significant 24% suppression. All patients with pain experienced a significant reduction of their pain (using a visual analog scale), and in four out of five it was clinically relevant, i.e., the patient is really helped by it. It is concluded that electrical stimulation of sensory cortices can be effective treatments of severe unilateral tinnitus and unilateral neuropathic pain in selected patients. The results suggest that similar pathophysiological mechanisms underlie some forms of these phantom sensations, and therefore, similar treatment such as electrical stimulation of the respective sensory cortices can suppress tinnitus and pain.

37. Trans-electrical Nerve Stimulation (TENS) for somatic tinnitus
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The somatic tinnitus syndrome includes those forms of tinnitus that are associated with a somatic disorder involving the head and upper neck. It has been suggested that physiological mechanisms where interactions occur between the somatosensory and auditory systems are the etiology for that kind of tinnitus. Trans-electrical nerve stimulation (TENS) of areas of skin close to the ear increases the activation of the dorsal cochlear nucleus through the somatosensory pathway and may augment the inhibitory role of this nucleus on the CNS and thereby ameliorate tinnitus. In a prospective descriptive study of 26 patients with the probable diagnosis of somatic tinnitus we found that TENS could improve the tinnitus in 46% of the participants (23% did not hear it anymore, and in 23% its intensity was reduced). VAS scores improved from 6.5 to 6.0 after 2 weeks of treatment (p<0.01). Patients used TENS at home for 2h, once per day during 2 weeks (alternating ramped burst, 150pps, with pulse duration of 100mus, amplitude 0-60mA; average TENS intensity was 27mA). Intermittent “typewriter” type of tinnitus was the most responsive. Somatic tinnitus without otologic disease had better response than tinnitus associated to otological causes (p=0.047).

D. Surgical treatment
38. Microvascular decompression operations
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Moving a blood vessel off the intracranial portion of the auditory nerve can successfully cure some individuals with specific forms of subjective tinnitus. This operation, known as microvascular decompression (MVD) is in general use to treat other hyperactive disorders such as hemifacial spasm (HFS) and trigeminal neuralgia (TGN) where the operation has a success rate of approximately 85%. MVD for tinnitus has lower success rate. MVD operations have also been used to treat some forms of vestibular disorders, disabling positional vertigo (DPV). In a study of treatment of a selected group of 72 patients with severe tinnitus and signs of change in the conduction properties of the auditory nerve 13 (18.2%) had total relief from tinnitus after MVD, 16 (22.2%) had marked improvement, 8 slight improvement and 33 (45.8%) no improvement. Two patients became worse (2.8%). There were 40 men and 32 women in the study group and there was considerable difference in the success rate for men and women. Fifty-five percent of the women and 29% of men showed relief or improvement.
The success of the operation depended on the length of time the participants in the study had had their tinnitus and it was best for those who had had tinnitus for less than 3 years. The success rate for bilateral tinnitus was much lower than for unilateral tinnitus.

39. Tinnitus in microvascular compression of the cochleovestibular nerve: A surgical pathophysiological approach to ABR changes
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Some forms of tinnitus are associated with a blood vessel being in close contact with the auditory nerve near its entrance into the brainstem. The outcome of operations for tinnitus, moving the blood vessel off the nerve (microvascular decompression operations, MVD) is less successful than microvascular decompression operations for other vascular conflict syndromes (hemifacial spasm, HFS, and trigeminal neuralgia, TGN). No generally accepted criteria exist for the selection of candidates for MVD for tinnitus. A pathophysiological approach for interpreting auditory brainstem response (ABR) changes is proposed as a basis for selection of tinnitus patients for the MVD operation. We followed changes in the ABR and the tinnitus in 78 patients with unilateral tinnitus, who had indications of having vascular conflicts of the eighth nerve. In 18 of these patients a blood vessel was removed of the auditory nerve and in 9 of these a correlation could be made between preoperative and postoperative clinical changes and ABR changes. In this retrospective study we found abnormalities in the amplitude of peak II and the interpeak latency (IPL) I-III of the ABR that were related to the duration of their tinnitus and its intensity. While no ABR changes could be detected during the first 2 years, after that period a decrease of the amplitude of peak II occurred, and a prolongation the IPL of peak I-III occurred in patients whose peak II had disappeared. The rate of IPL I-III increase slows down after 10 years. IPL I-III prolongation correlates with ipsilateral hearing loss at tinnitus frequency and worsens in time. This correlates with a worsening of the tinnitus associated with the worsening of the IPL I-III. Tinnitus frequency correlates to the frequency of maximal hearing loss and the more the hearing loss at tinnitus frequency the worse the tinnitus. Postoperative improvement of tinnitus correlated with postoperative improvement of peak II and postoperative improvement of hearing loss at the tinnitus frequency correlated with postoperative IPL I-III improvement. It is concluded that interpreting ABRs from a pathophysiological point of view can be beneficial for surgeons performing MVDs for tinnitus, especially with regard to timing of the surgery and interpretation of symptom presentation.

E. Cognitive Behavioral Therapy

40. Tinnitus Retraining Therapy
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Tinnitus retraining therapy (TRT) is a specific clinical method based on the neurophysiological model of tinnitus described by Jastreboff (Jastreboff, P.J. (1990). Neurosci. Res., 8: 221-254). The method is aimed at habituation of reactions evoked by tinnitus, and subsequently habituation of the tinnitus perception. Several other methods have been suggested for habituation of tinnitus, but in TRT two components that strictly follow the principles of the neurophysiological model of tinnitus are implemented and necessary: (1) counseling, aimed at reclassification of tinnitus to a category of a neutral signals and (2) sound therapy, aimed at weakening tinnitus-related neuronal activity as suggested by Jastreboff and Hazell (Jastreboff, P.J. and Hazell, J.W.P. (2004). Cambridge University Press, Cambridge). This chapter outlines the theoretical basis of TRT as well as comments on the clinical outcome of the use of TRT for different kinds of tinnitus.
41. Tinnitus activities Therapy  
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Tinnitus Activities Treatment includes counseling of the whole person, and considers individual differences and needs. We consider four areas: thoughts and emotions, hearing and communication, sleep, and concentration. We typically use Partial Masking Sound Therapy, with a noise or music set to the lowest level that provides relief. A picture-based approach facilitates engagement of the patient, and provides thorough and structured counseling. We engage the patient by including homework and activities to demonstrate understanding and facilitate progress.

42. An Overview of Sound Therapies  
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Many people with bothersome (suffering) tinnitus notice that their tinnitus changes in different acoustical surroundings, it is more intrusive in silence and less profound in the sound enriched environments. This observation led to the development of treatment methods for tinnitus utilizing sound. Many of these methods are still under investigation in respect to their specific protocol and effectiveness and only some have been objectively evaluated in clinical trials. This chapter will review therapies for tinnitus using sound stimulation.

43. Object identification and attention training for tinnitus treatment  
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We hypothesize that abnormal attention and auditory scene analysis contribute to the severity of tinnitus and that the incongruence between tinnitus and normal auditory perception is responsible for its resistance to traditional sound-based habituation therapies. New methods of treatment using auditory and visual attention training are proposed as a means to augment counseling and sound therapies for tinnitus management. Attention training has been demonstrated to improve an individuals' ability to attend to relevant sounds while ignoring distracters. The main aim of the current study was to determine the effectiveness of structured Auditory Object Identification and Localization (AOIL) tasks to train persons to ignore their tinnitus. The study looked at the effects of a 15-day (30min/day) take-home auditory training program on individuals with severe tinnitus. Pitch-matched tinnitus loudness levels (TLLs), tinnitus minimum masking levels (MMLs) and measures of attention were compared before and after the auditory training. The results of this study suggest that short-duration auditory training which actively engages attention, object identification and which requires a response from participants, reduces tinnitus. There was a greater effect on pitch-matched tinnitus MMLs than on actual TLLs. The reason(s) for this are unclear, although a correlation found between changes in MMLs and improvements in the ability to shift attention may be one underlying reason. Although this study followed a small number of participants over a limited time-span, it is believed that the training and accompanying model are a promising approach to investigate and treat some forms of tinnitus.

44. An extinction training for tinnitus  
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Recent accounts of tinnitus development and maintenance assign an important role to central mechanisms. Residual inhibition is a frequent phenomenon in individuals with tinnitus, and refers to the fact that tinnitus can temporarily be reduced by presenting sounds or noises that inhibit tinnitus for a limited time even after termination of the sound. This kind of stimulation-induced inhibition of tinnitus could potentially be used for treatment by combining it with additional interventions to enhance the extinction of tinnitus.
Here we propose a training program aimed at the amplification and the extension in time of residual inhibition as well as the extinction of negative emotional responses to the tinnitus. The program is tested alone or in combination with a pharmacological intervention that is aimed at decreasing central hyperactivity. Treatment effects are assessed by tinnitus questionnaires, electroencephalographic measures (reduction in the amplitude of the N(100) component of the event-related potential as an indicator of habituation) as well as skin conductance responses to 1000Hz tones or tinnitus-like tones. This training is an example of the use of centrally acting and mechanism-oriented tinnitus treatments.

45. Auditory discrimination therapy (ADT) for tinnitus management: clinical trial
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Auditory discrimination training (ADT) designs a procedure to increase cortical areas responding to trained frequencies (damaged cochlear areas with cortical misrepresentation) and to shrink the neighboring over-represented ones (tinnitus pitch). In a prospective descriptive study of 27 patients with high frequency tinnitus, the severity of the tinnitus was measured using a visual analog scale (VAS) and the tinnitus handicap inventory (THI). Patients performed a 10-min auditory discrimination task twice a day during one month. Discontinuous 4kHz pure tones were mixed randomly with short broadband noise sounds through an MP3 system. After the treatment mean VAS scores were reduced from 5.2 to 4.5 (p=0.000) and the THI decreased from 26.2% to 21.3% (p=0.000). Forty percent of the patients had improvement in tinnitus perception (RESP). Comparing the ADT group with a control group showed statistically significant improvement of their tinnitus as assessed by RESP, VAS, and THI.

46. Neurofeedback for treating tinnitus
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Many individuals with tinnitus have abnormal oscillatory brain activity. Led by this finding, we have developed a way to normalize such pathological activity by neurofeedback techniques (Weisz et al. (2005). PLoS Med., 2: e153). This is achieved mainly through enhancement of tau activity, i.e., oscillatory activity produced in perisylvian regions within the alpha frequency range (8-12Hz) and concomitant reduction in delta power range (0.5-4Hz). This activity is recorded from electrodes placed on the frontal scalp. We have found that modification of the tau-to-delta ratio significantly reduces tinnitus intensity. Participants who successfully modified their oscillatory pattern profited from the treatment to the extent that the tinnitus sensation became completely abolished. Overall, this neurofeedback training was significantly superior in reducing tinnitus-related distress than frequency discrimination training.

47. Residual Inhibition: Psychoacoustic properties, mechanisms, and applications
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Following offset of an appropriate masking stimulus, tinnitus may remain suppressed for a period, typically less than a minute. This phenomenon is known as „residual inhibition“ (RI). This chapter reviews the psychoacoustic properties of RI and their relation to hearing impairment, tinnitus spectra, and the spectra of masking stimuli. RI is also contrasted with tinnitus suppression produced by repetitive transcranial magnetic stimulation (rTMS) the cortical effects of which do not require the ear to reach the brain. Although the two procedures act in different ways, both may reduce tinnitus by interrupting abnormal synchronous activity among networks of neurons that generate tinnitus. Therapies that induce tinnitus suppression by these methods have been reported to reduce tinnitus distress by processes that are not well understood.
SECTION V
ASSESSMENTS OF TREATMENT RESULTS

48. Considerations for the design of clinical trials for tinnitus
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We review a few issues related to clinical trials for treating patients with tinnitus, including the study population, design, choice of measurement variables, and some new approaches to data analysis. We emphasize the importance of being aware of different subgroups of tinnitus patients, and that patients who have had tinnitus for less than 6 months could be more amenable to treatment than patients who have had their tinnitus for a longer period. We distinguish the tinnitus itself, from the reactions to the tinnitus. When the treatment is intended to reduce the tinnitus, we recommend measuring the magnitude of the tinnitus. We provide arguments and data to support the use of the Tinnitus Handicap Questionnaire as a measure of the reaction to the tinnitus. We suggest that the current quality of life measures are not valid for measuring lifestyle effects of alleviating tinnitus. Because tinnitus likely has different subgroups, and because tinnitus affects people differently, we believe data analysis should emphasize individuals, not groups. A clinically meaningful effect should represent a valid and reliable statistical change for an individual.

49. Tinnitus assessment instruments
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There is a wide range of assessment techniques for tinnitus, but no consensus has developed concerning how best to measure either the presenting features of tinnitus or the effects of tinnitus treatments. Standardization of reliable and valid tinnitus measures would provide many advantages including improving the uniformity of diagnostic and screening criteria between clinics and facilitating comparison of treatment outcomes obtained at different sites. This chapter attempts to clarify issues involved in developing self-report questionnaires for the assessment of tinnitus. While the tinnitus questionnaires that are currently available provide valuable information on which to base diagnostic and screening decisions, they were not originally developed in such a way as to maximize their sensitivity to treatment-related changes in tinnitus. As a result, their construct validity for measuring treatment benefit has not received appropriate attention. In this paper, special emphasis is devoted to the use of effect sizes as an estimate of the ability of questionnaires (and their individual items) to measure changes associated with treatment. We discuss the criteria relevant to evaluating the effectiveness of a questionnaire for diagnostic purposes vs. for treatment-evaluation purposes, and we present a detailed illustration of how the various criteria have been applied in a recent questionnaire development effort.
APPENDIX

Consensus for tinnitus patient assessment and treatment outcome measurement: Tinnitus Research Initiative meeting, Regensburg, July 2006


(Regensburg, Konstanz and Mannheim, Germany, Auckland, New Zealand, Volta Redonda and São Paulo, Brasil, Ystad, Sweden, Albany, NY, Portland, OR, Boston, MA, Richardson, TX and George-town, WA, USA, Milan and Padova, Italy, Antwerp, Belgium, Madrid, Spain, Paris, France and Bogota’, Colombia)

There is widespread recognition that consistency between research centres in the ways that patients with tinnitus are assessed and outcomes following interventions are measured would facilitate more effective co-operation and more meaningful evaluations and comparisons of outcomes. At the first Tinnitus Research Initiative meeting held in Regensburg in July 2006 an attempt was made through workshops to gain a consensus both for patient assessments and for outcome measurements. It is hoped that this will contribute towards better cooperation between research centres in finding and evaluating treatments for tinnitus by allowing better comparability between studies.
Recently published literature

I Epidemiology

Alexithymia, depression and tinnitus in elderly people.

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Objectives: Tinnitus is known to have an association with depression and other psychiatric disorders. As part of a larger epidemiological survey, we evaluated the associations among tinnitus, depression and alexithymia in a group of elderly people.

Methods: A survey of hearing loss, audiological rehabilitation and associated morbidity in a senior population was conducted in Turku, Finland. The study sample consisted of 583 participants aged between 70 and 85 years. The Toronto Alexithymia Scale (TAS-20) was used to measure alexithymia, whereas the 13-item version of the Beck Depression Inventory was used to measure depression; the subjective experience of tinnitus was queried with a questionnaire.

Results: Depression had a clear association with subjectively annoying tinnitus. Contrary to expectations, the TAS-20 score did not correlate with the severity of tinnitus. In fact, the highest TAS-20 scores were found among the subjects who had tinnitus but did not find it to be subjectively annoying. No significant association between high TAS-20 scores and hearing loss was found

Conclusion: Although we found an association between TAS-20 scores and the presence of tinnitus, alexithymia does not seem to be helpful in explaining tinnitus annoyance among elderly people.

The use of hearing protection devices by older adults during recreational noise exposure.

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A population-based study to assess the use of hearing protection devices by older adults during noisy recreational activities was performed. The population-based Epidemiology of Hearing Loss Study was designed to measure the prevalence of hearing loss in adults residing in Beaver Dam, Wisconsin. The use of hearing protection devices during noisy recreational activities was assessed by performing three examinations over a period of 10 years (1993-1995, no. of participants (n) = 3753, aged 48-92 years; 1998-2000, n = 2800, aged 53-97 years; 2003-2005, n = 2395, aged 58-100 years). The recreational activities included hunting, target shooting, woodworking/carpentry, metalworking, driving loud recreational vehicles, and performing yard work using either power tools or a chain saw. The prevalence of using hearing protection devices during any of these activities increased with time (9.5%, 15.0%, and 19.9% at baseline, 5 years, and 10 years, respectively). However, the use of hearing protection devices remained low for most activities. Those under the age of 65 were twice as likely to use hearing protection devices during noisy activities than were older adults. Men, those with a hearing handicap, and those with significant tinnitus were more likely to use hearing protection devices. Smokers and the less educated were less likely to use hearing protection devices. The results demonstrated that many adults expose themselves to potentially damaging recreational noise, leaving them at risk for hearing loss.
II Pathophysiology

Pathways involved in somatosensory electrical modulation of dorsal cochlear nucleus activity.
Brain Res. 2007 Sep 29; [Epub ahead of print]

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Our recent study has shown that somatosensory electrical stimulation may be useful to modulate sound-induced hyperactivity in the dorsal cochlear nucleus (DCN), a neural correlate of certain forms of tinnitus. Somatosensory electrical stimulation induced both suppressive and excitatory effects on neural activity in the DCN of both control and tone-exposed animals. However, it is unclear what neural pathways underlie the somatosensory electrical stimulation-induced effects on DCN activity. To address this issue, we conducted c-fos immunocytochemistry using hamsters and mapped neural activation in both auditory and non-auditory structures following transcutaneous electrical stimulation of the basal part of the pinna. We also conducted tracing experiments to investigate the anatomical relations between the DCN and structures that showed a significant increase in the number of Fos-positive neurons as a result of electrical stimulation. Electrical stimulation of the pinna induced significant increases in the number of Fos-positive neurons in the DCN, spinal trigeminal nucleus (Sp5), dorsal raphe nucleus (DR) and locus coeruleus (LC). Results of tracing experiments indicate that the DCN received inputs from the Sp5, DR and LC. The above results suggest that modulation of DCN activity through somatosensory electrical stimulation may involve both direct pathways via the Sp5 and indirect pathways via the DR and LC. Therefore, relieving tinnitus through somatosensory electrical stimulation may require manipulations of both auditory and non-auditory functions.

Evaluation of cochlear function in patients with tinnitus using spontaneous and transitory evoked otoacoustic emissions.

Montoya FS, Ibargüen AM, Del Rey AS, Fernández JM.

Objective: The aim of this paper has been to investigate the cochlear function and the basic properties of otoacoustic emissions (OAEs) in patients with tinnitus using Spontaneous Otoacoustic Emissions (SOAEs) and Transitory Evoked Otoacoustic Emissions (TEOAEs).

Materials and methods: We have analyzed the incidence, amplitude and spectral content of hearing thresholds, SOAEs and TEOAEs in a sample of 44 ears. We have measured incidence, intensity, frequency, number of peaks and amplitude of emission and their variability across frequency range from 500 to 5000 Hz. A correlation was determined between the OAEs results and the results obtained using hearing thresholds.

Results: We have not found statistically significant differences at 500, 1000, 2000, 4000 and 8000 Hz frequencies neither at mean hearing thresholds between the sample of ears with tinnitus and the sample of ears without tinnitus. SOAEs were only present in 1 of the 44 ears tested (2.27%) and it was a 17 dB SPL amplitude peak at 2770 Hz frequency. TEOAEs, however, were displayed in some frequency in all the ears. We have compared TEOAEs parameters between the sample of ears with tinnitus and the sample of ears without tinnitus in 500, 1000, 2000, 4000 and 5000 Hz frequencies, and we have only found statistically significant differences at 4000 Hz frequency, \( p = 0.02 \). Comparison of TEOAEs parameters between ears with tinnitus and ears without tinnitus in the same patient have only found statistically significant differences at 4000 Hz frequency, \( p = 0.011 \). In both cases there were not statistically significant differences at 500, 1000, 2000 and 5000 Hz frequencies nor at mean TEOAEs amplitudes for every group.

Conclusions: We have not found significant relations between tinnitus and OAEs registration.
Age-Related Hearing Loss in C57BL/6J Mice has both Frequency-Specific and Non-Frequency-Specific Components that Produce a Hyperacusis-Like Exaggeration of the Acoustic Startle Reflex.

J Assoc Res Otolaryngol. 2007 Oct 19; [Epub ahead of print]

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Auditory brainstem-evoked response (ABR) thresholds were obtained in a longitudinal study of C57BL/6J mice between 10 and 53 weeks old, with repeated testing every 2 weeks. On alternate weeks, acoustic startle reflex (ASR) amplitudes were measured, elicited by tone pips with stimulus frequencies of 3, 6, 12, and 24 kHz, and intensities from subthreshold up to 110 dB sound pressure level. The increase in ABR thresholds for 3 and 6 kHz test stimuli followed a linear time course with increasing age from 10 to 53 weeks, with a slope of about 0.7 dB/week, and for 48 kHz a second linear time course, but beginning at 10 weeks with a slope of about 2.3 dB/week. ABR thresholds for 12, 24, and 32 kHz increased after one linear segment with a 0.7 dB slope, then after a variable delay related to the test frequency, shifted to a second segment having slopes of 3-5 dB/week. Hearing loss initially reduced the ASR for all eliciting stimuli, but at about 6 months of age, the response elicited by intense 3 and 6 kHz stimuli began to increase to reach values about three times above normal, and previously subthreshold stimuli came to elicit vigorous responses seen at first only for the intense stimuli. This hyperacusis-like effect appeared in all mice but was especially pronounced in mice with more serious hearing loss. These ABR data, together with a review of histopathological data in the C57BL/6 literature, suggest that the non-frequency-specific slow time course of hearing loss results from pathology in the lateral wall of the cochlea, whereas the stimulus-specific hearing loss with a rapid time course results from hair cell loss. Delayed exaggeration of the ASR with hearing loss reveals a deficit in centrifugal inhibitory control over the afferent reflex pathways after central neural reorganization, suggesting that this mouse may provide a useful model of age-related tinnitus and associated hyperacusis.

[The role of cochlear neurotransmitters in tinnitus.]
[Article in German]
HNO. 2007 Oct 19; [Epub ahead of print]

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Pathologic changes in the cochlear neurotransmission, e.g. as a result of intensive noise exposure or ototoxic drugs, can be a factor in the development of tinnitus. The efficiency of inhibitory and excitatory neurotransmitters may then be modulated at the switching points. Glutamate is the most important afferent neurotransmitter within the inner ear. A massive glutamate release induced by cochlear damage may result in excitotoxicity and irrevocable cell death. Efferent cochlear neurotransmitters include dopamine, gammaaminobutyric acid (GABA), acetylcholine (ACH) and serotonin. Dopamine and GABA are inhibitory transmitters that may protect the cochlea from excitotoxicity. ACH, like GABA, reduces the stiffness of the outer hair cells and increases their motility. Serotonin is a neuromodulator of the cholinergic and GABAergic innervation within the cochlea and can inhibit glutamatergic impulses. Our understanding of neurotransmission in the cochlea has been extended by advances in molecular biology, which has given rise to new approaches in the treatment of tinnitus. As there are several types of tinnitus, differing in aetiology and development, our present challenge is to achieve precise identification of the cause in individual cases of tinnitus.
Physiology and phenomenology of tinnitus: Implications for treatment.

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We examine a contrast in understanding tinnitus and how this impacts on treatment approaches. First, a physiological account of tinnitus is described based on disinhibition and cortical remapping following injury at the receptor level, the analog for tinnitus being the 'phantom limb pain' phenomenon. Secondly, an experimental model of tinnitus is reviewed that relies on inference from conditioning animal behaviour. Arising from this, a role for conditioning in people distressed by tinnitus has been proposed, based on the unfounded premise that, for humans, tinnitus is a neutral stimulus, the distress being due to association with other stressful events. We critique this because we believe it influences approaches to tinnitus treatment. Finally, the phenomenology of tinnitus in the human case is analysed, with its nature illuminated via a series of distinctions with hearing impairment. Tinnitus can be intrinsically stressful for some people. Understanding this emphasizes the need to involve concepts and treatment in the area of clinical psychology. A flexible coalition between clinical audiologists and clinical psychologists is proposed as fruitful for tinnitus and related rehabilitation.

Inhibition of voltage-gated channel currents in rat auditory cortex neurons by salicylate.
Neuropharmacology. 2007 Aug 28; [Epub ahead of print]

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Salicylate is a medicine for anti-inflammation with a side effect of tinnitus. To understand the mechanisms of tinnitus induced by salicylate, we studied the effects of salicylate on voltage-gated ion channels and action potential firing rates in freshly dissociated rat pyramidal neurons in auditory cortex (AC) using the whole-cell patch technique. We found that salicylate reduced the voltage-gated sodium current (I(Na)), the delayed rectifier potassium current (I(K(DR))) and the L-type voltage-gated calcium current (I(Ca,L)) in concentration-dependent manner. An amount of 1mM salicylate shifted the steady-state inactivation curve of I(Na) negatively by about 5mV, shifted the steady-state activation and inactivation curve of I(K(DR)) negatively by approximately 14mV and 17mV, respectively, and shifted the steady-state activation curve of I(Ca,L) negatively by about 10mV. 1mM salicylate significantly increased the action potential firing rates, ultimately. From the results, we speculated that through affecting the voltage-gated ion channels in AC, an important position in auditory system, salicylate increased the firing rate of neurons and enhanced neuronal excitability on the one hand, increased the excitatory transmitters release and reduced the inhibitory transmitter release on the other hand, thus finally induced tinnitus.

Otoacoustic emissions, ear fullness and tinnitus in the recovery course of sudden deafness.
Auris Nasus Larynx. 2007 Sep 26; [Epub ahead of print]

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Objective: This study aimed to investigate how the symptoms of ear fullness, tinnitus and otoacoustic emissions (OAE) change in relation to the recovery course of pure tone audiometry thresholds (PTA) in sudden deafness (SD).
Methods: This study analyzed follow-up data on ear fullness, tinnitus and otoacoustic emissions of eight SD patients with good hearing improvement (Group A) and eight SD patients with poor hearing improvement (Group B) in an attempt to elucidate the behavior of these symptoms in their recovery course. This study was done until there was no change in the PTA for more than 1 week and hearing recovery was no longer expected.

Results: All patients from both groups had ear fullness and tinnitus in association with the onset of SD. However, these symptoms improved only in Group A, showing a significant relationship between PTA recovery and the improvement of ear fullness annoyance (P<0.05), presence of tinnitus (P<0.01), improvement in tinnitus loudness (P<0.01) and in tinnitus annoyance (P<0.01). No patients (Group A or B) had OAE responses at their first examination. In Group A, OAE responses appeared simultaneously with improvement of hearing levels in five patients (63%) and it appeared later than hearing levels improvement in the other three patients (37%) from Group A. No patient from Group B showed OAE response on follow-up.

Conclusion: SD patients with good hearing improvement (Group A) tended to have OAE responses and the sensations of the ear fullness and tinnitus improved almost simultaneously with hearing level improvement. Their PTA improvement occurred primarily in the low to mid frequencies, with high frequencies showing less recovery. When hearing recovery was not full, OAEs did not reappear for these frequencies. Patients with poor hearing improvement tended to have absent OAEs and persistent ear fullness and tinnitus.
well monitored hemodynamic conditions. This led to observe that the prevalence of this symptom, regardless of audiological features, was increased under “aggressive” antihypertensive therapy as well as in particularly severe degree of heart decompensation. These data represent a first step and encourage in searching for a profile of subject who could be more prone to the development of tinnitus with respect to the normal population, even in absence of pathological conditions. With this aim, echocardiography is thought to be able to yield useful informations in addition to standard and ambulatory blood pressure monitoring, in order to obtain a better definition of the correlations between cardiovascular function (and related changes) and inner ear insufficient perfusion.

**Acoustic injury and TRPV1 expression in the cochlear spiral ganglion.**

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Acoustic trauma not only produces temporary and permanent hearing loss but is a common cause of chronic tinnitus. Recent work indicated a possible role for the transient receptor potential channel vanilloid subfamily type 1 (TRPV1) in modulating the effects of cochlear injury. In our research, we investigated the effects of acoustic damage on TRPV1 expression in spiral ganglion neurons of adult rats. After exposing them unilaterally to noise, we extracted cochleas and processed the spiral ganglion for TRPV1 expression at four posttrauma intervals (2 hours, 24 hours, 12 days, and 16.9 months). We measured TRPV1 immunodensity in the apical, middle, and basal turns of the cochlea. We found a significant interaction (p = .039) between posttrauma interval and regional cochlear receptor expression: For survival intervals between 24 hours and 2 weeks, TRPV1 density increased in all cochlear regions; at the longest survival interval (16.9 months), TRPV1 density was dramatically reduced in the basal region. We also psychophysically tested the long-survival subjects, which showed evidence of 20-kHz tonal tinnitus. These results suggest that TRPV1 may participate after cochlear injury in a signal cascade that is responsible for the neuroplastic events leading to tinnitus and hyperacusis.

**Eyes as fenestrations to the ears: a novel mechanism for high-frequency and ultrasonic hearing.**

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Intense airborne ultrasound has been associated with hearing loss, tinnitus, and various nonauditory subjective effects, such as headaches, dizziness, and fullness in the ear. Yet, when people detect ultrasonic components in music, ultrasound adds to the pleasantness of the perception and evokes changes in the brain as measured in electroencephalograms, behavior, and imaging. How does the airborne ultrasound get into the ear to create such polar-opposite human effects? Surprisingly, ultrasound passes first through the eyes; thus, the eye becomes but another window into the inner ear.
Facial palsy and fallopian canal expansion associated with idiopathic intracranial hypertension.

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Objective: Describe neurotologic findings associated with idiopathic intracranial hypertension (IIH).
Study design: Retrospective.
Setting: Tertiary referral center.
Patients: Case of IIH (>250 mm water) presenting with unilateral facial palsy and enlargement of the fallopian canal on computed tomography and magnetic resonance imaging.
Intervention(s): Oral acetazolamide, corticosteroids, and cerebrospinal fluid drainage.
Main outcome measure(s): Intracranial pressure measurement, cranial nerve examination, audiometry, and symptom assessment.
Results: Audiometry revealed asymmetric sensorineural hearing loss. Enlargement of the fallopian canal with cerebrospinal fluid was evident on imaging studies. Partial resolution of IIH symptoms was achieved.
Conclusion: IIH is an enigmatic disease entity. Increased intracranial pressure usually presents with headache and pulsatile tinnitus and is occasionally associated with cranial neuropathies. Abducens palsy is most common, producing diplopia. Cranial nerve involvement is often asymmetric, producing false localizing signs. Facial paralysis is an uncommon sequela of IIH. Treatment of IIH consists of reducing intracranial pressure. Corticosteroids are recommended for treatment of facial paralysis.

Future thinking in tinnitus patients.

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Objective: The purpose of the study was to investigate future thinking in a group of tinnitus patients. It was predicted that participants in the tinnitus group would report fewer positive future events.
Methods: A cross-sectional design was used. Two groups of participants completed the test session: tinnitus patients (n=20) and healthy controls (n=20) without tinnitus. Participants completed measures of anticipation of future positive and negative experiences, anxiety and depression. In addition, participants with tinnitus completed a test of tinnitus annoyance.
Results: Tinnitus participants generated a greater number of negative future events compared to the controls. There was no difference between the groups on positive future events or on self-reported anxiety, but the tinnitus group scored higher on a depression measure. Controlling for depression scores removed the group difference.
Conclusions: While the groups differed on future thinking, the difference concerned negative events, which suggests that anxious information processing might be important in explaining tinnitus annoyance. Levels of depressive symptoms should, however, be considered.

Chloroquine ototoxicity.

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Chloroquine (CQ), a 4-aminoquinoline drug, has been largely used for the treatment of rheumatoid arthritis and other connective tissue diseases. Besides the well-known retinal toxicity, its use has been suspected of being associated to ototoxicity. Some reports have described mainly sensorineural hearing loss, tinnitus, sense of imbalance, and cochleovestibular manifestations. Differently from what occurs in retinopathy, in which there is a predominance of CQ toxicity, there are reports of alterations in hearing related to either CQ or hydroxychloroquine. Brain-evoked response audiometry seems to be the most sensitive test in detecting early manifestations of cochlear injury caused by CQ when still in a reversible stage. The reversibility of CQ ototoxicity has been debated, but there is suggestion that such complication can be corrected if the medication is stopped and appropriate therapy, with steroids and plasma expanders, is instituted.

**The origin of spontaneous activity in the developing auditory system.**


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Spontaneous activity in the developing auditory system is required for neuronal survival as well as the refinement and maintenance of tonotopic maps in the brain. However, the mechanisms responsible for initiating auditory nerve firing in the absence of sound have not been determined. Here we show that supporting cells in the developing rat cochlea spontaneously release ATP, which causes nearby inner hair cells to depolarize and release glutamate, triggering discrete bursts of action potentials in primary auditory neurons. This endogenous, ATP-mediated signalling synchronizes the output of surrounding inner hair cells, which may help refine tonotopic maps in the brain. Spontaneous ATP-dependent signalling rapidly subsides after the onset of hearing, thereby preventing this experience-independent activity from interfering with accurate encoding of sound. These data indicate that supporting cells in the organ of Corti initiate electrical activity in auditory nerves before hearing, pointing to an essential role for peripheral, non-sensory cells in the development of central auditory pathways.

**III Diagnostics**

**Prognostic factors for vestibular impairment in sensorineural hearing loss.**

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The clinical course and prognosis in sensorineural hearing loss (SNHL) may be even worse if vestibular system is also involved, especially due to near location of anatomical structures in the inner ear. The aim of the study was to determine prognostic value of some clinical, audiological and demographic factors associated with SNHL in predicting a possibility of vestibular impairment. The study was conducted on 124 consecutive patients (183 ears) diagnosed for sensorineural hearing loss during 1 year in our department. In all of them, audiological (pure-tone, speech and impedance audiometry, ABR) and ENG examinations (visual ocular-motor, positional, kinetic and caloric tests) were performed. The correlations between ENG outcome and the following variables associated with sensorineural hearing loss were investigated: audiological (degree and location of hearing loss, audiogram configuration), clinical (tinnitus, vertigo, dizziness) and demographic (age, sex) factors. Normal ENG was recorded in 26.6%, vestibular impairment of peripheral type in 38.7%, and central type in 34.7% of the patients. In a multivariate stepwise linear regression analysis, the degree of hearing loss was the main variable correlating with abnormal ENG result. Tinnitus and location of hearing loss were also found to be the two other variables which, to some minor extent, can influence the ENG outcome.
Peripheral vestibular impairment was observed more frequently in patients with residual hearing/deafness. The degree of hearing loss, presence of tinnitus and location of hearing loss are factors predicting the possibility of abnormal ENG outcome in sensorineural hearing loss.

**Provocation of Endolymphatic Hydrops With a Prick Test in Meniere’s Disease.**
Topuz B, Ogmen G, Ardiç FN, Kara CO.

This study was conducted to test the hypothesis that antigenic challenge is an important stimulative factor for an episode of endolymphatic hydrops. The study was held in a tertiary care center for patients with probable or definite Meniere’s disease. The prick test, which included dietary and inhalant allergens, was applied to all patients with a Multi-Test Applicator (Lincoln Diagnostics, Decatur, Ill). Patients were tested with electrocochleography before and after the prick test. The positive allergen was diluted in 1/10 of a prick test dose, and patients were provoked and tested again. A negative summating potential/action potential (SP/AP) amplitude ratio greater than 0.5 was used as the main outcome measure. Pretest, posttest, and postprovocation SP/AP amplitude ratios were compared. A total of 80 diseased and 16 normal ears of 48 patients with Meniere’s disease were assessed. All patients were found to be atopic, but none had allergic symptoms. No symptom like vertigo or fullness was seen after the prick test was performed. In all, 30 patients had tinnitus and fullness in the diseased ear, and 6 patients had vertigo after the provocation. The SP/AP ratio was greater than 0.50 in 23 diseased (29%) and 3 normal (19%) ears before the prick test. After the prick test, 62 diseased (78%) and 13 normal (81%) ears had endolymphatic hydrops. These numbers did not change much after the provocation. Results reported here support the role of antigenic stimulation for episodes of Meniere’s disease. Endolymphatic hydrops was the atopic reaction that occurred in most study patients.

**Applications of the marchbanks transcranial-cerebral sonography technique in neurootology: preliminary report.**
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Transcranial-cerebral sonography (TCCS) is a noninvasive technique that allows clinicians to detect nanoliter (billionths of a liter) displacements of the tympanic membrane. This technique was developed to assess cerebrospinal fluid (CSF) pressure in cases of shunted hydrocephalus; it takes advantage of the CSF connection to the inner ear through the cochlear aqueduct. The movements of the tympanic membrane that are observed in TCCS are those evoked by the acoustic stapedius reflex and those spontaneous movements generated by intracranial arterial, venous, and respiratory pulses transmitted through the inner ear to the stapes and thence to the tympanic membrane. Analysis of the amplitude and direction of these displacements has enabled neurosurgeons and neurologists to estimate CSF pressures accurately in patients evaluated by TCCS. TCCS allows for applications in neurootology, particularly in those patients who present with symptoms of pulsating tinnitus, dizziness and imbalance, or hearing loss. This preliminary report describes the test and its application in a series of patients whose diagnoses included pulsating tinnitus, idiopathic intracranial hypertension, Ménière's disease, perilymphatic fistula, perilymphatic hypertension, arterial stenosis, and Arnold-Chiari syndrome. We conclude that TCCS is a valuable addition to the armamentarium of neurootologists.
A critical analysis of tinnitus measuring methods.
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One of the main factors that make tinnitus treatment so difficult is the subjectivity of measuring methods and therapeutic monitoring. DATABASE: Our aim, in this study, is to make a critical analysis of tinnitus measuring methods. CONCLUSION: There is no consensus about tinnitus measuring methods, causing criticism in the methodology used in many papers. In Brazil, the simplest methods are the most used.

Facial palsy and fallopian canal expansion associated with idiopathic intracranial hypertension.
Brackmann DE, Doherty JK.
House Clinic and House Ear Institute, Los Angeles 90057, and University of California, San Diego, Division of Otolaryngology-Head & Neck Surgery, La Jolla, California, USA. dbrackmann@hei.org

Objective: Describe neurotologic findings associated with idiopathic intracranial hypertension (IIH).
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Results: Audiometry revealed asymmetric sensorineural hearing loss. Enlargement of the fallopian canal with cerebrospinal fluid was evident on imaging studies. Partial resolution of IIH symptoms was achieved.

Conclusion: IIH is an enigmatic disease entity. Increased intracranial pressure usually presents with headache and pulsatile tinnitus and is occasionally associated with cranial neuropathies. Abducens palsy is most common, producing diplopia. Cranial nerve involvement is often asymmetric, producing false localizing signs. Facial paralysis is an uncommon sequela of IIH. Treatment of IIH consists of reducing intracranial pressure. Corticosteroids are recommended for treatment of facial paralysis.

When tinnitus loudness and annoyance are discrepant: audiological characteristics and psychological profile.
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This study evaluates sociodemographic and clinical characteristics of patients reporting discrepant levels of tinnitus loudness and annoyance. 4958 subjects recruited from a national tinnitus association completed a comprehensive screening questionnaire including Klockhoff and Lindblom’s loudness grading system and the psychometric Mini-TQ (Tinnitus Questionnaire). There was a moderate correlation of 0.45 between loudness and annoyance. Of the subjects reporting very loud tinnitus, about one third had only mild or moderate annoyance scores. They were not different from those with high annoyance regarding age, gender and tinnitus duration, but annoyance was increased when subjects had additional hearing loss (OR = 1.71), vertigo/dizziness (OR = 1.94) or hyperacusis (OR = 4.96). Another significant predictor was history of neurological disease (OR = 3.16). Subjects reported low annoyance despite high loudness more often if not feeling low/depressed and not considering themselves as victims of their noises. A specific psychological profile was found to characterize annoyed tinnitus sufferers. Permanent awareness of the noises, decreased ability to ignore them and concentration difficulties were reported frequently even when overall annoyance scores were comparatively low.
It is concluded that the coexistence of tinnitus with hearing loss, vertigo/dizziness and hyperacusis as complicating otological conditions seems to be of clinical relevance for the prediction of high annoyance levels. Tinnitus loudness and annoyance are not necessarily congruent and should be assessed separately. (c) 2007 S. Karger AG, Basel.

Predicting Hyperacusis in Tinnitus Patients
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The goal of this study was to develop a model that predicts whether tinnitus patients would report hyperacusis based upon their audiometric thresholds and loudness discomfort levels (LDLs), measured at 1000, 2000, 4000, and 8000 Hz. Follow-up LDLs subsequent to tinnitus retraining therapy (TRT) were used to predict hyperacusis subsequent to treatment. Pretreatment and TRT follow-up audiometric thresholds and LDLs were analyzed for a group of 68 tinnitus patients who self-reported sound tolerance complaints and a group of 58 tinnitus patients who denied sound tolerance problems. A logistic regression model was implemented to determine which of the eight audiological measures (i.e., four threshold and four LDL measures) were essential in predicting the hyperacusis or tinnitus-only categorization. Predictions from the logistic regression model are compared with three versions of a published categorization scheme. The success of each model varied depending on the hearing-loss configuration, with poorest performance for sloping hearing losses. The logistic regression model was the best model overall. The logistic regression model predicted improvement for 54 of 68 (79%) self-reported hyperacusis patients following TRT treatment. The logistic regression model improves the prediction of hyperacusis in tinnitus patients and successfully predicts improvement in the majority of tinnitus patients following TRT treatment.

Disortion Product Otoacoustic Emission Levels and Input/Output-Growth Functions in Normal-Hearing Individuals with Tinnitus and/or Hyperacusis
Semin Hear 2007; 28: 303-318

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

Prognostic factors for vestibular impairment in sensorineural hearing loss
European Archives of Oto-Rhino-Laryngology

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The clinical course and prognosis in sensorineural hearing loss (SNHL) may be even worse if vestibular system is also involved, especially due to near location of anatomical structures in the inner ear. The aim of the study was to determine prognostic value of some clinical, audiological and demographic factors associated with SNHL in predicting a possibility of vestibular impairment. The study was conducted on 124 consecutive patients (183 ears) diagnosed for sensorineural hearing loss during 1 year in our department. In all of them, audiological (pure-tone, speech and impedance audiometry, ABR) and ENG examinations (visual ocular–motor, positional, kinetic and caloric tests) were performed. The correlations between ENG outcome and the following variables associated with sensorineural hearing loss were investigated: audiological (degree and location of hearing loss, audiogram configuration), clinical (tinnitus, vertigo, dizziness) and demographic (age, sex) factors. Normal ENG was recorded in 26.6%, vestibular impairment of peripheral type in 38.7%, and central type in 34.7% of the patients. In a multivariate stepwise linear regression analysis, the degree of hearing loss was the main variable correlating with abnormal ENG result. Tinnitus and location of hearing loss were also found to be the two other variables which, to some minor extent, can influence the ENG outcome. Peripheral vestibular impairment was observed more frequently in patients with residual hearing/deafness. The degree of hearing loss, presence of tinnitus and location of hearing loss are factors predicting the possibility of abnormal ENG outcome in sensorineural hearing loss.

Sleep Complaints in Elderly Tinnitus Patients: A Controlled Study.

Hebert S, Carrier J

Objectives: Sleep difficulties are among the most frequent complaints associated with tinnitus. Yet most studies reporting on this problem are rather succinct, and all of them lack proper age- and health-matched control subjects.

Design: The present study reports on 102 participants (51 with and 51 without tinnitus), assessed with the Pittsburgh Sleep Quality Index (PSQI), the Beck-II depression inventory, a hyperacusis questionnaire, and a tinnitus-reaction questionnaire (tinnitus group only). Participants were matched for health and relevant socioeconomic factors.

Results: Results show that tinnitus patients have greater self-reported sleep difficulties compared with control subjects, specifically sleep efficiency and sleep quality, and that high tinnitus-related distress is associated with greater sleep disturbance.

Conclusions: Rather than hearing loss, sleep complaints in this population are mainly explained by hyperacusis, a hallmark of tinnitus, and to a lesser extent by subclinical depressive symptoms.
IV Imaging

High frequency localised „hot spots“ in temporal lobes of patients with intractable tinnitus: A quantitative electroencephalographic (QEEG) study.

Neurosci Lett. 2007 Aug 22;

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Tinnitus, the perception of noise in the absence of an external auditory stimulus, is common, frequently distressing and often intractable. It is associated with a number of conditions including deafness but may arise spontaneously. Brain imaging studies indicate increased neuronal excitability and decreased density of benzodiazepine receptors in temporal (auditory) cortex but the source and mechanism of such changes are unknown. Various electroencephalographic (EEG) abnormalities involving temporal lobe and other brain areas have been described but recordings have been limited to standard EEG wave bands up to frequencies of 22Hz. This clinical study of otherwise healthy patients with intractable unilateral tinnitus, using quantitative EEG power spectral mapping (QEEG), identified discrete localised unilateral foci of high frequency activity in the gamma range (>40-80Hz) over the auditory cortex in eight patients experiencing tinnitus during recording. These high frequency „hot spots“ were not present in 25 subjects without tinnitus. The results suggest that further EEG investigations should include recordings in the gamma frequency range since such high frequency oscillations are believed to be necessary for perception. Identification of „hot spots“ in tinnitus patients would provide a means for monitoring the effects of new treatments. These findings may also provide a model for exploration of more complex phenomena such as verbal and musical hallucinations.

V Pharmacotherapy

Gabapentin effectiveness on the sensation of subjective idiopathic tinnitus: a pilot study.

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This prospective, placebo-controlled, double-blind clinical trial evaluated the effectiveness of gabapentin in decreasing subjective features of idiopathic subjective tinnitus in the patients. Pure-tone audiograms, laboratory test and personal histories were used to exclude any particular etiology of tinnitus. Participants were restricted to those with moderate to severe idiopathic subjective tinnitus for at least 6 months. A total of 30 participants received gabapentin in a graduated ascending dose series extending over 4 weeks (peak dose of 900 mg/day). There was not a significant subjective improvement in tinnitus annoyance for the patients (37%) versus controls (42%). Comparison between the results before and after intervention for patients and controls according to subjective response, tinnitus questionnaire, tinnitus severity index and the loudness perception by the patient showed no significant differences (P > 0.05). There is insufficient evidence to support the effectiveness of gabapentin in the treatment of tinnitus up to now.

Sulpiride and melatonin decrease tinnitus perception modulating the auditolimbic dopaminergic pathway.


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Objectives: Sulpiride and melatonin decrease dopamine activity. Sulpiride, a D2 antagonist of dopamine receptors, and melatonin, a pineal substance with antidopaminergic action, are administered to tinnitus patients to decrease tinnitus perception.

Design: A prospective, randomized, double-blinded, placebo-controlled study was done.


Methods: One hundred twenty patients consulted for subjective tinnitus. They were included randomly in four groups of 30. One group took sulpiride (50 mg/8 h) alone, the second group took melatonin (3 mg/24 h), the third group took the same doses of sulpiride (50 mg/8 h) plus melatonin (3 mg/24 h), and the fourth group took placebo (lactose 50 mg/8 h), all for 1 month. Ninety-nine patients completed the study.

Main outcome measures: Clinical history, tonal audiometry, tympanometry, and tinnitometry were done at the beginning and end of the study. Subjective grading of tinnitus perception and a visual analogue scale (0-10) were done for evaluation of results.

Results: Based on the subjective grading, tinnitus perception diminished by 56% in patients treated with sulpiride, by 40% in patients treated with melatonin, by 81% in patients treated with sulpiride plus melatonin, and by 22% in patients treated with placebo. Based on the visual analogue scale, tinnitus perception diminished from 7.7 to 6.3 in patients treated with sulpiride, to 6.5 in those treated with melatonin, to 4.8 in patients treated with sulpiride plus melatonin, and to 7.0 in those treated with placebo.

Conclusions: Sulpiride and melatonin reduce tinnitus perception, decreasing dopamine activity. The tinnitus auditolimbic dopaminergic pathway has broad therapeutic implications.

Carbamazepine reduces the behavioural manifestations of tinnitus following salicylate treatment in rats.

Acta Otolaryngol. 2007 Aug 22;:1-5 [Epub ahead of print]
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Conclusion: The results are consistent with the hypothesis that carbamazepine (CBZ) has efficacy against tinnitus in humans.

Objective: CBZ is an anti-epileptic drug that is widely used for the treatment of tinnitus. Despite this, there are relatively few clinical trials or preclinical studies supporting its efficacy. In an effort to increase the amount of information available on CBZ, the aim of this study was to investigate the efficacy of CBZ in salicylate-induced tinnitus in rats. Materials and methods. We investigated the effects of CBZ in an animal model of tinnitus induced by the injection of salicylate using a conditioned lick suppression paradigm.

Results: We found that CBZ, at a dose of 15 mg/kg i.p., but not at 5 mg/kg or 30 mg/kg, significantly suppressed the behavioural manifestations of tinnitus.

Intratympanic application of botulinum toxin: experiments in guinea pigs for excluding ototoxic effects.

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The aim of the study was to exclude ototoxic side effects of intratympanically applied botulinum toxin. The background is that a transection of the tensor tympani tendon (tenotomy) may relieve symptoms of tinnitus due to myoclonic tensor contractions. Moreover, there are certain indications that in some cases tenotomy may influence the course of Menière’s disease positively. In such cases, a temporary (probatory) inactivation of the muscle with botulinum toxin might be better than a definitive surgical solution. Although in theory botulinum toxin should not have ototoxic side effects, a study on animals (guinea pigs) should prove this assumption.
On eight guinea pigs (16 ears), the middle ear spaces (bullae) were opened and botulinum toxin was introduced. Hearing thresholds were measured via ABR recordings, prior to 1 and 3 weeks, respectively, after botulinum toxin application. Histological examinations of the middle ear mucosa were performed on each animal. In our series, the hearing thresholds remained essentially unchanged. Furthermore, no middle ear pathologies could be found in histology. No negative effects of botulinum toxin on hearing could be observed in our series. This is a precondition for the further development of the concept of intratympanic applications of the drug, to inactivate the tensor tympani muscle or for other options.

Clear Tinnitus, middle-ear pressure, and tinnitus relief: a prospective trial.

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Goal: Our goal was to establish the efficacy, in a 12-week period, of Clear Tinnitus for tinnitus relief in patients with tinnitus of the severe, disabling type.

Hypothesis: We hypothesized that tinnitus relief with Clear Tinnitus reflects improvement in the sensory component of the tinnitus complaint by controlling the factor of aeration of the middle ears and improving eustachian tube function.

Method: In a prospective clinical trial of a homeopathic preparation--Clear Tinnitus--we attempted to identify in 15 tinnitus patients (14 male, 1 female; mean age, 47.6 years) its clinical efficacy for establishing tinnitus relief for a 3-month period. We employed a descriptive data analysis method across dimensions of risk to evaluate a base of multidimensional evidence and establish support for our hypothesis. A medical-audiological tinnitus patient protocol completed by each patient identified the clinical type of tinnitus as predominantly cochlear, with a central and middle-ear component bilaterally. We identified fluctuation in middle-ear pressure (MEP) via patients’ clinical history, supported by physical examination and established with tympanometry, as a factor influencing the clinical course of the tinnitus in each patient.

Results: Eleven of 15 patients completed the study. Seven responders reported tinnitus relief; four did not respond. Descriptive data analysis failed to detect any trends in a change in response with audiometric tests across the hearing spectrum; thus, we could derive no coefficients of hearing change. Evaluation revealed high-frequency tinnitus in 11 patients. The Feldmann masking curve comparison at the start and end of the study showed no significant change in the 11 patients. There was no significant alteration in the minimum masking levels or loudness discomfort levels before and after the study. Tympanometry and MEP measurement indicated a significant difference in MEP with an improvement on average of -58.18 in the right ear and -40.90 in the left ear for the 11 patients. Quantitative electroencephalography analysis revealed a marked difference in the number of significant abnormal recordings between the different frequency bands, with the delta band significantly higher than the theta, alpha, and beta bands for both the overall cohort of patients (n = 11) and those reporting tinnitus relief (n = 7). The tinnitus outcome questionnaires--the tinnitus intensity index, the tinnitus annoyance index, and the tinnitus reaction questionnaire--revealed a significant difference for the patients (7 of 11) obtaining tinnitus relief. Results of the tinnitus stress test, the tinnitus handicap index, and the measurement of depression scale before and after the study were not statistically significant.

Conclusions: Patients who completed the study demonstrated with tympanometry a statistical and clinical significance in MEP improvement or maintenance of MEP (or both). Patients with tinnitus of the severe disabling type selected for this study and responding to Clear Tinnitus reported tinnitus relief accompanied by improvement in or maintenance of MEP of the middle ears. The statistical and clinical significance of Clear Tinnitus for establishing tinnitus relief remains to be established with a larger cohort of tinnitus patients.
Tinnitus treatment with Trazodone.
Dib GC, Kasse CA, Alves de Andrade T, Gurgel Testa JR, Cruz OL.
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Tinnitus is a common symptom, defined as a sound perception in absence of a sound stimulus. AIM: Evaluate if Trazodone, an antidepressant drug, which modulates serotonin at central neuronal pathways, is effective in controlling tinnitus. STUDY DESIGN: Prospective, double blind, randomized, placebo-controlled. MATERIALS AND METHODS: Study performed with patients presenting tinnitus. 85 patients were analyzed between February and June of 2005. 43 received trazodone and 42 placebo, for 60 days. The clinical criteria of analysis were tinnitus intensity, discomfort and life quality impact by tinnitus, using an analogue scale varying between 0 and 10, scored by patients before and after drug or placebo use. RESULTS: There was a significant improvement in intensity, discomfort and life quality in both groups after treatment; however, there was no significant difference between the drug and placebo groups. Patients with age equal or over 60 years presented better results after treatment. CONCLUSION: Trazodone was not efficient in controlling tinnitus in the patients evaluated under the doses utilized.

Modafinil enhances thalamocortical activity by increasing neuronal electrotonic coupling.
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Modafinil (Provigil, Modiodal), an antinarcoleptic and mood-enhancing drug, is shown here to sharpen thalamocortical activity and to increase electrical coupling between cortical interneurons and between nerve cells in the inferior olivary nucleus. After irreversible pharmacological block of connexin permeability (i.e., by using either 18beta-glycyrrhetinic derivatives or mefloquine), modafinil restored electrotonic coupling within 30 min. It was further established that this restoration is implemented through a Ca(2+)/calmodulin protein kinase II-dependent step.

VI Auditive Stimulation

The effect of unilateral multichannel cochlear implant on bilaterally perceived tinnitus.
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Conclusions: Available multichannel cochlear implants (CIs) provide effective tinnitus suppression. More sophisticated speech strategies are more effective than analogue or slow strategies. The mechanisms by which tinnitus is suppressed by CIs are unclear; however, both acoustic masking and reorganization of the right auditory association cortex induced by the CI are possible mechanisms. CI significantly reduced the tinnitus-related handicap as assessed by the Tinnitus handicap Inventory (THI). Objective: The objective of the study was to evaluate the effects of a unilateral CI on bilaterally perceived tinnitus. Patients and methods. Forty-one profoundly deaf patients implanted with a multichannel CI reporting bilateral tinnitus were evaluated. All patients were asked to complete a questionnaire that evaluated the presence, location and intensity of tinnitus before and after cochlear implantation.
Results: Seven patients (17%) reported the perception of a 'new tinnitus' after surgery. With the CI off tinnitus was abolished in 23 patients (56.1%) in the implanted ear and in 22 patients (53.6%) in the contralateral ear. With the CI on tinnitus was abolished in the ipsilateral ear in 27 patients (65.8%) and in the contralateral ear in 27 patients (65.8%). Statistical analysis showed a significant reduction of the total THI score and of each subscale score (p<0.001).

The efficacy of open molds in controlling tinnitus.

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Hearing aids may be a option to improve tinnitus and hearing loss. AIM: to evaluate tinnitus after one month use of BTE hearing aids with open molds and pressure vent molds in patients with symmetric sensorineural hearing loss.

Methods: 50 patients seen at our Tinnitus Clinic who presented bilateral tinnitus and hearing loss underwent a randomized blind crossover clinical trial: 26 first used BTE hearing aids with open molds, and the remaining 24 first used pressure vent molds. After 30 days using the first mold and a wash-out period, the type of earmold was changed and was applied for another 30-day-period. Tinnitus evaluation was done qualitatively (improved, unchanged and worsened) and quantitatively (variation on a numeric scale from 0 to 10).

Results: 82% of the cases reported improvement of tinnitus with at least one type of earmold; there was no significant difference in the reduction of discomfort due to tinnitus in the quantitative and qualitative evaluations. Although similar tinnitus control was obtained with both methods, 66% of the patients preferred the open mold. CONCLUSION: In a short-term evaluation improvement of tinnitus by the use of hearing aids does not depend on earmold ventilation.

Tinnitus modifications after cochlear implantation.

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Tinnitus can be defined as a phantom sensation in the absence of an external sound. In our study, we evaluated the effect of cochlear implant on tinnitus evolution. Among adult, postlingually deaf patients who underwent cochlear implantation at our clinic, we selected 20 subjects with pre-implantation tinnitus (group A) and 10 subjects without pre-implantation tinnitus (group B). Pre- and post-surgery tinnitus was assessed through two questionnaires: the first one dealing with tinnitus characteristics and psychosocial impact, and the second one represented by THI, an internationally validated score of evaluation of the effects of tinnitus on patient's emotions and activities of daily living. None of the patients belonging to group B developed tinnitus after surgery. As for group A, 40% of patients declared suppression of tinnitus, 30% attenuation of tinnitus after surgery, 25% reported tinnitus was unchanged and 5% reported worsening of tinnitus. In the nine patients with bilateral tinnitus (45%), after implantation tinnitus disappeared from both sides in four patients and attenuated bilaterally in four patients. A comparison between pre- and post-implantation THI scores showed decreased score in 65% of cases, unchanged score in 30% and increased score in 5%. The beneficial effect of cochlear implant on tinnitus, reported by a majority of patients, could be due to acoustic masking, to direct electrical stimulation of the acoustic nerve, and above all to a possible cochlear implantation dependent reorganization of the central auditory pathways and associative cerebral areas. In the light of these results, the authors propose (1) to include tinnitus in the selection criteria of which ear to implant; (2) to consider implantation eligibility for patients with bilateral severe hearing loss associated with severe tinnitus; and (3) to inform patients about the small risk of post-operative tinnitus worsening.
Secondary Treatment Benefits achieved by Hearing-Impaired Tinnitus Patients Using Aided Environmental Sound Therapy for Tinnitus Retraining Therapy: Comparisons with Matched Groups of Tinnitus Patients Using Noise Generators for Sound Therapy
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Tinnitus patients with hearing loss may use amplified environmental sound from hearing aids (HAs) for the sound therapy (ST) component of tinnitus retraining therapy (TRT). Sizable secondary treatment benefits, namely, incremental shifts in loudness discomfort levels (LDLs) and expansion of the auditory dynamic range (DR) for loudness, have been reported for tinnitus patients who use noise generators (NGs) for ST in TRT. The primary questions addressed in this study are (1) Then hearing-impaired tinnitus patients using amplified environmental sound for their ST also achieve significant secondary treatment benefits and, if so, (2) are these secondary effects of similar magnitude to those measured for tinnitus patients using NGs for their ST? An analysis of patient records in the University of Maryland Tinnitus and Hyperacusis Center (UMTHC) revealed TRT treatment-related changes in the LDL averaged 2.70 dB for a group of 25 aided hearing-impaired tinnitus patients. Corresponding treatment effects for four matched groups of tinnitus patients, who used NGs for their ST, ranged from 5.91 to 10.10 dB. The associated incremental changes in the DR averaged 0.60 dB for the aided tinnitus patients and from 4.10 to 9.23 dB for the matched groups of tinnitus patients who used NGs for their ST. These findings indicate that hearing-impaired tinnitus patients using aided environmental sound for TRT achieve smaller secondary treatment benefits than do tinnitus patients who use NGs for their ST.

Adaptive Recalibration of Chronic Auditory Gain
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This report follows up and extends an exploratory investigation of a hypothetical adaptive chronic gain (amplification of suprathreshold information) process within the auditory system. In theory, this hypothetical gain process is plastic and can be systematically modified and recalibrated. The idea of an adaptive auditory gain mechanism is a fundamental concept in the treatment of both tinnitus and hyperacusis with tinnitus retraining therapy (TRT). This notion, however, has gone virtually untested. The hypothesis of this research is that judgments of loudness provide a functional index of chronic auditory gain. Further, chronic auditory gain can be manipulated either upward or downward in a controlled way by prolonged reduction or enhancement in the levels of background sound to which a listener is exposed. To evaluate these assertions, 8 normal-hearing volunteers were assigned randomly to continuous (23 hours/day), chronic (4-week) external sound treatments. Participants were exposed either to low-level sound produced by bilateral in-the-ear noise generators (NGs) or were fitted bilaterally with sound-attenuating earplugs (EPs) in a sequential crossover design. Both treatments produced elevated audibility thresholds, mainly above 1000 Hz. The effects of each treatment type on loudness judgments were evaluated to test the following predictions: (1) The EPs would enhance the magnitude of perceived loudness and the resulting loudness growth functions would become steeper as a consequence of chronic sound attenuation (consistent with enhanced system gain in response to diminished peripheral sound input); whereas, (2) the NGs would reduce the magnitude of perceived loudness and the resul-
ting loudness growth functions would become shallower (consistent with diminished system gain in response to the elevated background input). Results after 4 weeks of each treatment were consistent with the above predictions, providing support for a plastic, chronic auditory gain process, and the use of sound therapy (i.e., NGs) in TRT.

VII Brain Stimulation

Do tonic and burst TMS modulate the lemniscal and extralemniscal system differentially?
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Introduction: Tinnitus is an auditory phantom percept related to tonic and burst hyperactivity of the auditory system. Two parallel pathways supply auditory information to the cerebral cortex: the tonotopically organised lemniscal system, and the non-tonotopic extralemniscal system, firing in tonic mode and burst mode respectively. Transcranial magnetic stimulation (TMS) is a non-invasive method capable of modulating activity of the human cortex, by delivering tonic or burst stimuli. Burst stimulation is shown to be more powerful in activating the cerebral cortex than tonic stimulation and bursts may activate neurons that are not activated by tonic stimulations.

Methods: The effect of both tonic and burst TMS in 14 placebo-negative patients presenting narrow band/white noise tinnitus were analysed.

Results: Our TMS results show that narrow band/white noise tinnitus is better suppressed with burst TMS in comparison to tonic TMS, t(13)=6.4, p=.000. For pure tone tinnitus no difference is found between burst or tonic TMS, t(13)=.3, ns.

Discussion: Based on the hypothesis that white noise is the result of hyperactivity in the non-tonotopic system and pure tone tinnitus of the tonotopic system, we suggest that burst stimulation modulates the extralemniscal system and lemniscal system and tonic stimulation only the lemniscal system.

Theta, alpha and beta burst transcranial magnetic stimulation: brain modulation in tinnitus.
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Introduction: Some forms of tinnitus are considered to be auditory phantom phenomena related to re-organization and hyperactivity of the auditory central nervous system. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive tool capable of modulating human brain activity, using single pulse or burst stimuli. Burst rTMS has only been performed in the theta range, and has not been used clinically. The authors analyze whether burst TMS at theta (5 Hz), alpha (10 Hz) and beta (20 Hz) frequencies can temporarily suppress narrow band noise/white noise tinnitus, which has been demonstrated to be intractable to tonic stimulation.

Methods: rTMS is performed both in tonic and burst mode in 46 patients contralateral to the tinnitus side, at 5, 10 and 20 Hz. Fourteen placebo negative rTMS responders are further analyzed.

Results: In 5 patients, maximal tinnitus suppression is obtained with theta, in 2 with alpha and in 7 with beta burst stimulation. Burst rTMS suppresses narrow band/white tinnitus much better than tonic rTMS t(13)=6.4, p<.000. Women experience greater suppression of their tinnitus with burst stimulation than men, t(12)=2.9, p<.05. Furthermore left sided tinnitus is perceived as more distressing on the TQ than right sided tinnitus, t(12)=3.2, p<.01. The lower the tinnitus pitch the more effectively rTMS suppresses tinnitus(r=-0.65, p<0.05).
**Discussion:** Burst rTMS can be used clinically, not only theta burst, but also alpha and beta burst. Burst rTMS is capable of suppressing narrow band/white noise tinnitus very much better than tonic rTMS. This could be due to the simple fact that burst neuromodulation is more powerful than tonic neuromodulation or to a differential effect of burst and tonic stimulation on the lemniscal and extralemniscal auditory system. In some patients only alpha or beta burst rTMS is capable of suppressing tinnitus, and theta burst not. Therefore in future rTMS studies it could be worthwhile not to limit burst stimulation to theta burst rTMS.

**Tuning the tinnitus percept by modification of synchronous brain activity.**

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**Purpose:** Tinnitus, the perception of sound without the presence of a physical stimulus, provides the opportunity to study neural codes of percepts without simultaneous processing of stimuli. Previously, we have found that tinnitus is associated with enhanced delta- and reduced tau-power in temporal brain regions. By operantly modifying corresponding aspects of spontaneous EEG activity, the aim of the present study was to corroborate the assumption that tinnitus should be reduced if patterns of ongoing synchronous brain activity are normalised.

**Methods:** In response to different variants of neurofeedback, a total of twenty-one patients produced significant changes in EEG frequency bands.

**Results:** Simultaneous alteration of both frequency bands was strongly related to changes in tinnitus intensity matched before and after the intervention ($r=-0.74$). In those two patients with the greatest modulatory success, the tinnitus sensation resided completely in response to the treatment. Comparing the neurofeedback-treated patients with a group of patients trained with a frequency discrimination task ($n=27$), the tinnitus relief in the neurofeedback group was significantly stronger.

**Conclusions:** This study supports the notion that altered patterns of intrinsic ongoing brain activity lead to phantom percepts and offer new routes to the treatment of tinnitus.

**Which tinnitus patients benefit from transcranial magnetic stimulation?**

Department of Otorhinolaryngology, University of Regensburg, Germany.

**Objectives:** Chronic tinnitus is associated with hyperactivity of the central auditory system. Low-frequency repetitive transcranial magnetic stimulation (rTMS) of the temporal cortex has been proposed as a treatment for chronic tinnitus. This study determined the factors that predict a beneficial outcome with rTMS treatment.

**Study Design:** Forty-five patients with chronic tinnitus underwent 10 sessions of low-frequency rTMS to their left auditory cortex. The treatment outcome was assessed with a tinnitus questionnaire. Therapeutic success was related to the patients’ clinical characteristics.

**Results:** A significant reduction in tinnitus complaints occurred after rTMS. In the questionnaire, 40% of the patients improved by five points or more. Treatment responders were characterized by shorter duration of tinnitus complaints and no hearing impairment.

**Conclusion:** Tinnitus-related neuroplastic changes might be less pronounced in patients with normal hearing and a short history of complaints. This could explain why those patients benefitted more from rTMS treatment.
The use of tDCS and CVS as methods of non-invasive brain stimulation.
Brain Res Rev. 2007 Aug 28; [Epub ahead of print]

Been G, Ngo TT, Miller SM, Fitzgerald PB.
Alfred Psychiatry Research Centre, The Alfred Hospital and Monash University School of Psychology, Psychiatry and Psychological Medicine, Commercial Rd, Melbourne, VIC 3004, Australia.

Transcranial direct current stimulation (tDCS) and caloric vestibular stimulation (CVS) are safe methods for selectively modulating cortical excitability and activation, respectively, which have recently received increased interest regarding possible clinical applications. tDCS involves the application of low currents to the scalp via cathodal and anodal electrodes and has been shown to affect a range of motor, somatosensory, visual, affective and cognitive functions. Therapeutic effects have been demonstrated in clinical trials of tDCS for a variety of conditions including tinnitus, post-stroke motor deficits, fibromyalgia, depression, epilepsy and Parkinson’s disease. Its effects can be modulated by combination with pharmacological treatment and it may influence the efficacy of other neurostimulatory techniques such as transcranial magnetic stimulation. CVS involves irrigating the auditory canal with cold water which induces a temperature gradient across the semicircular canals of the vestibular apparatus. This has been shown in functional brain-imaging studies to result in activation in several contralateral cortical and subcortical brain regions. CVS has also been shown to have effects on a wide range of visual and cognitive phenomena, as well as on post-stroke conditions, mania and chronic pain states. Both these techniques have been shown to modulate a range of brain functions, and display potential as clinical treatments. Importantly, they are both inexpensive relative to other brain stimulation techniques such as electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS).

Auditory cortex stimulation for tinnitus.

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Functional imaging techniques have demonstrated a relationship between the intensity of tinnitus and the degree of reorganization of the primary auditory cortex. Studies in experimental animals and humans have revealed that tinnitus is associated with a synchronized hyperactivity in the auditory cortex and proposed that the underlying pathophysiological mechanism is thalamocortical dysrhythmia; hence, decreased auditory stimulation results in decreased firing rate, and decreased lateral inhibition. Consequently, the surrounding brain area becomes hyperactive, firing at gamma band rates; this is considered a necessary precondition of auditory consciousness, and also tinnitus. Synchronization of the gamma band activity could possibly induce a topographical reorganization based on Hebbian mechanisms. Therefore, it seems logical to try to suppress tinnitus by modifying the tinnitus-related auditory cortex reorganization and hyperactivity. This can be achieved using neuronavigation-guided transcranial magnetic stimulation (TMS), which is capable of modulating cortical activity. If TMS is capable of suppressing tinnitus, the effect should be maintained by implanting electrodes over the area of electrophysiological signal abnormality on the auditory cortex. The results in the first patients treated by auditory cortex stimulation demonstrate a statistically significant tinnitus suppression in cases of unilateral pure tone tinnitus without suppression of white or narrow band noise. Hence, auditory cortex stimulation could become a physiologically guided treatment for a selected category of patients with severe tinnitus.
Transcranial magnetic stimulation elicits coupled neural and hemodynamic consequences.
Comment in:
Science. 2007 Sep 28;317(5846):1846.

Allen EA, Pasley BN, Duong T, Freeman RD.
Helen Wills Neuroscience Institute, Group in Vision Science, School of Optometry, University of California, Berkeley, CA 94720, USA.

Transcranial magnetic stimulation (TMS) is an increasingly common technique used to selectively modify neural processing. However, application of TMS is limited by uncertainty concerning its physiological effects. We applied TMS to the cat visual cortex and evaluated the neural and hemodynamic consequences. Short TMS pulse trains elicited initial activation (approximately 1 minute) and prolonged suppression (5 to 10 minutes) of neural responses. Furthermore, TMS disrupted the temporal structure of activity by altering phase relationships between neural signals. Despite the complexity of this response, neural changes were faithfully reflected in hemodynamic signals; quantitative coupling was present over a range of stimulation parameters. These results demonstrate long-lasting neural responses to TMS and support the use of hemodynamic-based neuroimaging to effectively monitor these changes over time.

VIII Behavioural Therapy

Tuning the tinnitus percept by modification of synchronous brain activity.

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Purpose: Tinnitus, the perception of sound without the presence of a physical stimulus, provides the opportunity to study neural codes of percepts without simultaneous processing of stimuli. Previously, we have found that tinnitus is associated with enhanced delta- and reduced tau-power in temporal brain regions. By operantly modifying corresponding aspects of spontaneous EEG activity, the aim of the present study was to corroborate the assumption that tinnitus should be reduced if patterns of ongoing synchronous brain activity are normalised.

Methods: In response to different variants of neurofeedback, a total of twenty-one patients produced significant changes in EEG frequency bands.

Results: Simultaneous alteration of both frequency bands was strongly related to changes in tinnitus intensity matched before and after the intervention (r=-0.74). In those two patients with the greatest modulatory success, the tinnitus sensation resided completely in response to the treatment. Comparing the neurofeedback-treated patients with a group of patients trained with a frequency discrimination task (n=27), the tinnitus relief in the neurofeedback group was significantly stronger.

Conclusions: This study supports the notion that altered patterns of intrinsic ongoing brain activity lead to phantom percepts and offer new routes to the treatment of tinnitus.

Use of a self-help book with weekly therapist contact to reduce tinnitus distress: a randomized controlled trial.

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**Objective:** Tinnitus distress can be reduced by means of cognitive-behavior therapy (CBT). To compensate for the shortage of CBT therapists, we aimed, in this study, to investigate the effects of a CBT-based self-help book guided by brief telephone support.

**Methods:** Seventy-two patients were randomized either to a self-help book and seven weekly phone calls or to a wait-list control condition, later on receiving the self-help book with less therapist support. The dropout rate was 7%. Follow-up data 1 year after completion of treatment were also collected (12% dropout). The Tinnitus Reaction Questionnaire (TRQ) was the main outcome measure, complemented with daily ratings of tinnitus and measures of insomnia, anxiety, and depression.

**Results:** On the TRQ, significant reductions were found in the treatment group both immediately following treatment and at 1-year follow-up. In the treatment group, 32% reached the criteria for clinical significance (at least 50% reduction of the TRQ) compared to 5% in the wait-list group. Directly after treatment, two out of five measures showed significant differences in favor of the treatment with more therapist support compared with the group who, after their waiting period, received little therapist support. The self-help treatment was estimated to be 2.6 (seven phone calls) and 4.8 (one phone call) times as cost-effective as regular CBT group treatment.

**Conclusions:** Guided self-help can serve as an alternative way to administer CBT for tinnitus. Preliminary results cast some doubts on the importance of weekly therapist contact. The effect size was somewhat smaller than for regular CBT, but on the other hand, the self-help seems far more cost-effective. Future studies should compare treatment modalities directly and explore cost-effectiveness more thoroughly.

**Secondary Benefits from Tinnitus Retraining Therapy: Clinically Significant Increases in Loudness Discomfort Level and Expansion of the Auditory Dynamic Range**

Semin Hear 2007; 28: 227-260

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In this report, the authors highlight clinically significant improvements in sound tolerance observed over the past decade among patients who were enrolled in tinnitus retraining therapy (TRT) at the University of Maryland Tinnitus and Hyperacusis Center. Pretreatment and TRT follow-up audiometric threshold, loudness discomfort level (LDL), and dynamic-range (DR) data are documented for (1) a group of 68 tinnitus patients who presented with primary complaints of sound intolerance, and (2) a second group of 70 patients who reported only tinnitus (and no sound tolerance problems). TRT-related increases in sound tolerance are (1) due to increases in LDLs and occur independently of changes in audiometric threshold, which were invariant with treatment; (2) statistically significant in tinnitus patients with and without sound tolerance problems, and with and without hearing loss; (3) observed among 81% of the patients with sound tolerance complaints and 44% of the patients who reported primary tinnitus; (4) independent of audiometric frequency over the range 1000 to 8000 Hz; and (5) seemingly independent of TRT treatment duration, which is consistent with recent experimental evidence of a rapid treatment effect (within the first month of TRT). The TRT treatment effects were clinically meaningful, offering new opportunities for expanding the auditory DR and improving sound tolerance in the general hearing-impaired population. The mechanism responsible for the plasticity underlying these treatment effects is uncertain, but appears consistent with a centrally mediated auditory gain control process. Sound tolerance problems were overpredicted among the authors’ sample of tinnitus-only patients when existing objective audiometric criteria were used. This finding promoted the development of a new predictive model for sound tolerance problems, which is described in a companion report.
Predicting Hyperacusis in tinnitus Patients
Semin Hear 2007; 28: 261-275

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The goal of this study was to develop a model that predicts whether tinnitus patients would report hyperacusis based upon their audiometric thresholds and loudness discomfort levels (LDLs), measured at 1000, 2000, 4000, and 8000 Hz. Follow-up LDLs subsequent to tinnitus retraining therapy (TRT) were used to predict hyperacusis subsequent to treatment. Pretreatment and TRT follow-up audiometric thresholds and LDLs were analyzed for a group of 68 tinnitus patients who self-reported sound tolerance complaints and a group of 58 tinnitus patients who denied sound tolerance problems. A logistic regression model was implemented to determine which of the eight audiological measures (i.e., four threshold and four LDL measures) were essential in predicting the hyperacusis or tinnitus-only categorization. Predictions from the logistic regression model are compared with three versions of a published categorization scheme. The success of each model varied depending on the hearing-loss configuration, with poorest performance for sloping hearing losses. The logistic regression model was the best model overall. The logistic regression model predicted improvement for 54 of 68 (79%) self-reported hyperacusis patients following TRT treatment. The logistic regression model improves the prediction of hyperacusis in tinnitus patients and successfully predicts improvement in the majority of tinnitus patients following TRT treatment.

IX Somatic Tinnitus
Pathways involved in somatosensory electrical modulation of dorsal cochlear nucleus activity.
Brain Res. 2007 Sep 29; [Epub ahead of print]

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Our recent study has shown that somatosensory electrical stimulation may be useful to modulate sound-induced hyperactivity in the dorsal cochlear nucleus (DCN), a neural correlate of certain forms of tinnitus. Somatosensory electrical stimulation induced both suppressive and excitatory effects on neural activity in the DCN of both control and tone-exposed animals. However, it is unclear what neural pathways underlie the somatosensory electrical stimulation-induced effects on DCN activity. To address this issue, we conducted c-fos immunocytochemistry using hamsters and mapped neural activation in both auditory and non-auditory structures following transcutaneous electrical stimulation of the basal part of the pinna. We also conducted tracing experiments to investigate the anatomical relations between the DCN and structures that showed a significant increase in the number of Fos-positive neurons as a result of electrical stimulation. Electrical stimulation of the pinna induced significant increases in the number of Fos-positive neurons in the DCN, spinal trigeminal nucleus (Sp5), dorsal raphe nucleus (DR) and locus coeruleus (LC). Results of tracing experiments indicate that the DCN received inputs from the Sp5, DR and LC. The above results suggest that modulation of DCN activity through somatosensory electrical stimulation may involve both direct pathways via the Sp5 and indirect pathways via the DR and LC. Therefore, relieving tinnitus through somatosensory electrical stimulation may require manipulations of both auditory and non-auditory functions.
Continuous peripheral nerve blockade for inpatient and outpatient postoperative analgesia in children.
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Background: This is an audit of the continuous peripheral nerve blockade (CPNB) program that was implemented at our institution to provide postoperative analgesia after orthopedic procedures in children.

Methods: We reviewed the departmental regional anesthesia registry and the medical records of consecutive children who received CPNB for postoperative analgesia at The Children’s Hospital of Philadelphia between February 2003 and July 2006. Patients were prospectively followed until cessation of the effects of CPNB and/or resolution of any related complications. Data collected contemporaneously included presence of sensory and motor blockade, pain scores in inpatients, opioid administration, and complications related to CPNB.

Results: A total of 226 peripheral nerve catheters were placed in 217 patients. One hundred eight patients (112 catheters) were discharged home with CPNB. The ages ranged from 4 to 18 yr (13.7 +/- 3.4). Local anesthetic solution (0.125% bupivacaine [n = 164], 0.1% ropivacaine [n = 12], or 0.15% ropivacaine [n = 27]) was infused at an initial rate of 2-12 mL/h based on patients’ weights and locations of catheters. The mean duration of local anesthetic infusion was 48.4 +/- 29.3 h (range 0-160 h). The percentage of patients who did not require any opioids in the first 8, 24, and 48 h after surgery was 56%, 26%, and 21%, respectively. The incidence of nausea and vomiting was 14% (13% in outpatients, 15% in inpatients). Complications were noted in 2.8% of patients. Three patients had prolonged numbness (>24 h) that resolved spontaneously; one developed superficial cellulitis that resolved with a course of antibiotics; one had difficulty removing the catheter at home and one developed tinnitus 24 h after starting CPNB that resolved quickly after clamping of the catheter followed by removal.

CONCLUSION: It is feasible to implement a CPNB program to provide an alternative method of inpatient and outpatient postoperative analgesia after orthopedic surgery in children when appropriate expertise is available. Patient and family education along with frequent follow-up are crucial to detect and address adverse events promptly.

Walker repair of the temporomandibular joint: a retrospective evaluation of 117 patients.
Griffitts TM, Collins CP, Collins PC, Beirne OR.
Research fellow, Collins Oral Surgery, Spokane, WA; and Student, Temple University School of Dentistry, Philadelphia, PA.

Purpose: This study evaluated the outcome of a high condylar shave with meniscal repositioning (Walker repair) in patients with internal derangement of the temporomandibular joint (TMJ). Changes in incisal opening, pain level, chewing ability, and preoperative TMJ symptoms (tinnitus, vertigo, and crepitus) were evaluated.

Patients and methods: A retrospective evaluation of 202 patients undergoing the Walker repair was completed using a questionnaire. A total of 117 patients responded to the questionnaire. Preoperative and postoperative examination findings, subjective questionnaire results, and panoramic radiographs were analyzed.

Results: The Walker repair resulted in a statistically significant (P < .001) decrease in pain by an average of 5.6 points on a scale of 0 to 10. The procedure also improved incisal opening by an average of 5.8 mm (P < .001). Improvements of 69% in tinnitus, 72% in vertigo, and 66% in crepitus were documented. Patients evaluated their motion, diet, comfort, and overall improvement; each area was rated as good or excellent by more than 90% of patients. The overall success rate for the Walker repair was 86%.
Conclusions: The Walker repair is an effective surgical treatment for internal derangement that significantly decreases pain level and increases incisal opening. No statistically significant difference in the success rate between unilateral and bilateral procedures was noted.

Otologic symptom improvement through TMD therapy.
Quintessence Int. 2007 Oct;38(9):e564-e571.

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Objectives: Some patients with a temporomandibular disorder (TMD) and coexisting otologic symptoms desire to know the probability of TMD therapy improving their otologic symptoms. The aim of this study was to determine a clinically valid method for identifying which otologic symptoms have a high probability of improving as a result of satisfactory TMD symptom improvement.

Method and Methods: Two hundred TMD patients with coexisting tinnitus, otalgia, dizziness, and/or vertigo were asked about their otologic symptom characteristics and associations and were given clinical tests, which were speculated to predict otologic symptom response from TMD therapy. The subjects received conservative TMD therapy in a manner thought to be most advantageous for their disorders. These potential assessment instruments were then evaluated for their ability to predict otologic symptom improvement.

Results: After satisfactory TMD symptom improvement was obtained, the percent of subjects reporting significant improvement or resolution of their tinnitus, otalgia, dizziness, and vertigo was 83%, 94%, 91%, and 100%, respectively. The chi-square and Fisher exact probability tests identified significant correlations for tinnitus, otalgia, and dizziness improvement with younger age; for tinnitus and otalgia improvement with subjects who related that the otologic symptom began when the TMD symptoms began, was worse when the TMD symptoms were worse, and was related to stress; and for dizziness improvement with subjects relating more severe TMD symptoms.

Conclusion: Asking TMD patients with coexisting otologic symptoms these specific questions will help practitioners identify which otologic symptoms have a high probability of benefiting from TMD therapy.

[Chronic tinnitus and craniomandibular disorders: Effectiveness of dental functional therapy on perceived tinnitus distress.]
[Article in German]
HNO. 2007 Aug 31; [Epub ahead of print]

Bösel C, Mazurek B, Haupt H, Peroz I.
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Background: Whether the co-occurrence of signs and symptoms of a craniomandibular disorder (CMD) and chronic tinnitus are coincidental or causal is controversial. Therefore, the effects of splint therapy and self-therapy on perceived tinnitus were evaluated.

Patients and methods: Fifty-nine patients with chronic tinnitus were divided into three groups. In a cross-over design, two groups received the two different treatments and were compared with a control group. All patients received the initial basic tinnitus therapy.

Results: No significant correlation was established between the groups receiving treatment and the control group that would validate a link between tinnitus and CMD.

Conclusion: The results of this study suggest a coincidental relationship between the two complexes of symptoms.
X Surgical Treatment

Microvascular decompression of cochlear nerve for tinnitus incapacity: pre-surgical data, surgical analyses and long-term follow-up of 15 patients. 
Eur Arch Otorhinolaryngol. 2007 Oct 2; [Epub ahead of print]

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The level of success of neurovascular decompression in ponto-cerebellar angle for hemifacial spasm and trigeminal neuralgia has already established the reality of the pathology to explain such symptoms. However, cochlear nerve compression syndrome by vascular loop is still a controversial topic. We have performed a retrospective cases review with long-term follow-up (5-7 years) concerning the results of microvascular decompression surgery of the cochlear nerve via an endoscopy assisted retrosigmoid approach on 15 patients suffering from unilateral incapacitating tinnitus with abnormal auditory brainstem response and an offending vessel on magnetic resonance imaging. During the surgery, a vascular compression was found on every patient. In a long-term follow-up, 53.3% (8 cases) of our tinnitus cases improved and 20% (3 cases) of them were completely cured. The ABR returned to normal in all patients who had good clinical results (diminished or disappeared tinnitus). When a vertebral artery loop (5 cases) was concerned we obtained 80% of good clinical results. No one showed amelioration or sudden aggravation of their hearing. Three cases required surgical correction of cerebrospinal fluid leak and one case developed spontaneously regressive swallowing problems. Such microvascular decompression surgery of the cochlear nerve appears to be successful in treating incapacitating tinnitus in particular when a vertebral artery loop is observed. Therefore, in such a case, one might recommend neurovascular decompression surgery, keeping in mind that the complications of this surgery should be minimized by a careful closure of the retrosigmoid approach. In order to ensure a better selection of patient more accurate cochlear nerve monitoring and functional MRI should be a promising assessment.

Walker repair of the temporomandibular joint: a retrospective evaluation of 117 patients.

Griffitts TM, Collins CP, Collins PC, Beirne OR.
Research fellow, Collins Oral Surgery, Spokane, WA; and Student, Temple University School of Dentistry, Philadelphia, PA

Purpose: This study evaluated the outcome of a high condylar shave with meniscal repositioning (Walker repair) in patients with internal derangement of the temporomandibular joint (TMJ). Changes in incisal opening, pain level, chewing ability, and preoperative TMJ symptoms (tinnitus, vertigo, and crepitus) were evaluated.

Patients and methods: A retrospective evaluation of 202 patients undergoing the Walker repair was completed using a questionnaire. A total of 117 patients responded to the questionnaire. Preoperative and postoperative examination findings, subjective questionnaire results, and panorex radiographs were analyzed.

Results: The Walker repair resulted in a statistically significant (P < .001) decrease in pain by an average of 5.6 points on a scale of 0 to 10. The procedure also improved incisal opening by an average of 5.8 mm (P < .001). Improvements of 69% in tinnitus, 72% in vertigo, and 66% in crepitus were documented. Patients evaluated their motion, diet, comfort, and overall improvement; each area was rated as good or excellent by more than 90% of patients. The overall success rate for the Walker repair was 86%.

Conclusions: The Walker repair is an effective surgical treatment for internal derangement that significantly decreases pain level and increases incisal opening. No statistically significant difference in the success rate between unilateral and bilateral procedures was noted.
Intralabyrinthine schwannomas: Symptoms and managements.
Auris Nasus Larynx. 2007 Sep 12; [Epub ahead of print]

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Department of Otorhinolaryngology Head & Neck Surgery, Xinhua Hospital, Shanghai, China.

**Objective:** To describe the characteristic presentations, radiologic findings and managements of the intralabyrinthine schwannomas.

**Method:** Retrospective review of patient records, their managements, and review of the literature.

**Result:** Four patients with a variety of otologic symptoms including hearing loss, vertigo, and tinnitus were found to have a schwannomas involving the labyrinth. In all cases, the inner ear lesions were preoperatively identified on magnetic resonance imaging, and the surgical removals were performed in all patients without serviceable hearing. The patients experienced improvement in their vertigo and tinnitus after surgery. Two patients were implanted the Bone-Anchored Hearing Aid (BAHA) to reconstruct the pseudo-stereophonic hearing.

**Conclusion:** Intralabyrinthine schwannomas are the rare tumours in the otology. The tumour can be removed by surgical approach, but we do not propose surgical excision for the patients with serviceable hearing. BAHA can give patients a post-operative monaural pseudo-stereophonic hearing.

[Labyrinthitis, or inflammatory pseudotumor after stapedectomy.]
[Article in French]
Ann Otolaryngol Chir Cervicofac. 2007 Aug 17; [Epub ahead of print]

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**Objectives:** To describe an extensive pseudotumor as a complication of stapes surgery.

**Methods:** Radiological workup and surgical exploration in a 38-year-old man suffering from post-operative hearing loss. The patient presented with tinnitus, inferior facial palsy, vertigo, and rapidly progressive hearing loss after his operation.

**Results:** The initial postoperative CT scan was normal. However, seven months after surgery, the CT scan showed an enlargement of the inner ear canal and complete vestibular destruction. The CISS sequence of the magnetic resonance imaging (MRI) enhanced after gadolinium injection revealed the presence of a mass filling the entire inner ear canal, the cochlear, the posterior labyrinth, and the middle ear. The aspect suggested an inflammatory pseudotumor. Surgical exploration confirmed the invasive aspect of the mass and pathological analysis revealed inflammatory tissue associated with microcalcifications.

**Discussion:** Hearing loss, vertigo, and tinnitus after stapes surgery require a radiologic workup. The CT scan is done first. It could be normal or eliminate other diagnoses. MRI may lead to a more precise diagnosis. It can reveal an inflammatory process of the inner ear after gadolinium injection. Surgical exploration is indicated in case of aggressive and extensive lesions.

**Conclusion:** In the context of hearing loss complicating otosclerosis surgery, an imaging workup should include a CT scan. In case of a suspected expansive and inflammatory mass, it should be completed by an MRI (CISS sequence and gadolinium injection). An inflammatory lesion of the inner ear could indicate extensive pseudotumor.
The effect of tympanoplasty on tinnitus in patients with conductive hearing loss: a six month follow-up.

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Tympanoplasty is done to eradicate ear pathology and to restore the conductive hearing mechanism (eardrum and ossicles). Some patients, however, do not tolerate tinnitus and question physicians about the results of surgery when tinnitus persists. AIM: to evaluate the progression of tinnitus in patients with conductive hearing loss after tympanoplasty.

STUDY DESIGN: a prospective cohort study.

Material and Methods: 23 consecutive patients with tinnitus due to chronic otitis media underwent tympanoplasty. The patients underwent a medical and audiological protocol for tinnitus before and after tympanoplasty.

RESULTS: 82.6% of patients had improvement or elimination of tinnitus after tympanoplasty. The mean score of postoperative intolerance to tinnitus (1.91 for 30 and 180 days) was significantly different from preoperative scores (5.26). As to hearing loss, patients improved medically 30 and 180 days after surgery (3.65 and 2.91) compared to the preoperative condition (6.56). Audiometry revealed improvement at all frequencies from 0.25 to 6KHz, except at 8KHz. The air-bone gap was closed or was within 10dB in 14 cases (61%). An intact tympanic membrane was achieved in 78% of the cases.

CONCLUSION: Aside from the classical improvement of hearing loss, tympanoplasty also offers good control of tinnitus.

Change in Hearing and Tinnitus in conservatively Managed Vestibular Schwannomas
Skull Base 2007; 17: 223-228

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2 Department of Otoneurological and Skull Base Surgery, Addenbrooke’s Cambridge University Hospital, Cambridge, England

Objectives: The aim of this study was to evaluate the change of hearing and tinnitus in a group of conservatively managed unilateral vestibular schwannomas (VS).

Design: Retrospective case series review. Setting: Tertiary referral otoneurological and skull base surgery department. Participants: Seventy patients affected by unilateral VS with at least two audigrams available were retrospectively evaluated.

Main outcome measures: Changes in pure tone average (PTA), speech discrimination score (SDS), and tinnitus were analyzed.

Results: At diagnosis 16 patients (22.9%) had a PTA of 0 to 30 dB and 38 (54.4%) a PTA of 0 to 50 dB. At the end of the follow-up period, 9 patients (12.9%) had a PTA of 0 to 30 dB and 27 (38.7%) had a PTA of 0 to 50 dB, representing a hearing preservation rate of 56% and 70%, respectively. Of patients with both tonal and speech audiometry, 71.4% with class A hearing (PTA < 30 dB/SDS > 70%) maintained their initial hearing and 60% with class A or B hearing (PTA < 50 dB/SDS > 50%) maintained this useful hearing. Forty-two patients (60%) did not show a significant growth in their tumor over the period of observation. In this group of patients the mean PTA after a mean follow-up time of 40 months decreased from 44 dB HL to 50.8 dB HL, with a yearly rate of 2.47 dB HL. The chance of maintaining a PTA of 0 to 30 dB in this group of patients was 57.1% and a PTA of 0 to 50 dB was 81.4%.

Conclusions: In this group of patients affected by VS and managed conservatively with a mean follow-up of 33.3 months, the risk of losing eligibility for hearing preservation surgery was lower than 30%.
Clear Tinnitus, middle-ear pressure, and tinnitus relief: a prospective trial.

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Goal: Our goal was to establish the efficacy, in a 12-week period, of Clear Tinnitus for tinnitus relief in patients with tinnitus of the severe, disabling type.

Hypothesis: We hypothesized that tinnitus relief with Clear Tinnitus reflects improvement in the sensory component of the tinnitus complaint by controlling the factor of aeration of the middle ears and improving eustachian tube function.

Method: In a prospective clinical trial of a homeopathic preparation—Clear Tinnitus—we attempted to identify in 15 tinnitus patients (14 male, 1 female; mean age, 47.6 years) its clinical efficacy for establishing tinnitus relief for a 3-month period. We employed a descriptive data analysis method across dimensions of risk to evaluate a base of multidimensional evidence and establish support for our hypothesis. A medical-audiological tinnitus patient protocol completed by each patient identified the clinical type of tinnitus as predominantly cochlear, with a central and middle-ear component bilaterally. We identified fluctuation in middle-ear pressure (MEP) via patients' clinical history, supported by physical examination and established with tympanometry, as a factor influencing the clinical course of the tinnitus in each patient.

Results: Eleven of 15 patients completed the study. Seven responders reported tinnitus relief; four did not respond. Descriptive data analysis failed to detect any trends in a change in response with audiometric tests across the hearing spectrum; thus, we could derive no coefficients of hearing change. Evaluation revealed high-frequency tinnitus in 11 patients. The Feldmann masking curve comparison at the start and end of the study showed no significant change in the 11 patients. There was no significant alteration in the minimum masking levels or loudness discomfort levels before and after the study. Tympanometry and MEP measurement indicated a significant difference in MEP with an improvement on average of -58.18 in the right ear and -40.90 in the left ear for the 11 patients. Quantitative electroencephalography analysis revealed a marked difference in the number of significant abnormal recordings between the different frequency bands, with the delta band significantly higher than the theta, alpha, and beta bands for both the overall cohort of patients (n = 11) and those reporting tinnitus relief (n = 7). The tinnitus outcome questionnaires—tinnitus intensity index, the tinnitus annoyance index, and the tinnitus reaction questionnaire—revealed a significant difference for the patients (7 of 11) obtaining tinnitus relief. Results of the tinnitus stress test, the tinnitus handicap index, and the measurement of depression scale before and after the study were not statistically significant.

Conclusions: Patients who completed the study demonstrated with tympanometry a statistical and clinical significance in MEP improvement or maintenance of MEP (or both). Patients with tinnitus of the severe disabling type selected for this study and responding to Clear Tinnitus reported tinnitus relief accompanied by improvement in or maintenance of MEP of the middle ears. The statistical and clinical significance of Clear Tinnitus for establishing tinnitus relief remains to be established with a larger cohort of tinnitus patients.
Review

The latest buzz on tinnitus.

Daugherty JA.
Silverstein Institute, Sarasota, Fla., USA.
Although often benign, tinnitus can cause significant psychological distress and may be a symptom of a life-threatening disease. Prompt diagnosis and knowledge of current treatment options are essential.

Others

[Quality of partnerships in patients with tinnitus.]
[Article in German]
HNO. 2007 Sep 15; [Epub ahead of print]

Stürz K, Viertler HP, Kopp M, Pfaffenberger N, Günther V.
Abteilung für Klinische Psychologie und Psychotherapeutische Ambulanz, Univ.-Klinik für Psychiatrie, Anichstraße 35, A-6020, Innsbruck, Österreich, verena.guenther@uki.at.

Background: Chronic tinnitus can massively impair the quality of life of patients affected with this disorder. Whether the constant ringing sounds and head noises heard by the sufferer have a stressful effect on the individual's partner has not been investigated so far.

Patients and methods: A total of 32 members of the Tyrolean tinnitus self-help group suffering from chronic tinnitus and their partners with whom they shared a common household for a minimum period of 2 years underwent psychological investigation with regard to their subjectively experienced tinnitus-related stress, the quality of their partnership, emotional support they received, style of communication with their partners, and depression.

Results: Our results show that it is not the extent of subjective tinnitus that is associated with impaired partnership quality, but rather the extent of tinnitus-associated depression.

Conclusions: The results suggest that in clinical practice, less emphasis should be placed on the dynamics of family and partnership aspects and more attention should be paid to the possible presence of symptoms of depression and their treatment.

Tinnitus school: an educational approach to tinnitus management based on a stress-reaction tinnitus model.

Alpini D, Cesarani A, Hahn A.
Scientific Institute S. Maria Nascente, Don Carlo Gnocchi Foundation, Milan, Italy.
dalpini@dongnocchi.it

Stress is a significant factor influencing the clinical course of tinnitus. The auditory system is particularly sensitive to the effects of various stress factors (chemical, oxidative, emotional, etc.). Different stages of reaction (alarm, resistance, exhaustion) lead to different characteristics of tinnitus and to different therapeutic approaches. Individual characteristics of stress reaction may explain different aspects of tinnitus in various patients with different responses to treatment, despite similar audiological and etiological factors. A model based on individual reactions to stress factors (stress-reaction tinnitus model, or SRTM) could explain tinnitus as an alarm signal. In each patient, stressors have to be identified during the alarm phase to prevent an evolution toward the resistance and exhaustion phases. In the exhaustion phase, chronic tinnitus is due to the organization of a paradoxical auditory memory and a pathologically shifted attention to tinnitus. The aim of our study is to describe a
therapeutic proposal based on the SRTM by taking an educational approach to management of chronic tinnitus. The educational aspect is emphasized; thus, we named our approach tinnitus school. Selection of appropriate patients and follow-up is based on psychometrics of tinnitus and stress questionnaires, including a tinnitus reaction questionnaire, a tinnitus cognitive questionnaire, and a 20-item perceived stress questionnaire. Tinnitus school is a three-phase program: counseling, training, and home training. Training is based on a tinnitus-fitted physiotherapeutic protocol.

XIV Case Reports

Dural arteriovenous fistula of the transverse-sigmoid sinus causing trigeminal neuralgia.
de Paula Lucas C, Zabramski JM.
Department of Neurology and Neurosurgery, Instituto de Neurologia de Goiânia, Goiás, Brazil.

The authors analysed an unusual case of dural arteriovenous fistula (DAVF) of the transverse-sigmoid sinus causing trigeminal neuralgia is presented. Although progression to almost continuous facial pain has been reported, symptoms may be indistinguishable from typical trigeminal neuralgia. The patient had a 6-year history of right-sided trigeminal neuralgia initially well controlled by medical management. He was referred for surgical management after 10 months of progressively worsening of symptoms. At the time of consultation, the patient complained of pulsatile tinnitus in the right ear. Computed tomography imaging and angiography demonstrated a DAVF involving the right transverse-sigmoid sinus junction with retrograde venous drainage. Surgical resection of the DAVF provided both angiographic cure and complete relief of all symptoms. The authors discuss the pathophysiology of trigeminal neuralgia in patients with a DAVF.

Continuous peripheral nerve blockade for inpatient and outpatient postoperative analgesia in children.
Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania 19104-4399, USA. ganesha@email.chop.edu

Background: This is an audit of the continuous peripheral nerve blockade (CPNB) program that was implemented at our institution to provide postoperative analgesia after orthopedic procedures in children.
Methods: We reviewed the departmental regional anesthesia registry and the medical records of consecutive children who received CPNB for postoperative analgesia at The Children's Hospital of Philadelphia between February 2003 and July 2006. Patients were prospectively followed until cessation of the effects of CPNB and/or resolution of any related complications. Data collected contemporaneously included presence of sensory and motor blockade, pain scores in inpatients, opioid administration, and complications related to CPNB.
Results: A total of 226 peripheral nerve catheters were placed in 217 patients. One hundred eight patients (112 catheters) were discharged home with CPNB. The ages ranged from 4 to 18 yr (13.7 +/- 3.4). Local anesthetic solution (0.125% bupivacaine [n = 164], 0.1% ropivacaine [n = 12], or 0.15% ropivacaine [n = 27]) was infused at an initial rate of 2-12 mL/h based on patients' weights and locations of catheters. The mean duration of local anesthetic infusion was 48.4 +/- 29.3 h (range 0-160 h). The percentage of patients who did not require any opioids in the first 8, 24, and 48 h after surgery was 56%, 26%, and 21%, respectively. The incidence of nausea and vomiting was 14% (13% in outpatients, 15% in inpatients). Complications were noted in 2.8% of patients. Three patients had prolonged numbness (>24 h) that resolved spontaneously; one developed superficial cellulitis that
resolved with a course of antibiotics; one had difficulty removing the catheter at home and one developed tinnitus 24 h after starting CPNB that resolved quickly after clamping of the catheter followed by removal.

**CONCLUSION:** It is feasible to implement a CPNB program to provide an alternative method of inpatient and outpatient postoperative analgesia after orthopedic surgery in children when appropriate expertise is available. Patient and family education along with frequent follow-up are crucial to detect and address adverse events promptly.

**Congenital cholesteatoma of mastoid origin.**
J Laryngol Otol. 2007 Oct 12;:1-5 [Epub ahead of print]

**Lee JH, Hong SJ, Park CH, Jung SH.**
Department of Otorhinolaryngology–Head and Neck Surgery, School of Medicine, Hallym University, Chuncheon, South Korea.

**Objective:** We report an extremely rare case of congenital cholesteatoma of mastoid origin.

**Case report:** A male patient was admitted with a one-month history of dizziness and headache, plus tinnitus in the right ear. Computed tomography scanning of the temporal bone showed destruction of the posterior wall of the external auditory canal by a lesion of soft tissue density in the right mastoid cavity, and also destruction of the bony plates of the posterior fossa and the sigmoid sinus, and of the mastoid tegmen. During surgery, a huge cholesteatoma sac was observed in the mastoid cavity, containing a large amount of keratinous material. The tegmen mastoideum and the bony plates of the posterior fossa and the sigmoid sinus were also observed to be destroyed. The skin and the tympanic membrane of the external auditory canal were intact, and the middle ear and aditus ad antrum mucosa were normal. The huge cholesteatoma sac was completely excised via a partial translabyrinthine approach, eradicating the superior and posterior semicircular canals. Conclusion: This case of congenital cholesteatoma of mastoid origin was diagnosed by clinical examination, radiological evaluation and surgical findings.

**Rupture of an aneurysm of the noncoronary sinus of Valsalva into the right atrium.**
Eur J Echocardiogr. 2007 Sep 27; [Epub ahead of print]

**Guenther F, von Zur Muhlen C, Lohrmann J, Bode C, Geibel A.**
Department of Cardiology and Angiology, University Hospital of Freiburg, Hugstetter Strasse 55, 79106 Freiburg, Germany. A 32-year-old woman presented to the emergency department after the sudden onset of palpitations, dyspnoea and left-sided tinnitus. Echocardiography revealed a ruptured aneurysm of the noncoronary sinus of Valsalva into the right atrium. Due to deterioration of right heart failure with rapidly progressive decline of systemic blood pressure, the patient underwent immediate surgery with a patch repair of the ruptured aneurysm. A few days later, the patient was discharged home in good condition.

**Intraneural perineurioma of the VIIth cranial nerve: case report.**
Neurosurgery. 2007 Sep;61(3):E652; discussion E652.

**Christoforidis M, Buhl R, Paulus W, Sepehrnia A.**
Department of Neurosurgery, Clemenshospital, Münster, Germany. mchristoforidis@web.de

**Objective:** The authors describe the clinical and pathological features of the second reported case of an intraneural perineurioma involving a major intracranial nerve and the first case of this entity involving the VIIth cranial nerve.

**Clinical presentation:** A 59-year-old woman presented with a long history of dizziness, tinnitus, hearing loss, and unstable gait. A magnetic resonance imaging scan revealed a small intrameatal lesion, which showed no clear progression from 2000 to 2006.
**Intervention:** As a result of worsening symptoms and a suspected vestibular schwannoma, an attempt of tumor resection through a retrosigmoid approach was performed. This revealed diffusely infiltrated and fusiform enlarged vestibular and cochlear nerves, with no identifiable border between the main tumor mass and normal nerve. An en bloc nerve-tumor mass excision was performed. The pathological findings confirmed the diagnosis of an intraneuronal perineurioma.

**Conclusion:** The experience with this unique case and the experience of others with the management of extracranial intraneural perineuriomas lead the authors to conclude that the most reasonable surgical management of this tumor at this location is a nerve-tumor cross-section resection.

**Neurofibromatosis type 2 associated with multiple cranial nerve schwannomas: a case report.**
Kulak Burun Bogaz Ihtis Derg. 2007;17(3):171-175.

**Halefoğlu AM.**
Department of Radiology, Sişli Etfal Training and Research Hospital, Istanbul, Turkey.
halefoglu@hotmail.com

A 16-year-old male patient complained of right-sided tinnitus and mild deafness of one-month history. He also had a family history of neurofibromatosis type 2 and a history of a prior operation for left vestibular schwannoma a year ago. Otoneurologic examination revealed moderate sensorineural hearing loss. Magnetic resonance imaging demonstrated multiple extra-axial enhancing masses in the vicinity of both hypoglossal nerves, the right vestibular nerve, the left vestibular nerve, the right trigeminal, the left oculomotor, and the right abducens nerves. These findings were evaluated as multiple cranial nerve schwannomas. The case was considered a rare manifestation of neurofibromatosis type 2 without any concomitant abnormality in the central nervous system. Symptomatic medical treatment was initiated and the patient was referred to the neurosurgery department.

**Echinococciosis presenting as an otogenic brain abscess: An unusual lesion of the middle ear cleft and temporal lobe.**
Auris Nasus Larynx. 2007 Sep 7; [Epub ahead of print]

**Llanes EG, Stibal A, Mühlethaler K, Vajtai I, Häusler R, Caversaccio M.**
Department of Otorhinolaryngology, Head and Neck Surgery, Inselspital (University Hospital), University of Berne, 3010 Berne, Switzerland.

This paper presents a case of a 28-year-old male with a seizure episode and a 4-year history of intermittent tinnitus on the left ear. On computed tomography and magnetic resonance imaging, a density with rim enhancement was found at the temporal lobe, associated with mastoid tegmen destruction and middle ear mass, indicating cholesteatoma with complicating brain abscess. Evacuation of the brain abscess was performed with a combined otolaryngologic and neurosurgical procedures (canal wall-down mastoidectomy and temporal craniotomy). The pathology turned out to be infestation with Echinococcus granulosus.

**[Tinnitus of vascular type. Diagnostic possibilities]**
[Article in Spanish]

**de García Hombre AM, Balderrama Caballero DH, Rodríguez Adrados F.**
Servicio de Otorrinolaringología, Hospital General de Fuerteventura, Puerto del Rosario.
aliadal@terra.es
It's defined tinnitus as an auditive perception of internal origin that it does not answer to vibratory external action. The rest of the sounds are considered as real biological noises and not properly as tinnitus. Tinnitus is a very common symptom in our practice. It is important to determine what causes it, since medical treatment is effective in some cases and prevents serious complications, severe bleeding and neurological consequence if any surgical treatment is carried out. We present two cases of tinnitus of vascular origen, the first caused by venous malformation and the second by an arterial one. We review the literature of this entity.

[Vogt Koyanagi Harada syndrome. Report of a case with hearing loss, tinnitus, vertigo associated to uveitis]
[Article in Spanish]
Pino Rivero V, Pardo Romero G, Rodriguez Carmona M, Iglesias González RJ, del Castillo Beneyto F.
Hospital Campo Arañuelo, Navalморal de la Mata, Cáceres. vicentepinorivero@terra.com

Vogt-Koyanagi-Harada sindrome is an autoimmune sistemic disease characterized by granulomatous bilateral uveitis with involvement of the central nervous system which can compromise the VIII cranial pair function producing tinnitus and neurosensorial hypoacusia. We report a case diagnosed in a young woman who also suffered episodes of vertigo. We review the literature of that pathology.

Treatment of a facial nerve neuroma with fractionated stereotactic radiotherapy.
McClelland S 3rd, Dusenbery KE, Higgins PD, Hall WA.
Department of Neurosurgery, University of Minnesota Medical School, Minneapolis, MN 55455, USA. mccl0285@umn.edu

BACKGROUND: Facial nerve neuromas are extremely rare and are often mistaken for acoustic neuromas when located near the vestibular nerve. Usually presenting with facial weakness and hearing loss, facial nerve neuromas of the cerebellopontine angle have commonly been managed by surgery. We present the first reported case of a facial nerve neuroma treated with fractionated stereotactic radiotherapy (FSRT).

METHODS: The patient was a 40-year-old woman who presented with tinnitus, dizziness and decreased hearing that was associated with a right intracanalicular mass on magnetic resonance imaging (MRI). She underwent a middle fossa craniotomy only to reveal a facial nerve tumor rather than an acoustic neuroma that was not resected due to the high risk of facial paralysis. Following surgery, her facial function worsened and was associated with tumor enlargement on MRI. She was referred for FSRT and received 54 Gy in daily 1.8-Gy fractions with a prescription isodose line of 90%.

RESULTS: Three months after treatment she had no worsening of her pretreatment symptoms, and at the 1-year follow-up, she experienced facial weakness improvement accompanied by an absence of tumor growth on MRI. These clinical and imaging findings persisted at 48 months of follow-up.

CONCLUSION: In the first report of a facial nerve neuroma treated with FSRT, this treatment resulted in excellent long-term (4-year) tumor control with improvement of pretreatment symptomatology and absence of morbidity. This report demonstrates the potential for using FSRT to treat facial nerve neuromas of the cerebellopontine angle that could otherwise be associated with significant operative morbidity. (c) 2007 S. Karger AG, Basel.
Synovial sarcoma of the temporomandibular joint area: report of a case.
Luo CW, Liu CJ, Chang KM.
Division of Oral and Maxillofacial Surgery, Department of Dentistry, Taipei Medical University Hospi-
tal, Taipei, Taiwan.

Synovial cell sarcoma is a relatively rare tumor of mesenchymal origin. It is a high-grade neoplasm
that microscopically shows a monophasic or biphasic cellular pattern and includes epithelial features
as well as supporting tissue features. Surgical excision is the primary mode of treatment. Postoperati-
ve radiotherapy and chemotherapy also is seen to be helpful. Between 3% and 10% of cases origin-
te in the head and neck. A review of relevant literature shows less than 10 cases of synovial cell sar-
coma of the temporomandibular joint area reported in the English literature. We report an additional
case of biphasic synovial cell sarcoma arising in the temporomandibular joint area, which caused ear
pain, tinnitus, and hearing loss, and we further discuss the clinical features, histopathology, differenti-
al diagnosis, and treatment modality.

Endolymphatic sac tumor demonstrated by intralabyrinthine hemorrhage. Case report.
Jagannathan J, Butman JA, Lonser RR, Vortmeyer AO, Zalewski CK, Brewer C, Oldfield EH,
Kim HJ.
Surgical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institu-
tes of Health, Bethesda, Maryland 20892-1414, USA.

Endolymphatic sac tumors (ELSTs) are locally invasive neoplasms that arise in the posterior petrous
bone and are associated with von Hippel-Lindau (VHL) disease. These tumors cause symptoms even
when microscopic in size (below the threshold for detectability on imaging studies) and can lead to
symptoms such as hearing loss, tinnitus, vertigo, and facial nerve dysfunction. While the mechanisms
of audiovestibular dysfunction in patients harboring ELSTs are incompletely understood, they have
critical implications for management. The authors present the case of a 33-year-old man with VHL
disease and a 10-year history of progressive tinnitus, vertigo, and left-sided hearing loss. Serial T1-
weighted magnetic resonance (MR) imaging and computed tomography scans revealed no evidence
of tumor, but fluid attenuated inversion recovery (FLAIR) MR imaging sequences obtained after
hearing loss demonstrated evidence of left intralabyrinthine hemorrhage. On the basis of progressive
disabling audiovestibular dysfunction (tinnitus and vertigo), FLAIR imaging findings, and VHL disease
status, the patient underwent surgical exploration of the posterior petrous region, and a small (2-mm)
ELST was identified and completely resected. Postoperatively, the patient had improvement of the
tinnitus and vertigo. Intralabyrinthine hemorrhage may be an early and the only neuroimaging sign of
an ELST in patients with VHL disease and audiovestibular dysfunction. These findings support tumor-
associated hemorrhage as a mechanism underlying the audiovestibular dysfunction associated with
ELSTs.

Endovascular stent placement of cervical internal carotid artery dissection related to a
seat-belt injury: a case report.
Nakagawa N, Akai F, Fukawa N, Yugami H, Kimoto A, Majima S, Taneda M.
Department of Neurosurgery, Kinki University School of Medicine, Osakasayama, Japan.
nakkan@neuro-s.med.kindai.ac.jp

Object: The incidence of carotid artery dissection related to blunt injury is very low, but the mortality
rate is high. Rapid diagnosis and proper treatments are discussed.
Clinical presentation: A 48-year-old woman presented diplopia and pulsating tinnitus of the left ear. An angiography showed a carotid cavernous fistula (CCF) and dissection of the extra-cranial internal carotid artery (ICA). To treat the dissection, a self-expanding endovascular stent was used. She has been followed for 6 years without any event and the ICA is patent.

Conclusion: Prompt diagnosis without delay and intimate follow-up is the key for the treatment of a carotid injury. Those patients who exhibit cervical bruits and/or seat-belt signs should be examined aggressively. Angioplasty with stents is amenable for patients with traumatic carotid dissections requiring vascular reconstruction in the acute stage.

Bilateral sudden profound hearing loss and vertigo as a unique manifestation of bilateral symmetric inferior pontine infarctions.

Bovo R, Ortore R, Ciorba A, Berto A, Martini A.
Department of Audiology, Ferrara University, Ferrara, Italy.

Objectives: We present a case of sudden bilateral profound deafness and vertigo, without any accompanying neurologic signs, secondary to bilateral infarctions of the cochlear and vestibular nuclei.

Methods: Vertigo, vomiting, tinnitus, and bilateral profound deafness suddenly developed in a 65-year-old woman without any accompanying neurologic signs. In particular, she did not present dysarthria, numbness, cranial nerve palsies, or visual or cerebellar signs.

Results: Magnetic resonance imaging of the brain revealed 2 fresh infarctions of 8 to 10 mm symmetrically localized in the posterolateral bulbopontine junction. Angiography revealed a complete occlusion of the basilar artery, with a well-represented backward flow of its distal portion from the carotid artery via posterior communicating arteries. Excluding a transient ischemic attack that occurred 16 days after the acute episode, the patient had had no other neurologic events at 8 months of follow-up.

Conclusions: Acute vertigo and sudden deafness in a patient with known cerebrovascular occlusive disease may represent the warning signs of an impending brain stem or cerebellar infarction, even when other neurologic signs are absent. These events are fortunately very rare, but should be considered by clinicians who see patients with vertigo.

Vertigo caused by a nasopharyngeal carcinoma.

Krause E, Hempel JM, Gürkov R.
Department of Otorhinolaryngology, Ludwig Maximilians University Munich, Marchioninistraße 15, 81377, Munich, Germany, eike.krause@med.uni-muenchen.de.

A case of a 63 year-old woman with acute vertigo, hearing loss and tinnitus caused by a nasopharyngeal carcinoma is reported. Despite a long-standing unilateral Eustachian tube dysfunction, only the occurrence of vertigo attacks lead to the diagnosis in this patient. Inner ear-related symptoms are rare in nasopharyngeal carcinoma and the disease is uncommon in Europe. Skull base tumors are an important differential diagnosis of labyrinth dysfunction that can be detected by MRI. A complete diagnostic work-up is necessary in patients with unilateral tube dysfunction, to allow early detection of this disorder.
Cochlear implantation for hearing loss associated with bilateral endolymphatic sac tumors in von Hippel-Lindau disease.

Surgical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892-1414, USA.

Objective: Bilateral endolymphatic sac tumors (ELSTs) are associated with von Hippel-Lindau disease and often underlie significant audiovestibular morbidity, including hearing loss.

Patient: This 44-year-old female von Hippel-Lindau disease patient presented with tinnitus, vertigo, and binaural hearing loss. Magnetic resonance and computed tomography imaging demonstrated bilateral ELSTs, and audiometry confirmed bilateral hearing loss.

Intervention: The patient underwent staged resection of the ELSTs (left then right). After resection of the left ELST and during the same operation, a cochlear implant was placed.

Main outcome measures: Clinical, audiometric, and imaging data.

Results: Postoperatively, the patient had resolution of tinnitus and vertigo with a significant implant-aided improvement in hearing.

Conclusion: Because of their unique anatomic and biologic features, resection of bilateral tumors and cochlear implantation in deaf ELST patients is a potential option to improve hearing and quality of life.
Clinical Trials

Source: clinicaltrials.gov

Safety and Effectiveness of Repetitive Transcranial Magnetic Stimulation in the Treatment of Tinnitus

<table>
<thead>
<tr>
<th>Current status</th>
<th>not yet open for patient recruiting</th>
</tr>
</thead>
</table>
| Sponsors and collaborators | University Hospital Tuebingen  
                                      German Research Foundation  
                                      CenTrial GmbH               |
| Information provided by | University Hospital Tuebingen |
| ClinicalTrials.gov Identifier | NCT00518024 |

Purpose

Tinnitus, i.e., the perception of sounds or noise in the absence of auditory stimuli, is a frequent and often severely disabling symptom of different disorders of the auditory system. There are currently no causal treatments. Using repetitive transcranial magnetic stimulation (rTMS), we have previously demonstrated that the temporoparietal cortex is critically involved in tinnitus perception and that tinnitus can be reduced by rTMS applied to these cortical regions. Therefore, it is reasonable to test rTMS as a potential new treatment strategy against tinnitus. At this stage, small pilot studies indicate some effect on tinnitus impairment but the reduction is predominantly reported to be transient, with high interindividual variability, and questionable clinical relevance. Moreover, the optimal stimulation area is unclear.

Here, we use theta burst stimulation (TBS), a new rTMS paradigm for the prolonged modulation of cortical activity. The aim of this study is to test safety and effectiveness of 4 weeks of daily bilateral TBS to two cortical areas on chronic tinnitus compared to sham-stimulation.

Condition(s)

Tinnitus

Interventions

Procedure: Repetitive Transcranial Magnetic Stimulation (rTMS)

Phase

Phase II

Study type and design

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

Number of arms in study

3

Official title:

Safety and Effectiveness of Bilateral Repetitive Transcranial Magnetic Stimulation (Theta Burst Stimulation) in the Treatment of Chronic Tinnitus

Primary Outcome Measures

Tinnitus severity (Tinnitus Questionnaire) [Time Frame: after the end of treatment]

Secondary Outcome Measures

Visual Analog Scale (Tinnitus Loudness); Visual Analog Scale (Tinnitus Annoyance); Visual Analog Scale (Tinnitus Change); Beck's Depression Inventory; Symptom Check List; Audiogram; Speech Audiometry [Time Frame: after end of treatment]

Total Enrollment Arms

48
| Total Enrollment Arms | 1) Experimental  
Bilateral theta burst stimulation to the secondary auditory cortex  
2) Experimental  
Bilateral theta burst stimulation to the tertiary auditory cortex  
3) Sham Comparator  
Bilateral theta burst stimulation to a non-cortical region |
|----------------------|--------------------------------------------------|
| Assigned Interventions | 1) Procedure: Repetitive Transcranial Magnetic Stimulation (rTMS)  
Bilateral Theta Burst Stimulation  
2) Procedure: Repetitive Transcranial Magnetic Stimulation (rTMS)  
Bilateral Theta Burst Stimulation  
3) Procedure: Repetitive Transcranial Magnetic Stimulation (rTMS)  
Bilateral Theta Burst Stimulation |
| Inclusion criteria | Subjective tinnitus > 6 mo, < 5 ys |
| Exclusion criteria | Objective tinnitus  
Seizures  
Brain trauma  
Brain surgery  
Pacemaker  
intake of: Benzodiazepines, antiepileptics, neuroleptics  
Suicidality |
| Gender Eligibility | Both |
| Age Eligibility | 18 Years-75 Years |
| Contact | Carola Arfeller, M.Sc.  
phone ++49 7071 29 Ext. 82294  
carola.arfeller@med.uni-tuebingen.de |
| Location | Christian Plewnia, M.D., Principal Investigator, University of Tuebingen, Department of General Psychiatry |
| Study ID Number | PL 525/1-1 |
| Last Updated | August 15, 2007 |
| Record first received | August 15, 2007 |
| ClinicalTrials.gov Identifier | NCT00518024 |
| Health Authority | Germany: Ethics Commission |
### Efficacy of Acetylcysteine in Patients Undergoing Surgery for Otosclerosis

<table>
<thead>
<tr>
<th>Current status</th>
<th>recruiting</th>
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</table>
| Sponsors and collaborators | Karolinska University Hospital  
Karolinska Institutet  
AstraZeneca |
| Information provided by | Karolinska University Hospital |
| ClinicalTrials.gov Identifier | NCT00525551 |

**Purpose**

In otosclerosis, one of the tiny bones of the middle ear is unable to move normally. Sounds cannot be transferred to the inner ear and a conductive hearing loss ensues. The disorder is usually treated by an operation where the bone is replaced by a prosthesis. This restores hearing at low sound frequencies. At high frequencies, surgery is less effective. The smaller effect at high frequencies is probably caused by surgically induced inner ear damage. Animal studies have shown that the drug acetylcysteine can protect the inner ear against damage. It is not known whether the drug has similar effects in humans. This study will assess the efficacy of acetylcysteine in patients undergoing surgery for otosclerosis.

**Condition(s)**

Otosclerosis

**Interventions**

Drugs: Acetylcysteine, NaCl

**Phase**

Phase IV

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

**Number of arms in study**

2

**Official Title**

Acetylcystein Vid Stapedotomi

**Primary outcome measures**

Hearing thresholds [Time Frame: one year]

**Secondary outcome measures**

Self-reported vertigo and tinnitus [Time Frame: one year]

**Total Enrollment**

110

**Arms**

1) Active Comparator  
2) Placebo Comparator

**Assigned Interventions**

1) Drug: Acetylcysteine 150 mg / kg body weight. Drug is dissolved in NaCl to a final volume of 300 mL. This volume is infused starting one hour prior to surgery, and continued 1 hour after the end of surgery  
2) Drug: NaCl 300 mL 0.9% NaCl

**Inclusion criteria**

Otosclerosis where surgery is planned  
Air / bone gap larger than 20 dB  
Normal middle ear status

**Exclusion criteria**

Hypersensitivity to acetylcysteine  
Deafness on the other ear  
Stapedotomy previously performed on the ear  
Pregnancy  
Asthma

**Study start**

September 2007

**Expected completion**

September 2010

**Gender Eligibility**

Both
Age Eligibility
18 Years and above

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Location
Karolinska University Hospital, Dept. Of Otorhinolaryngology, Stockholm, SE-171 76, Sweden; Recruiting

Study chairs or principal investigators
Dan Bagger-Sjoback, M.D., Ph.D., Study Chair, Karolinska University Hospital
Anders Fridberger, M.D., Ph.D., Principal Investigator, Karolinska Institutet

Study ID Numbers
KS-OAS1; EudraCT 2006-006243-31

Last Updated
September 4, 2007

Record first received
September 4, 2007

ClinicalTrials.gov Identifier
NCT00525551

Health Authority
Sweden: Medical Products Agency

Source: ISRCTN Register
Medical treatment of Meniere's disease with betahistine: a placebo-controlled, dose-finding study

Current status
ongoing

Sponsors and collaborators
University Hospital Grosshadern (Klinikum Grosshadern) (Germany)
Department of Neurology

Source of funding
German Federal Ministry of Education and Research (Bundesministerium fuer Bildung und Forschung [BMBF]) (Germany)

ISRCTN
ISRCTN44359668

Local reference number
04T-617

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

Condition
Meniere’s disease

Intervention
The trial comprises three arms:
1. Therapy with high-dose betahistine (3 x 48 mg)
2. Therapy with low-dose betahistine (2 x 24 mg)
3. Placebo
The total treatment time will be nine months with a three month follow-up. The trial is estimated to last three years (first patient in to last patient out).

Study type and design
Placebo-controlled, double-blind, randomised controlled trial.

Title of trial/grant title
Medical treatment of Meniere's disease with betahistine: a placebo-controlled, dose-finding study

Acronym:
BEMED
<table>
<thead>
<tr>
<th>Ethics approval</th>
<th>Ethics approval pending as of 13th August 2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Countries of recruitment</td>
<td>Germany</td>
</tr>
<tr>
<td>Primary Outcome Measures</td>
<td>Number of vertigo attacks in the three treatment arms during the last three months of the treatment period.</td>
</tr>
<tr>
<td>Secondary Outcome Measures</td>
<td>ISRCTN44359661. Number of vertigo attacks during the last three months of the total follow-up period</td>
</tr>
<tr>
<td></td>
<td>2. Median duration of vertigo attacks and median severity of vertigo attacks during the last three months of the treatment period and the last three months of the total follow-up period</td>
</tr>
<tr>
<td></td>
<td>3. Change of:</td>
</tr>
<tr>
<td></td>
<td>3.1. Peripheral vestibular function</td>
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<tr>
<td></td>
<td>3.2. Tinnitus intensity</td>
</tr>
<tr>
<td></td>
<td>3.3. Effect of tinnitus on quality of life</td>
</tr>
<tr>
<td></td>
<td>3.4. Subjective hearing loss</td>
</tr>
<tr>
<td></td>
<td>3.5. Objective hearing loss - determined by acoustic evoked potentials</td>
</tr>
<tr>
<td></td>
<td>3.6. Change of handicap/impairment due to vertigo or dizziness - assessed by the Dizziness Handicap Inventory (DHI) and the Vestibular Disorders Activities of Daily Living (VADL) score</td>
</tr>
<tr>
<td>Number of participants</td>
<td>84</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>1. Definite Meniere’s disease according to the American Academy of Ophthalmology and Otolaryngology, Head and Neck Surgery</td>
</tr>
<tr>
<td></td>
<td>1.1. Two or more attacks of vertigo, each lasting more than 20 minutes</td>
</tr>
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<td></td>
<td>1.2. Audiometrically documented hearing loss in at least one examination</td>
</tr>
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<td>1.3. Tinnitus or aural fullness in the affected ear</td>
</tr>
<tr>
<td></td>
<td>1.4. Other causes excluded</td>
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<tr>
<td></td>
<td>2. At least two attacks of Meniere’s disease per month for at least three subsequent months</td>
</tr>
<tr>
<td></td>
<td>3. Aged 18 to 80 years</td>
</tr>
<tr>
<td></td>
<td>4. Written informed consent to all protocol-specified procedures</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>1. Other vestibular disorders such as vestibular migraine or phobic postural vertigo</td>
</tr>
<tr>
<td></td>
<td>2. Contraindications for treatment with betahistine-dihydrochloride, such as:</td>
</tr>
<tr>
<td></td>
<td>2.1. Asthma bronchiale</td>
</tr>
<tr>
<td></td>
<td>2.2. Pheochromacytoma</td>
</tr>
<tr>
<td></td>
<td>2.3. Pregnancy or breast-feeding</td>
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<td></td>
<td>2.4. Severe dysfunction of kidneys or liver</td>
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<tr>
<td></td>
<td>2.5. Ulcer of the stomach or duodenum</td>
</tr>
<tr>
<td></td>
<td>2.6. Tumours</td>
</tr>
<tr>
<td></td>
<td>2.7. Severe coronary heart disease</td>
</tr>
<tr>
<td></td>
<td>2.8. Treatment with other antihistamines</td>
</tr>
<tr>
<td>Study start</td>
<td>01/11/2007</td>
</tr>
</tbody>
</table>
Prime stimulation as an enhancement of low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) for the treatment of tinnitus

Current status Completed

Sponsors and collaborators Regensburg District Clinic (Bezirksklinikum Regensburg) (Germany)

Source of funding Tinnitus Research Initiative (Germany)

ISRCTN ISRCTN03638520

Local reference number 01/194

Study hypothesis Low-frequency rTMS has been investigated for the treatment of hyperexcitability disorders such as auditory hallucinations and tinnitus. Experimental data indicate that the depressant effect of low-frequency rTMS can be enhanced by high frequency stimulation. In the proposed study we investigate whether priming improves therapeutic efficacy of low-frequency rTMS in a clinical application.

Condition Chronic tinnitus

Intervention Experimental intervention: Low frequency rTMS over the left auditory cortex with priming stimulation: 6Hz (90% motor threshold, 960 stimuli) followed by low frequency rTMS (110% motor threshold, 1Hz, 1040 stimuli/day) 5 days a week for two weeks.

Control intervention: Standard protocol of low frequency rTMS (110% motor threshold, 1Hz, 2000 stimuli/day), 5 days a week for two weeks.

Study type and design Randomized, controlled, parallel-design study

Title of trial/grant title Priming stimulation as an enhancement of low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) for the treatment of tinnitus

Acronym: NA

Ethics approval Ethics Committee of the University of Regensburg, University Clinic Regensburg (ref: 01/194). Approved on 19.12.2001 (amendment on 19.2.2007).

Countries of recruitment Germany
<table>
<thead>
<tr>
<th>Primary Outcome Measures</th>
<th>Change in tinnitus severity according to the Tinnitus Questionnaire of Goebel and Hiller (baseline vs day 12).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Outcome Measures</td>
<td>Reduction of tinnitus severity as measured by the Tinnitus Questionnaire of Goebel and Hiller (TQ; THI) during the follow-up period (screening versus baseline versus days 18, 59, 90)</td>
</tr>
<tr>
<td>Number of participants</td>
<td>32</td>
</tr>
</tbody>
</table>
| Inclusion criteria | 1. Female and male in- and outpatients  
2. Age 18-70 years  
3. Diagnosis of subjective chronic tinnitus  
4. Duration of tinnitus more than 6 months |
| Exclusion criteria | 1. Patients with conductive hearing loss of more than 15dB  
2. Objective tinnitus  
3. Treatable otologic disorder  
4. Involvement in other treatments for tinnitus at the same time  
5. Clinically relevant psychiatric comorbidity  
6. Clinically relevant unstable internal or neurological comorbidity  
7. History of or evidence of significant brain malformation or neoplasm, head injury  
8. Cerebral vascular events  
9. Neurodegenerative disorder affecting the brain or prior brain surgery  
10. Factors militating against the use of TMS (e.g. cardiac pace makers or other metal implants)  
11. Pregnancy |
| Study start | 01/03/2003 |
| Expected completion | 31/07/2007 |
| Contact | Dr Berthold Langguth, Bezirksklinikum Regensburg, Universitaetsstrasse 84, 93053 Regensburg  
www.bkr-regensburg.de |
| Last Updated | 30/10/2007 |
| ISRCTN | ISRCTN03638520 |