The Whole is More than the Sum of its Parts (Aristoteles)

When Matteo de Nora decided to found the TRI in 2006, it was one of his visions that the tinnitus field could move forward by connecting clinicians and researchers from many disciplines and many countries.

At that time the research structure in tinnitus was characterized by separate groups working largely in isolation. Interestingly, the places where interdisciplinary research happened were places where couples with different backgrounds worked together (e.g. Aage and Magrareta Moller, Pavel and Margaret Jastreboff, Jean Luc Puel and Cecile Nicolas-Puel, Jack Vernon and Mary Meikle and many more).

These couples were the “proof of principle” that interdisciplinary collaboration can move the tinnitus field forward. At the same time these couples demonstrated that interdisciplinary tinnitus research was still at the level of a “family business”. With the goal to “professionalize” interdisciplinary interaction TRI has organized six international meetings and many more small group workgroup meetings, which were all based on the interaction of researchers and clinicians with different backgrounds. Over 300 publications emerged from the activities of TRI. There is no doubt that these activities moved the tinnitus field significantly forward. This has contributed to a steadily increase of quantity and quality of tinnitus-related publications with a new maximum reached in 2012.

Figure: amount of tinnitus related publications per year.
The increasing recognition of tinnitus as a research field is also reflected by the fact that the 44th volume of the Springer Handbook of Auditory Research is devoted to tinnitus (see book review on page 8).

However, the critical question still remains: how much these activities have helped the millions of patients worldwide who suffer day after day from their tinnitus. Many explorative treatments have been attempted, most of which fail to help many patients, but some with success for a small group of them. Examples are carbamazepine for typewriter tinnitus, cochlear implants for unilaterally deaf patients, diverse brain stimulation approaches, neurofeedback or virtual reality treatment.

The study of Cima et al. which was published in Lancet this year and which received lots of media attention around the world, has demonstrated that a well-organized application of counseling, sound therapy and cognitive behavioral therapy in a stepped care process is much more efficient than treatment as usual. Thus the year 2012 has brought a clear statement against therapeutic nihilism and will hopefully overcome the attitude that “nothing can be done” for tinnitus.

Even though psychological and audiological treatments help many patients to habituate and to cope with tinnitus, most will say that they would prefer if the tinnitus sound was gone. Thus a cure for both the sound and the affective components remains the goal of research for 2013. The 7th TRI Meeting will be devoted to this goal and to all approaches that make tinnitus treatment more effective. It will take place in Valencia from May 15th to the 18th, 2013 under the motto “Tinnitus: a Treatable Disease”.

We hope to meet you all in Valencia to enjoy Spanish sun and paella, to foster knowledge exchange and networking and to speed up the quest for a cure.

Ana Belén Elgoyhen  Dirk De Ridder  Berthold Langguth  Sylvia Dorner-Mitschke
RESEARCH HIGHLIGHTS


By investigating the interaction between stress and CNS response patterns to cochlear damage this animal study aims at highlighting the relevance of stress in the generation of tinnitus.


By demonstrating diminished cortical inhibition and increased cortical excitation in an aging mouse model of tinnitus specifically in auditory cortical areas, this study sheds light on the neuronal mechanisms of tinnitus.


Cognitive impairment has been repeatedly documented in tinnitus patients. This study demonstrates that cognitive impairment as assessed by a short computerized test is an independent predictor for tinnitus handicap.


This serendipitous finding of tinnitus suppression after a discrete injury of the area of the locus caudate provides a hint for a potential target for the treatment of tinnitus by deep brain stimulation.


By demonstrating that baseline neuronal activity before noise trauma predicts tinnitus development after trauma, this animal study provides a potential explanation why some people with noise induced hearing loss develop tinnitus, whereas others don’t.


By demonstrating a correlation between oscillatory gamma activity in auditory cortex and tinnitus intensity on an individual level, this study confirms the relevance of cortical gamma activity in the pathophysiology of tinnitus.


In this “Opinion” article a testable model is proposed, which provides an explanation for neuroplastic processes associated with learning and disease.


By investigating people with gaze-evoked tinnitus and MRI, the effect of gaze on specific structures along the central auditory pathways could be identified. Observed findings are consistent with the thalamocortical dysrhythmia hypothesis of tinnitus.
Tinnitus: A Treatable Disease
Announcement

The 7th International TRI Tinnitus Conference will be held in May 15-18, 2013, in Valencia, Spain.

Please mark your calendars with this extraordinary event!

Congress Venue: SH Valencia Palace Hotel, Paseo Alameda 32, 46023 Valencia, Spain

Registration is open now!

Abstract submission for oral and poster presentation will be possible from December, 17th, 2012

**Oral Presentations** will cover unpublished preliminary or finalized data, novel ideas and techniques and are 15 minutes in length.

**Poster sessions** will also cover unpublished preliminary or finalized data, novel ideas and techniques, with the added value that viewers can study and restudy your information and discuss it with you one on one.

**Key Dates:** Deadline for all submissions and proposals: February 1, 2013
Early registration deadline is February 1, 2013

For more details please look at http://tri2013.tinnitusresearch.org

We are looking forward to seeing you all in Valencia, in May 2013!

**JM Láinez, J Marco, C Morera, Mi Pitarch, I Diges, D De Ridder, AB Elgoyhen, B Langguth**

2013 Conference Organizers

TRI Office Germany: Sylvia Dorner-Mitschke, Susanne Staudinger
E-mail: meetings@tinnitusresearch.org
Upcoming Meetings

Masterclass: Tinnitus & Hyperacusis in Adults and Children
When: January 22 – 24, 2013
Where: UCL Ear Institute, London, UK
Detailed Information: [http://www.ucl.ac.uk/ear/courses/shortcourses/aamc/aamc-pages/tinnitusandhyperacusis](http://www.ucl.ac.uk/ear/courses/shortcourses/aamc/aamc-pages/tinnitusandhyperacusis)

36th MidWinter Meeting of the Association for Research in Otolaryngology (ARO)
When: February 16 – 20, 2013
Where: Baltimore, MD, USA
Detailed Information: [http://www.aro.org/mwm/mwm.html](http://www.aro.org/mwm/mwm.html)

1st International Conference on Hyperacusis: Causes, Evaluation, Diagnosis and Treatment
When: March 01 – 02, 2013
Where: Birkbeck College, University of London, London, UK
Detailed Information: [http://www.royalsurrey.nhs.uk/advanced-audiology-seminars](http://www.royalsurrey.nhs.uk/advanced-audiology-seminars)

Tinnitus & Hyperacusis Therapy Masterclass
When: March 04 – 08, 2013
Where: Birkbeck College, University of London, London, UK
E-Mail: hashir.aazh@nhs.net
Detailed Information: [http://tinnitustherapy.org.uk/](http://tinnitustherapy.org.uk/)

AIA-DAGA 2013 Conference on Acoustics
including the 40th Italian (AIA) Annual Conference on Acoustics and the 39th German Annual Conference on Acoustics (DAGA)
When: March 18 – 21, 2013
Where: Meran, Italy

AudiologyNOW! 2013
When: April 03 – 06, 2013
Where: Anaheim, CA, USA
Detailed Information: [http://www.audiologynow.org/](http://www.audiologynow.org/)
84. Jahresversammlung der Deutschen Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V.
When: May 08 – 12, 2013
Where: Nuernberg Convention Center, Nuernberg, Germany
Detailed Information: http://www.hno.org/veranstaltungen/ankuendigungen.html

7th INTERNATIONAL TRI CONFERENCE ON TINNITUS 2013
Tinnitus: A Treatable Disease?
When: May 15 – 18, 2013
Where: Valencia, Spain
Detailed Information: http://tri2013.tinnitusresearch.org

11th European Symposium on Paediatric Cochlear Implantation
When: May 23 – 26, 2013
Where: Lütfi Kirdar Convention and Exhibition Center Rumeli Building, Istanbul, Turkey
Detailed Information: http://www.espci2013.net

20th IFOS World Congress
When: June 01 – 05, 2013
Where: Seoul, Korea
Detailed Information: http://www.ifosseoul2013.com/

ICA 2013, 165th Meeting of the Acoustical Society of America, 52nd Meeting of the Canadian Acoustical Association and the 21st International Congress on Acoustics
When: June 02 – 07, 2013
Where: Montreal, Quebec, Canada
Detailed Information: http://www.ica2013montreal.org/

When: June 16 – 20, 2013
Where: Washington Trade and Convention Center, Seattle, WA, USA
Detailed Information: http://www.humanbrainmapping.org/i4a/pages/index.cfm?pageid=3298

13th International Conference on Cochlear Implants and Other Implantable Auditory Technologies
When: June 18 – 21, 2013
Where: Munich, Germany
Detailed Information: http://www.ci2014muc.info/
11th EFAS Congress
When: June 19 – 22, 2013
Where: Budapest, Hungary
Detailed Information: http://www.efas2013.eu/

117th American Academy of Otolaryngology, Head and Neck Surgery Annual Meeting & OTO EXPO
When: September 29 – October 02, 2013
Where: Vancouver, BC, CA
Detailed Information: http://www.entnet.org/

58th International Congress of Hearing Aid Acousticians EUHA
When: October 16 – 18, 2013
Where: Convention Center Nürnberg, Germany
Detailed Information: http://www.euha.org

28. Politzer Society Meeting
When: November 13 – 17, 2013
Where: Susesi Resort, Antalya, Turkey
Detailed Information: http://www.politzer2013.org

ASHA 2013 Annual Convention
When: November 14 – 16, 2013
Where: Chicago, IL, USA
Detailed Information: http://www.asha.org/Events/convention/Future-Conventions/
This book has very recently been published and constitutes a part of the Springer Handbook of Auditory Research (SHAR) Series. This series has been originally initiated in 1992 for the purpose to provide comprehensive reviews of fundamental topics in auditory research. The SHAR sequence aims at all individuals with interest in hearing research including advanced students, post-doctoral researchers, and clinical investigators. The volumes are intended both to introduce new investigators to important aspects of hearing science and to help established investigators to better understand the fundamental theories and data in fields of hearing that they may not normally follow closely. Each volume of this series presents a particular topic comprehensively and is intended to serve as a guide to the literature and as an “appetizer” for going deeper into detail.

The presented book contains almost 300 pages and focuses both on neural mechanisms of tinnitus and its behavioral consequences. Roughly, it is divided in two different parts, the first of them (Chapters 2-7) mainly concentrating on the underlying pathophysiology of tinnitus derived from basic research, the second one (Chapters 8-11) targeting research and potential therapies in humans.

After an opening chapter by Eggermont and Zeng, which provides historical reflections on current issues in tinnitus and its research, the first part of the book covers animal research that has led to increased understanding of the underlying mechanisms of the generation of tinnitus. In Chapter 2, Heffner and Heffner evaluate the behavioral tests for animals currently employed in tinnitus research. In Chapter 3, Knipper, Müller and Zimmermann discuss etiologies of tinnitus in the context of molecular changes in the peripheral auditory system, in subcortical areas, and in the auditory cortex. This is followed by Chapter 4 by Nouvian, Eybalin, and Puel, who argue that the auditory nerve is a potential tinnitus generator through recruitment of N-methyl-D-aspartate receptors at the first auditory synapse. In Chapter 5, Dehmel, Koehler, and Shore discuss the role of the dorsal cochlear nucleus as an interaction node between auditory and somatosensory neural activity in inducing tinnitus. In Chapter 6, Robertson and Mulders address the role of the inferior colliculus in tinnitus. Chapter 7 contains a discussion by Eggermont of the role of auditory cortex in sound perception in general and tinnitus in particular.

The first chapter of the second part of the book (Chapter 8) by Melcher describes the study of tinnitus in humans by means of brain imaging to measure human brain function and structure. In Chapter 9, Moore dissects the psychophysics of tinnitus, particularly that of pitch, loudness, and masking. In Chapter 10, Noreña emphasizes the view that tinnitus results from central changes due to sensory deprivation, which results in increases spontaneous activity and/or synchrony in auditory centers. Finally, in Chapter 11, Langguth, de Ridder, Kleinjung, and Elgoyhen review the effects of transcranial magnetic stimulation, direct electrical brain stimulation, and pharmacological interventions in tinnitus patients.

Overall evaluation: This book is suitable and highly recommendable both for the reader who wants to gather targeted pieces of information about certain tinnitus-related topics and is in need for a guide to current literature, as well as for the reader who wants to become familiar with the topic of tinnitus itself and is in need for a comprehensible and curt introduction. Due to its clear formal structure it may be used chapter-wise, but may be read at one go as well. The editors have perfectly managed to link animal and basic research to clinical approaches and we are sure that this book will be very helpful to broaden the view both for investigators and clinicians already working in the field of tinnitus and to draw the attention of individuals originally interested in other aspects of hearing. For sure, it will enable the reader to gain a deeper understanding of tinnitus without the need of gathering single pieces of information on his/her own and extracting pubmed-listed original research as a first step.

Peter Kreuzer
University of Regensburg
Recently published literature (articles of authors who are collaborating with TRI are marked in blue)

0 Special Topic

No publications this time.

I Epidemiology


Lin SW, Lin YS, Weng SF, Chou CW.

*Department of Pharmaceutical Science, University of British Columbia, Vancouver, Canada; †Department of Otolaryngology, School of Medicine, Taipei Medical University, Taipei City; ‡Department of Otolaryngology, and §Department of Medical Research, Chi Mei Medical Center; ¶Department of Hospital and Health Care Administration, Chia-Nan University of Pharmacy and Science; and ¶¶Department of Endocrinology, Chi Mei Medical Center, Tainan City, Taiwan, Republic of China.

OBJECTIVES: To explore the risk of development of sudden sensorineural hearing loss (SSHL) among diabetes mellitus patients. STUDY DESIGN: A retrospective cohort study. SETTING: Population-based study of Taiwan National Health Insurance Research Database. PATIENTS: Approximately 26,556 newly diagnosed diabetic patients and 26,556 comparison subjects without diabetes mellitus were selected from claims made during 2000 to 2004. MAIN OUTCOME MEASURES: The incidence of sudden sensorineural hearing loss (SSHL) at the end of 2009 was determined. RESULTS: The incidence of SSHL was 1.54-fold higher in the diabetic group compared with the nondiabetic group (1.29 versus 0.78 per 1,000 person-years), and using Cox proportional hazard regressions, the adjusted hazard ratio (HR) was 1.592 (95% confidence interval [CI], 1.295-1.957). The risk of developing SSHL increased substantially to an HR of 2.060 (95% CI, 1.051-4.037), for patients who required triple antidiabetic medication compared with diabetic patients treated with a single antidiabetic drug. An increased risk of developing SSHL, with adjusted HRs of 1.574 (95% CI, 1.091-2.271) and 2.842 (95% CI, 1.880-4.295), was observed in diabetic patients with newly diagnosed comorbidities of retinopathy or retinopathy combined with renal insufficiency, which are both expected to reflect the severity of diabetes. CONCLUSION: Diabetes mellitus was significantly associated with an increased risk of developing SSHL. Coronary heart disease or retinopathy comorbidities in diabetic patients seemed to be associated with an increased risk of developing SSHL. The risk of developing SSHL increased with the severity of diabetes.

Migraine is a risk factor for sudden sensorineural hearing loss: A nationwide population-based study.
Cephalalgia. 2012 Nov 28. [Epub ahead of print]


Department of Otorhinolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taiwan.

Background: The pathophysiology of idiopathic sudden sensorineural hearing loss (SSNHL) is poorly understood. Few case reports have proposed a possible link between migraine and SSNHL. Objectives: This study aimed to explore the risk of idiopathic SSNHL in patients with migraine in a nationwide, population-based cohort study. Methods: We identified patients with migraine from the Taiwan National Health Insurance Research Database (NHIRD) between 2000 and 2009. Each migraine patient was matched with four randomly selected subjects without migraine for age, sex, and comorbidities. Both cohorts were followed up until the end of 2009. We compared the incidence rates of SSNHL in the two cohorts and identified the risk factors. Results: A total of 10,280 migraine patients and 41,120 matched controls were enrolled with
a median follow-up of five years. The migraine cohort had a greater risk of developing SSNHL than the matched cohort (81.6 vs. 45.7 per 100,000 person-years, incidence rate ratio (IRR) = 1.8; 95% confidence interval (CI) 1.22-2.61, p = 0.002). The Cox proportional hazards analysis revealed that among migraine subjects, comorbidity with hypertension was associated with a trend of developing SSNHL (hazard ratio (HR) = 1.92, 95% CI 0.97-3.79, p = 0.06). Conclusions: This population-based study demonstrates that migraine is associated with an increased risk of idiopathic SSNHL, which, however, is a rare condition.

Estimating Young Australian Adults’ Risk of Hearing Damage From Selected Leisure Activities.
Ear Hear. 2012 Sep 12. [Epub ahead of print]

Beach E, Williams W, Gilliver M.

OBJECTIVE: Several previous studies have attempted to estimate the risk of noise-induced hearing loss from loud leisure noise. Some of these studies may have overestimated the risk because they used noise estimates taken from the higher end of reported levels. The aim of the present study was to provide a realistic estimate of the number of young Australian adults who may be at risk of hearing damage and eventual hearing loss from leisure-noise exposure. DESIGN: Average noise levels at five high-noise leisure activities, (1) nightclubs; (2) pubs, bars, and registered clubs; (3) fitness classes; (4) live sporting events; (5) concerts and live music venues, were calculated using 108 measurements taken from a large database of leisure noise measurements. In addition, an online survey was administered to a convenience sample of 1000 young adults aged 18 to 35 years, who reported the time spent at these leisure activities and the frequency with which they undertook the activities. They also answered questions about tinnitus and their perceived risk of hearing damage. Although the survey data cannot be considered representative of the population of young Australian adults, it was weighted to this population in respect of age, gender, education, and location. The survey data and the average noise levels were used to estimate each individual's annual noise exposure, and in turn, estimate those at risk of hearing damage from leisure-noise exposure. RESULTS: For the majority of participants (n = 868), the accumulated leisure noise level was within the acceptable workplace limit. However, 132 participants or 14.1% (population weighted) were exposed to an annual noise dose greater than the acceptable workplace noise limit. By far, the main source of high-risk leisure noise was from nightclubs. Those with more leisure-noise exposure experienced more tinnitus and perceived themselves to be more at risk than those with lower noise exposures. CONCLUSIONS: It is recommended that nightclub operators reduce noise levels, display warnings, and provide earplugs for patrons and employees. Health promoters should focus their attention on those young adults who are most at risk and provide them with targeted practical advice about reducing their leisure-noise exposure and avoiding hearing loss.

Characterization of tinnitus in Nigeria.

Sogebi OA.

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OBJECTIVE: This study aimed to characterize tinnitus in middle aged and elderly out-patients attending a specialized clinic in a developing country. METHODS: A cross sectional study of patients attending the ear, nose and throat (ENT) clinic of Olabisi Onabanjo University Teaching Hospital, OOUTH Sagamu, Nigeria. Data was collected with the use of a structured questionnaire. Data collected included socio demographics, medical history including experience of tinnitus, PTAs, BMI and BP. Data was analyzed using SPSS version 17.0. RESULTS: 79 patients had complaints of tinnitus thus making a crude prevalence of 14.5%, the prevalence increased steadily along the age groups. 51.9% of patients experienced tinnitus for a short period. 53.2% of the patients had symptoms referable to only one ear, while 54.4% had discrete as opposed to multiple types of tinnitus. Occurrence of intermittent symptoms was experienced by 75.9% of the patients and 70.9% were non-pulsatile in nature. Tinnitus was significantly associated with abnormal
audiographic pattern, global increased hearing thresholds, high tone hearing loss, vertigo, hypertension and obesity. CONCLUSION: Tinnitus character was majorly short term, unilateral, discrete, intermittent, and non-pulsatile in nature, and it is associated with otological, audiological, anthropometric and cardiovascular anomalies. The characteristics of tinnitus in Nigerian patients were similar to those described in developed countries, but the major risk factors for tinnitus except hearing impairment, may be different from the latter. Copyright © 2012 Elsevier Ireland Ltd. All rights reserved.

Troublesome tinnitus in childhood and adolescence: Data from expert centres (Article in press)

Baguley, D.M.a, Bartnik, G.b, Kleinjung, T.c, Savastano, M.d, Hough, E.A.a

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b Tinnitus Clinic, Institute of Physiology and Pathology of Hearing, Warsaw, Poland
c Interdisciplinary Tinnitus Clinic, University of Regensburg, Germany
d Padua University Hospital, Padua, Italy

Objective: Whilst there are several published studies of the prevalence of troublesome tinnitus in childhood and adolescence (indicating that up to a sixth may experience bothersome tinnitus), there is sparse information regarding incidence. Methods: In this study a retrospective case review of patients aged under 18 with a primary complaint of tinnitus seen in 2009 was undertaken in four European clinics known to accept such referrals. Results: A total of 88 young persons with a primary complaint of tinnitus were seen in 2009 by these services, and this represents 3.8% of the paediatric clinical workload of these services and 0.3% of the total clinical workload in that year. The overwhelming majority (93%) of cases were aged 10 years or over at presentation. In only 16 cases (18%) was the tinnitus classified as severe by the reviewing clinician. Tinnitus was accompanied by hyperacusis in 34 cases (39%). Conclusions: Whilst tinnitus in childhood or adolescence can be severe, this is rarely seen in the clinic. Epidemiological data for childhood tinnitus reported previously should be interpreted with caution, as it is dissonant with the data presented in the current study. This may represent an unmet need in the population, but it may also be the case that the incidence of tinnitus in childhood and adolescence is low. Crown Copyright © 2012.

Hearing ability and self-reported hearing disorders in orchestral musicians (Conference Paper)

Lund, S.P.a, Persson, R.a, Kristiansen, J.a, Nielsen, P.M.b, Gade, A.C.c

a National Research Centre for the Working Environment, Copenhagen, Denmark.
b Akustik Aps, Copenhagen, Denmark.
c Gade and Mortensen Akustik A/S, Charlottenlund, Denmark.

This study examined the relationship between objective measures of hearing thresholds (HT) and distortion product oto-acoustic emissions (DPOAE) and self-reported hearing ability, tinnitus and hyperacusis. The participants were 50 opera-orchestral musicians that were at elevated risk of noise induced hearing loss (NIHL). Self rating of hearing ability on a scale seems to be preferential to categorical question regarding hearing loss (yes/no) in questionnaires for professional orchestral musicians, and is primarily associated with changes in both HT and DPOAE in the 3-6 kHz frequency range like NIHL in industrial workers. Reports of daily tinnitus daily were associated in with increase in HT at 6 kHz, but sporadic tinnitus (weekly or monthly) were not associated with any consistent changes in HT or DPOAE. The fraction of musicians reporting hyperacusis (yes/no) did not have worse hearing in the assessments than the rest of the musicians.
II Pathophysiology

Noise-Induced Inner Hair Cell Ribbon Loss Disturbs Central Arc Mobilization: A Novel Molecular Paradigm for Understanding Tinnitus.


Molecular Physiology of Hearing, Hearing Research Centre Tübingen (THRC), Department of Otolaryngology, University of Tübingen, Elfriede-Aulhorn-Str. 5, 72076, Tübingen, Germany.

Increasing evidence shows that hearing loss is a risk factor for tinnitus and hyperacusis. Although both often coincide, a causal relationship between tinnitus and hyperacusis has not been shown. Currently, tinnitus and hyperacusis are assumed to be caused by elevated responsiveness in subcortical circuits. We examined both the impact of different degrees of cochlear damage and the influence of stress priming on tinnitus induction. We used (1) a behavioral animal model for tinnitus designed to minimize stress, (2) ribbon synapses in inner hair cells (IHCs) as a measure for deafferentation, (3) the integrity of auditory brainstem responses (ABR) to detect differences in stimulus-evoked neuronal activity, (4) the expression of the activity-regulated cytoskeletal protein, Arc, to identify long-lasting changes in network activity within the basolateral amygdala (BLA), hippocampal CA1, and auditory cortex (AC), and (5) stress priming to investigate the influence of corticosteroid on trauma-induced brain responses. We observed that IHC ribbon loss (deafferentation) leads to tinnitus when ABR functions remain reduced and Arc is not mobilized in the hippocampal CA1 and AC. If, however, ABR waves are functionally restored and Arc is mobilized, tinnitus does not occur. Both central response patterns were found to be independent of a profound threshold loss and could be shifted by the corticosterone level at the time of trauma. We, therefore, discuss the findings in the context of a history of stress that can trigger either an adaptive or nonadaptive brain response following injury.

Flavoprotein autofluorescence imaging was used to examine auditory cortical synaptic responses in aged animals with behavioral evidence of tinnitus and hearing loss. Mice were exposed to noise trauma at 1-3 months of age and were assessed for behavioral evidence of tinnitus and hearing loss immediately after the noise trauma and again at 24-30 months of age. Within 2 months of the final behavioral assessment, auditory cortical synaptic transmission was examined in brain slices using electrical stimulation of putative thalamocortical afferents, and flavoprotein autofluorescence imaging was used to measure cortical activation. Noise-exposed animals showed a 68% increase in amplitude of cortical activation compared with controls (p = 0.008), and these animals showed a diminished sensitivity to GABA(A)ergic blockade (p = 0.008, using bath-applied 200 nm SR 95531 [6-Imino-3-(4-methoxyphenyl)-1(6H)-pyridazinobutanoic acid hydrobromide]). The strength of cortical activation was significantly correlated to the degree of tinnitus behavior, assessed via a loss of gap detection in a startle paradigm. The decrease in GABA(A) sensitivity was greater in the regions of the cortex farther away from the stimulation site, potentially reflecting a greater sensitivity of corticocortical versus thalamocortical projections to the effects of noise trauma. Finally, there was no relationship between auditory cortical activation and activation of the somatosensory cortex in the same slices, suggesting that the increases in auditory cortical activation were not attributable...
to a generalized hyperexcitable state in noise-exposed animals. These data suggest that noise trauma can cause long-lasting changes in the auditory cortical physiology and may provide specific targets to ameliorate the effects of chronic tinnitus.

Hyperexcitability of inferior colliculus neurons caused by acute noise exposure.


Department of Otolaryngology-Head and Neck Surgery, General Hospital of PLA, Beijing, People’s Republic of China; Center for Hearing and Deafness, Department of Communicative Disorders and Sciences, State University of New York at Buffalo, Buffalo, New York.

Noise exposure is one of the most common causes of hearing loss. Recent studies found that noise exposure-induced cochlear damage may change the excitability and tonotopic organization of the central auditory system (CAS). This plasticity was suspected to be related to tinnitus and hyperacusis. However, how cochlear damage affects CAS function and causes these neurologic diseases is still not clear. CAS function is activity dependent, so we hypothesize that a restricted cochlear lesion might disrupt the balance of excitation and inhibition in the CAS and thereby affect its neural activity. To test this hypothesis, we studied the effects of narrow-band noise exposure on the firing properties of neurons in the inferior colliculus (IC), which has complex neural circuits and plays an important role in sound processing. We found that noise exposure (20 kHz, 105 dB SPL, 30 min) caused a dramatic decrease of the characteristic frequency in about two-thirds of high-frequency neurons with/without causing a significant threshold shift. The noise exposure also caused an increase in firing rate of the low-frequency neurons at suprathreshold levels, whereas it dramatically decreased the firing rate of the high-frequency neurons. Our results suggest that acute high-frequency noise exposure may increase low-frequency responsiveness by causing hyperexcitability of low-frequency neurons. The functional change of the low-frequency neurons may be related to the disruption of side-band inhibition at the noise exposure frequencies caused by cochlear damage. © 2012 Wiley Periodicals, Inc. Copyright © 2012 Wiley Periodicals, Inc.

Somatosensory projections to cochlear nucleus are upregulated after unilateral deafness.

Zeng C, Yang Z, Shreve L, Bledsoe S, Shore S.

Kresge Hearing Research Institute, Department of Otolaryngology, and Department of Molecular and Integrative Physiology, University of Michigan, Ann Arbor, Michigan 48109-0506.

The cochlear nucleus (CN) receives innervation from auditory and somatosensory structures, which can be identified using vesicular glutamate transporters, VGLUT1 and VGLUT2. VGLUT1 is highly expressed in the magnocellular ventral CN (VCN), which receives auditory nerve inputs. VGLUT2 is predominantly expressed in the granule cell domain (GCD), which receives nonauditory inputs from somatosensory nuclei, including spinal trigeminal nucleus (Sp5) and cuneate nucleus (Cu). Two weeks after unilateral deafening VGLUT1 is significantly decreased in ipsilateral VCN while VGLUT2 is significantly increased in the ipsilateral GCD (Zeng et al., 2009), putatively reflecting decreased inputs from auditory nerve and increased inputs from nonauditory structures in guinea pigs. Here, we wished to determine whether the upregulation of VGLUT2 represents increases in the number of somatosensory projections to the CN that are maintained for longer periods of time. Thus, we examined concurrent changes in VGLUT levels and somatosensory projections in the CN using immunohistochemistry combined with anterograde tract tracing three and six weeks following unilateral deafening. The data reveal that unilateral deafness leads to increased numbers of VGLUT2–colabeled Sp5 and Cu projections to the ventral and dorsal CN. These findings suggest that Sp5 and Cu play significant and unique roles in cross-modal compensation and that, unlike after shorter term deafness, neurons in the magnocellular regions also participate in the compensation. The enhanced glutamatergic somatosensory projections to the CN may play a role in neural spontaneous hyperactivity associated with tinnitus.
Forskolin induced increase in spontaneous activity of auditory brainstem neurons is comparable to acoustic stimulus evoked responses.

Shaikh AG, Finlayson PG.
Department of Neurology, Case Western Reserve University, Cleveland, OH. Electronic address: aasefshaikh@gmail.com.

Contemporary proposals for the pathophysiology of tinnitus due to cochlear damage underscore increased spontaneous activity of auditory brainstem neurons. One of the several consequences of the cochlear injury is the activation of the ERK pathway, suppression of phosphodiesterase E activity, and putatively setting a long-term increase in intracellular levels of cyclic AMP at central auditory neurons. Local application of forskolin also increases intracellular cyclic AMP and spontaneous neural activity. We measured the effects of locally applied forskolin on spontaneous firing rate of isolated neurons in the peri-olivary region of the superior olive complex in anesthetized adult Long Evan rats. Forskolin induced increase in spontaneous neural activity was comparable to supra-threshold tone evoke neural responses. These results are viewed in context of hyperexcitability as a correlate of tinnitus. Copyright © 2012. Published by Elsevier Ireland Ltd.

Acoustic stimulation promotes DNA fragmentation in the Guinea pig cochlea.

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Apoptosis can be described as programmed cell death. Apoptosis regulates cell turnover and is involved in various pathological conditions. The characteristic features of apoptosis are shrinkage of the cell body, chromatin condensation, and nucleic acid fragmentation. During apoptosis, double-stranded DNA is broken down into single-stranded DNA (ssDNA) by proteases. Acoustic trauma is commonly encountered in otorhinolaryngology clinics. Intense noise can cause inner ear damage, such as hearing disturbance, tinnitus, ear fullness, and decreased speech discrimination. In this study, we used immunohistochemical and electrophysiological methods to examine the fragmentation of DNA in the cochleas of guinea pigs that had been exposed to intense noise. Twenty-four guinea pigs weighing 250 to 350 g were used. The animals were divided into 4 groups: (I) a control group (n=6), (II) a group that was exposed to noise for 2 hours (n=6), (III) a group that was exposed to noise for 5 hours (n=6), and (IV) a group that was exposed to noise for 20 hours. The stimulus was a pure tone delivered at a frequency of 2 kHz. The sound pressure level was 120 dB SPL. No threshold shifts were apparent in group I. Group II showed a significant elevation of the hearing threshold (ANOVA, p<0.05(∗)). The ABR threshold level was also significantly elevated immediately after the acoustic stimulation in groups III and IV (ANOVA, p<0.01(∗∗)). In groups I, II, and IV, the lateral wall of the ear did not show immunoreactivity to ssDNA but did in group III. No immunoreactivity was apparent in the organ of Corti in group I or II. However, the supporting cells and outer hair cells in groups III and IV showed reactions for ssDNA. The fine structure of the organ of Corti had been destroyed in group IV. The lateral wall showed immunoreactivity for ssDNA only in group III, whereas the organ of Corti showed reactions for ssDNA in groups III and IV. Our study suggests that apoptotic changes occur in patients that suffer acoustic trauma. Once the apoptotic pathway has started, it is irreversible. Thus, early diagnosis and treatment are necessary. Earplugs should also be worn at rock concerts.
Predisposition for and prevention of subjective tinnitus development.

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Dysfunction of the inner ear as caused by presbyacusis, injuries or noise traumata may result in subjective tinnitus, but not everyone suffering from one of these diseases develops a tinnitus percept and vice versa. The reasons for these individual differences are still unclear and may explain why different treatments of the disease are beneficial for some patients but not for others. Here we for the first time compare behavioral and neurophysiological data from hearing impaired Mongolian gerbils with (T) and without (NT) a tinnitus percept that may elucidate why some specimen do develop subjective tinnitus after noise trauma while others do not. Although noise trauma induced a similar permanent hearing loss in all animals, tinnitus did develop only in about three quarters of these animals. NT animals showed higher overall cortical and auditory brainstem activity before noise trauma compared to T animals; that is, animals with low overall neuronal activity in the auditory system seem to be prone to develop tinnitus after noise trauma. Furthermore, T animals showed increased activity of cortical neurons representing the tinnitus frequencies after acoustic trauma, whereas NT animals exhibited an activity decrease at moderate sound intensities by that time. Spontaneous activity was generally increased in T but decreased in NT animals. Plastic changes of tonotopic organization were transient, only seen in T animals and vanished by the time the tinnitus percept became chronic. We propose a model for tinnitus prevention that points to a global inhibitory mechanism in auditory cortex that may prevent tinnitus genesis in animals with high overall activity in the auditory system, whereas this mechanism seems not potent enough for tinnitus prevention in animals with low overall activity. Free PMC Article.

Multi-sensory integration in brainstem and auditory cortex.

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Tinnitus is the perception of sound in the absence of a physical sound stimulus. It is thought to arise from aberrant neural activity within central auditory pathways that may be influenced by multiple brain centers, including the somatosensory system. Auditory-somatosensory (bimodal) integration occurs in the dorsal cochlear nucleus (DCN), where electrical activation of somatosensory regions alters pyramidal cell spike timing and rates of sound stimuli. Moreover, in conditions of tinnitus, bimodal integration in DCN is enhanced, producing greater spontaneous and sound-driven neural activity, which are neural correlates of tinnitus. In primary auditory cortex (A1), a similar auditory-somatosensory integration has been described in the normal system (Lakatos et al., 2007), where sub-threshold multisensory modulation may be a direct reflection of subcortical multisensory responses (Tyll et al., 2011). The present work utilized simultaneous recordings from both DCN and A1 to directly compare bimodal integration across these separate brain stations of the intact auditory pathway. Four-shank, 32-channel electrodes were placed in DCN and A1 to simultaneously record tone-evoked unit activity in the presence and absence of spinal trigeminal nucleus (Sp5) electrical activation. Bimodal stimulation led to long-lasting facilitation or suppression of single and multi-unit responses to subsequent sound in both DCN and A1. Immediate (bimodal response) and long-lasting (bimodal plasticity) effects of Sp5-tone stimulation were facilitation or suppression of tone-evoked firing rates in DCN and A1 at all Sp5-tone pairing intervals (10, 20, and 40ms), and greater suppression at 20ms pairing-intervals for single unit responses. Understanding the complex relationships between DCN and A1 bimodal processing in the normal animal provides the basis for studying its disruption in hearing loss and tinnitus models. This article is part of a Special Issue entitled: Tinnitus Neuroscience. Published by Elsevier B.V.
Increased intensity discrimination thresholds in tinnitus subjects with a normal audiogram.

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Recent auditory brain stem response measurements in tinnitus subjects with normal audiograms indicate the presence of hidden hearing loss that manifests as reduced neural output from the cochlea at high sound intensities, and results from mice suggest a link to deafferentation of auditory nerve fibers. As deafferentation would lead to deficits in hearing performance, the present study investigates whether tinnitus patients with normal hearing thresholds show impairment in intensity discrimination compared to an audiometrically matched control group. Intensity discrimination thresholds were significantly increased in the tinnitus frequency range, consistent with the hypothesis that auditory nerve fiber deafferentation is associated with tinnitus.

Interactions between the vestibular nucleus and the dorsal cochlear nucleus: Implications for tinnitus.

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The peripheral auditory and vestibular systems are recognized to be closely related anatomically and physiologically; however, less well understood is the interaction of these two sensory systems in the brain. A number of previous studies in different species have reported that the dorsal and ventral cochlear nuclei receive direct projections from the primary vestibular nerve and one previous study had reported projections from the vestibular nucleus to the dorsal cochlear nucleus (DCN) in rabbit. Recently, Barker et al. (2012 PLoS One. 7(5): e35955) have reported new evidence that the lateral vestibular nucleus (LVN) projects to the DCN in rat and that these synapses are mediated by glutamate acting on AMPA and NMDA receptors. These recent findings, in addition to the earlier ones, suggest that the auditory and vestibular systems may be intimately connected centrally as well as peripherally and this may have important implications for disorders such as tinnitus. Copyright © 2012 Elsevier B.V. All rights reserved.

[Changes of gamma-amino butyric acid and electrophysiology inferior colliculus after noise exposure in guinea pig].
[Article in Chinese].


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OBJECTIVE: To explore the changes of inferior collicular (IC) neurons after noise exposure cochlea injury in guinea pig to elucidate the encoding mechanism of pure tones, observe the changes of IC gamma-amino butyric acid (GABA) after cochlear damage by acoustic trauma and understand the possible mechanism of symptoms such as noise-induced tinnitus, hyperacusis and loudness recruitment. METHODS: The responses of IC neurons to pure tone stimuli were observed in guinea pig at Day 1 and Days 11-21 after cochlear damage induced by noise exposure. And the IC neurons of normal guinea pig were assigned as the controls. Reverse transcription-polymerase chain reaction (RT-PCR) was used to measure the concentrations of GABA(A) and GABA(B) receptors. RESULTS: (1) The types of frequency reaction area
(FRA) in the experiment group were the same as those in the control group (V-shape 84.8%, W-shape 8.9%, N-shape 6.3%). But the percentages of types were markedly different at Day 1 (V-shape 63.9%, W-shape 18.1%, N-shape, 18.1%) and Days 11-21 (V-shape 84.2%, W-shape 12.3%, N-shape 3.5%) after noise exposure. (2) After noise exposure, there was a marked fault in characteristic frequency (CF) and depth function map corresponding to 4 kHz (noise frequency). The rake ratio of CF and depth linear function map in the experiment group was lower than that of the control group. The control group, Day 1 and Days 11-21 after noise exposure, the rake ratios were 6.6, 5.8, 5.2 respectively. (3) GABA(A)/GABA(B) receptors decreased markedly at Days 1, 11 and 21 post-exposure compared to normal controls. And the values increased gradually with the prolonged time after exposure. The above findings conformed to the changes of electrophysiology of IC. CONCLUSIONS: After acoustic trauma, the responses of IC neurons to pure tone stimuli change with the elongation of time. It may be explained by the changes of IC GABA receptors after noise exposure.

**GDNF and BDNF gene interplay in chronic tinnitus.**


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**BACKGROUND:** Glial cell-derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF) play key roles in the early development of the central auditory pathway and the inner ear. Both have been successfully employed to treat experimental forms of hearing loss and are likely to operate in a broad spectrum of auditory phenotypes, including phantom perceptions of sound. We conducted a genetic association study addressing five biallelic candidate variants in 240 Caucasian subjects who had been diagnosed with tinnitus for more than 6 months. **FINDINGS:** Allele frequencies were determined for three GDNF and two BDNF markers, including a functional missense substitution (V66M). When data were compared to previously examined control populations, no significant allelic associations were noted after corrections for multiple testing. However, using a multiple regression approach and scores from a validated self-report questionnaire, GDNF and BDNF genotypes jointly predicted tinnitus severity in women (N=69, uncorrected p=0.04) but not in men (N=171, n.s.). **CONCLUSIONS:** The present findings serve as an incentive for further explorations of neurotrophic factors’ role in predicting clinical features of tinnitus. Possible implications of sexually dimorphic at-risk genotypes are discussed with regard to hearing and neural plasticity. Free PMC Article.

**Harnessing plasticity to understand learning and treat disease.**


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A large body of evidence suggests that neural plasticity contributes to learning and disease. Recent studies suggest that cortical map plasticity is typically a transient phase that improves learning by increasing the pool of task-relevant responses. Here, I discuss a new perspective on neural plasticity and suggest how plasticity might be targeted to reset dysfunctional circuits. Specifically, a new model is proposed in which map expansion provides a form of replication with variation that supports a Darwinian mechanism to select the most behaviorally useful circuits. Precisely targeted neural plasticity provides a new avenue for the treatment of neurological and psychiatric disorders and is a powerful tool to test the neural mechanisms of learning and memory. Copyright © 2012 Elsevier Ltd. All rights reserved.
Analysis of inner ear potassium recycling genes as potential factors associated with tinnitus.

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Tinnitus is defined as a perception of sound in the absence of an external acoustic stimulus. Several factors are known to influence tinnitus, e.g. hearing loss, noise exposure, age, and hypertension. As only certain individuals develop tinnitus in the presence of the above risks and in approximately 50% of cases tinnitus is not attributed to any particular cause, the question arose whether this inter-individual susceptibility to tinnitus could be explained by the influence of genetic factors. OBJECTIVES: To test the hypothesis that genetic variability in genes of the potassium recycling pathway is associated with increased susceptibility to tinnitus. MATERIALS AND METHODS: The study group consisted of 626 subjects exposed to occupational noise (128 with tinnitus and 498 without tinnitus). 99 single nucleotide polymorphisms were investigated in 10 genes involved in the potassium recycling pathway in the inner ear, previously selected as putative noise-induced hearing loss (NIHL) candidate genes. RESULTS: Nominally significant associations were obtained for 2 variants in KCNE1 (potassium voltage-gated channel, Isk-related family, member 1) and SLC12A2 (solute carrier family 12, member 2) genes. The first gene contributed to tinnitus that developed independently of hearing loss, while the second one was associated with increased susceptibility to noise-induced hearing loss. CONCLUSIONS: Present findings lend support to the notion of potassium recycling pathway genes as possible risk modifiers of tinnitus in individuals with and without hearing loss. Due to the lack of replication in other independent populations these results should be seen as suggestive.

The Relation between Perception and Brain Activity in Gaze-Evoked Tinnitus.

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Tinnitus is a phantom sound percept that can be severely disabling. Its pathophysiology is poorly understood, partly due to the inability to objectively measure neural correlates of tinnitus. Gaze-evoked tinnitus (GET) is a rare form of tinnitus that may arise after vestibular schwannoma removal. Subjects typically describe tinnitus in the deaf ear on the side of the surgery that can be modulated by peripheral eye gaze. This phenomenon offers a unique opportunity to study the relation between tinnitus and brain activity. We used functional magnetic resonance imaging in humans to show that in normal-hearing control subjects, peripheral gaze results in inhibition of the auditory cortex, but no detectable response in the medial geniculate body (MGB) and inferior colliculus (IC). In patients with GET, peripheral gaze (1) reduced the cortical inhibition, (2) inhibited the MGB, and (3) activated the IC. Furthermore, increased tinnitus loudness is represented by increased activity in the cochlear nucleus (CN) and IC and reduced inhibition in the auditory cortex (AC). The increase of CN and IC activity with peripheral gaze is consistent with models of plastic reorganization in the brainstem following vestibular schwannoma removal. The activity decrease in the MGB and the reduced inhibition of the AC support a model that attributes tinnitus to a dysrhythmia of the thalamocortical loop, leading to hypometabolic theta activity in the MGB. Our data offer the first support of this loop hypothesis of tinnitus, independent of the initial experiments that led to its formulation.
Salicylate-induced cochlear impairments, cortical hyperactivity and re-tuning, and tinnitus.

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High doses of sodium salicylate (SS) have long been known to induce temporary hearing loss and tinnitus, effects attributed to cochlear dysfunction. However, our recent publications reviewed here show that SS can induce profound, permanent, and unexpected changes in the cochlea and central nervous system. Prolonged treatment with SS permanently decreased the cochlear compound action potential (CAP) amplitude in vivo. In vitro, high dose SS resulted in a permanent loss of spiral ganglion neurons and nerve fibers, but did not damage hair cells. Acute treatment with high-dose SS produced a frequency-dependent decrease in the amplitude of distortion product otoacoustic emissions and CAP. Losses were greatest at low and high frequencies, but least at the mid-frequencies (10-20 kHz), the mid-frequency band that corresponds to the tinnitus pitch measured behaviorally. In the auditory cortex, medial geniculate body and amygdala, high-dose SS enhanced sound-evoked neural responses at high stimulus levels, but it suppressed activity at low intensities and elevated response threshold. When SS was applied directly to the auditory cortex or amygdala, it only enhanced sound evoked activity, but did not elevate response threshold. Current source density analysis revealed enhanced current flow into the supragranular layer of auditory cortex following systemic SS treatment. Systemic SS treatment also altered tuning in auditory cortex and amygdala; low frequency and high frequency multiunit clusters up-shifted or down-shifted their characteristic frequency into the 10-20 kHz range thereby altering auditory cortex tonotopy and enhancing neural activity at mid-frequencies corresponding to the tinnitus pitch. These results suggest that SS-induced hyperactivity in auditory cortex originates in the central nervous system, that the amygdala potentiates these effects and that the SS-induced tonotopic shifts in auditory cortex, the putative neural correlate of tinnitus, arises from the interaction between the frequency-dependent losses in the cochlea and hyperactivity in the central nervous system. Copyright © 2012. Published by Elsevier B.V.

Preliminary studies on differential expression of auditory functional genes in the brain after repeated blast exposures.

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The mechanisms of central auditory processing involved in auditory/vestibular injuries and subsequent tinnitus and hearing loss in Active Duty servicemembers exposed to blast are not currently known. We analyzed the expression of hearingrelated genes in different regions of the brain 6 h after repeated blast exposures in mice. Preliminary data showed that the expression of the deafness-related genes otoferlin and otoancorin wassignificantly changed in the hippocampus after blast exposures. Differential expression of cadherin and protocadherin genes, which are involved in hearing impairment, was observed in the hippocampus, cerebellum, frontal cortex, and midbrain after repeated blasts. A series of calcium-signaling genes that are known to be involved in auditory signal processing were also found to be significantly altered after repeated blast exposures. The hippocampus and midbrain showed significant increase in the gene expressionof hearing loss-related antioxidant enzymes. Histopathology of the auditory cortex showed more significant injury in the inner layer compared to the outer layer. In summary, mice exposed to repeated blasts showed injury to the auditory cortex and significant alterations in multiple genes in the brain known to be involved in age- or noise-induced hearing impairment.
The relationship between distortion product otoacoustic emissions and extended high-frequency audiometry in tinnitus patients. Part 1: Normally hearing patients with unilateral tinnitus.


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Background: The aim of this study was to evaluate distortion product otoacoustic emissions (DPOAEs) and extended high-frequency (EHF) thresholds in a control group and in patients with normal hearing sensitivity in the conventional frequency range and reporting unilateral tinnitus. Material/Methods: Seventy patients were enrolled in the study: 47 patients with tinnitus in the left ear (Group 1) and 23 patients with tinnitus in the right ear (Group 2). The control group included 60 otologically normal subjects with no history of pathological tinnitus. Pure-tone thresholds were measured at all standard frequencies from 0.25 to 8 kHz, and at 10, 12.5, 14, and 16 kHz. The DPOAEs were measured in the frequency range from approximately 0.5 to 9 kHz using the primary tones presented at 65/55 dB SPL. Results: The left ears of patients in Group 1 had higher median hearing thresholds than those in the control subjects at all 4 EHF, and lower mean DPOAE levels than those in the controls for almost all primary frequencies, but significantly lower only in the 2-kHz region. Median hearing thresholds in the right ears of patients in Group 2 were higher than those in the right ears of the control subjects in the EHF range at 12.5, 14, and 16 kHz. The mean DPOAE levels in the right ears were lower in patients from Group 2 than those in the controls for the majority of primary frequencies, but only reached statistical significance in the 8-kHz region. Conclusions: Hearing thresholds in tinnitus ears with normal hearing sensitivity in the conventional range were higher in the EHF region than those in non-tinnitus control subjects, implying that cochlear damage in the basal region may result in the perception of tinnitus. In general, DPOAE levels in tinnitus ears were lower than those in ears of non-tinnitus subjects, suggesting that subclinical cochlear impairment in limited areas, which can be revealed by DPOAEs but not by conventional audiometry, may exist in tinnitus ears. For patients with tinnitus, DPOAE measures combined with behavioral EHF hearing thresholds may provide additional clinical information about the status of the peripheral hearing.

Design and evaluation of tinnitus synthesis methods: From spectral to spatial matching.


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PURPOSE: This study was designed to investigate methods to help patients suffering from unilateral tinnitus synthesizing an auditory replica of their tinnitus. MATERIALS AND METHODS: Two semi-automatic methods (A and B) derived from the auditory threshold of the patient and a method (C) combining a pure tone and a narrow band-pass noise centred on an adjustable frequency were devised and rated on their likeness over two test sessions. A third test evaluated the stability over time of the synthesized tinnitus replica built with method C, and its proneness to merge with the patient's tinnitus. Patients were then asked to try and control the lateralisation of this single percept through the adjustment of the tinnitus replica level. RESULTS: The first two tests showed that seven out of ten patients chose the tinnitus replica built with method C as their preferred one. The third test, performed on twelve patients, revealed pitch tuning was rather stable over a week interval. It showed that eight patients were able to consistently match the central frequency of the synthesized tinnitus (presented to the contralateral ear) to their own tinnitus, which
Effects of tensor tympani muscle contraction on the middle ear and markers of a contracted muscle.


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OBJECTIVES/HYPOTHESIS: Many otologic disorders have been attributed to dysfunction of the tensor tympani muscle, including tinnitus, otalgia, Meniere's disease and sensorineural hearing loss. The objective of this study was to determine adequate stimuli for tensor tympani contraction in humans and determine markers of the hypercontracted state that could be used to detect this process in otologic disease. STUDY DESIGN: Multiple types of studies. METHODS: Studies included 1) measuring middle ear impedance changes in response to orbital puffs of air, facial stroking, and self-vocalization; 2) measuring changes in stapes and eardrum vibrations and middle ear acoustic impedance in response to force loading of the tensor tympani in fresh human cadaveric temporal bones; 3) measuring changes in acoustic impedance in two subjects who could voluntarily contract their tensor tympani, and performing an audiogram with the muscle contracted in one of these subjects; and 4) developing a lumped parameter computer model of the middle ear while simulating various levels of tensor tympani contraction. RESULTS: Orbital jets of air are the most effective stimuli for eliciting tensor tympani contraction. As markers for tensor tympani contraction, all investigations indicate that tensor tympani hypercontraction should result in a low-frequency hearing loss, predominantly conductive, with a decrease in middle ear compliance. CONCLUSIONS: These markers should be searched for in otologic pathology states where the tensor tympani is suspected of being hypercontracted. Copyright © 2012 The American Laryngological, Rhinological, and Otological Society, Inc.

Interaural Differences of Distortion Product Otoacoustic Emission Amplitudes in Patients with Unilateral Tinnitus.


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Objective: We aimed to determine whether abnormalities in outer hair cell (OHC) function were related to tinnitus through interaural comparison of distortion product otoacoustic emissions (DPOAEs). Study Design: Cross-sectional study. Setting: Tertiary care university teaching hospital. Participants: Twenty-seven patients with unilateral tinnitus and pure-tone average of both ears ≤25 dB hearing loss (HL) at 500, 1000, 2000, and 4000 Hz were included. Subjects and Methods: Pure-tone thresholds observed at 500 to 16,000 Hz and DPOAE amplitudes at f2 frequencies of 1001 to 6348 Hz were compared between the tinnitus ears and nontinnitus ears in patients with unilateral tinnitus. Results: The pure-tone averages (13 ± 6 dB HL) in the nontinnitus ears were similar to those (15 ± 6 dB HL) in the tinnitus ears. There were no differences in pure-tone averages at all frequencies tested. While the DPOAE amplitudes measured at f2 frequencies of 1001 to 3174 Hz in tinnitus ears were not different from those in the nontinnitus ears, the tinnitus ears showed significantly reduced DPOAE amplitudes when compared with the nontinnitus ears at frequencies of 4004 to 6348 Hz. Conclusion: OHC dysfunction was correlated with tinnitus at high frequencies, and DPOAE amplitudes can provide additional information about cochlear dysfunction, which is complementary to pure-tone audiometry.
Cognitive speed as an objective measure of tinnitus.

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OBJECTIVES/HYPOTHESIS: Subjective, chronic tinnitus is a common but poorly understood condition. The heterogeneity within tinnitus has hindered the development of functional severity measures and effective treatment. Tinnitus at least partially results from maladaptive cortical processes that are associated with cognitive deficits. This study examined whether cognitive processing speed might serve as a novel objective measure of tinnitus severity, and whether the psychiatric comorbidities of depression and somatization are predictive of self-reported tinnitus severity.

STUDY DESIGN: Cross-sectional study of 92 chronic tinnitus participants.

METHODS: The Tinnitus Handicap Inventory (THI) captured the self-reported severity of tinnitus. Cognitive processing speed was objectively measured by the Brain Speed Test (BST), a short computerized test from Posit Science. Somatization and depression were captured by the Whiteley-7 and Patient Health Questionnaire-9 scales. The results of these tests were combined into a Composite Psychiatric State (CPS) variable. The ability of BST z score and CPS level to predict THI was assessed.

RESULTS: There was a significant correlation (r = 0.54, P < .001) between BST z scores and THI in those with bothersome tinnitus (THI ≥ 30). Additionally, BST z score was correlated with the validated neurocognitive tests. Multivariate analysis identified BST z score and CPS level as independent predictors of THI.

CONCLUSIONS: In severe tinnitus, BST provides an objective measure of the functional impact of tinnitus. Cognitive processing speed and psychiatric state are independent predictors of self-reported tinnitus severity. These measures help define clinical subgroups within tinnitus: one subgroup whose functional impact is primarily cognitive and another whose functional impact is primarily psychiatric.


[Mental Distress and Quality of Life in Tinnitus Patients.]
[Article in German]
Laryngorhinootologie. 2012 Oct 22. [Epub ahead of print]

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Tinnitus is a disease with a high prevalence that is often combined with psychiatric comorbidity. The aim of this study was to identify the dimensions of quality of life in which tinnitus patients are especially affected, and how these affections change during a therapy, including a hyperbaric oxygen therapy. 120 patients suffering from tinnitus were examined at 3 time points: at the beginning (t1) and the end (t2) of a 2-week hyperbaric oxygen therapy, and 4 weeks later (t3). The following questionnaires were adopted: Hospital Anxiety and Depression Scale, Multidimensional Fatigue Inventory, and the quality of life instrument EORTC QLQ-C30. Compared with the general population, tinnitus patients were impaired in all areas of quality of life. The greatest differences were found in the scales Social, Cognitive, Emotional and Role Functioning and in the field of financial difficulties with effect sizes of about 1.5. During the therapy, the scores improved, reaching roughly the middle between the initial patients' scores and the values of the general population. The directly assessed subjective improvement due to the therapy was only marginally correlated with the differences in the questionnaires. Since there was no control group without hyperbaric oxygen therapy, the results do not justify conclusions about the effectiveness of this therapy. However, the findings document multiple impairments of the patients (especially psycho-social disturbances) and show hints for supportive offers. © Georg Thieme Verlag KG Stuttgart New York.
The influence of high frequency hearing loss on the distortion product otoacoustic emissions in tinnitus subjects with normal hearing threshold (0.25-8kHz).

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AIM OF THE STUDY: To evaluate the influence of high frequency hearing loss (>8000Hz) on distortion product otoacoustic emissions registered in the frequency range from 0.5 to 8kHz. MATHERIAL AND METHODS: 280 ears with tinnitus and normal hearing (0.25-8kHz) divided into 3 groups depending on the degree of high frequency hearing loss: group A - hearing threshold up to 20dB for 10, 12.5, 14 and 16kHz (68 ears); group B - hearing threshold 25-40dB HL for at least one of four EHfs (93 ears); group C - hearing threshold above 40dB HL for at least one of four EHFs (119 ears). For each group mean audiogram and DP-gram were obtained and statistical analysis was used for comparison across these groups. RESULTS: Mean DPOAE values in group C were significantly lower in comparison with group A for the frequency range 2-8kHz, and in comparison with group B were significantly lower for the frequency range 4-8kHz.
CONCLUSIONS: High frequency hearing loss (above 8kHz) has a relevant influence on distortion product otoacoustic emissions registered at frequencies below 8kHz in tinnitus patients. The greater is hearing loss above 8kHz, the lower is DPOAE value below 8kHz. Copyright © 2012 Polish Otorhinolaryngology - Head and Neck Surgery Society. All rights reserved.

Tinnitus assessment by means of standardized self-report questionnaires: Psychometric properties of the Tinnitus Questionnaire (TQ), the Tinnitus Handicap Inventory (THI), and their short versions in an international and multi-lingual sample.

Zeman F, Koller M, Schecklmann M, Langguth B, Landgrebe M.

BACKGROUND: Tinnitus research in an international context requires standardized and validated questionnaires in different languages. The aim of the present set of analyses was the reassessment of basic psychometric properties according to classical test theory of self-report instruments that are being used within the multicentre Tinnitus Research Initiative (TRI) database project. METHODS: 1318 patients of the TRI Database were eligible for the analyses. The basic psychometric properties reliability, validity, and sensitivity of Tinnitus Handicap Inventory (THI), Tinnitus Questionnaire (TQ) and Tinnitus Beeinträchtigungs Fragebogen (i.e., Tinnitus Impairment Questionnaire, TBF-12) were assessed by the use of Cronbach’s alpha, corrected item-total correlations, correlation coefficients and standardized response means.
RESULTS: Throughout the languages, all questionnaires showed high internal consistencies (Cronbach’s alpha > 0.79) and solid item-total correlations, as well as high correlations among themselves (around 0.8) and in combination with the self-reported tinnitus severity. However, some paradoxical correlations between individual items of the TBF-12, constructed as a shortform of the THI, and the corresponding THI-items were seen. Standardized Response Means (SRM) were low if tinnitus did not change, and between 0.3 and 1.09 for improved or worsened tinnitus complaints, indicating the sensitivity of the measures.
CONCLUSIONS: All investigated instruments have high internal consistency, high convergence and discriminant validity and good change sensitivity in an unselected large multinational clinical sample and thus appear appropriate to evaluate the effects of tinnitus treatments in a cross-cultural context.
Evaluation of Masking Effects on Speech Perception in Patients With Unilateral Chronic Tinnitus Using the Hearing in Noise Test.
Otol Neurotol. 2012 Sep 19. [Epub ahead of print]

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OBJECTIVE: To verify that tinnitus itself could disturb speech perception and to evaluate the effects of masking noise on speech perception ability in the patients with normal hearing but unilateral chronic tinnitus using the hearing in noise test. STUDY DESIGN: Prospective, nonrandomized study. MATERIALS AND METHODS: Between June 2009 and May 2011, we enrolled 20 patients with normal hearing and subjective unilateral tinnitus that had persisted for more than 12 months, along with 20 healthy controls of the same age. All subjects were evaluated using audiologic examinations, the tinnitus handicap inventory, and the Korean version of the Hearing in Noise Test (K-HINT) to assess characteristics of tinnitus and speech perception ability in various noisy situations. RESULTS: Reception threshold for speech (RTS) in a quiet environment and signal-to-noise ratio (SNR) in various conditions of noise were significantly higher in the tinnitus than in the control group, regardless of whether noise came from the front, right, or left (p < 0.05). When the tinnitus group was subdivided according to the site of noise exposure, the mean SNR of the contralateral noise group was -7.9 ± 1.4 dB, which was significantly higher than the ipsilateral noise (-9.1 ± 1.8 dB) or control group (right, -10.0 ± 0.6 dB; left, -10.1 ± 0.5 dB) (p < 0.05). In addition, there was no significant difference between ipsilateral noise and control groups. CONCLUSION: From this study, we showed that tinnitus itself could adversely affect speech perception ability by increasing both RTS and SNR in the tinnitus patients in comparison with healthy controls. In addition, we suggest that proper level of noise on the site of tinnitus might be helpful to increase speech perception in the patients who experience chronic subjective tinnitus.

Imaging of the temporal bone: a symptom-based approach.

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Some of the symptoms associated with the temporal bone diseases are nonspecific, whereas others overlap with each other. Careful history and physical examination is of paramount importance for the localization of these disorders to a certain anatomic structure. Imaging plays a critical role in diagnosis, treatment planning, and follow-up of diseases of the temporal bone. This article discusses the common diseases associated with the temporal bone in a symptom-based approach. The categories reviewed are otalgia, hearing loss, tinnitus, and vertigo. Representative imaging features of the common abnormalities in each category are discussed. When a disease is associated with more than one symptom, it is included under the predominant symptom. We also provide guidelines for the preferred imaging modalities in certain clinical scenarios. Copyright © 2013 Elsevier Inc. All rights reserved.
The validity and reliability of Tinnitus Handicap Inventory Thai Version

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Objective: Demonstrate the reliability and validity of the Tinnitus Handicap Inventory Thai Version (THI-T), a self-report measure of tinnitus. Material and Method: A cross-sectional psychometric validation study was used to determine internal consistency reliability and validity of the Tinnitus Handicap Inventory Thai Version at the Otoneurology clinic at Tertiary care center. The crosscultural adaptation of the Tinnitus Handicapped Inventory English version (Newman et al, 1996) was translated into Thai version following the steps indicated by Guillemin et al. The reliability was constructed by using Cronbach’s coefficient alpha. The validity was analyzed by the correlation between Tinnitus Handicap Inventory Thai version and the 36-items short form health survey and visual analog scale using Spearman and Pearson test. Results: The result showed good internal consistency reliabilities of total, functional, emotional, and catastrophic scale (α = 0.902, 0.804, 0.831 and 0.661, respectively) of Tinnitus Handicap Inventory Thai Version. Spearman correlation showed the significant correlation of Tinnitus Handicap Inventory to 36-items short form health survey and visual analog scale. Conclusion: Tinnitus Handicap Inventory Thai Version will be a vigorous tool in evaluating tinnitus patients as well as monitoring the progress of their symptoms.

Anatomical anomalies of the vertebral and carotid arteries in patients with vertigo and hearing disorders (Article in press)

Anatomical anomalies of the vertebral and carotid arteries in patients with vertigo and hearing disorders (Article in press)

Introduction: The aim of this work was the analysis of the frequency and type of anatomical anomalies of the arteries to the cranium such as vertebral arteries and carotid arteries in patients with vertigo and hearing disorders. Material and methods: Between 2007 and 2011, in the Department of Otolaryngology and Laryngological Oncology, the number of the patients diagnosed due to vertigo and hearing disorders amounted to 2,167. In CT-angiogram anatomical anomalies were confirmed in 29 of these patients. The studied group included 22 women aged 22-68 and 7 men aged 21-53. Each patient underwent a subjective and objective structured laryngological interview, audiological and otoneurological examinations, laboratory tests, USG and angio-CT of the arteries to the cranium. Results: The most common anatomical anomaly of the arteries to the cranium was hypoplasia of the right vertebral artery in 58.7% of the cases, out of which 51.7% in women and 6.9% in men. Hypoplasia of the left vertebral artery was diagnosed in 24.7% of the studied group, 13.8% of women and 10.3% of men. Hypoplasia of the right internal carotid artery was found in 3.4% of the female patients while hypoplasia of the left internal carotid artery was identified in 6.8% of the studied cases, 3.4% of women and 3.4% of men. Hypoplasia of the right common carotid artery was confirmed in 3.4% of the male patients whereas critical stenosis of the left subclavian artery with the subclavian steal syndrome was found in 3.4% of the studied female patients. Tinnitus was reported in 88.2% of the patients with diagnosed right vertebral artery hypoplasia, and in 58.8% vertigo and in 52.9% hearing disorders were confirmed. Tinnitus was the most common complaint in the studied group, both in men and women. Less frequent complaints referred to vertigo (65.5% altogether) and hearing impairment (55.2% altogether). Conclusions: In the analyzed group, diagnosed anatomical anomalies were not indications for vascular surgery nor neurosurgery, therefore, the applied treatment was strictly conservative. © 2012.
The Tinnitus Handicap Inventory as a Screening Test for Psychiatric Comorbidity in Patients with Tinnitus.

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BACKGROUND: Psychiatric comorbidity is common in patients who seek help for tinnitus. The perceived severity of tinnitus correlates closer to psychological and general health factors than to audiometrical parameters. Audiologists need valid screening tools in order to identify patients with psychiatric disorders and to tailor treatment in a multidisciplinary setting. The tinnitus handicap inventory (THI) has gained widespread acceptance as a self-report measure of tinnitus handicap. In several studies, THI test score correlates with the level of psychopathologic distress. The aim of our study was to investigate the predictive power of the test THI in relation to psychiatric disorders. METHODS: We recruited 156 patients with chronic tinnitus who have requested help at our tinnitus center. All patients underwent psychiatric evaluation, the diagnosis was made in agreement with the DSMIV-TR criteria; all patients filled out the following questionnaires: THI, Symptomatic Check List-90-Revised (SCL-90-R) and Stress-related Vulnerability Scale (VRS). Sensibility and specificity of tests as screening tool for psychiatric disorders was evaluated using Receiver Operating Characteristic (ROC) curve. RESULTS: Sixty-eight patients (prevalence: 43.59%) were found to be affected by a psychiatric disorder. AUC = 0.792 (p > 0.001) shows that THI is a moderately accurate test to individuate psychiatric affected people among our sample. We identified a score of 36 at THI (sensibility = 86.76%; specificity = 59.09%) as an appropriate cut-off point. CONCLUSIONS: If a patient reports a THI score greater than 36, the audiologist should supplement diagnostic studies with a psychiatric evaluation. Copyright © 2012 The Academy of Psychosomatic Medicine. Published by Elsevier Inc. All rights reserved.

The Role of Fear-Avoidance Cognitions and Behaviors in Patients with Chronic Tinnitus.
Cogn Behav Ther. 2012 Dec 3. [Epub ahead of print]

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The current study investigated the role of fear-avoidance—a concept from chronic pain research—in chronic tinnitus. A self-report measure the "Tinnitus Fear-Avoidance Cognitions and Behaviors Scale (T-FAS)" was developed and validated. Furthermore, the role of fear-avoidance behavior as mediator of the relationship between anxiety sensitivity and tinnitus handicap was investigated. From a clinical setting, N = 373 patients with chronic tinnitus completed questionnaires assessing tinnitus handicap (Tinnitus Handicap Inventory), anxiety, depression (Hospital Anxiety and Depression Scale), anxiety sensitivity (Anxiety Sensitivity Index-3), personality factors (Big Five Inventory-10), and fear-avoidance. To analyze the psychometric properties, principal component analysis with parallel component extraction and correlational analyses were used. To examine a possible mediating effect, hierarchical regression analysis was applied. The principal component analysis resulted in a three-factor solution: Fear-avoidance Cognitions, Tinnitus-related Fear-Avoidance Behavior, and Ear-related Fear-Avoidance Behavior. Internal consistency was satisfactory for the total scale and all subscales. High correlations between tinnitus-related handicap scales, depressive and anxiety symptoms, and the T-FAS were found, whereas associations with personality factors were low. Moreover, results indicate a significant partial mediation of fear-avoidance behaviors in the relationship between anxiety sensitivity and the cognitive dimension of tinnitus handicap. Results show that fear-avoidance behavior plays an important role in tinnitus handicap. More attention should be paid to this concept in research and clinical practice of psychotherapy for chronic tinnitus.
Accuracy of tinnitus pitch matching using a web-based protocol.

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OBJECTIVES: We investigated the accuracy of a web-based protocol for tinnitus frequency matching compared to that of tinnitus pitch matching performed by an audiologist using an audiometer in an anechoic chamber. METHODS: Twenty subjects underwent tinnitus frequency-matching in a random order using an audiometer in an anechoic chamber and using web-based software with a multiple-choice protocol in octave or half-octave steps from 250 Hz to 12,000 Hz and a slider in 25-Hz steps from 20 to 20,000 Hz. Octave challenge testing was performed. The participants were asked to indicate which protocol resulted in the closest match to their tinnitus frequency. RESULTS: The median tinnitus frequency was 6,000 Hz (range, 2,000 to 12,000 Hz) with use of the audiometer and self-directed multiple-choice protocol. With the slider, the median frequency was 5,925 Hz (range, 1,850 to 16,000 Hz). The patients with a tinnitus frequency higher than 12,000 Hz experienced a greater level of satisfaction when using the computer-based slider system. Five patients experienced octave confusion with self-directed multiple-choice tinnitus matching that was corrected accurately after the octave challenge step. CONCLUSIONS: A web-based protocol for tinnitus frequency matching is as accurate as a standard audiometric protocol. An octave challenge test might be necessary for patient-directed tinnitus frequency matching.

IV Imaging

Neuromagnetic index of hemispheric asymmetry predicting long-term outcome in sudden hearing loss.
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The neuromagnetic index of hemispheric asymmetry in terms of ipsilateral/contralateral ratio at acute stage was previously revealed to prognosticate the 1-month hearing outcome of acute unilateral idiopathic sudden sensorineural hearing loss (ISSNHL), showing a dynamic relationship between top- and down-levels of auditory pathway. However, the prognostic effect of reorganization pattern for the long-term results remained elusive. This study aimed to probe the prognosticating relevance of hemispheric asymmetry to the hearing at chronic stage of ISSNHL. Using magnetoencephalography (MEG), inter-hemispheric differences in peak dipole of N100m responses to monaural tones were evaluated in 21 controls and 21 ISSNHL patients at initial and final (12months later) stages. Predictive value of hemispheric asymmetry was assessed by correlating hearing level and ipsilateral/contralateral ratio (I/C) of N100m latency and amplitude. Healthy-side dominance of N100m was observed in ISSNHL initially, and remained in three final prognostic subgroups (complete, partial, and no recovery) of ISSNHL. The initial I/C(amplitude) on affected-ear stimulation strongly correlated with the hearing level of final stage in ISSNHL. However, there was no prognostic effect of hemispheric asymmetry pattern for the 12-month hearing improvement. The heterogeneity between neuromagnetic index and hearing levels possibly echoed different pathogeneses of ISSNHL. Since a restored hearing status did not necessarily lead toward a normal functional organization, the dynamics of hemispheric asymmetry could actually index a central resilient reorganization in the brain for sound processing in ISSNHL. Our finding showed not only a clinically relevant measure to predict final hearing of ISSNHL, but also a linkage between central plasticity and cochlear lesion. This finding suggests a new perspective, and perhaps new interventions, to diagnose and treat unilateral ISSNHL. Copyright © 2012. Published by Elsevier Inc.
Functional MRI evidence for a role of ventral prefrontal cortex in tinnitus.
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It has long been known that subjective tinnitus, a constant or intermittent phantom sound perceived by 10 to 15% of the adult population, is not a purely auditory phenomenon but is also tied to limbic-related brain regions. Supporting evidence comes from data indicating that stress and emotion can modulate tinnitus, and from brain imaging studies showing functional and anatomical differences in limbic-related brain regions of tinnitus patients and controls. Recent studies from our lab revealed altered blood oxygen level-dependent (BOLD) responses to stimulation at the tinnitus frequency in the ventral striatum (specifically, the nucleus accumbens) and gray-matter reductions (i.e., anatomical changes) in ventromedial prefrontal cortex (vmPFC), of tinnitus patients compared to controls. The present study extended these findings by demonstrating functional differences in vmPFC between 20 tinnitus patients and 20 age-matched controls. Importantly, the observed BOLD response in vmPFC was positively correlated with tinnitus characteristics such as subjective loudness and the percent of time during which the tinnitus was perceived, whereas correlations with tinnitus handicap inventory scores and other variables known to be affected in tinnitus (e.g., depression, anxiety, noise sensitivity, hearing loss) were weaker or absent. This suggests that the observed group differences are indeed related to the tinnitus percept and not to an affective reaction to tinnitus. The results further corroborate vmPFC as a region of high interest for tinnitus research. Copyright © 2012 Elsevier B.V. All rights reserved.

Single-subject oscillatory gamma responses in tinnitus.
Brain. 2012 Sep 13. [Epub ahead of print]

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This study used magnetoencephalography to record oscillatory activity in a group of 17 patients with chronic tinnitus. Two methods, residual inhibition and residual excitation, were used to bring about transient changes in spontaneous tinnitus intensity in order to measure dynamic tinnitus correlates in individual patients. In residual inhibition, a positive correlation was seen between tinnitus intensity and both delta/theta (6/14 patients) and gamma band (8/14 patients) oscillations in auditory cortex, suggesting an increased thalamocortical input and cortical gamma response, respectively, associated with higher tinnitus states. Conversely, 4/4 patients exhibiting residual excitation demonstrated an inverse correlation between perceived tinnitus intensity and auditory cortex gamma oscillations (with no delta/theta changes) that cannot be explained by existing models. Significant oscillatory power changes were also identified in a variety of cortical regions, most commonly midline lobar regions in the default mode network, cerebellum, insula and anterior temporal lobe. These were highly variable across patients in terms of areas and frequency bands involved, and in direction of power change. We suggest a model based on a local circuit function of cortical gamma-band oscillations as a process of mutual inhibition that might suppress abnormal cortical activity in tinnitus. The work implicates auditory cortex gamma-band oscillations as a fundamental intrinsic mechanism for attenuating phantom auditory perception. Free full text.
The Relation between Perception and Brain Activity in Gaze-Evoked Tinnitus.

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Tinnitus is a phantom sound percept that can be severely disabling. Its pathophysiology is poorly understood, partly due to the inability to objectively measure neural correlates of tinnitus. Gaze-evoked tinnitus (GET) is a rare form of tinnitus that may arise after vestibular schwannoma removal. Subjects typically describe tinnitus in the deaf ear on the side of the surgery that can be modulated by peripheral eye gaze. This phenomenon offers a unique opportunity to study the relation between tinnitus and brain activity. We used functional magnetic resonance imaging in humans to show that in normal-hearing control subjects, peripheral gaze results in inhibition of the auditory cortex, but no detectable response in the medial geniculate body (MGB) and inferior colliculus (IC). In patients with GET, peripheral gaze (1) reduced the cortical inhibition, (2) inhibited the MGB, and (3) activated the IC. Furthermore, increased tinnitus loudness is represented by increased activity in the cochlear nucleus (CN) and IC and reduced inhibition in the auditory cortex (AC). The increase of CN and IC activity with peripheral gaze is consistent with models of plastic reorganization in the brainstem following vestibular schwannoma removal. The activity decrease in the MGB and the reduced inhibition of the AC support a model that attributes tinnitus to a dysrhythmia of the thalamocortical loop, leading to hypometabolic theta activity in the MGB. Our data offer the first support of this loop hypothesis of tinnitus, independent of the initial experiments that led to its formulation.

V Pharmacotherapy

Current pharmacological treatments for tinnitus.
Expert Opin Pharmacother. 2012 Nov 4. [Epub ahead of print]

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Introduction: Tinnitus, the phantom perception of sound, is a highly prevalent disorder and treatment is elusive. Areas covered: This review focuses on clinical research regarding pharmacological treatments for tinnitus. The authors searched PubMed databases for English language articles related to pharmacological treatment of tinnitus, published through August 2012. The keywords "tinnitus AND pharmacological treatment" and "tinnitus AND drugs" were used. The search focused on clinical trials, but was complemented by other articles and information from clinical trial registries. Expert opinion: Despite the significant unmet clinical need for a safe and effective drug for tinnitus relief, there is currently no EMA- or FDA-approved drug on the market. Even a drug that produces a small but significant effect would have a huge therapeutic impact. At present, evidence-based pharmacological approaches are limited to the treatment of comorbidities such as depression, anxiety, or insomnia. In the last few years there have been significant advances in the understanding of the pathophysiology of the different forms of tinnitus, the establishment of valid animal models, and the development of clinical trial methodology. A glimpse of hope is appearing in the horizon as an increasing number of pharmaceutical industries now have compounds targeting tinnitus in their pipeline.
The effect of naltrexone on the perception and distress in tinnitus: an open-label pilot study.

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Objective: Tinnitus is a perceived sensation of sound without actual acoustic stimulation. Currently there are no standardized drug therapies for the treatment of tinnitus patients. A potential novel treatment for chronic tinnitus is naltrexone. Tinnitus can be considered an auditory phantom phenomenon similar to phantom pain. Naltrexone acts predominantly on μ-opioid receptors which are present in multiple areas of the brain, including the thalamus, dorsal part of the anterior cingulate, insula, amygdala, nucleus accumbens, and ventromedial to orbitofrontal cortex. These areas overlap with the areas involved in tinnitus-related distress. The aim of the present study is to investigate three doses of naltrexone, namely 5, 12.5, and 50 mg and determine their influence on tinnitus complaints. We conducted a 4-week single-center, open-label treatment study. Subjects and methods: 86 patients received the drug treatment, while 30 patients received no treatment. Results: Overall tinnitus distress was significantly reduced for the drug treatment group, while for the waiting control group this was not the case. No significant effect could be obtained for tinnitus intensity. A closer look at the data indicates that this effect is mainly generated due to a significant difference in the 50 mg drug treatment group for tinnitus distress. Conclusion: our results indicate that naltrexone might have an effect on tinnitus distress and more particularly higher doses of naltrexone.

The evaluation of ozone and betahistine in the treatment of tinnitus.
Eur Arch Otorhinolaryngol. 2012 Oct 26. [Epub ahead of print]

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The aim of the study is to evaluate the effectiveness of ozone and betahistine treatments in the treatment of tinnitus. Sixty-eight patients were enrolled in this randomized, prospective controlled study. The ozone group consisted of 27, betahistine group consisted of 26 and control group consisted of 15 patients. The patients in ozone group received 10 sessions of ozone treatment via major autohemotherapy. Betahistine group received 48 mg/day betahistine tablets per oral for 3 months duration. The control group was followed up without any treatment given. The evaluation of tinnitus was made by tinnitus loudness and tinnitus handicap inventory (THI). The changes in findings from baseline to 3rd and 6th months were assessed, and the group results were compared. Comparison of the initial mean tinnitus loudness and 3 and 6 months after treatment in each of the three groups did not reveal a significant difference. The comparison between the groups in terms of the improvement of tinnitus loudness was not significant (p = 0.821). Comparison of the initial mean THI and 3 and 6 months after treatment revealed a significant difference in ozone and betahistine groups but not in the control group. When the delta (Δ) THI (the change of mean THI between the initial and 6th month) was compared between the groups, there was no significant difference. This randomized controlled study investigating the effects of ozone in tinnitus tries to shed light to a new method of treatment in tinnitus. The findings of the study does not provide enough evidence to support ozone and betahistine as a treatment for tinnitus and further research on the subject is necessary.
Efficacy of 3 Different Steroid Treatments for Sudden Sensorineural Hearing Loss: A Prospective, Randomized Trial.
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Objectives
We treated patients with idiopathic sudden sensorineural hearing loss (ISSNHL) with several protocols on an outpatient department (OPD) basis. The study compared the efficacy of 3 different steroid treatments for ISSNHL. Study Design
A prospective randomized controlled study.
Setting
Tertiary referral center.
Methods
A total of 60 patients diagnosed with ISSNHL were treated through OPD. They were randomly and equally divided into 3 groups based on therapy: oral steroid for 10 days (group I), intratympanic dexamethasone injection (ITDI) 4 times (group II), and both (group III). Pure-tone average (PTA) was measured by taking 4 frequencies (0.5, 1, 2, and 3 kHz). Hearing change was evaluated by comparing pre- and posttreatment PTAs. Recovery rate was assessed by American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) Clinical Practice Guidelines.

Results
The hearing gain was 12.8 ± 15.4 decibels (dB) in group I, 12.1 ± 14.6 dB in group II, and 21.9 ± 26.2 dB in group III. The recovery rate was 60% in groups I and III and 55% in group II. The overall recovery rate was 58.3% (35 of 60 patients). There was no significant difference in hearing gain and recovery rates for the 3 groups. Frequency-specific hearing gain also did not differ significantly among groups.

Conclusion
Three different treatment protocols (oral steroid, ITDI, or the combination) resulted in similar hearing recovery rates. Therefore, OPD-based systemic and/or local steroid therapy can be recommended as an initial treatment in ISSNHL.

Corticosteroid Therapy for Hearing and Balance Disorders.
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This review addresses the current status of steroid therapies for hearing and vestibular disorders and how certain misconceptions may be undermining the efficacy in restoring normal ear function, both experimentally and clinically. Specific misconceptions addressed are that steroid therapy is not effective, steroid-responsive hearing loss proves an underlying inflammatory problem in the ear, and steroids only have application to the hearing disorders listed below. Glucocorticoid therapy for hearing and balance disorders has been employed for over 60 years. It is recommended in cases of sudden hearing loss, Menière's disease, immune-mediated hearing loss, and any vestibular dysfunction suspected of having an inflammatory etiology. The predominant steroids employed today are dexamethasone, prednisone, prednisolone, and methylprednisolone. Despite years of use, little is known of the steroid responsive mechanisms in the ear that are influenced by glucocorticoid therapy. Furthermore, meta-analyses and clinical study reviews occasionally question whether steroids offer any benefit at all. Foremost in the minds of clinicians is the immune suppression and anti-inflammatory functions of steroids because of their efficacy for autoimmune hearing loss. However, glucocorticoids have a strong binding affinity for the mineralocorticoid (aldosterone) and glucocorticoid receptors, both of which are prominent in the ear. Because the auditory and vestibular end organs require tightly regulated endolymph and perilymph fluids, this ion homeostasis role of the mineralocorticoid receptor cannot be overlooked in both normal and pathologic functions of the ear. The function of the glucocorticoid receptor is to provide anti-inflammatory and antiapoptotic signals by mediating survival factors. Anat Rec, 2012. © 2012 Wiley Periodicals, Inc. Copyright © 2012 Wiley Periodicals, Inc.
Trauma-Associated Tinnitus: Audiological, Demographic and Clinical Characteristics.


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BACKGROUND: Tinnitus can result from different etiologies. Frequently, patients report the development of tinnitus after traumatic injuries. However, to which extent this specific etiologic factor plays a role for the phenomenology of tinnitus is still incompletely understood. Additionally, it remains a matter of debate whether the etiology of tinnitus constitutes a relevant criterion for defining tinnitus subtypes. OBJECTIVE: By investigating a worldwide sample of tinnitus patients derived from the Tinnitus Research Initiative (TRI) Database, we aimed to identify differences in demographic, clinical and audiological characteristics between tinnitus patients with and without preceding trauma. MATERIALS: A total of 1,604 patients were investigated. Assessment included demographic data, tinnitus related clinical data, audiological data, the Tinnitus Handicap Inventory, the Tinnitus Questionnaire, the Beck Depression Inventory, various numeric tinnitus rating scales, and the World Health Organisation Quality of Life Scale (WHOQoL). RESULTS: Our data clearly indicate differences between tinnitus patients with and without trauma at tinnitus onset. Patients suffering from trauma-associated tinnitus suffer from a higher mental burden than tinnitus patients presenting with phantom perceptions based on other or unknown etiologic factors. This is especially the case for patients with whiplash and head trauma. Patients with posttraumatic noise-related tinnitus experience more frequently hyperacousis, were younger, had longer tinnitus duration, and were more frequently of male gender. CONCLUSIONS: Trauma before tinnitus onset seems to represent a relevant criterion for subtypization of tinnitus. Patients with posttraumatic tinnitus may require specific diagnostic and therapeutic management. A more systematic and - at best - standardized assessment for hearing related sequelae of trauma is needed for a better understanding of the underlying pathophysiology and for developing more tailored treatment approaches as well. Free PMC Article.

Ondansetron in patients with tinnitus: randomized double-blind placebo-controlled study.
Eur Arch Otorhinolaryngol. 2012 Sep 22. [Epub ahead of print]


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The aim of this study was to assess the effect of ondansetron on symptoms of patients with subjective tinnitus accompanied by sensorineural hearing loss or normal hearing. Sixty patients with a chief complaint of tinnitus (with duration of more than 3 months) were equally randomized to ondansetron or placebo for 4 weeks. The dose of ondansetron was gradually increased from 4 mg/day (one tablet) to 16 mg/day (4 tablets) during 12 days and then continued up to 4 weeks. The exact number of tablets was prescribed in the placebo group. Patients underwent audiologic examinations and filled questionnaires at baseline and after 4 weeks of treatment. Our primary outcomes were changes in Tinnitus Handicap Inventory questionnaire (THI), Tinnitus Severity Index (TSI) and visual analog scale (VAS) scores. Our secondary outcomes were the changes in depression and anxiety based on Hospital Anxiety and Depression (HADS) questionnaire, side effects, tinnitus loudness matching, tinnitus pitch matching, pure tone audiometry and speech recognition threshold (SRT). In the ondansetron and placebo groups, 27 and 26 patients completed the study, respectively. The changes in VAS (P = 0.934), THI (P = 0.776), anxiety (P = 0.313) and depression (P = 0.163) scores were not different between the groups. TSI score decreased significantly in the ondansetron compared with the placebo group (P = 0.004). Changes in tinnitus loudness matching (P = 0.75) and pitch matching (P = 0.56) did not differ between the two groups. Ondansetron, but not placebo, decreased the SRT threshold (right, P < 0.001; left, P = 0.043) and mean PTA (right, P = 0.006; left, P < 0.001). In conclusion, ondansetron reduces the severity of tinnitus hypothetically through cochlear amplification.  

back to content
Antidepressants for patients with tinnitus.

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BACKGROUND: This is an update of a Cochrane review first published in The Cochrane Library in Issue 4, 2006 and previously updated in 2009. Tinnitus is described as the perception of sound or noise in the absence of real acoustic stimulation. It has been compared with chronic pain, and may be associated with depression or depressive symptoms which can affect quality of life and the ability to work. Antidepressant drugs have been used to treat tinnitus in patients with and without depressive symptoms.

OBJECTIVES: To assess the effectiveness of antidepressants in the treatment of tinnitus and to ascertain whether any benefit is due to a direct tinnitus effect or a secondary effect due to treatment of concomitant depressive states.

SEARCH METHODS: We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; PsycINFO; CINAHL; Web of Science; BIOSIS; ICTR; and additional sources for published and unpublished trials. The date of the most recent search was 5 January 2012.

SELECTION CRITERIA: Randomised controlled clinical studies of antidepressant drugs versus placebo in patients with tinnitus.

DATA COLLECTION AND ANALYSIS: Two authors critically appraised the retrieved studies and extracted data independently. Where necessary we contacted study authors for further information.

MAIN RESULTS: Six trials involving 610 patients were included. Trial quality was generally low. Four of the trials looked at the effect of tricyclic antidepressants on tinnitus, investigating 405 patients. One trial investigated the effect of a selective serotonin reuptake inhibitor (SSRI) in a group of 120 patients. One study investigated trazodone, an atypical antidepressant, versus placebo. Only the trial using the SSRI drug reached the highest quality standard. None of the other included trials met the highest quality standard, due to use of inadequate outcome measures, large drop-out rates or failure to separate the effects on tinnitus from the effects on symptoms of anxiety and depression. All the trials assessing tricyclic antidepressants suggested that there was a slight improvement in tinnitus but these effects may have been attributable to methodological bias. The trial that investigated the SSRI drug found no overall improvement in any of the validated outcome measures that were used in the study although there was possible benefit for a subgroup that received higher doses of the drug. This observation merits further investigation. In the trial investigating trazodone, the results showed an improvement in tinnitus intensity and in quality of life after treatment, but in neither case reached statistical significance. Reports of side effects including sedation, sexual dysfunction and dry mouth were common.

AUTHORS’ CONCLUSIONS: There is as yet insufficient evidence to say that antidepressant drug therapy improves tinnitus.

Effect of high dose intravenous vitamin C on idiopathic sudden sensorineural hearing loss: a prospective single-blind randomized controlled trial.
Eur Arch Otorhinolaryngol. 2012 Dec 4. [Epub ahead of print]

Kang HS, Park JJ, Ahn SK, Hur DG, Kim HY.
Yeil ENT, Changwon, South Korea.

The aim of this prospective single-blind randomized controlled study was to evaluate the therapeutic efficacy of high dose intravenous vitamin C (HDVC) added to systemic steroid in patients with idiopathic sudden sensorineural hearing loss (ISSNHL). Between August 2010 and August 2011, 72 ISSNHL patients who participated in this study were randomly allocated to two groups: 36 to a control group, members of which were given systemic steroid treatment for 15 days, and 36 to a HDVC group, members of which were given HDVC (200 mg/kg/day) for 10 days in addition to steroid therapy followed by oral vitamin C (2,000 mg) for 30 days after discharge. Finally, we analyzed each group: 35 as a control group and 32 as a HDVC group. Auditory evaluations were performed by pure tone audiometry (PTA) before and ~1 month after treatment using Siegel's criteria. HDVC group showed significantly greater complete and
partial recovery improvement \((p = 0.035)\). In addition, the complete recovery rate in the HDVC group was more than twice that of the control group \((p = 0.031)\). In the HDVC group, PTA improved from 67.6 ± 19.8 dB HL before treatment to 37.1 ± 28.8 dB HL at 1 month after treatment, whereas in the control group, PTA improved from 70.3 ± 12.4 to 47.6 ± 25.2 dB HL, which represented a significant intergroup difference \((p = 0.030)\). In conclusion, HDVC may enhance hearing recovery in ISSNHL patients, which suggests that HDVC reduces levels of reactive oxygen metabolites produced by inner ear ischemia or inflammation, and that HDVC could be considered for the treatment of ISSNHL.


**Inner ear drug delivery using nano/micro particles.**

Oto-Rhino-Laryngology Tokyo Volume 55, Issue SUPPL. 1, August 2012, Pages 11-14

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One major reason for the difficulty in the treatment of inner ear disorders is that only a tiny fraction of drug molecules administrated systemically or intratympanically arrive in the inner ear. Several approaches to override this difficulty are discussed. Steroid encapsulated in Stealth-type nano particles made of biodegradable polymer and coated with poly-ethylene glycol was injected intravenously after noise exposure to induce hearing impairment in guinea pigs. Delivery via Stealth particles resulted in a higher tissue concentration of the steroid in the inner ear and better hearing recovery compared to the steroid alone or encapsulated in non-coated nano particles. Lidocaine, a potential tinnitus attenuator, was encapsulated in microparticles made of biodegradable polymer. The microparticles were placed on the round window membrane (RWM) in guinea pigs, and achieved controlled and sustained delivery of lidocaine into the inner ear. Biodegradable gelatin hydrogels saturated with insulin-like growth factor 1 (IGF-1) were placed on the RWM, and showed a protective effect after inner ear damages in rodents. In humans, a phase I/II clinical trial has been completed in which gelatin hydrogels with IGF-1 were applied to the RWM. Patients with sudden onset hearing impairment, in whom treatment with a 7-day systemic steroid failed, were included in the trial. Hearing recovery was better than the historical control (hyperbaric oxygen therapy as a rescue treatment after the failure of systemic steroids), and no major adverse events were observed. The phase II randomized trial to test the effectiveness of the treatment compared to intratympanic steroids is being conducted in 9 institutes in Japan.

**VI Auditive Stimulation**

**Sound therapy (masking) in the management of tinnitus in adults.**


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**BACKGROUND:** This is an update of a Cochrane Review first published in The Cochrane Library in Issue 12, 2010. Tinnitus is described as the perception of sound or noise in the absence of real acoustic stimulation. Numerous management strategies have been tried for this potentially debilitating, heterogeneous symptom. External noise has been used as a management tool for tinnitus, in different capacities and with different philosophical intent, for over a century. **OBJECTIVES:** To assess the effectiveness of sound-creating devices (including hearing aids) in the management of tinnitus in adults. Primary outcome measures were changes in the loudness or severity of tinnitus and/or impact on quality of life. Secondary outcome measures were change in pure-tone auditory thresholds and adverse effects of treatment. **SEARCH METHODS:** We searched the Cochrane ENT Group Trials Register; CENTRAL; PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTR and additional sources for published and unpublished trials. The date of the most recent search was 8 February 2012. **SELECTION CRITERIA:**
Prospective randomised controlled trials recruiting adults with persistent, distressing, subjective tinnitus of any aetiology in which the management strategy included maskers, noise-generating device and/or hearing aids, used either as the sole management tool or in combination with other strategies, including counselling.

DATA COLLECTION AND ANALYSIS: Two authors independently examined the 387 search results to identify studies for inclusion in the review, of which 33 were potentially relevant. The update searches in 2012 retrieved no further potentially relevant studies. Both authors extracted data independently. MAIN RESULTS: Six trials (553 participants) are included in this review. Studies were varied in design, with significant heterogeneity in the evaluation of subjective tinnitus perception, with different scores, scales, tests and questionnaires as well as variance in the outcome measures used to assess the improvement in tinnitus sensation/quality of life. This precluded meta-analysis of the data. There was no long-term follow-up. We assessed the risk of bias as medium in three and high in three studies. Following analysis of the data, no significant change was seen in the loudness of tinnitus or the overall severity of tinnitus following the use of sound therapy compared to other interventions such as patient education, ‘relaxation techniques’, ‘tinnitus coping strategies’, counselling, ‘tinnitus retraining’ and exposure to environmental sounds. No side effects or significant morbidity were reported from the use of sound-creating devices. AUTHORS’ CONCLUSIONS: The limited data from the included studies failed to show strong evidence of the efficacy of sound therapy in tinnitus management. The absence of conclusive evidence should not be interpreted as evidence of lack of effectiveness. The lack of quality research in this area, in addition to the common use of combined approaches (hearing therapy plus counselling) in the management of tinnitus are, in part, responsible for the lack of conclusive evidence. Other combined forms of management, such as tinnitus retraining therapy, have been subject to a Cochrane Review. Optimal management may involve multiple strategies.

Tinnitus pitch, masking, and the effectiveness of hearing aids for tinnitus therapy.
Int J Audiol. 2012 Nov 5. [Epub ahead of print]

McNeill C, Távora-Vieira D, Alnafjan F, Searchfield GD, Welch D.

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Objective: To assess the benefits of hearing aids on tinnitus according to the tinnitus reaction questionnaire (TRQ; Wilson et al, 1991), to verify whether the degree of masking provided by the hearing aid influenced the TRQ score, to examine whether the matched tinnitus pitch predicted the effectiveness of hearing aids in masking tinnitus, and to determine whether prescription of high-frequency amplification might be desirable in tinnitus management when tinnitus pitch is high. Design and study sample: A retrospective evaluation of the clinical outcomes of 70 tinnitus patients fitted with hearing aids was undertaken. The primary outcome measure was the TRQ, with a secondary subjective measure of tinnitus masking. Results: Participants who achieved masking with their hearing aids had greater reduction in TRQ scores. Masking was more likely to be achieved when participants had good low-frequency hearing and tinnitus pitch fell into the frequency range of the hearing aids. Conclusions: The results support the use of hearing aids for tinnitus management, and suggest that masking may be a significant contributor to hearing aid success, implying that high-frequency amplification may be effective in high-pitch tinnitus.
Does enriched acoustic environment in humans abolish chronic tinnitus clinically and electrophysiologically? A double blind placebo controlled study.


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Animal research has shown that loss of normal acoustic stimulation can increase spontaneous firing in the central auditory system and induce cortical map plasticity. Enriched acoustic environment after noise trauma prevents map plasticity and abolishes neural signs of tinnitus. In humans, the tinnitus spectrum overlaps with the area of hearing loss. Based on these findings it can be hypothesized that stimulating the auditory system by presenting music compensating specifically for the hearing loss might also suppress chronic tinnitus. To verify this hypothesis, a study was conducted in three groups of tinnitus patients. One group listened just to unmodified music (i.e. active control group), one group listened to music spectrally tailored to compensate for their hearing loss, and a third group received music tailored to overcompensate for their hearing loss, associated with one (in presbycusis) or two notches (in audiometric dip) at the edge of hearing loss. Our data indicate that applying overcompensation to the hearing loss worsens the patients' tinnitus loudness, the tinnitus annoyance and their depressive feelings. No significant effects were obtained for the control group or for the compensation group. These clinical findings were associated with an increase in current density within the left dorsal anterior cingulate cortex in the alpha2 frequency band and within the left pregenual anterior cingulate cortex in beta1 and beta2 frequency band. In addition, a region of interest analysis also demonstrated an associated increase in gamma band activity in the auditory cortex after overcompensation in comparison to baseline measurements. This was, however, not the case for the control or the compensation groups. In conclusion, music therapy compensating for hearing loss is not beneficial in suppressing tinnitus, and overcompensating hearing loss actually worsens tinnitus, both clinically and electrophysiologically. Copyright © 2012. Published by Elsevier B.V.

Tinnitus in patients with profound hearing loss and the effect of cochlear implantation.

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The objectives of this study were to characterize the features of tinnitus in patients with profound sensorineural hearing loss and to evaluate the effect of cochlear implantation (CI) on their tinnitus. Medical records were reviewed for 35 patients who underwent CI, and completed tinnitus questionnaire between March 2003 and August 2011. Of them, 22 had tinnitus prior to CI (62.9 %) and the tinnitus group was older than the non-tinnitus group (47.5 ± 15.1 vs. 28.9 ± 15.2). The mean tinnitus handicap inventory (THI) score of the tinnitus group was 50.5 ± 28.7 before surgery, and the mean THI score and visual analogue scale (VAS) scores for loudness, annoyance, effect on life, and awareness decreased significantly after CI, with a mean follow-up period of 10.7 months. Tinnitus was completely eliminated in ten patients (45.5 %) and THI scores decreased in all patients. In a correlation analysis of the decrease in THI scores, preoperative VAS scores for loudness, awareness, effect on life, and annoyance, as well as preoperative THI scores, were highly correlated with the degree of decrease in THI scores postoperatively. The auditory performance of patients older than 40 years did not differ from that of younger patients, but their tinnitus was more improved after CI. In conclusion, tinnitus is a common complaint in patients with cochlear implants, and is more prevalent in elderly implantees. In the present study, CI improved tinnitus in all patients, although the most severe cases had the greatest benefit.
The Mozart effect in patients suffering from tinnitus.

Department of Sensory Organs.

Abstract
Conclusion: The study suggests that Mozart therapy could be a valid alternative to the common sound therapy methods in tinnitus patients. Objectives: The aim of the study was to evaluate the presence of the Mozart effect as indexed by a variation in tinnitus intensity and tolerability. Method: Sixty-two individuals aged between 22 and 78 years, reporting tinnitus for at least 1 year, were enrolled for the study. All patients attended a 1 h cognitive behavioral counseling session and listened to Mozart's sonata k448 for 1 h per day for a month. Afterwards patients listened to Beethoven's Für Elise sonata for 1 h per day for a month. To evaluate the general stress level, the impact of tinnitus on patients’ quality of life, and the intensity of tinnitus, patients were invited to participate in three tests: the Measure du Stress Psychologique (MSP) questionnaire, the Tinnitus Handicap Inventory (THI), and a 0 to 10 visual analog scale (VAS). Results: For all the parameters investigated, MSP, THI, and intensity, there was a general significant improvement between the pre- and post-listening evaluation. A significant improvement, as regards THI and intensity, could already be appreciated after a single exposure to Mozart's sonata.

Cochlear implantation in the elderly.
Cochlear Implants Int. 2012 Sep 18. [Epub ahead of print]

OBJECTIVES: To analyse complications and outcome of cochlear implant (CI) treatment in seniors receiving CIs during a 10-year period. METHODS: A total of 28 patients, 79 years or older (mean age 81.6 years), were evaluated and compared with a younger group of 76 patients, 20-60 years old (mean age 48.9 years). A retrospective study of the patients' records was performed. Data on per- and post-operative complications, pre- and post-operative speech perception, estimated cognitive skills, and social situation was extracted. A subjective score was assessed and correlated with post-operative performance. RESULTS: No severe per- or post-operative surgical complications were noted. Speech perception improved significantly after surgery (P < 0.001). The younger age group showed better results post-operatively for monosyllabic words (P < 0.01) compared with the older group with no difference seen for bi-syllabic words. In both the groups, there were no significant differences between patients living with or without social support. DISCUSSION: CI surgery for patients 79 years or older was well tolerated. Patients benefited greatly from the device with improved hearing. CI should not be denied older individuals who are otherwise in good health. Non-use in the elderly was associated with post-operative vertigo and tinnitus, severe disease and limited social support.

A systematic review of the effectiveness and cost-effectiveness of bilateral multichannel cochlear implants in adults with severe-to-profound hearing loss.

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Background: In the UK, approximately 10 000 people have cochlear implants, more than 99% with a unilateral implant. Evidence shows that adults implanted bilaterally may benefit from binaural advantages; however, systematic review evidence is limited. Objectives of the review: To conduct a systematic review to discover the evidence for effectiveness and cost-effectiveness of using bilateral cochlear implants in adults with severe-to-profound hearing loss by comparing their effectiveness with unilateral cochlear implantation or unilateral cochlear implantation and acoustic hearing aid in the contralateral ear. Type of
Systematic review. Search strategy: This examined 16 electronic databases, plus bibliographies and references for published and unpublished studies. Evaluation method: Abstracts were independently assessed against inclusion criteria by two researchers, and disagreements were resolved. Selected papers were then retrieved and further independently assessed in a similar way. Included studies had their data extracted by one reviewer and checked by another. Results: Searches yielded 2892 abstracts producing 19 includable studies. Heterogeneity between studies precluded meta-analysis. However, all studies reported that bilateral cochlear implants improved hearing and speech perception: one randomised controlled trial found a significant binaural benefit over the first ear alone for speech and noise from the front (12.6 ± 5.4%, P < 0.001) and when noise was ipsilateral to the first ear (21 ± 6%, P < 0.001); and another found a significant benefit for spatial hearing at 3 and 9 months post-implantation compared with pre-implantation [mean difference (sd) scores: 3 months = 1.46 (0.83-2.09), P < 0.01]. Quality of life results varied, showing bilateral implantation may improve quality of life in the absence of worsening tinnitus. Limited cost-effectiveness evidence showed that bilateral implantation is probably only cost-effective at a willingness-to-pay threshold above £62 000 per quality adjusted life year. Conclusions: Despite inconsistency in the quality of available evidence, the robustness of systematic review methods gives weight to the positive findings of included studies demonstrating that bilateral implantation is clinically effective in adults but unlikely to be cost-effective. © 2012 Blackwell Publishing Ltd.

VII Brain Stimulation

Surgical brain modulation for tinnitus: the past, present and future.
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Tinnitus treatment has traditionally been restricted to ENT surgeons, audiologists, psychologists and psychiatrists. Recently, both basic and clinical research has focused on the brain's involvement in the generation of tinnitus, opening the tinnitus field up to neurologists and neurosurgeons specialized in the field of tinnitus. Non-pulsatile tinnitus can be considered an auditory phantom phenomenon, analogous to phantom pain, both with regards to pathophysiological mechanisms, clinical characteristics, and treatment approaches. Thus the understanding of tinnitus has benefited a lot from translating available knowledge of the somatosensory (pain) system to the auditory system. A literature review of neuromodulatory approaches to tinnitus is integrated in a single center's experience with invasive neuromodulation treatments for tinnitus. This is compared to findings from neuromodulatory treatment of chronic pain syndromes. The past, present and future options for functional neurosurgical approaches are outlined.

In the past only destructive approaches were used, consisting of nerve lesions and frontal lobotomies. Presently neurostimulation trials are ongoing evaluating the effect of auditory cortex stimulation, frontal cortex stimulation, thalamic (VIM) and caudate stimulation as well as amygdalohippocampal stimulation, yielding suppression rates between 10 and 70%. Further potentially promising targets include the anterior cingulate, the medial geniculate bodies (MGB), the periaqueductal gray/ tectal longitudinal column (PAG/ TLC), the dorsal cochlear nucleus, as well as the C2 and trigeminal nerve. Understanding tinnitus and its potential neuromodulation treatments is relatively simple for a neurosurgeon specialized in pain or a pain physician, based on the pathophysiological and clinical analogies. Similarly to pain a multidisciplinary approach can be advocated, and in view of the epidemiology and amount of suffering associated with this enigmatic symptom further investment in possible neuromodulation treatments is warranted.
A neuronal network model for simulating the effects of repetitive transcranial magnetic stimulation on local field potential power spectra.


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Repetitive transcranial magnetic stimulation (rTMS) holds promise as a non-invasive therapy for the treatment of neurological disorders such as depression, schizophrenia, tinnitus, and epilepsy. Complex interdependencies between stimulus duration, frequency and intensity obscure the exact effects of rTMS stimulation on neural activity in the cortex, making evaluation of and comparison between rTMS studies difficult. To explain the influence of rTMS on neural activity (e.g. in the motor cortex), we use a neuronal network model. The results demonstrate that the model adequately explains experimentally observed short term effects of rTMS on the band power in common frequency bands used in electroencephalography (EEG). We show that the equivalent local field potential (eLFP) band power depends on stimulation intensity rather than on stimulation frequency. Additionally, our model resolves contradictions in experiments. [Free PMC Article](https://doi.org/10.1371/journal.pone.0049097).

**Hearing safety of long-term treatment with theta burst stimulation.**


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BACKGROUND: Repetitive transcranial magnetic stimulation (rTMS) for the experimental treatment of tinnitus or auditory hallucinations aims at a modulation of cortical activity in areas of auditory perception and processing. Continuous theta burst stimulation (cTBS) is a patterned rTMS paradigm with lower stimulation intensity and shorter stimulus duration that is increasingly used for the optimization of rTMS-treatment paradigms. Possible interference with physiological brain function and the noise emitted by the rTMS device might induce relevant unwanted impairment of hearing and speech perception. OBJECTIVE/HYPOTHESIS: Here, we investigate the audiological safety of long-term, bilateral cTBS for the treatment of auditory phantom perception. METHODS: Forty-eight patients with chronic tinnitus were treated for four weeks with bilateral continuous theta burst stimulation to the temporal (n = 16), temporoparietal (n = 16) or a non-cortical control (n = 16) site. Measurements in these patients were obtained before and four weeks after treatment. The rTMS-induced noise was measured at various frequency levels. RESULTS: No evidence was found for auditory threshold shifts or alterations in the perception of speech in quiet or in background noise by bilateral, long-term theta burst stimulation to the temporal or temporoparietal cortex with a loudness of up to 84 dB SPL (A). CONCLUSIONS: Theta burst stimulation of the temporal and temporoparietal cortex appears to be safe with respect to hearing and speech perception. These data provide evidence for the audiological safety of rTMS in the experimental treatment of auditory phantom perception. Copyright © 2012 Elsevier Inc. All rights reserved.
Transcranial direct current stimulation in tinnitus patients: a systemic review and meta-analysis.

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Although transcranial direct current stimulation (tDCS) has already been used to manage tinnitus patients, paucity of reports and variations in protocols preclude a comprehensive understanding. Hence, we conducted a meta-analysis based on systemic review to assess effectiveness of tDCS in tinnitus management and to compare stimulation parameters. PubMed was searched for tDCS studies in tinnitus. For randomized controlled trials (RCTs), a meta-analysis was performed. A total of 17 studies were identified and 6 of them were included in the systemic review and 2 RCTs were included in the meta-analysis. Overall 39.5% responded to active tDCS with a mean tinnitus intensity reduction of 13.5%. Additionally, left temporal area (LTA) and bifrontal tDCS indicated comparable results. Active tDCS was found to be more effective than sham tDCS for tinnitus intensity reduction (Hedges’ g = .77, 95% confidence interval 0.23-1.31). The efficacy of tDCS in tinnitus could not be fully confirmed by the current study because of the limited number of studies, but all studies included in the current systemic review and meta-analysis demonstrated significant tinnitus intensity improvement. Therefore, tDCS may be a promising tool for tinnitus management. Future RCTs in a large series regarding the efficacy as well as the comparison between LTA- and bifrontal tDCS are recommended. Free PMC Article.

Directing Neural Plasticity to Understand and Treat Tinnitus.

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The functional organization of cortical and subcortical networks can be altered by sensory experience. Sensory deprivation destabilizes neural networks resulting in increased excitability, greater neural synchronization and increased spontaneous firing in cortical and subcortical neurons. This pathological activity is thought to generate the phantom percept of chronic tinnitus. While sound masking, pharmacotherapy and cortical stimulation can temporarily suppress tinnitus for some patients, these interventions do not eliminate the pathological activity that is responsible for tinnitus. A treatment that could reverse the underlying pathology would be expected to be effective in alleviating the symptoms, if not curative. Targeted neural plasticity can provide the specificity required to restore normal neural activity in dysfunctional neural circuits that are assumed to underlie many forms of tinnitus. The forebrain cholinergic system and the noradrenergic system play a significant role in modulating cortical plasticity. Stimulation of the vagus nerve is known to activate these neuromodulatory pathways. Our earlier studies have demonstrated that pairing sounds with either nucleus basalis of Meynert (NB) stimulation or vagus nerve stimulation (VNS) generates highly specific and long lasting plasticity in auditory cortex neurons. Repeatedly pairing tones with brief pulses of VNS reversed the physiological and behavioral correlates of tinnitus in noise exposed rats. We also recently demonstrated that VNS modulates synchrony and excitability in the auditory cortex at least in part by activation of muscarinic acetylcholine receptors, suggesting that acetylcholine is involved in the mechanism of action of VNS. These results suggest that pairing sounds with VNS provides a new avenue of treatment for some forms of tinnitus. This paper discusses neuromodulation as treatment for tinnitus with a focus on the potential value of pairing VNS with sound stimulation as a treatment of chronic tinnitus. Copyright © 2012. Published by Elsevier B.V.
A stroke of silence: tinnitus suppression following placement of a deep brain stimulation electrode with infarction in area LC.

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Department of Neurological Surgery and

The authors report on a case of tinnitus suppression following deep brain stimulation (DBS) for Parkinson disease. A perioperative focal vascular injury to area LC, a locus of the caudate at the junction of the head and body of the caudate nucleus, is believed to be the neuroanatomical correlate. A 56-year-old woman underwent surgery for implantation of a DBS lead in the subthalamic nucleus to treat medically refractory motor symptoms. She had comorbid tinnitus localized to both ears. The lead trajectory was adjacent to area LC. Shortly after surgery, she reported tinnitus suppression in both ears. Postoperative MRI showed focal hyperintensity of area LC on T2-weighted images. At 18 months, tinnitus localized to the ipsilateral ear remained completely silenced, and tinnitus localized to the contralateral ear was substantially suppressed due to left area LC injury. To the authors' knowledge, this is the first report of a discrete injury to area LC that resulted in bilateral tinnitus suppression. Clinicians treating patients with DBS may wish to include auditory phantom assessment as part of the neurological evaluation.

A neurophysiological insight into the potential link between transcranial magnetic stimulation, thalamocortical dysrhythmia and neuropsychiatric disorders.

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Altered neural oscillations and their abnormal synchronization are crucial factors in the pathophysiology of several neuropsychiatric disorders. There is increasing evidence that the perturbation with an abnormal increase of spontaneous thalamocortical neural oscillations lead to a phenomenon termed Thalamocortical dysrhythmia (TCD) which underlies the symptomatology of a variety of neurological and psychiatric disorders including Parkinson's disease, schizophrenia, epilepsy, neuropathic pain, tinnitus, major depression and obsessive-compulsive disorder. In addition, repetitive transcranial magnetic stimulation (rTMS) is a non-invasive neurophysiological tool that has been shown to both induce a modulation of neural oscillations and alleviate a wide range of human neuropsychiatric pathologies. However, little is known about the precise electrophysiological mechanisms behind the therapeutic effect of rTMS and its potential to improve abnormal oscillations across diverse neuropsychiatric disorders. Here we show, using combined rTMS and surface electroencephalography (EEG), a short lasting frequency-dependant rTMS after-effect on thalamocortical rhythmic interplay of low-frequency oscillations in healthy humans at rest. In particular, high-frequency rTMS (10Hz) induces a transient synchronised activity for delta and theta rhythms thus mimicking the pathological TCD-like oscillations. In contrast, rTMS 1 and 5Hz have the opposite outcome of de-synchronising low-frequency brain rhythms. These results lead to a new neurophysiological insight of basic mechanisms underlying neurological and psychiatric disorders and a probable electrophysiological mechanism underlying the therapeutic effects of rTMS. Thus, we propose the use of rTMS and EEG as a platform to test possible treatments of TCD phenotypes by restoring proper neural oscillations across various neuropsychiatric disorders. Copyright © 2012. Published by Elsevier Inc.
TMS by double-cone coil prefrontal stimulation for medication resistant chronic depression: A case report.

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A double-cone coil with large angled windings has been developed to modulate deeper brain areas such as the anterior cingulate cortex (ACC). Abnormal resting state activity in the pregenual ACC (pgACC), dorsal ACC (dACC) and subgenual ACC (sgACC) has been observed in depression. A patient with medication resistant chronic depression received ten sessions of transcranial magnetic stimulation (TMS) (10 Hz, 2000 stimuli/session) using a double-cone coil placed over the supplementary motor area, targeting the anterior cingulate. Source localized EEG recordings were conducted pre- and post-TMS. The Beck Depression Inventory (BDI-II) improved by 27%, and the two subscales of the Hospital Anxiety Depression Scale (HADS), namely depression (40%) and anxiety (33%) improved as well. Along with the clinical improvement  electrophysiological resting state activity changed in the dACC and sgACC in this patient in comparison to a normative group. The results of this case report further support the involvement of pgACC, dACC and sgACC activity in the pathophysiology of depression and indicate that modulation of neural activity in this area by high frequency TMS with a double-cone coil might represent a new promising approach in the treatment of medication resistant chronic depression.

EEG Driven tDCS Versus Bifrontal tDCS for Tinnitus.

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Tinnitus is the perception of a sound in the absence of any objective physical sound source. Transcranial Direct Current Stimulation (tDCS) induces shifts in membrane resting potentials depending on the polarity of the stimulation: under the anode gamma band activity increases, whereas under the cathode the opposite occurs. Both single and multiple sessions of tDCS over the dorsolateral prefrontal cortex (DLPFC; anode over right DLPFC) yield a transient improvement in tinnitus intensity and tinnitus distress. The question arises whether optimization of the tDCS protocol can be obtained by using EEG driven decisions on where to place anode and cathode. Using gamma band functional connectivity could be superior to gamma band activity as functional connectivity determines the tinnitus network in many aspects of chronic tinnitus. Six-hundred-seventy-five patients were included in the study: 265 patients received tDCS with cathodal electrode placed over the left DLPFC and the anode placed overlying the right DLPFC, 380 patients received tDCS based on EEG connectivity, and 65 received no tDCS (i.e., waiting list control group). Repeated measures ANOVA revealed a significant main effect for pre versus post measurement. Bifrontal tDCS in comparison to EEG driven tDCS had a larger reduction for both tinnitus distress and tinnitus intensity. Whereas the results of the bifrontal tDCS seem to confirm previous studies, the use of gamma band functional connectivity seems not to bring any advantage to tDCS for tinnitus suppression. Using other potential biomarkers, such as gamma band activity, or theta functional connectivity could theoretically be of use. Further studies will have to elucidate whether brain state based tDCS has any advantages over "blind" bifrontal stimulation. Free PMC Article.
Transcranial Direct Current Stimulation Intensity and Duration Effects on Tinnitus Suppression.
Neurorehabil Neural Repair. 2012 Oct 2. [Epub ahead of print]

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BACKGROUND: Perception of sound in the absence of an external auditory source is called tinnitus, which may negatively affect quality of life. Anodal transcranial direct current stimulation (tDCS) of the left temporoparietal area (LTA) was explored for tinnitus relief. OBJECTIVE: This pilot study examined tDCS dose (current intensity and duration) and response effects for tinnitus suppression. METHODS: Twenty-five participants with chronic tinnitus and a mean age of 54 years took part. Anodal tDCS of LTA was carried out. Current intensity (1 mA and 2 mA) and duration (10 minutes, 15 minutes, and 20 minutes) were varied and their impact on tinnitus measured. RESULTS: tDCS was well tolerated. Fifty-six percent of participants (14) experienced transient suppression of tinnitus, and 44% of participants (11) experienced long-term improvement of symptoms (overnight-less annoyance, more relaxed, and better sleep). There was an interaction between duration and intensity of the stimulus on the change in rated loudness of tinnitus, F(2, 48) = 4.355, P = .018, and clinical global improvement score, F(2, 48) = 3.193, P = .050, after stimulation. CONCLUSIONS: Current intensity of 2 mA for 20 minutes was the more effective stimulus parameter for anodal tDCS of LTA. tDCS can be a potential clinical tool for reduction of tinnitus, although longer term trials are needed.

Effects of individual alpha rTMS applied to the auditory cortex and its implications for the treatment of chronic tinnitus.

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An increasing amount of studies apply repetitive transcranial magnetic stimulation (rTMS) to treat chronic tinnitus, yet the neurophysiological impacts have remained largely obscure. Several studies show that endogenous brain rhythms may be enhanced via diverse brain stimulation techniques applying rhythmic stimulation. Here, we investigated in normal hearing participants whether application of rTMS (left auditory cortex) with an individualized alpha frequency was capable of increasing alpha activity in stimulated auditory regions in a sustained manner. Behavioral intensity discrimination performance worsened for the rTMS group as compared to Sham. Electroencephalography (EEG) data, however, clearly show that this functional inhibition is not accompanied by increases of auditory cortical alpha. Even though more pronounced power reductions for the rTMS group were observed at slower frequencies (delta to theta range) at stimulated and other sites of the left hemisphere, they were unrelated to behavioral changes. Our results also strongly suggest that the amount of power modulations at these slower frequencies is strongly dependent on pre-rTMS power, thus supporting current state-dependency notions. Strong relationships to behavioral changes were in particular observed for anterior cingulate cortex (ACC) beta power and posterior cingulate cortex (PCC) beta connectivity. Moreover, these beta band measures were strongly inter-related and when viewed together specifically sensitive to behavioral changes in the rTMS group. We conclude that currently alpha frequency rTMS is not a promising avenue for the treatment of chronic tinnitus and that beneficial effects could be mediated via nonauditory systems. Our study argues for the value of combined EEG-TMS studies when investigating the impacts of rTMS. Hum Brain Mapp, 2012. © 2012 Wiley Periodicals, Inc. Copyright © 2012 Wiley Periodicals, Inc.
Multiple coils in a conducting liquid for deep and whole-brain transcranial magnetic stimulation. II. Multiple-frequency excitation (Conference Paper).
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We present a system comprising multiple coils immersed in a conducting liquid allowing for unprecedented deep, whole-brain transcranial magnetic stimulation (TMS). The system exploits a configuration of large-coils with dedicated spatial asymmetries in order to spare current induction in the retinas and in the human trunk, optimizing deep-brain stimulation down to the center of the brain. The resulting axially-induced currents of this system are prone to magnetic steering by means of dipole and quadrupole-focusing electromagnet (DC) assemblies, with its viability also analyzed in this work. Finite-element methods were applied onto a spherical head model complemented by an ellipsoidal torso. The head model comprises skin, skull, cerebral spinal fluid, and brain tissue. Results, not yet comprising the magnetic-steering capability of the system, show deep-brain induced currents reaching 53% at 10-cm penetration (brain center) in respect to surface (cortex) maximum. For comparison, state-of-the-art published data reach 47% relative induction at 8-cm depth only. This system counterparts well-known limiting effects occurring due to the enhancement of current densities at the brain/surface interface by immersing the stimulating coils (and partially the head of the patient) into a conducting liquid such as an electrolyte solution or a liquid metal. These results may potentially enhance clinical applicability of TMS in a number of pathologies such as Alzheimer's disease, parkinsonism, depression, sleep disorders, pain management, stroke rehabilitation, tinnitus, trigeminal neuralgia, brain palsy, and prevention and resolution of epileptic seizures, among others. © 2012 IEEE.

Multisite rTMS for the Treatment of Chronic Tinnitus: Stimulation of the Cortical Tinnitus Network-A Pilot Study.
Brain Topogr. 2012 Dec 11. [Epub ahead of print]
Lehner A, Schecklmann M, Poeppl TB, Kreuzer PM, Vielsmeier V, Rupprecht R, Landgrebe M, Langguth B.

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Low-frequency repetitive transcranial magnetic stimulation (rTMS) of the auditory cortex has been shown to significantly reduce tinnitus severity in some patients. There is growing evidence that a neural network of both auditory and non-auditory cortical areas is involved in the pathophysiology of chronic subjective tinnitus. Targeting several core regions of this network by rTMS might constitute a promising strategy to enhance treatment effects. This study intends to test the effects of a multisite rTMS protocol on tinnitus severity. 45 patients with chronic tinnitus were treated with multisite stimulation (left dorsolateral prefrontal, 2,000 stimuli, 20 Hz; left temporoparietal, 1,000 stimuli, 1 Hz; right temporoparietal, 1,000 stimuli, 1 Hz). Results were compared with a historical control group consisting of 29 patients who received left temporal stimulation (2,000 stimuli, 1 Hz). Both groups were treated on ten consecutive working days. Tinnitus severity was assessed at three time points: at baseline, after the last treatment session (day 12) and after a follow-up period of 90 days. A change of tinnitus severity over time was tested using repeated measures ANOVA with the between-subjects factor treatment group. Both groups improved similarly from baseline to day 12. However, there was a difference on day 90: the multisite stimulation group showed an overall
improvement whereas patients receiving temporal stimulation returned to their baseline level of tinnitus severity. These pilot data suggest that multisite rTMS is superior to temporal rTMS and represents a promising strategy for enhancing treatment effects of rTMS in tinnitus. Future studies should explore this new protocol with respect to clinical and neurobiological effects in more detail.

Transcutaneous vagus nerve stimulation in tinnitus: a pilot study.

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Abstract Conclusions: This pilot study shows that transcutaneous vagus nerve stimulation (tVNS), if combined with sound therapy (ST), reduces the severity of tinnitus and tinnitus-associated distress. Our magnetoencephalography (MEG) results show that auditory cortical activation can be modulated by the application of tVNS. Thus, tVNS might offer a new avenue to treat tinnitus and tinnitus-associated distress.

Objectives: Recent studies suggest that tinnitus can be improved by tailored ST or by VNS plus ST. Our aims were to study whether tVNS has therapeutic effects on patients with tinnitus and, additionally, if tVNS has effects on acoustically evoked neuronal activity of the auditory cortex. Methods: The clinical efficacy was studied by a short-term tVNS plus ST trial in 10 patients with tinnitus using disease-specific and general well-being questionnaires. tVNS was delivered to the left tragus. The acute effects of tVNS were evaluated in eight patients in the MEG study in which the N1m response was analyzed in terms of source level amplitude and latency in the presence or absence of tVNS. Results: The treatment with tVNS plus ST produced improved mood and decreased tinnitus handicap scores, indicating reduced tinnitus severity. The application of tVNS decreased the amplitude of auditory N1m responses in both hemispheres.

VIII Behaviorial Therapy

Mindfulness-and body-psychotherapy-based group treatment of chronic tinnitus: a randomized controlled pilot study.

Kreuzer PM, Goetz M, Holl M, Schecklmann M, Landgrebe M, Staudinger S, Langguth B.

BACKGROUND: Tinnitus, the perception of sound in absence of an external acoustic source, impairs the quality of life in 2% of the population. Since in most cases causal treatment is not possible, the majority of therapeutic attempts aim at developing and strengthening individual coping and habituation strategies. Therapeutic interventions that incorporate training in mindfulness meditation have become increasingly popular in the treatment of stress-related disorders. Here we conducted a randomized, controlled clinical study to investigate the efficacy of a specific mindfulness- and body-psychotherapy based program in patients suffering from chronic tinnitus. METHODS: Thirty-six patients were enrolled in this pilot study. The treatment was specifically developed for tinnitus patients and is based on mindfulness and body psychotherapy. Treatment was performed as group therapy at two training weekends that were separated by an interval of 7 weeks (eleven hours/weekend) and in four further two-hour sessions (week 2, 9, 18 and 22). Patients were randomized to receive treatment either immediately or after waiting time, which served as a control condition. The primary study outcome was the change in tinnitus complaints as measured by the German Version of the Tinnitus Questionnaire (TQ). RESULTS: ANOVA testing for the primary outcome showed a significant interaction effect time by group (F = 7.4; df = 1,33; p = 0.010). Post hoc t-tests indicated an amelioration of TQ scores from baseline to week 9 in both groups (intervention group: t = 6.2; df = 17; p < 0.001; control group: t = 2.5; df = 16; p = 0.023), but the intervention group improved more than the control group. Groups differed at week 7 and 9, but not at week 24 as far as the TQ score was concerned. CONCLUSIONS: Our results suggest that this mindfulness- and body-psychotherapy-based approach is feasible in the treatment of tinnitus and merits further evaluation in clinical studies with larger sample sizes. The study is registered with clinicaltrials.gov (NCT01540357). Free Article.
Acceptance and commitment therapy - pathways for general practitioners.

Smout M.

Acceptance and commitment therapy (ACT) focuses on helping patients to behave more consistently with their own values and apply mindfulness and acceptance skills to their responses to uncontrollable experiences. OBJECTIVE: This article presents an overview of ACT, its evidence base and how general practitioners can apply ACT consistent practice in the primary care setting. It describes pathways for general practitioners to develop further expertise in the approach. DISCUSSION: Acceptance and commitment therapy has been associated with improved outcomes in patients with chronic pain (comparable to cognitive behaviour therapy) and several studies suggest that it may be useful in patients with mild to moderate depression. Preliminary evidence of benefit has also been shown in the setting of obsessive-compulsive disorder, psychosis, smoking, tinnitus, epilepsy and emotionally disordered eating after gastric band surgery. Acceptance and commitment therapy starts with a discussion about what the patient wants and how they have tried to achieve these aims. Strategies previously used to avoid discomfort are discussed. Psychoeducation in ACT involves metaphors, stories and experiential exercises to demonstrate the uncontrollability and acceptability of much psychological experience. In its final phase, ACT resembles traditional behaviour therapy consisting of goal setting and graduated activity scheduling toward goals directed by values.

The effectiveness of training in Introvision as a method of improving health: a review of empirical results (Article in press)

[Gesundheitsförderung durch Introvision als Methode der mentalen Selbstregulation: eine zusammenfassende Übersicht über empirische Forschungsergebnisse]


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This article gives an overview on five empirical studies on the effects of training in Introvision on improving health. Introvision is a newly developed, research based method of mental self-regulation aiming at resolving inner conflicts. To put it briefly, Introvision is a method of combining principles of cognitive behavior therapy with a special kind of mindfulness, thus aiming at extinguishing the habitual coupling of core cognitions with heightened arousal, tension and inhibition. In this article, two general hypotheses on the effects of Introvision on health are developed based on the theory of mental introference. The results of three controlled empirical studies show that introvision leads to significant improvement in reducing chronic health problems. Specifically, there were significant improvements (1) of hearing (in case of presbyacusis), (2) in lessening the strain of tinnitus and (3) in reducing and resolving chronic neck tensions. Also, training in Introvision led to significant long-term reduction of chronic stress (prae, post) in various groups (e.g. high-performance sports, managers). After the ending of training in Introvision, chronic stress was decreased even further significantly (post vs. follow-up). © 2012 VS Verlag für Sozialwissenschaften.
An Internet-Based Cognitive-Behavioural Training for Acute Tinnitus: Secondary Analysis of Acceptance in Terms of Satisfaction, Trial Attrition and Non-usage Attrition.
Cogn Behav Ther. 2012 Dec 3. [Epub ahead of print]

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Objectives: Recent studies on tinnitus have focused on the efficacy of Internet-based interventions. Other core features of the quality of service, e.g. acceptance and attrition, have often been overlooked. This study analyses Internet-based training regarding acceptance and attrition in a trial on minimal-contact interventions for acute tinnitus. Whenever possible, we give information on other forms of training for comparison. Methods: In a randomised controlled trial with 337 participants, 87 persons took part in the Internet training. Results: The participants were as satisfied with the Internet-based training as with a face-to-face group training. There was a 34.48% dropout from the Internet-based training (dropout attrition). The training attrition from the Internet-based training was even higher at 64.4%. Conclusions: Two out of three indicators for acceptance-satisfaction and dropout attrition-provide comparable results between the Internet-based training and a face-to-face group training. The third indicator, training attrition, shows a better result for the group training. Future research should focus on attrition in order to enhance the overall effectiveness of training.

Pilot study to develop telehealth tinnitus management for persons with and without traumatic brain injury.


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Tinnitus, or “ringing in the ears,” affects 10%-15% of adults; cases can be problematic and require lifelong management. Many people who have experienced traumatic brain injury (TBI) also experience tinnitus. We developed Progressive Tinnitus Management (PTM), which uses education and counseling to help patients learn how to self-manage their reactions to tinnitus. We adapted PTM by delivering the intervention via telephone and by adding cognitive-behavioral therapy. A pilot study was conducted to evaluate the feasibility and potential efficacy of this approach for individuals with and without TBI. Participants with clinically significant tinnitus were recruited into three groups: probable symptomatic mild TBI (n = 15), moderate to severe TBI (n = 9), and no symptomatic TBI (n = 12). Participants received telephone counseling (six sessions over 6 months) by an audiologist and a psychologist. Questionnaires were completed at baseline, 12 weeks, and 24 weeks. All groups showed trends reflecting improvement in self-perceived functional limitations due to tinnitus. A follow-up randomized clinical study is underway.
We examined the prevalence, severity, etiology, and treatment of audiology problems among Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) Veterans with mild traumatic brain injury (TBI). A retrospective chart review was performed of 250 Veterans with mild TBI. Results of a comprehensive second-level mild TBI evaluation and subsequent visits to audiology were evaluated. We found the vast majority (87%) of Veterans reported some level of hearing disturbance and those involved in blast injuries reported a higher incidence of hearing disturbance than those with other injury etiologies. Audiology referrals were given to 75 Veterans and 37 attended. At this visit, Veterans reported tinnitus (75.7%) and hearing loss (59.8%). Nearly half (48.6%) of Veterans were diagnosed with conductive hearing loss, sensorineural hearing loss, or central auditory dysfunction. An additional 24.3% of Veterans had subclinical levels of auditory dysfunction. Our study has highlighted the increased prevalence of hearing loss among OIF/OEF Veterans and, thus, the need for appropriate referrals and treatment. Strategies to address perceived stigma associated with hearing loss may increase attendance at follow-up visits. Additionally, while only a third of audiograms were found to be abnormal, advanced testing resulted in a significant percentage of our population being diagnosed with auditory dysfunction.

IX Somatic Tinnitus

Somatosensory projections to cochlear nucleus are upregulated after unilateral deafness.

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The cochlear nucleus (CN) receives innervation from auditory and somatosensory structures, which can be identified using vesicular glutamate transporters, VGLUT1 and VGLUT2. VGLUT1 is highly expressed in the magnocellular ventral CN (VCN), which receives auditory nerve inputs. VGLUT2 is predominantly expressed in the granule cell domain (GCD), which receives nonauditory inputs from somatosensory nuclei, including spinal trigeminal nucleus (Sp5) and cuneate nucleus (Cu). Two weeks after unilateral deafening VGLUT1 is significantly decreased in ipsilateral VCN while VGLUT2 is significantly increased in the ipsilateral GCD (Zeng et al., 2009), putatively reflecting decreased inputs from auditory nerve and increased inputs from nonauditory structures in guinea pigs. Here, we wished to determine whether the upregulation of VGLUT2 represents increases in the number of somatosensory projections to the CN that are maintained for longer periods of time. Thus, we examined concurrent changes in VGLUT levels and somatosensory projections in the CN using immunohistochemistry combined with anterograde tract tracing three and six weeks following unilateral deafening. The data reveal that unilateral deafness leads to increased numbers of VGLUT2-colabeled Sp5 and Cu projections to the ventral and dorsal CN. These findings suggest that Sp5 and Cu play significant and unique roles in cross-modal compensation and that, unlike after shorter term deafness, neurons in the magnocellular regions also participate in the compensation. The enhanced glutamatergic somatosensory projections to the CN may play a role in neural spontaneous hyperactivity associated with tinnitus.
Multi-sensory integration in brainstem and auditory cortex.
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Tinnitus is the perception of sound in the absence of a physical sound stimulus. It is thought to arise from aberrant neural activity within central auditory pathways that may be influenced by multiple brain centers, including the somatosensory system. Auditory-somatosensory (bimodal) integration occurs in the dorsal cochlear nucleus (DCN), where electrical activation of somatosensory regions alters pyramidal cell spike timing and rates of sound stimuli. Moreover, in conditions of tinnitus, bimodal integration in DCN is enhanced, producing greater spontaneous and sound-driven neural activity, which are neural correlates of tinnitus. In primary auditory cortex (A1), a similar auditory-somatosensory integration has been described in the normal system (Lakatos et al., 2007), where sub-threshold multisensory modulation may be a direct reflection of subcortical multisensory responses (Tyll et al., 2011). The present work utilized simultaneous recordings from both DCN and A1 to directly compare bimodal integration across these separate brain stations of the intact auditory pathway. Four-shank, 32-channel electrodes were placed in DCN and A1 to simultaneously record tone-evoked unit activity in the presence and absence of spinal trigeminal nucleus (Sp5) electrical activation. Bimodal stimulation led to long-lasting facilitation or suppression of single and multi-unit responses to subsequent sound in both DCN and A1. Immediate (bimodal response) and long-lasting (bimodal plasticity) effects of Sp5-tone stimulation were facilitation or suppression of tone-evoked firing rates in DCN and A1 at all Sp5-tone pairing intervals (10, 20, and 40ms), and greater suppression at 20ms pairing-intervals for single unit responses. Understanding the complex relationships between DCN and A1 bimodal processing in the normal animal provides the basis for studying its disruption in hearing loss and tinnitus models. This article is part of a Special Issue entitled: Tinnitus Neuroscience. Published by Elsevier B.V.

Nocturnal masseter muscle activity is related to symptoms and somatization in temporomandibular disorders.
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OBJECTIVE: Temporomandibular disorders (TMD) have often been related to sleep bruxism and elevated nocturnal masseter muscle activity (NMMA). However, previous studies have revealed controversial results, and the role of somatization, depression and anxiety has not been studied in this context. The aim of this study was to investigate the association between NMMA and pain intensity, TMD related symptoms, somatoform symptoms, depression, and anxiety in chronic TMD. METHODS: Thirty-six subjects with chronic painful TMD, 34 subjects with pain free bruxism, and 36 healthy controls recorded their nocturnal masseter muscle activity during three consecutive nights with portable devices. In addition, participants completed pain diaries and questionnaires. Diagnoses were established using the research diagnostic criteria for TMD. RESULTS: Subjects with chronic TMD reported a reduced general health state (p<.001), higher levels of somatoform symptoms (p<.001), depression (p<.05), and anxiety (p<.001) compared to control subjects with or without sleep bruxism. The amount of NMMA did not differ significantly between the groups. In subjects with TMD, pain intensity was not related to NMMA. However, higher NMMA was related to higher intensity of jaw related symptoms such as headache or tinnitus, and higher somatization in general. CONCLUSION: Chronic TMD is associated with elevated levels of psychopathology. These findings suggest a common link between NMMA, somatization, and symptom intensity in chronic TMD. Copyright © 2012 Elsevier Inc. All rights reserved.
Surgical Treatment

Is there any predictor for tinnitus outcome in different types of otologic surgery?
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Our objective was to determine the effect of different types of otologic surgeries on tinnitus symptoms. Our study consisted of 63 patients who were operated between January and June 2011. Variables such as age, sex, presence of systemic diseases, location and size of the perforation, duration of dry period, type of otologic surgery, peroperative presence of cholesteatoma, tympanosclerotic plaques and ossicular chain discontinuity were evaluated. Audiologic evaluation by pure tone audiometry and assessment of THI scores were conducted before surgery and 12 weeks after surgery. There was a very significant difference between preoperative and postoperative mean THI scores (p < 0.01). There was no significant effect of presence of ossicular discontinuity, cholesteatoma, tympanosclerotic plaques, type of surgery or duration of symptoms on the difference of preoperative and postoperative THI scores (p > 0.05). There was a significant positive relationship between audiological gain and THI scores (r = 0.355, p < 0.01). In our study, we investigated the relationship between many types of otologic surgeries including some preoperative and peroperative pathological findings and tinnitus. As a result, we found that postoperative audiologic gain is an important factor determining outcome of tinnitus in these types of otologic surgeries.

Cochlin-tomoprotein (CTP) detection test identified perilymph leakage preoperatively in revision stapes surgery.

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Perilymphatic fistula (PLF) is defined as an abnormal leakage between perilymph from the labyrinth to the middle ear. Symptoms include hearing loss, tinnitus, and vertigo. The standard mode of PLF detection is intraoperative visualization of perilymph leakage and fistula, which ostensibly confirms the existence of PLF. Other possible methods of diagnosis include confirmation of pneumolabyrinth via diagnostic imaging. Recently, a cochlinc-tomoprotein (CTP) detection test has been developed that allows definitive diagnosis of PLF-related hearing loss. We report the case of a 45-year-old man who presented with right-sided tinnitus, hearing loss, and dizziness 30 years after stapes surgery. Middle ear lavage was performed after myringotomy. A preoperative diagnosis of PLF was reached using the CTP detection test. Intraoperative observations included a necrotic long process of the incus, displaced wire piston, and fibrous tissue in the oval window. Perilymph leakage was not evident. The oval window was closed with fascia, and vertigo disappeared within 2 weeks postoperatively. When PLF is suspected after stapes surgery, the CTP detection test can be a useful, highly sensitive, and less invasive method for preoperative diagnosis. Copyright © 2012. Published by Elsevier Ireland Ltd.
Surgical resection of endolymphatic sac tumors in von Hippel-Lindau disease: Findings, results, and indications.


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OBJECTIVES/HYPOTHESIS: To define the surgical treatment and outcomes of von Hippel-Lindau (VHL) disease-associated endolymphatic sac tumors (ELSTs), we analyzed consecutive VHL patients who underwent ELST resection. STUDY DESIGN: Retrospective investigation of consecutive VHL patients who underwent resection of ELSTs at a clinical research center between 1999 and 2010. METHODS: Analysis of serial clinical examinations, audiograms, imaging studies, and operative findings were analyzed. RESULTS: Thirty-one consecutive patients with ELSTs (15 males, 16 females) underwent resection of 33 tumors (mean follow-up, 49.9 ± 48.0 months; range, 1.0-116 months). One patient had bilateral ELST resections and one patient underwent reoperation for recurrence. Mean age at surgery was 38.2 ± 10.2 years (range, 12-67 years). Whereas 29 ears (88%) had direct radiographic evidence of an ELST, four ears (12%) did not. Mean tumor size was 1.3 ± 1.1 cm (range, 0.2-5.2 cm). Whereas two patients (two ears, 6%) were asymptomatic, 29 patients (31 ears, 94% of ears) had associated audiovestibular symptoms, including sensorineural hearing loss (28 ears, 84%), tinnitus (24 ears, 73%), and vertigo (21 patients, 68%). Postoperatively, hearing was stabilized (27) or improved (three) in 97% of 31 ears. Complete tumor resection was achieved in 30 ears (91% of 33 ears). Complications included cerebrospinal fluid leak in two ears (6%) and transient lower cranial nerve palsy in one ear (3%). CONCLUSIONS: Surgical resection of ELSTs can be performed with hearing preservation and a reduction in audiovestibular dysfunction. Early surgical resection can prevent or decrease disabling audiovestibular symptoms, enhance the opportunity for complete resection, and preserve hearing. Laryngoscope, 2012. Copyright © 2012 The American Laryngological, Rhinological, and Otological Society, Inc.

Prognosis of tinnitus after acoustic neuroma surgery - Surgical management of postoperative tinnitus.


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OBJECT: Tinnitus is a bothersome symptom for patients with acoustic neuroma. We studied the possibility of surgical control of postoperative tinnitus associated with acoustic neuroma. METHODS: Postoperative changes and prognosis of tinnitus were studied in 367 patients treated surgically via a lateral suboccipital retrosigmoid approach. RESULTS: Postoperative prognosis of tinnitus was: resolved in 20%, improved in 22%, unchanged in 35%, changed in 10%, and worsened in 14% of 290 patients who had preoperative tinnitus, and no tinnitus in 78% and appeared in 22% of 77 patients without preoperative tinnitus. Prognosis of postoperative tinnitus was influenced by age, tumor size, preoperative hearing acuity, types of preoperative hearing disturbance, and conditions of the cochlear nerve after tumor resection. Worse prognosis of postoperative tinnitus in the preoperative tinnitus group was found in younger patients, smaller tumor size, better preoperative hearing function, and normal or retrocochlear type of hearing disturbance. Regarding the conditions of the cochlear nerve after tumor resection, prognosis of tinnitus was significantly worse in the group of anatomically preserved cochlear nerve without useful hearing than in the group of cut cochlear nerve. CONCLUSIONS: Deciding whether to cut the cochlear nerve during acoustic neuroma...
surgery by referring to a flowchart we proposed in cases where hearing preservation is not intended or judged less possible contributes to controlling postoperative tinnitus. However, regardless of whether the cochlear nerve was cut intraoperatively, tinnitus remained unchanged in 37% of patients, suggesting that their tinnitus originates in the brainstem or post-brainstem pathways before surgery, and it is considered difficult to control postoperative tinnitus in these cases. Copyright © 2012. Published by Elsevier Inc.

A novel approach for surgical repair of dehiscent high jugular bulb (Article in press)
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No abstract available.

Fractionated stereotactic radiotherapy for acoustic neuromas: A prospective monocenter study of about 158 cases.


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PURPOSE: To evaluate long-term outcomes and efficacy of fractionated stereotactic radiotherapy in the treatment of acoustic neuromas. MATERIAL AND METHODS: Between January 1996 and December 2009, 158 acoustic neuromas were treated by FSR in 155 patients. They received a dose of 50.4Gy, with a safety margin of 1-2mm with a median tumor volume at 2.45mL (range: 0.17-12.5mL) and a median follow-up duration at 60months (range: 24-192). RESULTS: FSR was well tolerated in all patients with mild sequelae consisting in radiation-induced trigeminal nerve impairments (3.2%), Grade 2 facial neuropathies (2.5%), new or aggravated tinnitus (2.1%) and VP shunting (2.5%). The treatment failed in four patients (2.5%) who had subsequent surgery respectively at 20, 38, 45 and 84months post-FSR. The local tumor control rates were respectively 99.3%, 97.5% and 95.2% at 3, 5 and >7-year of follow-up. For initial Gardner-Robertson Grade 1 and 2 ANs, the preservation of useful hearing was possible in 54% of the cases; only Grade 1 ANs had stabilized during the course of the follow-up with 71% >7years. However, hearing preservation was not correlated to the initial Koos Stage and to the radiation dose delivered to the cochlea. Tinnitus (70%), vertigo (59%), imbalance (46%) and ear mastoid pain (43%) had greatly improved post-FRS in most patients. Tumor control, hearing preservation and FRS toxicity were quite similar in patients with NF2, cystic acoustic neuroma, prior surgical resection and Koos Stage 4 AN. No secondary tumors were observed. CONCLUSION: FSR is a safe and effective therapeutic for acoustic neuromas and could be an alternative to microsurgery. Compared to radiosurgery, there are no contraindications for fractioned doses of stereotactic radiotherapy especially for Stage-4 tumors and patients at high risk of hearing loss. Copyright © 2012 Elsevier Ireland Ltd. All rights reserved.
Role of Gamma Knife surgery in the treatment of intracranial dural arteriovenous fistulas.

Hanakita S, Koga T, Shin M, Shojima M, Igaki H, Saito N.

Departments of Neurosurgery and.

Objective: The goal of this study was to assess the efficacy of Gamma Knife surgery (GKS) in the management of dural arteriovenous fistulas (dAVFs). Methods: The authors performed a retrospective analysis of a group of 22 patients who underwent GKS for dAVFs at the University of Tokyo Hospital between 1991 and 2009. The patients underwent CT or MR imaging with contrast enhancement every 6 months after GKS; when obliteration of a dAVF was indicated by these images, patients also underwent angiography. Follow-up in these patients ranged from 12 months to 100 months (median 33 months) after GKS. Results: Obliteration of the dAVF was confirmed by neuroimaging in 12 patients (55%). According to a Kaplan-Meier analysis, obliteration rates for the dAVFs were 51% at 3 years and 80% at 5 years. The obliteration rate for lesions without cortical venous drainage (CVD) was 86%, which was significantly higher than the rate for dAVFs with CVD (47%) (p = 0.007). Hemorrhage at presentation (p = 0.03), a target volume less than 1.5 cm³ (p = 0.009), and Cognard Type III or IV dAVF (p = 0.005) were factors associated with a higher obliteration rate. Among 10 patients whose dAVFs were not obliterated by the initial GKS, 5 patients underwent additional treatment and complete obliteration was achieved in all. Relief of tinnitus was obtained in 5 (83%) of 6 patients with transverse-sigmoid sinus dAVFs, and ophthalmic symptoms improved in 2 (67%) of 3 patients with cavernous sinus dAVFs. No patient experienced interval hemorrhage or radiation-induced complications after treatment. Conclusions: Gamma Knife surgery is a safe and effective treatment for dAVF. It can be a first line of therapy in the multidisciplinary treatment strategy for dAVFs, especially when significant morbidity is anticipated with other therapeutic options. One should be very careful about recommending GKS for patients harboring dAVFs with CVD because of the expected natural history of such a lesion and the possibility of other therapeutic options.

XI Holistic

Acupuncture at local and distant points for tinnitus: study protocol for a randomized controlled trial.

Shi GX, Han LL, Liu LY, Li QQ, Liu CZ, Wang LP.

Background: Tinnitus is the perception of a sound in the absence of an objective physical source. Up to now, there is no generally accepted view about how these phantom sounds come about, and also no efficient treatment. Patients are turning to complementary or alternative medical therapies, such as acupuncture. Based on the theory of traditional Chinese medicine, acupoints located on both the adjacent and distal area of the disease can be needled to treat disease. Furthermore, the way of combining acupoints is for strengthening the curative effect. We aim to evaluate the efficacy of acupuncture at local points in combination with distal points in subjective tinnitus patients. Method: This trial is a randomized, single-blind, controlled study. A total of 112 participants will be randomly assigned to one of four treatment groups receiving acupuncture treatment for 4 weeks. The primary outcome measure is subjective tinnitus loudness and annoyance perception, which is graded using the Visual Analogue Scale (VAS). The assessment is at baseline (before treatment initiation), 4 weeks after the first acupuncture session, and 8 weeks after the first acupuncture session. Discussion: Completion of this trial will help to identify whether acupuncture at local acupoints in combination with distal acupoints may be more effective than needling points separately.

Trial registration International Standard Randomized Controlled Trial Number Register: ISRCTN29230777. Free full text.
Surgical brain modulation for tinnitus: the past, present and future.

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Tinnitus treatment has traditionally been restricted to ENT surgeons, audiologists, psychologists and psychiatrists. Recently, both basic and clinical research has focused on the brain's involvement in the generation of tinnitus, opening the tinnitus field up to neurologists and neurosurgeons specialized in the field of tinnitus. Non-pulsatile tinnitus can be considered an auditory phantom phenomenon, analogous to phantom pain, both with regards to pathophysiological mechanisms, clinical characteristics, and treatment approaches. Thus the understanding of tinnitus has benefited a lot from translating available knowledge of the somatosensory (pain) system to the auditory system. A literature review of neuromodulatory approaches to tinnitus is integrated in a single center's experience with invasive neuromodulation treatments for tinnitus. This is compared to findings from neuromodulatory treatment of chronic pain syndromes. The past, present and future options for functional neurosurgical approaches are outlined. In the past only destructive approaches were used, consisting of nerve lesions and frontal lobotomies. Presently neurostimulation trials are ongoing evaluating the effect of auditory cortex stimulation, frontal cortex stimulation, thalamic (VIM) and caudate stimulation as well as amygdalohippocampal stimulation, yielding suppression rates between 10 and 70%. Further potentially promising targets include the anterior cingulate, the medial geniculate bodies (MGB), the periaqueductal gray/ tectal longitudinal column (PAG/ TLC), the dorsal cochlear nucleus, as well as the C2 and trigeminal nerve. Understanding tinnitus and its potential neuromodulation treatments is relatively simple for a neurosurgeon specialized in pain or a pain physician, based on the pathophysiological and clinical analogies. Similarly to pain a multidisciplinary approach can be advocated, and in view of the epidemiology and amount of suffering associated with this enigmatic symptom further investment in possible neuromodulation treatments is warranted.

Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus.

Bennett MH, Kertesz T, Perleth M, Yeung P, Lehm JP.

Department of Anaesthesia, Prince of Wales Hospital, Randwick, Australia. m.bennett@unsw.edu.au.

BACKGROUND: This is an update of a Cochrane Review first published in The Cochrane Library in Issue 1, 2005 and previously updated in 2007 and 2009. Idiopathic sudden sensorineural hearing loss (ISSHL) is common and has a significant effect on quality of life. Hyperbaric oxygen therapy (HBOT) may improve oxygen supply to the inner ear and result in an improvement in hearing. OBJECTIVES: To assess the benefits and harms of HBOT for treating ISSHL and/or tinnitus. SEARCH METHODS: We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; Database of Randomised Trials in Hyperbaric Medicine (DORCHIM); CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. The date of the most recent search was 2 May 2012, following previous searches in 2009, 2007 and 2004. SELECTION CRITERIA: Randomised studies comparing the effect on ISSHL and tinnitus of HBOT and alternative therapies. DATA COLLECTION AND ANALYSIS: Three authors evaluated the quality of trials using the 'Risk of bias' tool and extracted data from the included trials. MAIN RESULTS: Seven trials contributed to this review (392 participants). The studies were small and of generally poor quality. Pooled data from two trials did not show any significant improvement in the chance of a 50% increase in hearing threshold on pure-tone average with HBOT (risk ratio (RR) with HBOT 1.53, 95% confidence interval (CI) 0.85 to 2.78, P = 0.16), but did show a significantly increased chance of a 25% increase in pure-tone average (RR 1.39, 95% CI 1.05 to 1.84, P = 0.02).
was a 22% greater chance of improvement with HBOT, and the number needed to treat (NNT) to achieve one extra good outcome was 5 (95% CI 3 to 20). There was also an absolute improvement in average pure-tone audiometric threshold following HBOT (mean difference (MD) 15.6 dB greater with HBOT, 95% CI 1.5 to 29.8, \( P = 0.03 \)). The significance of any improvement in tinnitus could not be assessed. There were no significant improvements in hearing or tinnitus reported for chronic presentation (six months) of ISSHL and/or tinnitus. AUTHORS’ CONCLUSIONS: For people with acute ISSHL, the application of HBOT significantly improved hearing, but the clinical significance remains unclear. We could not assess the effect of HBOT on tinnitus by pooled analysis. In view of the modest number of patients, methodological shortcomings and poor reporting, this result should be interpreted cautiously. An appropriately powered trial is justified to define those patients (if any) who can be expected to derive most benefit from HBOT. There is no evidence of a beneficial effect of HBOT on chronic ISSHL or tinnitus and we do not recommend the use of HBOT for this purpose. Update of Cochrane Database Syst Rev. 2007;(1):CD004739.

Sound therapy (masking) in the management of tinnitus in adults.

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BACKGROUND: This is an update of a Cochrane Review first published in The Cochrane Library in Issue 12, 2010. Tinnitus is described as the perception of sound or noise in the absence of real acoustic stimulation. Numerous management strategies have been tried for this potentially debilitating, heterogeneous symptom. External noise has been used as a management tool for tinnitus, in different capacities and with different philosophical intent, for over a century. OBJECTIVES: To assess the effectiveness of sound-creating devices (including hearing aids) in the management of tinnitus in adults. Primary outcome measures were changes in the loudness or severity of tinnitus and/or impact on quality of life. Secondary outcome measures were change in pure-tone auditory thresholds and adverse effects of treatment. SEARCH METHODS: We searched the Cochrane ENT Group Trials Register; CENTRAL; PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. The date of the most recent search was 8 February 2012. SELECTION CRITERIA: Prospective randomised controlled trials recruiting adults with persistent, distressing, subjective tinnitus of any aetiology in which the management strategy included maskers, noise-generating device and/or hearing aids, used either as the sole management tool or in combination with other strategies, including counselling. DATA COLLECTION AND ANALYSIS: Two authors independently examined the 387 search results to identify studies for inclusion in the review, of which 33 were potentially relevant. The update searches in 2012 retrieved no further potentially relevant studies. Both authors extracted data independently. MAIN RESULTS: Six trials (553 participants) are included in this review. Studies were varied in design, with significant heterogeneity in the evaluation of subjective tinnitus perception, with different scores, scales, tests and questionnaires as well as variance in the outcome measures used to assess the improvement in tinnitus sensation/quality of life. This precluded meta-analysis of the data. There was no long-term follow-up. We assessed the risk of bias as medium in three and high in three studies. Following analysis of the data, no significant change was seen in the loudness of tinnitus or the overall severity of tinnitus following the use of sound therapy compared to other interventions such as patient education, ‘relaxation techniques’, ‘tinnitus coping strategies’, counselling, ‘tinnitus retraining’ and exposure to environmental sounds. No side effects or significant morbidity were reported from the use of sound-creating devices. AUTHORS’ CONCLUSIONS: The limited data from the included studies failed to show strong evidence of the efficacy of sound therapy in tinnitus management. The absence of conclusive evidence should not be interpreted as evidence of lack of effectiveness. The lack of quality research in this area, in addition to the common use of combined approaches (hearing therapy plus counselling) in the management of tinnitus are, in part, responsible for the lack of conclusive evidence. Other combined forms of management, such as tinnitus retraining therapy, have been subject to a Cochrane Review. Optimal management may involve multiple strategies.
Tinnitus evaluation in primary care.

Ruppert SD, Fay VP.

Susan D. Ruppert is a professor and assistant dean at The University of Texas Health Science Center at Houston, School of Nursing. Vaunette P. Fay is a professor at The University of Texas Health Science Center at Houston, School of Nursing.

Tinnitus is a common, yet poorly understood problem. This symptom has many causes, both benign as well as serious. Patients can experience significant changes in quality-of-life related to symptom severity and duration. This article explores causes of tinnitus, evaluation in a primary care setting, and management strategies.

Ringing in my ears: tinnitus in pregnancy.

Smith S, Hoare D.

NIHR Nottingham Hearing Biomedical Research Unit.

A number of ear, nose and throat symptoms are often associated with pregnancy, which although transient (most will disappear after birth), can have a significant impact on the woman's quality of life. It is essential therefore that midwives are aware of how such symptoms might present during pregnancy, in order to appropriately inform women and safely manage those symptoms. Tinnitus, the most common ear symptom experienced by women during pregnancy, for some will be a distressing experience and for others may indicate more serious conditions such as pre eclampsia, requiring careful monitoring and confident management.

Tinnitus-related neural activity: theories of generation, propagation, and centralization.

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The neuroscience of tinnitus represents an ideal model to explore central issues in brain functioning such as the formation of auditory percepts, in addition to opening up new treatment avenues for the condition in the long-term. The present review discusses the origin and nature of tinnitus-related neural activity. First, we review evidence for the hypothesis that tinnitus is caused by the central nervous system changes induced by sensory deprivation, even when hearing loss is not visible in the audiogram. Second, we suggest that changes in neural activity in individual central structures may not be sufficient to underlie the tinnitus percept. Instead, we propose that tinnitus may arise from functional alterations at multiple levels which promote abnormal propagation of neural activity throughout the network involved in auditory perception. In this context, functional coupling within and between central auditory structures may be especially important to consider. Investigating how sensory deprivation affects functional coupling between areas, which might be reflected in changes in temporal coherence of intrinsic ongoing activity patterns, may give critical insights into the mechanisms of tinnitus. Copyright © 2012. Published by Elsevier B.V.
Recurrent Spontaneous Attacks of Dizziness.

Lempert T.

Purpose of Review: This article describes the common causes of recurrent vertigo and dizziness that can be diagnosed largely on the basis of history. Recent Findings: Ninety percent of spontaneous recurrent vertigo and dizziness can be explained by six disorders: (1) Ménière disease is characterized by vertigo attacks, lasting 20 minutes to several hours, with concomitant hearing loss, tinnitus, and aural fullness. Aural symptoms become permanent during the course of the disease. (2) Attacks of vestibular migraine may last anywhere from minutes to days. Most patients have a previous history of migraine headaches, and many experience migraine symptoms during the attack. (3) Vertebrobasilar TIAs affect older adults with vascular risk factors. Most attacks last less than 1 hour and are accompanied by other symptoms from the posterior circulation territory. (4) Vestibular paroxysmia is caused by vascular compression of the eighth cranial nerve. It manifests itself with brief attacks of vertigo that recur many times per day, sometimes with concomitant cochlear symptoms. (5) Orthostatic hypotension causes brief episodes of dizziness lasting seconds to a few minutes after standing up and is relieved by sitting or lying down. In older adults, it may be accompanied by supine hypertension. (6) Panic attacks usually last minutes, occur in specific situations, and are accompanied by choking, palpitations, tremor, heat, and anxiety. Less common causes of spontaneous recurrent vertigo and dizziness include perilymph fistula, superior canal dehiscence, autoimmune inner ear disease, otosclerosis, cardiac arrhythmia, and medication side effects. Summary: Neurologists need to venture into otolaryngology, internal medicine, and psychiatry to master the differential diagnosis of recurrent dizziness.

Ménière’s disorder: A short history (Review).

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The authors discuss early reports probably related to Ménière’s disorder, a short account of the contribution and life of Prosper Menière and the developments and terminological confusions following that time. We consider various approaches that have been made to the treatment of the condition and briefly mention some famous people who have suffered from the condition. © 2012 Informa Healthcare.

Early noise exposure and subsequent age-related hearing loss: A review (Conference Paper).

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The author recently chaired a committee of the Institute of Medicine which was charged with examining the evidence regarding noise-induced hearing loss (and tinnitus) in U.S. military veterans since World War II. A central question addressed was whether noise exposure as a young adult would impact subsequent age-related hearing loss. At the time, there were very few data available to address this issue. In fact, there were relatively few longitudinal studies of hearing thresholds in adults published at the time of the report and most had little information about the impact of prior noise history on the progression of hearing loss.
Since the publication of the committee's report in 2006, several longitudinal studies of hearing loss have been published for older adults. In addition, there has been at least one animal study and three human studies published in which the specific issue of the effect of prior noise exposure on subsequent age-related hearing loss had been examined. The results of these studies will be reviewed in this presentation, as well as the implications of these studies for issues critical to the study of hearing loss from occupational noise, such as the additivity of age-related and noise-induced hearing loss.

XIII Others

Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus.

Bennett MH, Kertesz T, Perleth M, Yeung P, Lehm JP.
Department of Anaesthesia, Prince of Wales Hospital, Randwick, Australia. m.bennett@unsw.edu.au

BACKGROUND: This is an update of a Cochrane Review first published in The Cochrane Library in Issue 1, 2005 and previously updated in 2007 and 2009. Idiopathic sudden sensorineural hearing loss (ISSHL) is common and has a significant effect on quality of life. Hyperbaric oxygen therapy (HBOT) may improve oxygen supply to the inner ear and result in an improvement in hearing. OBJECTIVES: To assess the benefits and harms of HBOT for treating ISSHL and/or tinnitus. SEARCH METHODS: We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; Database of Randomised Trials in Hyperbaric Medicine (DORCTHIM); CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. The date of the most recent search was 2 May 2012, following previous searches in 2009, 2007 and 2004. SELECTION CRITERIA: Randomised studies comparing the effect on ISSHL and tinnitus of HBOT and alternative therapies. DATA COLLECTION AND ANALYSIS: Three authors evaluated the quality of trials using the 'Risk of bias' tool and extracted data from the included trials. MAIN RESULTS: Seven trials contributed to this review (392 participants). The studies were small and of generally poor quality. Pooled data from two trials did not show any significant improvement in the chance of a 50% increase in hearing threshold on pure-tone average with HBOT (risk ratio (RR) with HBOT 1.53, 95% confidence interval (CI) 0.85 to 2.78, P = 0.16), but did show a significantly increased chance of a 25% increase in pure-tone average (RR 1.39, 95% CI 1.05 to 1.84, P = 0.02). There was a 22% greater chance of improvement with HBOT, and the number needed to treat (NNT) to achieve one extra good outcome was 5 (95% CI 3 to 20). There was also an absolute improvement in average pure-tone audiometric threshold following HBOT (mean difference (MD) 15.6 dB greater with HBOT, 95% CI 1.5 to 29.8, P = 0.03). The significance of any improvement in tinnitus could not be assessed. There were no significant improvements in hearing or tinnitus reported for chronic presentation (six months) of ISSHL and/or tinnitus. AUTHORS’ CONCLUSIONS: For people with acute ISSHL, the application of HBOT significantly improved hearing, but the clinical significance remains unclear. We could not assess the effect of HBOT on tinnitus by pooled analysis. In view of the modest number of patients, methodological shortcomings and poor reporting, this result should be interpreted cautiously. An appropriately powered trial is justified to define those patients (if any) who can be expected to derive most benefit from HBOT. There is no evidence of a beneficial effect of HBOT on chronic ISSHL or tinnitus and we do not recommend the use of HBOT for this purpose. Update of Cochrane Database Syst Rev. 2007;(1):CD004739.
Application of distortion product otoacoustic emissions to inflation of the eustachian tube in low frequency tinnitus with normal hearing.

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OBJECTIVE: This study was designed to investigate the applications of distortion product otoacoustic emissions to assess the efficacy of eustachian tube inflation on low frequency tinnitus with normal hearing.

METHODS: Ninety-four patients (155 ears) suffering from subjective tinnitus with normal hearing sensitivity participated in this study. Control group consists of fifty volunteers (100 ears) without tinnitus. They were subjected to full history taking, otoscopy, basic audiologic evaluation and distortion product otoacoustic emissions (DPOAE). As for the patients with decreased DPOAE amplitude over a limited frequency range from 0.5 to 1kHz, we offered nose dropping and tubal inflation for a week and DPOAE was preformed again. The patients were followed up for a month. RESULTS: 34.8% DPOAE-gram showed decreased amplitude at the frequencies from 0.5 to 1kHz in tinnitus group and "the ring" is mostly lower in pitch. Among the patients accepted the treatment of eustachian tube inflation, 16.7% the tinnitus disappeared, no recurrence within one month; 66.67% the tinnitus reduced within one month. 95.5% the amplitude of DPOAE showed improved over the limited frequency. 16.7% the tinnitus still existed. CONCLUSION: The changes of the mechanical properties of ossicular chain or the tympanic membrane influenced by tympanum pressure may cause tinnitus, which is sub-clinical prior to the changes of audiometry and tympanometry. The low frequency tinnitus may gain transitory relief from ringing with the tubal inflation. DPOAE was proved to be a useful tool in the evaluation of the efficacy of tubal inflation on low frequency tinnitus with normal hearing. Copyright © 2012 Elsevier Ireland Ltd. All rights reserved.

A suggested model for decision-making regarding hearing conservation: Towards a systems theory approach.

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Objective: The aim of the study was to investigate potential health promotion variables associated with adolescents’ hearing protection use at concerts. Study sample: The sample consisted of 242 upper secondary school students aged 15-19 years. Design: Variables defined by the theory of planned behaviour (TPB) and health belief model were tested in this quantitative study. Results: Fifty-three percent of the adolescents reported that they used hearing protection at concerts to some degree, and 33 individuals (14%) reported that they used hearing protection in 50% of cases or more. The average degree of hearing protection use was reported to be 17% of the visits at concerts. Norms, perceived control, barriers, and noise sensitivity were associated with attitudes towards loud music. In addition, norms, barriers, permanent tinnitus, and noise sensitivity were significantly correlated with hearing protection use. However, intention was not significantly correlated with hearing protection use. Conclusions: From a systems theoretical approach it can be suggested that preventive strategies must consider more levels than just the individual, in order to achieve long lasting behavioural changes in adolescents’ listening habits. To be able to get useful knowledge about preventive strategies, it is necessary to add context-specific variables into generic models such as TPB.
Application of Ozone Therapy in the Vestibulocochlear Syndrome.
Rev Recent Clin Trials. 2012 Sep 7. [Epub ahead of print]

Menéndez S, Del Cerro A, Alvarez T, Hernández F.
National Center for Scientific Research. POBox 6414, Havana City, Cuba.

The aim of this study was to evaluate the efficacy of ozone therapy in the treatment of 50 patients with peripheral vestibulocochlear syndrome. Ozone was injected in the cervical region C2-C3, for 20 sessions. Evaluation criteria was based in the evolution of nystagmus, tinnitus, hearing loss and vertigo. Also, oxidative stress parameters were measured. Results demonstrated that patient improvements, according to vertigo, hearing loss, tinnitus and nystagmus, were of 90, 80, 65 and 100 %, respectively. These patients were initially under condition of systemic oxidative stress, however, at the end of the study a redox balance was achieved. No side effects were observed.

Observations From a Musician With Hearing Loss.
Trends Amplif. 2012 Nov 30. [Epub ahead of print]

Einhorn R.

Extensive personal experience with professional recording and audio signal processing technology has enabled the author to continue his music career after experiencing sudden sensorineural hearing loss. The iPhone™ is one such device that has been found useful for many music and general listening situations that would otherwise be intractable. Additional techniques and technologies are described that the author has found useful for specific situations, including music composition, rehearsal, and enjoyment.

Learning for Everyday Life: Students' standpoints on loud sounds and use of hearing protectors before and after a teaching-learning intervention.
International Journal of Science Education Volume 34, Issue 16, November 2012, Pages 2583-2606

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Researchers have highlighted the increasing problem of loud sounds among young people in leisure-time environments, recently even emphasizing portable music players, because of the risk of suffering from hearing impairments such as tinnitus. However, there is a lack of studies investigating compulsory-school students' standpoints and explanations in connection with teaching interventions integrating school subject content with auditory health. In addition, there are few health-related studies in the international science education literature. This paper explores students' standpoints on loud sounds including the use of hearing-protection devices in connection with a teaching intervention based on a teaching-learning sequence about sound, hearing and auditory health. Questionnaire data from 199 students, in grades 4, 7 and 8 (aged 10-14), from pre-, post- and delayed post-tests were analysed. Additionally, information on their experiences of tinnitus as well as their listening habits regarding portable music players was collected. The results show that more students make healthier choices in questions of loud sounds after the intervention, and especially among the older ones this result remains or is further improved one year later. There are also signs of positive behavioural change in relation to loud sounds. Significant gender differences are found; generally, the girls show more healthy standpoints and expressions than boys do. If this can be considered to be an outcome of students' improved and integrated knowledge about sound, hearing and health, then this emphasizes the importance of integrating health issues into regular school science. © 2012 Copyright Taylor and Francis Group, LLC.
Music exposure and hearing health education: A review of knowledge, attitude, and behaviour in adolescents and young adults (Review).

Zhao, F.a, French, D.a, Manchaiah, V.K.b, Liang, M.a, Price, S.M.c

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Introduction: Adolescents and young adults have been shown to be the age group most at risk of music-induced hearing loss (MIHL), which is already evident and increasing among this group. Objective: The purpose of this review is to provide further insight into the effectiveness of education programmes on attitude and behaviour towards loud music exposure in adolescents and young adults, and to suggest positive and influential ways of delivering hearing health education. Methods: Literature searches were conducted using various databases, including PubMed, Google Scholar and Cumulative Index to Nursing and Allied Health Literature (CINAHL). Authors went through the abstracts of these articles to identify those which were potentially relevant; subsequently the full articles were retrieved. Results: This review highlights the dangers of significant exposure to music on hearing mechanics in adolescents and young adults, and shows that this danger continues to increase with modern music culture. Because the consequences are not immediate, it is difficult for the young to perceive the seriousness of a problem that may not present itself for many years. Conventional education may go a little way in helping to raise awareness but a raised awareness of consequences does not, in itself, change behaviour. There is a significant gap in literature regarding effective methods of education that will inspire attitude change, and have a bearing on actions. Conclusion: This review has concluded that there is a lack of understanding of how to best influence and educate adolescents and young adults in a way that will motivate and encourage a change in listening habits. It is of vital importance that these groups are made aware of the immediate and future dangers, and how changes in listening behaviour do not necessarily lower their enjoyment. © The Author(s) 2011.

Are parents aware of their children's hearing complaints?

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Faculdade de Ciências Médicas, Universidade Estadual de Campinas.

The accuracy of parents' impressions about their child's hearing status is variable and may not correspond to the child's complaints. AIM: To investigate children's self-reported hearing symptoms and parents' impressions about it. METHODS: 477 children (2nd to 5th grades of elementary schools) were interviewed and parents answered a survey at home. There were 393 matches between the children's interview and the parent's survey. RESULTS: 29% of the children reported trouble in understanding what people said, 12.7% had four or more ear infections, 21.7% had continuous tinnitus (positive association with history of exposure to loud sounds, p = 0.0007), 3.8% had pulsatile tinnitus and 2.9% had auditory hallucinations. 28.5% were annoyed by loud sounds (associated with tinnitus, p = 0.0142, and gender, p = 0.0029) 10.4% had had audiological tests, and the determinant factors were history of ear infections (p < 0.001) and parents' concern about their child's hearing (p = 0.043). Parents and their own child's responses were significantly different. CONCLUSIONS: Children's auditory complaints were prevalent and relevant, but most of them had never had an audiological evaluation and most parents were not aware of their child's complaints. Sound intolerances and auditory hallucinations should be considered in clinical and audiological examinations. Free Article.
Inhibition of oscillation in a plastic neural network model of tinnitus therapy using noise stimulus (Conference Paper).


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Tinnitus is the perception of phantom sounds in the ears or in the head. Accordingly sound therapy for tinnitus has been used. To account for mechanisms of tinnitus generation and the clinical effects of sound therapies from the viewpoint of neural engineering, we have proposed a plastic neural network model for the human auditory system. We found that this model has a bistable state, i.e., a stable oscillatory state and a stable equilibrium (non-oscillatory) state coexist at a certain parameter region. This paper describes inhibition of the oscillation for various kinds of noise stimuli, because noise stimuli are presented to tinnitus sufferers for therapeutic purposes. Through several numerical simulations it was shown that noise stimulus can inhibit the oscillation (similar to residual inhibition as seen in clinical studies), however, the oscillation is not inhibited in all cases, i.e., the effect of inhibition is not pervasive as in the case of inhibition in clinical cases.

XIV Case Reports

Sexual asphyxia causing blunt carotid artery injury and Horner's syndrome.

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Objective: To highlight a rare cause of Horner's syndrome, and to review the management of blunt carotid artery injury. Method: Literature search via PubMed for related articles. Results: Horner's syndrome and blunt carotid artery injury are rare phenomena; sexual asphyxia as a cause has not previously been reported. This case is also the first of its kind to have radiological evidence of injury to the external carotid artery but not the internal carotid artery. In Horner's syndrome, additional symptoms of ipsilateral headache or neck pain, tinnitus, or any cerebral ischaemic symptoms should raise suspicion of blunt carotid injury. Conclusion: Blunt carotid artery injury is a potentially fatal condition and can present without radiological evidence. Early recognition and management with anticoagulants or antiplatelet drugs is crucial to prevent mortality and morbidity.
Intralabyrinthine schwannomas (ILSs) are rare benign neoplasms arising from distal branches of the cochlear, superior vestibular, or inferior vestibular nerves. We report on a case of ILS with extensions to the round window niche and internal auditory canal (IAC) in a 47-year-old male. The patient noticed sudden hearing loss and tinnitus in his left ear at the age of 36, received steroid therapies, but was left with complete deafness. He had suffered from repetitive vertigo attacks for 6 months at 41. At 46 when he presented with deterioration of his left tinnitus, he was finally diagnosed as having ILS on enhanced MRI and constructive interference in steady-state analysis. The tumor was located in all turns of cochlea, vestibule, and the fundus of the IAC. Because follow-up MRI suggested growth of the IAC tumor, we performed total removal of the tumor via the translabyrinthine and transcanal approaches. The tumor had invaded only the cochlear nerve in the IAC and appeared in the round window niche in the middle ear. Pathological examination showed an Antoni A type schwannoma with fibrous changes of the semicircular canals. We should remember this inner.

Bilateral sudden sensorineural hearing loss as an initial presentation of myelodysplastic syndrome.

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This study reports an unusual case in which myelodysplastic syndrome presented bilateral sudden sensorineural hearing loss as the first symptom of the disease. The aural symptoms and signs such as tinnitus, dizziness, and hearing impairment of a hematologic disease are common. However, sudden hearing loss as the first manifestation of a hematologic disease is extremely rare. A 76-year-old woman presented with bilateral sudden hearing loss. The patient was found to have myelodysplastic syndrome during a workup for her hearing loss. Unfortunately, the patient's hearing loss did not improve after the medical treatment. Copyright © 2012 Elsevier Inc. All rights reserved.

Bilateral objective tinnitus in an infant with tuberous sclerosis.

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This is the first report of objective tinnitus presenting as audible spontaneous otoacoustic emission in a patient with tuberous sclerosis. The tinnitus was loud, continuous, and high pitched: 7757.8 and 6257.8Hz. The auditory system may be dysfunctional in patients with tuberous sclerosis. Possible causes of tinnitus in these patients are abnormal myelination and dysfunctional axons and neurons associated with tuberous sclerosis. A disturbance of the outer hair cells or the MOC efferent fibers innervating the outer hair cells is considered to be the source of the loud spontaneous otoacoustic emission. Copyright © 2012 Elsevier Ireland Ltd. All rights reserved.
Familial Intracranial Dural Arteriovenous Fistulas.
Neurosurgery. 2012 Nov 12. [Epub ahead of print]

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BACKGROUND AND IMPORTANCE: Intracranial dural arteriovenous fistulas (DAVF) are acquired abnormal communications between dural arteries and veins. Risk factors for development include sinus thrombosis and hypercoagulability, such as occurs in heritable thrombophilias. While there have been reports of other types of vascular anomalies (such as cavernous and arteriovenous malformations) occurring in families, to our knowledge there have been no reports of familial intracranial DAVFs. We describe the first two cases of intracranial DAVFs occurring in first-degree relatives. CLINICAL PRESENTATION: A 66 year-old woman presented with an 18-month history of bilateral pulsatile tinnitus. Neurological examination was significant for a prominent pulsatile bruit over the left mastoid region. Laboratory studies demonstrated heterozygosity for Prothrombin G20210A mutation. Imaging disclosed a large left Type I Borden DAVF involving the distal transverse-sigmoid sinus junction. She underwent uncomplicated stereotactic radiosurgery to the fistula that led to complete resolution of her tinnitus and the fistula. A 73 year-old woman, the sister of the previous patient, presented with a 24-month history of pulsatile tinnitus affecting the left ear. Laboratory studies demonstrated heterozygosity for the Prothrombin G20210A mutation. Imaging revealed a left Type I Borden DAVF involving the left transverse and sigmoid sinuses. The patient's symptoms resolved spontaneously without treatment. Repeat imaging revealed interval involution of the fistula. CONCLUSION: We describe two sisters who were heterozygous for Prothrombin G20210A mutation and found to have DAVFs. Clinicians should be aware of the potential for these fistulas to congregate in first-degree relatives via heritable thrombophilias such as the Prothrombin G20210A mutation.

Sudden sensorineural hearing loss associated with internal carotid artery pseudoaneurysm: causal or incidental?
Eur Arch Otorhinolaryngol. 2012 Oct 5. [Epub ahead of print]

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Sudden deafness is acute onset of impaired hearing which develops within hours to few days. The commonly accepted audiometric criterion is a decrease in hearing of ≥30 dB, affecting at least three consecutive frequencies. Hearing loss is thought to involve several causative factors, including internal ear circulatory disturbances. We report the case of a female with an internal carotid artery (ICA) pseudoaneurysm in the distal cervical tract and unilateral sudden sensorineural hearing loss (SSNHL). As putative risk vascular factor, the patient had history of migraine since youth. Extensive screenings for autoimmune, rheumatic diseases, virological, and microbiological infections were negative. The patient denied recent cervical trauma. Furosemide and oral prednisone were given with initial benefit and withdrawn in 3 weeks. The patient experienced short-lasting episodes of headache, tinnitus, vertigo. Five weeks after first onset, she underwent magnetic resonance imaging (MRI) angiogram which revealed fusiform dilatation of left ICA in the cervical tract. It can be proposed, but it remains to be proved, that the pseudoaneurysm of the cervical ICA plays a role in the patient SSNHL in relation to turbulent flow or thromboembolism of branches to the inner ear.
Nasopharyngeal tuberculosis presenting with auditory symptoms.

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We present an unusual case of a 54-year-old Chinese lady presenting to the ears, nose and throat clinic after family members noticed that her hearing had progressively deteriorated over the preceding weeks. She also complained of tinnitus. Examination of the ears, nose and throat was unremarkable. Flexible nasoendoscopy demonstrated swelling in the postnasal space, which, following biopsy, was shown to be pathognomonic of tuberculosis. This was successfully treated with multidisciplinary input and the patient made a complete recovery.


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A 28-year-old woman consulted for disabling pulsatile tinnitus. Clinical examination suggested a venous etiology. An aneurysm of the transverse-sigmoid sinus was identified on computed tomography angiography (CTA) and confirmed by digital subtraction angiography. Endovascular occlusion of the aneurysm with detachable coils permanently eliminated the bruit. Thus, this report is of a new case of pulsatile tinnitus caused by an aneurysm of the transverse-sigmoid sinus, with a focus on a literature review and etiopathophysiology. Embryological studies suggest that these aneurysms represent a partial remnant of the petrosquamous sinus. Copyright © 2012. Published by Elsevier Masson SAS.

External auditory canal paraganglioma: an atypical presentation.
J Laryngol Otol. 2012 Oct 1;1-3. [Epub ahead of print]

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Objective: We present the first published description of a painful paraganglioma of the external auditory canal. Atypical histopathology made the diagnosis difficult. We discuss the potential pitfalls of clinical diagnosis and treatment of such a case. Clinical presentation: A 49-year-old woman presented with left-sided otalgia, hearing loss and tinnitus. Physical examination revealed a firm swelling arising from the superior portion of the left external auditory canal. A clinical diagnosis of otitis externa was made. Intervention: There was minimal response to medical treatment. The swelling was aspirated, leading to brisk bleeding. A tumour was suspected from the computed tomography scan, and confirmed by a biopsy. The patient underwent excision of the paraganglioma. The histopathology was atypical, making diagnosis difficult. Conclusion: Such unusual masses of the external ear should always be borne in mind, especially when dealing with atypical presentations of commonly encountered diseases. Clinicians should have a low threshold for early intervention with imaging and biopsy.
Pulsatile tinnitus as the sole manifestation of an internal carotid artery aneurysm successfully treated by coil embolization.

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Pulsatile tinnitus is tinnitus that coincides with the patient's heartbeat. It constitutes a small portion of all tinnitus, but it is often the first or sole manifestation of a serious disease in the nervous system. Aneurysm of the internal carotid artery is known as a rare cause of pulsatile tinnitus and, in the main, aneurysms of the petrous portion have been reported as a cause of pulsatile tinnitus. We present an interesting case of pulsatile tinnitus that was caused by a paracclinoid aneurysm in this report and discuss clinical features and treatment of paracclinoid aneurysm. Free full text.

Capillary hemangioma of the middle ear: one case report and review of the literature.

Nouri H, Harkani A, Elouali Idrissi M, Rochdi Y, Aderdour L, Oussehal A, Raji A.

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Hemangiomas are rare benign vascular tumors; there are several types including the capillary hemangiomas, we present the case of an exceptional localization of capillary hemangioma in the middle ear. We report the case of a 60-year-old female which consults for episodes of pulsatile tinnitus, otorragies, and hearing loss of the left ear. The clinical examination revealed a reddish polypoid mass in the left external auditory canal, the radiological tests showed a vascular mass in the middle left ear. The tumor was surgically removed, the histological study revealed a capillary hemangioma. The incidence of hemangiomas in the temporal bone, especially in the middle ear, is exceptional. Medical imaging guides to the vascular nature of these tumors that make confusion with other vascular tumors such as tympanic paragangliomas. The management is often surgical and the final diagnosis is histological. Free PMC Article.
Sensorineural Hearing Loss due to Air Bag Deployment.

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Deployment of the air bag in a passenger vehicle accident rarely causes otologic injuries. However, sensorineural hearing loss induced by air bag deployment is extremely rare, with only a few cases reported in the English literature. A 38-year-old man involved in a traffic accident while driving his car at 40 km/hour presented with right sensorineural hearing loss and tinnitus, without associated vertigo. Pure-tone audiometry demonstrated elevated thresholds of 30 dB and 25 dB at 4 kHz and 8 kHz, respectively, on the right side. Air bag deployment in car accidents is associated with the risk of development of sensorineural hearing loss. Free PMC Article.

Pontomedullary white epidermoid: a rare cause of tinnitus.

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Intracranial epidermoid cysts are relatively rare congenital inclusion cysts. They are the third most common cerebellopontine angle cistern mass after vestibular schwannoma and meningioma. White epidermoid is a rare variant. We present the first case, to our knowledge, of a white epidermoid cyst anterior to the pontomedullary junction, emphasising its imaging appearance, location and the importance of pre-operative diagnosis, which may reduce operative complications. Free full text.

Dural-cavernous fistulas revealed by bilateral alternating third and sixth nerve palsies (Article in press).
[Fistule durale carotido-caverneuse révélée par une paralysie bilatérale à bascule des troisièmes et sixièmes nerfs crâniens].
Journal Francais d'Ophtalmologie 2012.

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A 74-year-old male was referred for disequilibrium, associated with right third and sixth nerve palsies observed 2 weeks after head trauma with no loss of consciousness. On clinical examination, 4 months after the injury, contralateral (left) third and sixth nerve palsies were observed, while ocular motility was now normal on the right side. The remainder of the ophthalmological examination was normal. Upon further history, tinnitus was found to have been present since the trauma, and auscultation of the preauricular area demonstrated a systolic bruit. Cerebral angiogram confirmed the presence of bilateral dural-cavernous fistulas. Clinical features of indirect or dural-cavernous fistulas and therapeutic options proposed in the literature are reviewed. © 2012.

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We describe a case of a 67-year-old woman with severe disabling right-sided tinnitus, mild hyperacusis, and headache. The tinnitus was associated with sudden right hearing loss and vertigo, which occurred about 18 months before. Magnetic resonance imaging (MRI) resulted in normal anatomical structures of the cochlea and of the cranial nerves showing a partial empty sella syndrome with suprasellar cistern hernia. Angio-MR revealed a bilateral contact between the anterior-inferior cerebellar artery (AICA) and the acoustic-facial nerve with a potential neurovascular conflict. Surgery was considered unnecessary after further evaluations. The right ear was successfully treated with a combination device (hearing aid plus sound generator). Shortly after a standard fitting procedure, the patient reported a reduction of tinnitus, hyperacusis, and headache which completely disappeared at the follow-up evaluation after 3, 6, and 12 months. This paper demonstrates that the combination device resulted in a complete tinnitus and hyperacusis suppression in a patient with unilateral sensorineural sudden hearing loss. Our paper further supports the restoration of peripheral sensory input for the treatment of tinnitus associated with hearing loss in selected patients.

Endolymphatic sac tumors: experience of three cases.
Eur Arch Otorhinolaryngol. 2012 Dec 5. [Epub ahead of print]

Bastier PL, de Mones E, Marro M, Elkhatib W, Franco-Vidal V, Liguoro D, Darrouzet V.

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OBJECTIVES: To describe the clinical features, radiological findings, treatment and outcomes of three cases of endolymphatic sac tumors (ELST).METHODS: Retrospective analysis of three cases of ELST. RESULTS: The first patient had a large ELST invading the labyrinth after a long history of vertigo. He was recurrence-free 1 year after retrolabyrinthine surgical removal. In the second case, an acute peripheral facial nerve paralysis associated with ipsilateral sensorineural hearing loss led to the diagnosis. A translabyrinthine approach was used to remove the tumor, which recurred three times over 10 years. The third patient was a young woman suffering from von Hippel-Lindau (VHL) disease and referred for a sudden sensorineural hearing loss due to an intralabyrinthine hemorrhage secondary to a 2 mm-large endolymphatic sac-confined ELST. Her hearing was totally lost after the deafness recurred 1 month after this first episode. MRI demonstrated a small bilateral ELST. The patient refused surgery on the deaf side. CONCLUSION: ELST are difficult to diagnose due to the wide variety of their presentations. Patients with ELST should be screened for VHL disease. Dural invasion and tumor hypervascularization increase the risk of local recurrences after surgery. Early surgical resection may lead to complete tumor removal and inner ear preservation.

[Decompensated chronic tinnitus and high-dose benzodiazepine dependence : Between Scylla and Charybdis.]

Bonnet U.

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No abstract available.
Type IV Ehlers-Danlos syndrome presenting as recurrent, bilateral carotid dissections.

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Vascular (type IV) Ehlers-Danlos is an autosomally dominant inherited condition that results from a defect in type III collagen production. It can result in vascular complications such as rupture and dissection, as well as gastrointestinal and uterine rupture. We present the case of a 17-year-old girl who presented with transient neurological signs and pulsatile tinnitus secondary to carotid dissection 1 year after suffering from a stroke caused also by a carotid dissection on the contralateral side. We managed acutely and investigated for an underlying connective tissue disorder. Genetic analysis of COL3A1 was performed and a heterozygous missense, non-conservative mutation of c.970G>A was detected. This replication mutation has previously been associated with type IV Ehlers-Danlos syndrome.

Acute labyrinthitis secondary to aural tick infestation.

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Aural tick usually manifests as intolerable otalgia. The severity of pain makes the patient to seek early treatment. Other uncommon symptoms include inner ear dysfunctions such as vertigo and tinnitus. The diagnosis is established by clinical examination either by otoscopic evidence of the tick itself, or its fecal remnant. We report a case of patient with acute labyrinthitis features with concurrent otoscopic findings of tick fecal material.

Successful Amelioration of Tinnitus in a Stroke Patient by Low-dose Gabapentin.

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Bilaterally progressive tinnitus and hearing impairment occurred in a hypertensive patient shortly after an episode of right ganglionic hemorrhage. Audiometric tests showed a mixed sensorineural and conduction hearing loss. When low-dose gabapentin was administrated for the pre-existing postherpetic thoracic neuralgia, the tinnitus dramatically improved but recurred after discontinuation of the drug. Hearing function did not change. In view of a controversy of gabapentin and tinnitus in previous trials, the findings in this patient support that low-dose gabapentin benefits the subgroup of tinnitus patients with secondary contributing factors, such as stroke. Copyright © 2012 National Stroke Association. Published by Elsevier Inc. All rights reserved.
Glomus jugulare tumor appeared with tinnitus and hoarseness
[Tinnitus ve ses kisiklik bulgularıyla ortaya çıkan glomus jugulare tümörü]

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Glomus jugulare tumors are arising from the jugulare bulb in the jugular foramen of the temporal bone and may spread to the middle ear. Glomus jugulare is a rare and highly vascular neural residue tumors that have benign features and grouped in the glomus tumors. Glomus caroticum, glomus vagale, glomus tympanicum and glomus jugulare both are inside this disease group also called as paraganglioma or chemodectoma. Women are more often and left side localization is frequent in this tumor. Glomus jugulare tumor has a slow progression and temporary pause periods on the symptoms; therefore findings lead delays on the diagnosis. 62-year-old female patient with tinnitus for 3 years was admitted to hospital because of developing a new hoarseness. This study reveals a glomus tumor that is a rare cause of tinnitus and new developed hoarseness caused by cranial nerve infiltration and examined with radiological findings.

A case of ear pick injury in which 3D-CT was useful for diagnosis and treatment.

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We report on a case of injury caused by an ear pick in which 3D-CT was useful for diagnosis and determining the treatment. The patient was a 36-year-old woman who complained of tinnitus and hearing loss in the left since she had pushed an ear pick into the ear. The eardrum had no abnormalities at the time of the first medical examination. However, 3D-CT revealed disruption in the incudomalleolar joint, transposition of the malleus. Traumatic ossicular disruption was diagnosed. The disruption in the incudomalleolar joint and coalescence of the handle of the malleus and the incus long process were identified during a tympanoplasty, as observed on 3D-CT scans. Ossicular chain reconstruction (II-c type) by PORP was performed between the incus and eardrum. Postoperative hearing improved markedly. Therefore, we conclude that to obtain good hearing improvement it is desirable to undertake surgery for traumatic ossicular disruption and that the surgical procedure can be decided on the basis of accurate diagnosis with 3D-CT.

XV Specific Forms of Tinnitus

Prevalence of musical hallucinations in patients referred for audiometric testing.

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OBJECTIVE: To assess the prevalence of musical hallucinations in patients referred for audiometric testing and to analyze associations with age, sex, degree of hearing loss, asymmetrical hearing loss, and tinnitus. METHODS: Patients referred for audiometric testing underwent a semi-structured interview on tinnitus and musical hallucinations. RESULTS: Out of 194 patients, most of whom had mild to moderate hearing loss, seven (3.6%) had musical hallucinations. Significant associations were found with female sex and predominant left-sided hearing impairment, but not with age, severity of hearing loss, or tinnitus. CONCLUSION: This study offers no evidence that age is a risk factor. Musical hallucinations seem to be prevalent in women with predominant left-sided hearing impairment.
Effects of tensor tympani muscle contraction on the middle ear and markers of a contracted muscle.


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OBJECTIVES/HYPOTHESIS: Many otologic disorders have been attributed to dysfunction of the tensor tympani muscle, including tinnitus, otalgia, Meniere’s disease and sensorineural hearing loss. The objective of this study was to determine adequate stimuli for tensor tympani contraction in humans and determine markers of the hypercontracted state that could be used to detect this process in otologic disease. STUDY DESIGN: Multiple types of studies. METHODS: Studies included 1) measuring middle ear impedance changes in response to orbital puffs of air, facial stroking, and self-vocalization; 2) measuring changes in stapes and eardrum vibrations and middle ear acoustic impedance in response to force loading of the tensor tympani in fresh human cadaveric temporal bones; 3) measuring changes in acoustic impedance in two subjects who could voluntarily contract their tensor tympani, and performing an audiogram with the muscle contracted in one of these subjects; and 4) developing a lumped parameter computer model of the middle ear while simulating various levels of tensor tympani contraction. RESULTS: Orbital jets of air are the most effective stimuli for eliciting tensor tympani contraction. As markers for tensor tympani contraction, all investigations indicate that tensor tympani hypercontraction should result in a low-frequency hearing loss, predominantly conductive, with a decrease in middle ear compliance. CONCLUSIONS: These markers should be searched for in otologic pathology states where the tensor tympani is suspected of being hypercontracted. Copyright © 2012 The American Laryngological, Rhinological, and Otological Society, Inc.

Midterm outcome of risedronate therapy for patients with Paget’s disease of bone in the central part of Japan.

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Although Paget’s disease of bone (PDB) is common in western countries, it is extremely rare in Asian ones including Japan. Recently, oral risedronate (17.5 mg once daily) was approved in Japan as a treatment of PDB besides calcitonin and etidronate. However, there are few data regarding the efficacy of this agent, dose for patients with PDB in Japan, or the durability of its effect. The purpose of this study was to evaluate the midterm outcome of oral risedronate (17.5 mg once daily) for patients with PDB in Japan. Seventeen patients with PDB were treated with risedronate (17.5 mg once daily) for 8 weeks. Efficacy and its durability were accessed based on serum total alkaline phosphatase (ALP) and symptoms. Risedronate effectively suppressed bone turnover evaluated with serum total ALP in all patients. In 8 of 10 patients with bone pain, risedronate reduced the pain. On the other hand, tinnitus and hearing loss did not disappear but somewhat improved. None of the patients suffered severe complications. Seven of 17 patients required readministration of oral bisphosphonate (risedronate, six; alendronate, one) due to elevated total ALP at 27 months (mean ranging from 9 to 39 months) after the initial administration of risedronate. Treatment of oral risedronate (17.5 mg once daily) for 8 weeks is safe and effective for patients with PDB in Japan. However, the durability of its effect is limited in some patients.
Does 'Cochlear Ménière's Disease' Exist? An Electrocochleographic and Audiometric Study.

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Introduction: According to current diagnostic criteria, patients exhibiting only cochlear symptoms without vertigo cannot be diagnosed with Ménière's disease (MD). The recently reported Ménière's Disease Index (MDI) combines audiometric and electrocochleographic parameters in a multidimensional measure correlating with the clinical degrees of MD. Materials and Methods: Twenty-one patients with hearing loss, tinnitus and aural fullness, but without vertigo, underwent transtympanic electrocochleography. Based on the previously reported formula, the MDI value for every patient was calculated. Results: Mean MDI value was 5.7 on a scale from 0 (mean value of non-MD patients) to 10 (mean value of definite MD patients). Conclusions: We can thus hypothesize that, based on audiology and electrocochleography, 'cochlear MD' patients may represent a separate clinical entity with Ménière-like pathophysiology or underlying endolymphatic hydrops. Copyright © 2012 S. Karger AG, Basel.

Auditory and otological manifestations in adults with HIV/AIDS.

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Objectives: This study describes the prevalence and nature of auditory and otological manifestations in adults with HIV/AIDS through clinical examinations and self-reported symptoms across stages of disease progression. Design: Descriptive cross-sectional group design. Study sample: Two hundred HIV positive adult patients (56.5% male; 43.5% female; mean age: 37.99 ± 6.66 years) attending the Infectious Disease Clinic of a tertiary referral hospital in Pretoria, South Africa were included. Patients were interviewed, medical files were reviewed, and clinical examinations, including otoscopy, tympanometry, pure-tone audiometry, and distortion product otoacoustic emissions, were conducted. A matched HIV negative control group was used to compare hearing loss prevalence. Results: Tinnitus (26%), vertigo (25%) hearing loss (27.5%), otalgia (19%), and ear canal pruritis (38%) were prevalent self-reported symptoms. Abnormalities in otoscopy, tympanometry, and otoacoustic emissions were evident in 55%, 41%, and 44% of patients respectively. Pure-tone average (PTA) hearing loss > 25 dBHL was evident in 14% of patients and 39% for hearing loss > 15 dBHL (PTA). Significant differences across average thresholds in the HIV positive and HIV negative control group was present. An increase in self reported vertigo, self reported hearing loss, OAE abnormalities, and hearing loss (PTA > 15 dBHL and PTA > 25 dBHL) was seen with disease progression but was not statistically significant. A significant increase (p < .05) in sensorineural hearing loss was however evident with disease progression. Conclusions: Auditory and otological symptoms are more common in patients with HIV with a general increase of symptoms, especially sensorineural hearing loss, towards advanced stages of disease progression.
Ménière's disorder: A short history (Review)

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The authors discuss early reports probably related to Ménière's disorder, a short account of the development and developments and terminological confusions following that time. We consider various approaches that have been made to the treatment of the condition and briefly mention some famous people who have suffered from the condition. © 2012 Informa Healthcare.


Olivetto, E.a, Simoni, E.a, Guaran, V.a, Astolfi, L.a, Martini, A.ab

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Ménière's disease is a disabling disorder presenting with crises of aural fullness, tinnitus, hearing loss and vertigo. The hallmark of the pathology is a labyrinthine hydrops, but its pathogenesis remains unclear. This unknown aetiology explains the lack of a good pharmacological treatment. Here, we wish to evaluate the different parameters that can be involved in the progression of the disease, focusing on vascular disorders, production of reactive oxygen species and the relationship between the endolymph and haematic perfusion. We know that the blood supply must be adequate to guarantee the establishment of the endocochlear potential and the production of endolymph, so aberrant microcirculation may be an aetiological factor for Ménière's disease. © 2012 Informa Healthcare.

Enhanced Vestibulo-ocular Reflex to Electrical Vestibular Stimulation in Meniere's Disease.

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Meniere's disease is characterized by sporadic episodes of vertigo, nystagmus, fluctuating sensorineural hearing loss, tinnitus and aural pressure. Since Meniere's disease can affect different regions of the vestibular labyrinth, we investigated if electrical vestibular stimulation (EVS) which excites the entire vestibular labyrinth may be useful to reveal patchy endorgan pathology. We recorded three-dimensional electrically evoked vestibulo-ocular reflex (eVOR) to transient EVS using bilateral, bipolar 100-ms current steps at intensities of 0.9, 2.5, 5.0, 7.5 and 10.0 mA with dual-search coils in 12 unilateral Meniere's patients. Their results were compared to 17 normal subjects. Normal eVOR had tonic and phasic spatiotemporal properties best described by the torsional component, which was four times larger than horizontal and vertical components. At EVS onset and offset of 8.9 ms latency, there were phasic eVOR initiation (M = 1.267 °/s(2)) and cessation (M = -1.675 °/s(2)) acceleration pulses, whereas during the constant portion of the EVS, there was a maintained tonic eVOR (M = 9.1 °/s) at 10 mA. However in Meniere's disease, whilst latency of EVS onset and offset was normal at 9.0 ms, phasic eVOR initiation (M = 1,720 °/s(2)) and cessation (M = -2,523 °/s(2)) were enlarged at 10 mA. The initiation profile was a bimodal response, whilst the cessation profile frequently did not return to baseline. The tonic eVOR (M = 20.5 °/s) exhibited a ramped enhancement of about twice normal at 10 mA. Tonic eVOR enhancement was present for EVS
>0.9 mA and disproportionately enhanced the torsional, vertical and horizontal components. These eVOR abnormalities may be a diagnostic indicator of Meniere’s disease and may explain the vertigo attacks in the presence of declining mechanically evoked vestibular responses.

**Evaluation of the cases with intracranial hypertension**

[Duzce Medical Journal Volume 14, Issue 2, 2012, Pages 37-40](#)

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**Objective**: In this study clinical findings of patients, who diagnosed with IIH in Duzce Univesity Research and Teaching Hospital Neurology Clinic were investigated. Materials and Methods: Treatment and follow-up of 23 patients were examined with diagnosis of IIH from the records. The study was based on modified Dandy criteria. The patients who were performed lumbar puncture and were done cranial imaging included in the study. Results: The patients diagnosed with IIH were 78.3% female and 21.7% male. The most common reason for admission was headache and it was accompanied by blurred vision, visual of limitation, temporary loss of vision, eye pain, double vision, nausea, dislike of light, dizziness and tinnitus. 60.9% of the patients were obese. Five patients without papilledema were diagnosed with IIH. The cranial imagings were in normal limits except for empty cella. In treatment, the patients were given acetozolamide, methylprednisolone and/or topiramate. The follow-up period was arranged in 3-6 months. In the process, there were not any patients who had loss of vision. Conclusion: Continuity in atypical cases of headache, if they have obesity, there should be further examination in mind of an IIH diagnosis. Early diagnosis and treatment are import to prevent the possible loss of vision. © 2012 Düzce Medical Journal.

**Clinical features of intracranial vestibular schwannomas (Review).**

[Oncology Letters Volume 5, Issue 1, 2012, Pages 57-62.](#)


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The aim of the present study was to discuss the clinical features of intracranial vestibular schwannomas and to evaluate the symptoms and signs as well as their correlation with tumor extension. The records of 1,009 patients who were treated in Shanghai Huashan Hospital were reviewed retrospectively. According to the Samii classification of 1997, the patients were grouped into a T3 and a T4 group based on the radiological findings. We focused our analysis on the incidence of subjective disturbances versus objective morbidity, and symptomatology versus tumor size and extension. Of the 1,009 cases, 424 patients (42.0%) were defined as T3 while 585 patients (58%) were defined as T4. The most frequent clinical symptoms were hearing loss (85.8%), facial numbness (48.9%), ataxia (44.6%), tinnitus (40.1%), deafness (26.3%) and facial paralysis (21.1%). The ratios of gender, vertigo and facial paralysis were significantly different between the T3 and T4 groups (P<0.05); however, none of the clinical symptoms had a positive likelihood ratio (PLR) greater than 10 for T4 prediction. The most frequent cranial nerve disturbance was associated with the cochlear nerve (92.6%) and trigeminal nerve (53.5%). Disturbance of the facial nerve was more severe in T3 than T4 patients (P<0.05). Hearing deficit, facial paresthesia, ataxia and tinnitus are key symptoms of huge vestibular schwannomas. Cochlear, trigeminal and facial nerves were the most commonly affected cranial nerves in cases of large tumors. Gender and tumor size were associated with tumor extension. Although the predictive value was limited, the symptoms of vertigo, facial paralysis and hearing loss may be indicators of tumor growth.
Clinical and Audio Vestibular Profile of Meniere's Disease in a Tertiary Care Centre in India.

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The aims of this study are to determine the frequency of patients presenting with Meniere's Disease (MD) in an Indian setting, using the American Academy of Otolaryngology-Head and Neck Surgery (AAO) diagnostic criteria, and to describe the clinical and audio vestibular profiles of these patients. The study was based on prospective case series design in the settings of a tertiary referral hospital. The study included all consecutive patients aged between 5 and 75 years presenting with the history of hearing loss, vertigo, tinnitus and or aural fullness as participants, satisfying inclusion and exclusion criteria for MD (AAO 1995) recruited over a 12 month period. Main outcome measures comprised the evaluation of epidemiological profile, clinical features, and results of audio vestibular investigations like Pure Tone Audiometry with and without glycerol, Impedance Audiometry, Electrocochleography (ECohG), Distortion Product Otoacoustic Emission and Electronystagmography (ENG). The results of the study are as follows: The frequency of MD was 15.6%, being commoner in males than females (2.6:1) and occurring more in the age group 40-49 years among males and 30-39 years among females. High frequency tinnitus was commoner than low frequency tinnitus. Extra tympanic ECohG had a positive predictive value of 76% for endolymphatic hydrops. ENG was useful for demonstrating canal paresis pattern of nystagmus in 61%. Indian patients with MD commonly present to tertiary care at the functional level scale of 3. The results of this study revealed that the frequency of MD is not as low in the Indian ENT setting as earlier believed. There is a high chance of missing cases in the routine ENT outpatient clinic setting unless a structured proforma incorporating the AAO 1995 diagnostic criteria is used. © 2011 Association of Otolaryngologists of India.

Hearing loss and acquired immune deficiency syndrome: systematic review.

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PURPOSE: To investigate the occurrence of hearing loss in individuals with HIV/AIDS and their characterization regarding type and degree. RESEARCH STRATEGY: It was conducted a systematic review of the literature found on the electronic databases PubMed, EMBASE, ADOLEC, IB ECS, Web of Science, Scopus, Lilacs and SciELO. SELECTION CRITERIA: The search strategy was directed by a specific question: "Is hearing loss part of the framework of HIV/AIDS manifestations?", and the selection criteria of the studies involved coherence with the proposed theme, evidence levels 1, 2 or 3, and language (Portuguese, English and Spanish). DATA ANALYSIS: We found 698 studies. After an analysis of the title and abstract, 91 were selected for full reading. Out of these, 38 met the proposed criteria and were included on the review. RESULTS: The studies reported presence of conductive, sensorineural, and mixed hearing loss, of variable degrees and audiometric configurations, in addition to tinnitus and vestibular disorders. The etiology can be attributed to opportunistic infections, ototoxic drugs or to the action of virus itself. The auditory evoked potentials have been used as markers of neurological alterations, even in patients with normal hearing. CONCLUSION: HIV/AIDS patients may present hearing loss. Thus, programs for prevention and treatment of AIDS must involve actions aimed at auditory health.
XVI Animal Models

Noise-Induced Inner Hair Cell Ribbon Loss Disturbs Central Arc Mobilization: A Novel Molecular Paradigm for Understanding Tinnitus.


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Increasing evidence shows that hearing loss is a risk factor for tinnitus and hyperacusis. Although both often coincide, a causal relationship between tinnitus and hyperacusis has not been shown. Currently, tinnitus and hyperacusis are assumed to be caused by elevated responsiveness in subcortical circuits. We examined both the impact of different degrees of cochlear damage and the influence of stress priming on tinnitus induction. We used (1) a behavioral animal model for tinnitus designed to minimize stress, (2) ribbon synapses in inner hair cells (IHCs) as a measure for deafferentation, (3) the integrity of auditory brainstem responses (ABR) to detect differences in stimulus-evoked neuronal activity, (4) the expression of the activity-regulated cytoskeletal protein, Arc, to identify long-lasting changes in network activity within the basolateral amygdala (BLA), hippocampal CA1, and auditory cortex (AC), and (5) stress priming to investigate the influence of corticosteroid on trauma-induced brain responses. We observed that IHC ribbon loss (deafferentation) leads to tinnitus when ABR functions remain reduced and Arc is not mobilized in the hippocampal CA1 and AC. If, however, ABR waves are functionally restored and Arc is mobilized, tinnitus does not occur. Both central response patterns were found to be independent of a profound threshold loss and could be shifted by the corticosterone level at the time of trauma. We, therefore, discuss the findings in the context of a history of stress that can trigger either an adaptive or nonadaptive brain response following injury.

Diminished cortical inhibition in an aging mouse model of chronic tinnitus.

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Flavoprotein autofluorescence imaging was used to examine auditory cortical synaptic responses in aged animals with behavioral evidence of tinnitus and hearing loss. Mice were exposed to noise trauma at 1-3 months of age and were assessed for behavioral evidence of tinnitus and hearing loss immediately after the noise trauma and again at 24-30 months of age. Within 2 months of the final behavioral assessment, auditory cortical synaptic transmission was examined in brain slices using electrical stimulation of putative thalamocortical afferents, and flavoprotein autofluorescence imaging was used to measure cortical activation. Noise-exposed animals showed a 68% increase in amplitude of cortical activation compared with controls (p = 0.008), and these animals showed a diminished sensitivity to GABA(A)ergic blockade (p = 0.008, using bath-applied 200 nm SR 95531 [6-Lmino-3-(4-methoxyphenyl)-1(6H)-pyridazinebutanoic acid hydrobromide]). The strength of cortical activation was significantly correlated to the degree of tinnitus behavior, assessed via a loss of gap detection in a startle paradigm. The decrease in GABA(A) sensitivity was greater in the regions of the cortex farther away from the stimulation site, potentially reflecting a greater sensitivity of corticocortical versus thalamocortical projections to the effects of noise trauma. Finally, there was no relationship between auditory cortical activation and activation of the somatosensory cortex in the same slices, suggesting that the increases in auditory cortical activation were not attributable
to a generalized hyperexcitable state in noise-exposed animals. These data suggest that noise trauma can cause long-lasting changes in the auditory cortical physiology and may provide specific targets to ameliorate the effects of chronic tinnitus.

**Hyperexcitability of inferior colliculus neurons caused by acute noise exposure.**


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Noise exposure is one of the most common causes of hearing loss. Recent studies found that noise exposure-induced cochlear damage may change the excitability and tonotopic organization of the central auditory system (CAS). This plasticity was suspected to be related to tinnitus and hyperacusis. However, how cochlear damage affects CAS function and causes these neurologic diseases is still not clear. CAS function is activity dependent, so we hypothesize that a restricted cochlear lesion might disrupt the balance of excitation and inhibition in the CAS and thereby affect its neural activity. To test this hypothesis, we studied the effects of narrow-band noise exposure on the firing properties of neurons in the inferior colliculus (IC), which has complex neural circuits and plays an important role in sound processing. We found that noise exposure (20 kHz, 105 dB SPL, 30 min) caused a dramatic decrease of the characteristic frequency in about two-thirds of high-frequency neurons with/without causing a significant threshold shift. The noise exposure also caused an increase in firing rate of the low-frequency neurons at suprathreshold levels, whereas it dramatically decreased the firing rate of the high-frequency neurons. Our results suggest that acute high-frequency noise exposure may increase low-frequency responsiveness by causing hyperexcitability of low-frequency neurons. The functional change of the low-frequency neurons may be related to the disruption of side-band inhibition at the noise exposure frequencies caused by cochlear damage. © 2012 Wiley Periodicals, Inc. Copyright © 2012 Wiley Periodicals, Inc.

**Acoustic stimulation promotes DNA fragmentation in the Guinea pig cochlea.**

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Apoptosis can be described as programmed cell death. Apoptosis regulates cell turnover and is involved in various pathological conditions. The characteristic features of apoptosis are shrinkage of the cell body, chromatin condensation, and nucleic acid fragmentation. During apoptosis, double-stranded DNA is broken down into single-stranded DNA (ssDNA) by proteases. Acoustic trauma is commonly encountered in otorhinolaryngology clinics. Intense noise can cause inner ear damage, such as hearing disturbance, tinnitus, ear fullness, and decreased speech discrimination. In this study, we used immunohistochemical and electrophysiological methods to examine the fragmentation of DNA in the cochleas of guinea pigs that had been exposed to intense noise. Twenty-four guinea pigs weighing 250 to 350 g were used. The animals were divided into 4 groups: (I) a control group (n=6), (II) a group that was exposed to noise for 2 hours (n=6), (III) a group that was exposed to noise for 5 hours (n=6), and (IV) a group that was exposed to noise for 20 hours. The stimulus was a pure tone delivered at a frequency of 2 kHz. The sound pressure level was 120 dB SPL. No threshold shifts were apparent in group I. Group II showed a significant elevation of the hearing threshold (ANOVA, p<0.05(∗∗)). The ABR threshold level was also significantly elevated immediately after the acoustic stimulation in groups III and IV (ANOVA, p<0.01(∗∗)). In groups I, II, and IV, the lateral wall of the ear did not show immunoreactivity to ssDNA but did in group III. No immunoreactivity was apparent in the organ of Corti in group I or II. However, the supporting cells and outer hair cells in groups III and IV showed reactions for ssDNA. The fine structure of the organ of Corti had been destroyed in group IV. The lateral wall showed immunoreactivity for ssDNA only in group III, whereas the organ of

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A low cost setup for behavioral audiometry in rodents.
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In auditory animal research it is crucial to have precise information about basic hearing parameters of the animal subjects that are involved in the experiments. Such parameters may be physiological response characteristics of the auditory pathway, e.g. via brainstem audiometry (BERA). But these methods allow only indirect and uncertain extrapolations about the auditory percept that corresponds to these physiological parameters. To assess the perceptual level of hearing, behavioral methods have to be used. A potential problem with the use of behavioral methods for the description of perception in animal models is the fact that most of these methods involve some kind of learning paradigm before the subjects can be behaviorally tested, e.g. animals may have to learn to press a lever in response to a sound. As these learning paradigms change perception itself (1,2) they consequently will influence any result about perception obtained with these methods and therefore have to be interpreted with caution. Exceptions are paradigms that make use of reflex responses, because here no learning paradigms have to be carried out prior to perceptual testing. One such reflex response is the acoustic startle response (ASR) that can highly reproducibly be elicited with unexpected loud sounds in naïve animals. This ASR in turn can be influenced by preceding sounds depending on the perceptibility of this preceding stimulus: Sounds well above hearing threshold will completely inhibit the amplitude of the ASR; sounds close to threshold will only slightly inhibit the ASR. This phenomenon is called pre-pulse inhibition (PPI) (3,4), and the amount of PPI on the ASR gradually depends on the perceptibility of the pre-pulse. PPI of the ASR is therefore well suited to determine behavioral audiograms in naïve, non-trained animals, to determine hearing impairments or even to detect possible subjective tinnitus percepts in these animals. In this paper we demonstrate the use of this method in a rodent model (cf. also ref. (5)), the Mongolian gerbil (Meriones unguiculatus), which is a well know model species for startle response research within the normal human hearing range (e.g. (6)).

Altered Neuronal Intrinsic Properties and Reduced Synaptic Transmission of the Rat's Medial Geniculate Body in Salicylate-Induced Tinnitus.
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Sodium salicylate (NaSal), an aspirin metabolite, can cause tinnitus in animals and human subjects. To explore neural mechanisms underlying salicylate-induced tinnitus, we examined effects of NaSal on neural activities of the medial geniculate body (MGB), an auditory thalamic nucleus that provides the primary and immediate inputs to the auditory cortex, by using the whole-cell patch-clamp recording technique in MGB slices. Rats treated with NaSal (350 mg/kg) showed tinnitus-like behavior as revealed by the gap prepulse inhibition of acoustic startle (GPIAS) paradigm. NaSal (1.4 mM) decreased the membrane input resistance, hyperpolarized the resting membrane potential, suppressed current-evoked firing, changed the action potential, and depressed rebound depolarization in MGB neurons. NaSal also reduced the excitatory and inhibitory postsynaptic response in the MGB evoked by stimulating the brachium of the inferior colliculus. Our results demonstrate that NaSal alters neuronal intrinsic properties and reduces the synaptic transmission of the MGB, which may cause abnormal thalamic outputs to the auditory cortex and contribute to NaSal-induced tinnitus. Free PMC Article.
Predisposition for and prevention of subjective tinnitus development.

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Dysfunction of the inner ear as caused by presbyacusis, injuries or noise traumata may result in subjective tinnitus, but not everyone suffering from one of these diseases develops a tinnitus percept and vice versa. The reasons for these individual differences are still unclear and may explain why different treatments of the disease are beneficial for some patients but not for others. Here we for the first time compare behavioral and neurophysiological data from hearing impaired Mongolian gerbils with (T) and without (NT) a tinnitus percept that may elucidate why some specimen do develop subjective tinnitus after noise trauma while others do not. Although noise trauma induced a similar permanent hearing loss in all animals, tinnitus did develop only in about three quarters of these animals. NT animals showed higher overall cortical and auditory brainstem activity before noise trauma compared to T animals; that is, animals with low overall neuronal activity in the auditory system seem to be prone to develop tinnitus after noise trauma. Furthermore, T animals showed increased activity of cortical neurons representing the tinnitus frequencies after acoustic trauma, whereas NT animals exhibited an activity decrease at moderate sound intensities by that time. Spontaneous activity was generally increased in T but decreased in NT animals. Plastic changes of tonotopic organization were transient, only seen in T animals and vanished by the time the tinnitus percept became chronic. We propose a model for tinnitus prevention that points to a global inhibitory mechanism in auditory cortex that may prevent tinnitus genesis in animals with high overall activity in the auditory system, whereas this mechanism seems not potent enough for tinnitus prevention in animals with low overall activity. Free PMC Article.

Multi-sensory integration in brainstem and auditory cortex.

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Tinnitus is the perception of sound in the absence of a physical sound stimulus. It is thought to arise from aberrant neural activity within central auditory pathways that may be influenced by multiple brain centers, including the somatosensory system. Auditory-somatosensory (bimodal) integration occurs in the dorsal cochlear nucleus (DCN), where electrical activation of somatosensory regions alters pyramidal cell spike timing and rates of sound stimuli. Moreover, in conditions of tinnitus, bimodal integration in DCN is enhanced, producing greater spontaneous and sound-driven neural activity, which are neural correlates of tinnitus. In primary auditory cortex (A1), a similar auditory-somatosensory integration has been described in the normal system (Lakatos et al., 2007), where sub-threshold multisensory modulation may be a direct reflection of subcortical multisensory responses (Tyll et al., 2011). The present work utilized simultaneous recordings from both DCN and A1 to directly compare bimodal integration across these separate brain stations of the intact auditory pathway. Four-shank, 32-channel electrodes were placed in DCN and A1 to simultaneously record tone-evoked unit activity in the presence and absence of spinal trigeminal nucleus (Sp5) electrical activation. Bimodal stimulation led to long-lasting facilitation or suppression of single and multi-unit responses to subsequent sound in both DCN and A1. Immediate (bimodal response) and long-lasting (bimodal plasticity) effects of Sp5-tone stimulation were facilitation or suppression of tone-evoked firing rates in DCN and A1 at all Sp5-tone pairing intervals (10, 20, and 40ms), and greater suppression at 20ms pairing-intervals for single unit responses. Understanding the complex relationships between DCN and A1 bimodal processing in the normal animal provides the basis for studying its disruption in hearing loss and tinnitus models. This article is part of a Special Issue entitled: Tinnitus Neuroscience. Published by Elsevier B.V.
OBJECTIVE: To explore the changes of inferior collicular (IC) neurons after noise exposure cochlea injury in guinea pig to elucidate the encoding mechanism of pure tones, observe the changes of IC gamma-aminobutyric acid (GABA) after cochlear damage by acoustic trauma and understand the possible mechanism of symptoms such as noise-induced tinnitus, hyperacusis and loudness recruitment. METHODS: The responses of IC neurons to pure tone stimuli were observed in guinea pig at Day 1 and Days 11-21 after cochlear damage induced by noise exposure. And the IC neurons of normal guinea pig were assigned as the controls. Reverse transcription-polymerase chain reaction (RT-PCR) was used to measure the concentrations of GABA(A) and GABA(B) receptors. RESULTS: (1) The types of frequency reaction area (FRA) in the experiment group were the same as those in the control group (V-shape 84.8%, W-shape 8.9%, N-shape 6.3%). But the percentages of types were markedly different at Day 1 (V-shape 63.9%, W-shape 18.1%, N-shape, 18.1%) and Days 11-21 (V-shape 84.2%, W-shape 12.3%, N-shape 3.5%) after noise exposure. (2) After noise exposure, there was a marked fault in characteristic frequency (CF) and depth function map corresponding to 4 kHz (noise frequency). The rake ratio of CF and depth linear function map in the experiment group was lower than that of the control group. The control group, Day 1 and Days 11-21 after noise exposure, the rake ratios were 6.6, 5.8, 5.2 respectively. (3) GABA(A)/GABA(B) receptors decreased markedly at Days 1, 11 and 21 post-exposure compared to normal controls. And the values increased gradually with the prolonged time after exposure. The above findings conformed to the changes of electrophysiology of IC. CONCLUSIONS: After acoustic trauma, the responses of IC neurons to pure tone stimuli change with the elongation of time. It may be explained by the changes of IC GABA receptors after noise exposure.
**Clinical Trials**
**Source: www.clinicaltrials.gov (December 20, 2012)**

**Efficacy of Antiviral Medications in Controlling Vertigo Attacks of Patients With Meniere’s Disease.**

This study is currently recruiting participants.
Study NCT01729767
Information provided by (Responsible Party): Tehran University of Medical Sciences
First Received on November 14, 2012.

Meniere's disease is a chronic illness that affects a substantial number of patients every year worldwide. The disease is characterized by intermittent episodes of vertigo lasting from minutes to hours, with fluctuating sensorineural hearing loss, tinnitus, and aural pressure. It has recently been suggested that viral etiologies specially Herpes virus might be the underlying reason. The investigators study is a randomized, double-blinded placebo-controlled clinical trial in Amiralam Hospital. In this study the primary objective is to assess efficacy of Acyclovir in control of symptoms in patients with Meniere's disease specially their vertigo attacks. Inclusion criteria would be patient's willingness to participate in the study and follow ups, being 18 years old or older, having at least 2 vertigos per month each at least 20 min, interfering with function, and not on medication for Meniere's disease for at least 3 months before the trial. They should not have any history of allergy to Acyclovir, renal insufficiency or Creatinine above 1.5 mg/dl, hepatic enzymes more than three times normal, serious uncontrolled illness, be pregnant or nursing or have previous surgeries on Endolymphatic Sac. Participants will be randomly placed in 2 different arms getting either Acyclovir 400 mg or placebo (inert ingredient). They will take the medication for 10 days 5 times a day, then 3 times a day for next 10 days, and 2 times a day for the last 10 days. Patients will report changes in their symptoms 10 days after initiating the drug and in 1, 3, 6 month intervals.

**Prevention of Noise-induced Damage by Use of Antioxidants.**

This study is currently recruiting participants.
ClinicalTrials.gov Identifier: NCT01727492
Information provided by (Responsible Party): Ethisch Comité UZ Antwerpen, University Hospital, Antwerp
First received: September 28, 2012

The current study is a double-blinde placebo-controlled cross-over study verifying the preventive effect of antioxidants on noise-induced hearing loss (NIHL) and noise-induced tinnitus (NIT). The antioxidants comprise of a mixture of magnesium and n-acetylcystein which should be taken 1h before leisure noise above 100dB for at least 30 minutes.

**The Effects of Caffeine on Vestibular Evoked Myogenic Potentials in Healthy Subjects.**

This study is ongoing, but not recruiting participants.
Study NCT01693809.
Information provided by (Responsible Party): Ana Maria Almeida de Sousa, Hospital do Servidor Publico Estadual.
First Received on September 20, 2012.

The principal aim of this study is to evaluate the presence of changes in cervical vestibular evoked myogenic potentials (VEMPC) after acute intake of caffeine in healthy subjects. Secondarily, it wants to standardize normal values exam VEMPC in otorhinolaryngology service of the hospital.