EDITORIAL

“You can recognize a really good idea by the fact that it seems impossible to realize from the outset”
(A. Einstein)

The end of a year is always a good opportunity to reflect about the past years and make plans about the future.

Where are we now with TRI and what have we accomplished in the last years? The aim of TRI was to bring researchers and clinicians from many different disciplines together in order to find a cure for tinnitus.

The first part of this idea has been accomplished pretty well. With the yearly TRI meeting we frequently bring hundreds of researchers together for a tinnitus conference. The TRI newsletter reaches over 4'500 scientists and the TRI webpage provides at www.tinnitusresearch.org a lot of valuable up to date content for experts in the field. The public awareness for tinnitus has increased and there are more and more articles in the public media covering tinnitus. As a consequence, also the funding for tinnitus research has increased and this year we started the first large-scale project funded by the European Union (www.tinnet.tinnitusresearch.net).

The second part of the aim is still pending. Many different approaches for tinnitus treatment have been tried in the last years, but there is still no general cure for tinnitus available. The right idea has just not been thought, but the seeds have been planted. The sudden insight, or the stroke of genius that solves a problem never comes falling out of nowhere. It is usually the result of a sequence of many smaller right ideas culminating in a eureka moment after a lot of intensive preliminary work. In another quote from one of the most prolific inventors ever, Thomas Alva Edison: “genius is 10% inspiration and 90% perspiration”.

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With the above cited phrases, Einstein suggests that we should look for ideas that seem impossible to realize, and Edison adds that we should subsequently work hard at realizing them. Thus, even if you as a tinnitus researcher have an idea that seems impossible, embrace it, and discuss it with the TRI community. A united approach might make it work. It is only by sharing the specific expertise each of us has that the impossible becomes possible.

So, let us keep up the good networking and do not shy away of the seemingly impossible. We should not be worried to fail many times, the alternative not to try is definitively not the better option. Nature evolves by mistakes, tinnitus will ultimately be solved by the many mistakes, the many failed trials from which we learn. Let’s go for the impossible, but united, by trial and error, and we will emerge with a solution.

Ana Belén Elgoyhen    Dirk De Ridder    Berthold Langguth

Winfried Schlee    Sylvia Dorner-Mitschke
RESEARCH HIGHLIGHTS

The authors Lee and Godfrey provide an exhaustive review of neurotransmitter changes in the central auditory system as response to cochlear ablation, noise trauma or ototoxic medications. They propose that any imbalance of the neurotransmitter system can be related to auditory dysfunction.

Blood tests on 30 tinnitus patients were analysed with respect to interleukin-1β (IL1β), interleukin-6 (IL6), tumor necrosis factor-α (TNFα) and a brain-derived neutrotrophic factor (BDNF). The authors reported highly significant associations between TNFα and the subjectively measured tinnitus loudness.

The authors present a double-blind randomized clinical trial on 35 tinnitus patients and tested a combination of computer-based cognitive training (using auditory stimulation) with D-cycloserine medication. D-cycloserine is a partial NMDA agonist that has been used in numerous studies as a neuroplasticity-enhancing drug. The results of this study suggest that D-cycloserine can also be used in tinnitus to enhance treatment effects related to the computer-based training.
Travel Awards for Students

Application Deadline: December 30, 2014

The Kresge Hearing Research Institute and Department of Otolaryngology at the University of Michigan have generously agreed to sponsor ten students with travel awards of $500 each. In order to apply for the awards please complete and submit the application by December 30, 2014 to TRI2015Committee@umich.edu

Successful applicants will be announced in March 2015 by email. Travel awards will be sent out immediately after the conference.

Registration and Abstract Submission at the Conference Website
http://tri2015.org

Local Committee
Richard Altschuler, PhD
Gabriel Corfas, PhD
Kara Leyzac, PhD
Silvana Papagerakis, MD, PhD
Susan Shore, PhD (Symposium Chair)

Scientific Committee
Anthony Cacace, PhD
Jennifer Melcher, PhD
Larry Roberts, PhD
Jinsheng Zhang, PhD
Upcoming Meetings

Meetings exclusively dedicated to Tinnitus are marked red.

January 2015

**Masterclass: Tinnitus Hyperacusis in Adults and Children**

When: January 20 – 22, 2015  
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)

February 2015

**BTA Tinnitus Advisor Training**

When: February 06 – 07, 2015  
Where: Sheffield, UK  
Detailed Information: [www.tinnitus.org.uk/tinnitus-adviser-training](http://www.tinnitus.org.uk/tinnitus-adviser-training)

**ARO (The Association for Research in Otolaryngology) 38th MidWinter Meeting**

When: February 21 – 25, 2015  
Where: Baltimore, MD, USA  
Detailed Information: [http://www.aro.org/mwm/mwm.html](http://www.aro.org/mwm/mwm.html)

March 2015

**18. Jahrestagung der Deutschen Gesellschaft für Audiologie (DGA e.V.)**

When: March 04 – 07, 2015  
Where: Bochum, Germany  

**42nd Annual AAS Scientific and Technology Conference of the American Auditory Society**

When: March 05 – 07, 2015  
Where: Chaparral Suites in Scottsdale, AZ, USA  

**BTA Assessment and Management of Tinnitus in Children**

When: March 13– 14, 2015  
Where: Kenwood Hall Hotel, Sheffield, UK  
Tinnitus & Hyperacusis Therapy Masterclass
When: March 16 - 20, 2015
Where: Birkbeck College, University of London, UK
Detailed Information: http://tinnitustherapy.org.uk/

10th Asia Pacific Symposium on Cochlear Implants and Related Sciences
When: April 30 – May 03, 2015
Where: Beijing, China

AudiologyNOW! 2015
When: May 25 – 28, 2015
Where: San Antonio, TX, USA
Detailed Information: www.audiologynow.org

12th EFAS Congress
When: May 27 – 30, 2015
Where: Istanbul, Turkey
Detailed Information: http://www.efas2015.org/

8th INTERNATIONAL TRI TINNITUS CONFERENCE
Tinnitus: from cochlea to brain and back
When: June 07 – 10, 2015
Where: Ann Arbor, MI, USA
Detailed Information: http://www.tinnitusresearch.org

23th Annual Management of the Tinnitus Patient Course
When: June 12 – 13, 2015
Where: University of Iowa, IA, USA
Detailed Information: http://www.medicine.uiowa.edu/oto/tinnituscourse/

OHBM 2015: 21st Annual Meeting of the Organization for Human Brain Mapping
When: June 14 – 18, 2015
Where: Honolulu, Hawaii, USA
Detailed Information: http://www.humanbrainmapping.org/i4a/pages/index.cfm?pageid=3298
17th International Symposium on Hearing (ISH)
(The meeting is a sequel to the meeting held in Cambridge in 2012)
When:    June 15 – 19, 2015
Where:   Familiehotel Paterswalde, Groningen, NL
Detailed Information:  http://www.ish2015.nl

BTA Advisor Training
When:    June 26 – 27, 2015
Where:   London, UK
Detailed Information:  www.tinnitus.org.uk/tinnitus-adviser-training

30th Politzer Society Meeting
When:    June 30 – 05, 2015
Where:   Niigata, Japan
Detailed Information:  http://www.c-linkage.co.jp/politzer2015/

2nd International Conference on Hyperacusis
When:    July 09 – 10, 2015
Where:   Birkbeck College, University of London, UK
Detailed Information:  http://hyperacusisresearch.co.uk/

BTA Advisor Training
When:    October 09 – 10, 2015
Where:   Sheffield, UK
Detailed Information:  www.tinnitus.org.uk/tinnitus-adviser-training

7th International Symposium on Meniere's Disease and Inner Ear Disorders
When:    October 17 – 20, 2015
Where:   Rome, Italy
Detailed Information:  https://www.etouches.com/ehome/76981/155439/?&
Recently published literature (articles of authors who are collaborating with TRI are marked in blue)

I Epidemiology


Martinez C¹, Wallenhorst C, McFerran D, Hall DA.

¹Institute for Epidemiology, Statistics and Informatics GmbH, Frankfurt, Germany; 2Colchester Hospital University NHS Foundation Trust, Colchester, Essex, United Kingdom; 3National Institute for Health Research (NIHR) Nottingham Hearing Biomedical Research Unit, University of Nottingham, Nottingham, United Kingdom; and 4Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, United Kingdom.

OBJECTIVE: To investigate the incidence of tinnitus that burdens the health service in England. DESIGN: This was an observational study of 4.7 million residents of England under 85 years of age who were at risk for developing clinically significant tinnitus (sigT). SigT was defined by a discharge from hospital with a primary diagnosis of tinnitus, or a primary care recording of tinnitus with subsequent related medical follow-up within 28 days. The database used was the Clinical Practice Research Datalink and individual records were linked to additional data from the Hospital Episode Statistics. The observational period was from January 1, 2002 to December 31, 2011. Age-, gender-, and calendar year-specific incidence rates for and cumulative incidences of sigT were estimated and a projection of new cases of sigT between 2012 and 2021 was performed. RESULTS: There were 14,303 incident cases of sigT identified among 26.5 million person-years of observation. The incidence rate was 5.4 new cases of sigT per 10,000 person-years (95% confidence interval: 5.3 to 5.5). The incidence rate did not depend on gender but increased with age, peaking at 11.4 per 10,000 in the age group 60 to 69 years. The annual incidence rate of sigT increased from 4.5 per 10,000 person-years in 2002 to 6.6 per 10,000 person-years in 2011. The 10-year cumulative incidence of sigT was 58.4 cases (95% confidence interval: 57.4 to 59.4) per 10,000 residents. Nearly 324,000 new cases of sigT are expected to occur in England between 2012 and 2021. CONCLUSIONS: Tinnitus presents a burden to the health care system that has been rising in recent years. Population-based studies provide crucial underpinning evidence; highlighting the need for further research to address issues around effective diagnosis and clinical management of this heterogeneous condition. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
II Pathophysiology

Glutamic Acid Decarboxylase Levels in the Cochlear Nucleus of Rats with Acoustic Trauma-Induced Chronic Tinnitus.
Zheng Y1, Dixon S2, MacPherson K2, Smith PF2.
1 Dept of Pharmacology and Toxicology, School of Medical Sciences, and the Brain Health Research Centre, University of Otago, Dunedin, New Zealand. Electronic address: yiwen.zheng@otago.ac.nz.
Tinnitus is the perception of phantom sounds, a phenomenon believed to be due to abnormal neuronal activity in auditory regions of the CNS such as the brainstem cochlear nucleus (CN). One possible mechanism for the abnormal neuronal activity in the CN, supported by recent animal studies, is a decrease in GABAergic inhibition. One possible explanation for this is a decrease in the enzyme responsible for the synthesis of GABA, glutamic acid decarboxylase (GAD). In this study we used immunohistochemistry to analyse the levels of GAD in the dorsal and ventral CN of rats that had been exposed to noise trauma and had been confirmed to exhibit psychophysical evidence of tinnitus (at 17.5 weeks post-exposure) using a conditioned behavioural task. At 22 weeks following noise trauma or sham treatment, the levels of GAD in the dorsal and ventral CN were not significantly different. This result suggests that acoustic trauma that can cause chronic tinnitus is not associated with changes in GAD in the CN at 22 weeks post-exposure. Copyright © 2014 Elsevier Ireland Ltd. All rights reserved.

Relationship between tinnitus pitch and edge of hearing loss in individuals with a narrow tinnitus bandwidth.
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1* National Institute for Health Research (NIHR) Nottingham Hearing Biomedical Research Unit, Nottingham, UK.
Objective: Psychoacoustic measures of tinnitus, in particular dominant tinnitus pitch and its relationship to the shape of the audiogram, are important in determining and verifying pathophysiological mechanisms of the condition. Our previous study postulated that this relationship might vary between different groups of people with tinnitus. For a small subset of participants with narrow tinnitus bandwidth, pitch was associated with the audiometric edge, consistent with the tonotopic reorganization theory. The current study objective was to establish this relationship in an independent sample. Design: This was a retrospective design using data from five studies conducted between 2008 and 2013. Study sample: From a cohort of 380 participants, a subgroup group of 129 with narrow tinnitus bandwidth were selected. Results: Tinnitus pitch generally fell within the area of hearing loss. There was a statistically significant correlation between dominant tinnitus pitch and edge frequency; higher edge frequency being associated with higher dominant tinnitus pitch. However, similar to our previous study, for the majority of participants pitch was more than an octave above the edge frequency. Conclusions: The findings did not support our prediction and are therefore not consistent with the reorganization theory postulating tinnitus pitch to correspond to the audiometric edge.
Successful treatment of sudden sensorineural hearing loss assures improvement of accompanying tinnitus.

Rah YC¹, Park KT, Yi YJ, Seok J, Kang SI, Kim YH.

¹ Department of Otorhinolaryngology-Head and Neck Surgery, Boramae Medical Center, Seoul National University College of Medicine, Seoul, South Korea.

OBJECTIVES/HYPOTHESIS: To investigate the long-term outcomes of accompanying tinnitus after steroid therapy for patients with sudden sensorineural hearing loss (SSNHL). STUDY DESIGN: Retrospective chart review and survey. METHODS: Fifty patients diagnosed with SSNHL accompanied by tinnitus were enrolled and divided into two groups-satisfied and unsatisfied-according to the degree of improvement of tinnitus after SSNHL treatment. Subjective improvement of tinnitus and hearing status were investigated before and 6 months after SSNHL treatment. Hearing improvement was assessed using criteria from our previous study and Siegel's criteria. The change of tinnitus was assessed using a visual analogue scale for tinnitus intensity and frequency. RESULTS: Patients with more severe initial hearing loss had less chance of hearing recovery (P = .05). The satisfied group included significantly more cases with better hearing recovery after SSNHL treatment than the unsatisfied group (P = .049). Pure-tone threshold and speech discrimination scores were significantly better in the satisfied group than in the unsatisfied group after SSNHL treatment (P = .033 and P = .018, respectively), although the two groups showed no definitive differences before treatment. CONCLUSIONS: Optimal and successful treatment of SSNHL may be an important factor in obtaining favorable long-term control of tinnitus accompanied by SSNHL. LEVEL OF EVIDENCE: 4. Laryngoscope, 2014. © 2014 The American Laryngological, Rhinological and Otological Society, Inc.

Noise exposure immediately activates cochlear mitogen-activated protein kinase signaling.

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Noise-induced hearing loss (NIHL) is a major public health issue worldwide. Uncovering the early molecular events associated with NIHL would reveal mechanisms leading to the hearing loss. Our aim is to investigate the immediate molecular responses after different levels of noise exposure and identify the common and distinct pathways that mediate NIHL. Previous work showed mice exposed to 116 decibels sound pressure level (dB SPL) broadband noise for 1 h had greater threshold shifts than the mice exposed to 110 dB SPL broadband noise, hence we used these two noise levels in this study. Groups of 4-8-week-old CBA/CaJ mice were exposed to no noise (control) or to broadband noise for 1 h, followed by transcriptome analysis of total cochlear RNA isolated immediately after noise exposure. Previously identified and novel genes were found in all data sets. Following exposure to noise at 116 dB SPL, the earliest responses included up-regulation of 243 genes and down-regulation of 61 genes, while a similar exposure at 110 dB SPL up-regulated 155 genes and down-regulated 221 genes. Bioinformatics analysis indicated that mitogen-activated protein kinase (MAPK) signaling was the major pathway in both levels of noise exposure. Nevertheless, both qualitative and quantitative differences were noticed in some MAPK signaling genes, after exposure to different noise levels. Cacna1b, Cacna1g, and Pla2g6, related to calcium signaling were down-regulated after 110 dB SPL exposure, while the fold increase in the expression of Fos was relatively lower than what was observed after 116 dB SPL exposure. These subtle variations provide insight on the factors that may contribute to the differences in NIHL despite the activation of a common pathway. Free full text.
Genetic variations in protocadherin 15 and their interactions with noise exposure associated with noise-induced hearing loss in Chinese population.

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Objectives: The purpose of this study was to examine the associations between genetic variations in the Protocadherin 15 gene (PCDH15) and the risk to noise induced hearing loss (NIHL) in a Chinese population. Methods: A case-control study was conducted with 476 noise-sensitive workers (NIHL) and 475 noise-resistant workers (normal) matched for gender, years of noise exposure, and intensity of noise exposure. 13 tag single-nucleotide polymorphisms in PCDH15 were genotyped using nanofluidic dynamic arrays on the Fluidigm platform. Multiple logistic regression was used to analyze the associations of genetic variations of PCDH15 with NIHL adjusted by age, smoking/drinking status, and cumulative noise exposure and their interactions with noise exposure. Results: The allele frequency and genotypes of rs1104085 were significantly associated with the risk of NIHL (P=0.009 and 0.005 respectively). The subjects carrying variant alleles (CT or CC) of rs11004085 had a decreased the risk for NIHL (adjusted odds ratio=0.587, 95% confidence interval 0.409-0.842) compared with subjects who had the wild-type (TT) homozygotes. The interactions were found between the SNPs of rs1100085, rs10825122, rs1930146, rs2384437, rs4540756, and rs2384375 and noise exposure. Conclusions: Genetic variations of PCDH15 and their interactions with occupational noise exposure are associated with genetic susceptibility to NIHL and modify the risk of noise induced hearing loss. Copyright © 2014 The Authors. Published by Elsevier Inc. All rights reserved.

From Development to Disease: Diverse Functions of Nmda-Type Glutamate Receptors in the Lower Auditory Pathway.

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N-methyl-D-aspartate receptors (NMDA-Rs) are located at each synapse in the lower auditory pathway of mammals and avians. Characterized by a slow and long-lasting excitatory response upon glutamate activation, their existence in a sensory system biologically engineered for speed and precision seems counterintuitive. In this review we consider the diverse functions of NMDA-Rs. Their developmental regulation and unique subunit composition in the inner ear promote protective and neurotropic roles following acute insult by regulating AMPA-R expression and assisting in the restoration of synaptic inputs. This contrasts with chronic damage where overactivation of NMDA-Rs is implicated in neuronal death. These functions are thought to be involved in auditory diseases, including noise-induced hearing loss, neural presbycusis, and tinnitus via aberrant excitation. A more traditional role emerges in the developing auditory brainstem, where NMDA-Rs are downregulated and switch subunit composition with maturation. Their biophysical properties also contribute to synaptic dynamics resembling long-term plasticity and at mature synapses; they support reliable auditory processing by increasing the probability of action potential generation, regulating first-spike latency, and maintaining reliable action potential firing. Thus, NMDA-R functions in the lower auditory pathway are diverse, contributing to synaptic development, plasticity, temporal processing, and diseases. Copyright © 2014 The Authors. Published by Elsevier Ltd.. All rights reserved.
Biological correlates of tinnitus-related distress: An exploratory study.

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During the process of tinnitus diagnostics, various psychometric instruments are used to measure tinnitus-related distress. The aim of present work was to explore whether candidates for biological correlates of the tinnitus-related distress could be found in peripheral blood of patients and if so, whether there was association between them and psychometric scores that reflect tinnitus-related distress. The concentrations of interleukin-1β (IL1β), interleukin-6 (IL6), tumor necrosis factor-α (TNFα) and a brain-derived neutrotrophic factor (BDNF) were measured in serum of 30 patients diagnosed with chronic tinnitus and tested for correlation with psychometric scores collected on the same day. Spearman's correlation analyses detected significant positive association between the concentrations of tumor necrosis factor α and tinnitus loudness, total perceived stress, tension and depression and a negative association between tumor necrosis factor α and a psychometric score "joy". Concentrations of interleukin-1β correlated with the awareness grade of tinnitus. The correlation between visual analogue scale (VAS) "loudness" and tumor necrosis factor α as well as between "joy" and tumor necrosis factor α retained their significance (p < 0.00167) after the application of Bonferroni correction for multiple testing. Partial correlations removing the effects of age, hearing loss and the duration of tinnitus verified the results obtained using Spearman correlation. We conclude that measuring the concentrations of selected circulating cytokines could possibly become an additional objective element of tinnitus diagnostics in the future. Copyright © 2014 Elsevier B.V. All rights reserved.

Cochlear and Brainstem Audiologic Findings in Normal Hearing Tinnitus Subjects in Comparison with Non-Tinnitus Control Group.

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While most tinnitus cases have some degree of hearing impairment, a small percent of the patients admitted to Ear, Nose and Throat Clinics or Hearing Evaluation Centers are those who complain of tinnitus despite having normal hearing thresholds. Present study was performed in order to better understanding of the probable causes of tinnitus and to investigate possible changes in the cochlear and auditory brainstem function in normal hearing patients with chronic tinnitus. Altogether, 63 ears (31 ears with tinnitus and 32 ears without tinnitus) were examined. The prevalence of transient evoked otoacoustic emissions and characteristics of the auditory brainstem response components including wave latencies and wave amplitudes was determined in the two groups and analyzed with appropriate statistical methods. There was no difference between the prevalence of transient evoked emissions in the two groups. The mean difference between absolute latencies of waves I, III and V was less than 0.1 ms between the two groups that were not statistically significant. Also, the interpeak latency values of I-III, III-V and I-V in both groups had no significant difference. Only the V/I amplitude ratio in the tinnitus group was significantly larger than the other group (p =0.04). The changes observed in amplitude of waves, especially in the later ones, can be considered as an Audiologic finding in normal hearing tinnitus subjects and its possible role in generation of tinnitus in these patients must be investigated.
Intronic Variants in the NFKB1 Gene May Influence Hearing Forecast in Patients with Unilateral Sensorineural Hearing Loss in Meniere’s Disease.

Cabrera S1, Sanchez E2, Requena T3, Martinez-Bueno M4, Benitez J4, Perez N5, Trinidad G6, Soto-Varela A7, Santos-Perez S7, Martin-Sanz E8, Fraile J9, Perez P10, Alarcon-Riquelme ME3, Batuecas A11, Espinosa-Sanchez JM12, Aran I13, Lopez-Escamez JA14.

1 Otology & Neurotology Group CTS495, Department of Genomic Medicine- Centro de Genómica e Investigación Oncológica - Pfizer/Universidad de Granada/Junta de Andalucía (GENYO), Granada, Spain.

Meniere’s disease is an episodic vestibular syndrome associated with sensorineural hearing loss (SNHL) and tinnitus. Patients with MD have an elevated prevalence of several autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis and psoriasis), which suggests a shared autoimmune background. Functional variants of several genes involved in the NF-κB pathway, such as REL, TNFAIP3, NFKB1 and TNIP1, have been associated with two or more immune-mediated diseases and allelic variations in the TLR10 gene may influence bilateral afebrilection and clinical course in MD. We have genotyped 716 cases of MD and 1628 controls by using the ImmunoChip, a high-density genotyping array containing 186 autoimmune loci, to explore the association of immune system related-loci with sporadic MD. Although no single nucleotide polymorphism (SNP) reached a genome-wide significant association (p<10-8), we selected allelic variants in the NF-κB pathway for further analyses to evaluate the impact of these SNPs in the clinical outcome of MD in our cohort. None of the selected SNPs increased susceptibility for MD in patients with uni or bilateral SNHL. However, two potential regulatory variants in the NFκB1 gene (rs3774937 and rs4648011) were associated with a faster hearing loss progression in patients with unilateral SNHL. So, individuals with unilateral MD carrying the C allele in rs3774937 or G allele in rs4648011 had a shorter mean time to reach hearing stage 3 (>40 dB HL) (log-rank test, corrected p values were p=0.009 for rs3774937 and p=0.003 for rs4648011, respectively). No variants influenced hearing in bilateral MD. Our data support that the allelic variants rs3774937 and rs4648011 can modify hearing outcome in patients with MD and unilateral SNHL. Free Article.

Otologic outcomes after blast injury: the Boston marathon experience.

1*Department of Otology and Laryngology, Harvard Medical School, U.S.A.

OBJECTIVE: Otologic trauma was the most common physical injury sustained after the April 15, 2013, Boston Marathon bombings. The goal of this study is to describe the resultant otologic morbidity and to report on early outcomes. STUDY DESIGN: Multi-institutional prospective cohort study. METHODS: Children and adults seen for otologic complaints related to the Boston Marathon bombings comprised the study population. Participants completed symptom assessments, quality-of-life questionnaires, and audiograms at initial and 6-month visits. Otologic evaluation and treatment, including tympanoplasty results, were reviewed. RESULTS: More than 100 patients from eight medical campuses have been evaluated for blast-related otologic injuries; 94 have enrolled. Only 7% had any otologic symptoms before the blasts. Ninety percent of hospitalized patients sustained tympanic membrane perforation. Proximity to blast (RR = 2.7, p < 0.01) and significant nonotologic injury (RR = 2.7, p < 0.01) were positive predictors of perforation. Spontaneous healing occurred in 38% of patients, and tympanoplasty success was 86%. After oral steroid therapy in eight patients, improvement in hearing at 2 and 4 KHz was seen, although changes did not reach statistical significance. Hearing loss, tinnitus, hyperacusis, and difficulty hearing in noise remain persistent and, in some cases, progressive complaints for patients. Otologic-specific quality of life was impaired in this population. CONCLUSION: Blast-related otologic injuries constitute a major source of ongoing morbidity after the Boston Marathon bombings. Continued follow-up and care of this patient population are warranted.
Tinnitus is characterized by an auditory perception of sound, with no stimuli from the external environment. Tinnitus is an increasingly significant complaint, affecting 10-17% of the world population. As a symptom, it should always be considered with pathology in the auditory system. Our study aims to assess the relationship of this symptom with the presence of a stapedial reflex and the phenomenon of recruitment. Medical records of patients complaining of subjective tinnitus during their first consultation in the Outpatient Clinic of the Unicamp Teaching Hospital, in Brazil, between 2011 and 2012 were analyzed. We carried out a study with 65 non-randomized tinnitus individuals using questionnaires, clinical and audiological evaluations. The visual analogue scale was used to characterize the degree of disturbance caused by tinnitus. Statistical tests were performed using the IBM SPSS Statistics 19. No association was found between tinnitus and the presence of acoustic reflex or phenomenon of recruitment. We concluded that there is no relationship between tinnitus, the phenomenon of recruitment or the presence of an acoustic reflex.

INTRODUCTION: Tinnitus includes all the sounds perceived by the patient, without any external stimulus that affects all aspects of life; there is no cure for most patients. Given that tinnitus and hearing of the ear are common complaints of patients in clinics and due to the impossibility of cure at the present time, it is necessary to set up common causes of tinnitus to solve social problems and present optimal solutions. The purpose of this study was to determine the causes of tinnitus in patients referred to ENT Clinic of Imam Khomeini Hospital in Urmia, 2012-2013. MATERIALS & METHODS: This is a cross-sectional analytic study that was performed on 184 patients with tinnitus referred to ENT clinic of Imam Khomeini Hospital, Urmia. After examination, audiometry performed and questionnaires of tinnitus patients were completed. The results were analyzed by statistical SPSS software. RESULTS: The study included 111 males and 73 females and the mean age was 50.6 years. 168 patients (91.3%) had non-pulsatile tinnitus and the rest had pulsatile tinnitus. The mean hearing loss in patients was 31.4 dB, 79.9% were of sensory neurons kind, and 12.5% of patients did not show any hearing loss in audiometry. In total, 90.2% of the cases were detected; most causes of tinnitus were noise (19.6%), ototoxicity (16.8%) and presbycusis (16.3%). The most common causes of tinnitus were noise with 31.5% in males and ototoxicity with 27.4% in females. Between age and hearing loss of patients, there was a significant relationship (0.001> P-value), but there was no significant relationship between gender and degree of hearing loss. DISCUSSION: The most common cause of tinnitus (NIHL) is quite predictable, except by accident, you can completely avoid by reducing noise levels on the source and ear protection. By reasonable prescription of ototoxic medications particularly antibiotics can reduce the prevalence of tinnitus that causes sleep disorders and concentration problems, depression and anxiety and help the public health.
Is human T-lymphotropic virus type 1 infection associated with hearing loss?

Bakhshaee M¹, Sorouri A, Shoeibi A, Boustani R, Golhasani-Keshtan F, Amali A, Rajati M.

¹ Sinus and Surgical Endoscopic Research Center.

OBJECTIVES/HYPOTHESIS: Human T-lymphotropic virus type 1 (HTLV-1) infection is endemic in the northeast area of Iran. Although various neurological disturbances have been reported in HTLV-1 infection, possible audiovestibular involvement during this infection has not yet been studied. STUDY DESIGN: Case control study. METHODS: Sixty-eight cases in three groups including 24 HTLV-1-infected patients with HTLV-1- associated myelopathy/tropical spastic paraparesis (HAM/TSP) (group 1), 23 HTLV-1-infected cases without clinical presentation (group 2), and 21 normal individuals (group 3) entered our study. A complete history of hearing-related disorders and a profile of audiologic tests, including pure-tone audiometry (PTA) with high frequencies, speech reception threshold (SRT), and auditory brainstem response (ABR) were taken. RESULTS: Subjective audiovestibular complaints of participants showed a significant difference among HAM/TSP patients and the two other groups regarding hearing loss and tinnitus, but not vertigo or aural fullness. Hearing evaluation by SRT and PTA in all frequencies showed a significant difference between HAM/TSP patients (group 1) and the controls (group 3). The difference was also significant between asymptomatic cases (group 2) and the controls only in PTA frequencies above 4 kHz. Auditory brainstem-evoked potential did not show any significant differences among the groups regarding latency of I, III, and V waves and interwave differences. CONCLUSIONS: HTLV-1 infection, particularly in those with a clinical presentation, appears to accompany hearing loss. Based on the results of PTA and ABR tests, this study may suggest a cochlear source of hearing impairment rather than neural problems. LEVEL OF EVIDENCE: 3b. Laryngoscope, 2014. © 2014 The American Laryngological, Rhinological and Otological Society, Inc.

Glucocorticoids stimulate endolymphatic water reabsorption in inner ear through aquaporin 3 regulation.
Pflugers Arch. 2014 Oct 23. [Epub ahead of print]

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Menière's disease, clinically characterized by fluctuating, recurrent, and invalidating vertigo, hearing loss, and tinnitus, is linked to an increase in endolymph volume, the so-called endolymphatic hydrops. Since dysregulation of water transport could account for the generation of this hydrops, we investigated the role of aquaporin 3 (AQP3) in water transport into endolymph, the K-rich, hyperosmotic fluid that bathes the apical ciliated membrane of sensory cells, and we studied the regulatory effect of dexamethasone upon AQP3 expression and water fluxes. The different AQP subtypes were identified in inner ear by RT-PCR. AQP3 was localized in human utricle and mouse inner ear by immunohistochemistry and confocal microscopy. Unidirectional transepithelial water fluxes were studied by means of 3H2O transport in murine EC5v vestibular cells cultured on filters, treated or not with dexamethasone (10-7 M). The stimulatory effect of dexamethasone upon AQP3 expression was assessed in EC5v cells and in vivo in mice. AQP3 was unambiguously detected in human utricle and was highly expressed in both endolymph secretory structures of the mouse inner ear, and EC5v cells. We demonstrated that water reabsorption, from the apical (endolymphatic) to the basolateral (perilymphatic) compartments, was stimulated by dexamethasone in EC5v cells. This was accompanied by a glucocorticoid-dependent increase in AQP3 expression at both messenger RNA (mRNA) and protein level, presumably through glucocorticoid receptor-mediated AQP3 transcriptional activation. We show that glucocorticoids enhance AQP3 expression in human inner ear and stimulate endolymphatic water reabsorption. These findings should encourage further clinical trials evaluating glucocorticoids efficacy in Menière's disease.
Middle fossa arachnoid cysts and inner ear symptoms: Are they related?

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BACKGROUND: Arachnoid cysts most frequently occur in the middle cranial fossa and when they are symptomatic, patients present with central nervous symptoms. Nevertheless, a large proportion of arachnoid cysts are incidentally diagnosed during neuroimaging in cases with nonspecific symptoms.

REPORT OF CASES: The cases of two males with middle cranial fossa arachnoid cysts with nonspecific inner ear symptoms were retrospectively reviewed. The first patient presented with mild headache, nausea, vertigo, unsteadiness, and tinnitus on the left ear while the second patient's main complaint was left sided tinnitus. Both patients (initially managed for peripheral disorders) underwent a thorough clinical and electrophysiological evaluation. Because of the patients' persistent clinical symptoms, and indications of CNS disorder in the first case, neuroimaging by brain MRI was performed revealing a middle cranial fossa arachnoid cyst in both patients. CONCLUSION: Occasionally, patients with arachnoid cysts may present with mild, atypical or intermittent and irrelevant symptoms which can mislead diagnosis. Otorhinolaryngologists should be aware of the fact that atypical, recurrent or intermittent symptoms may masquerade a CNS disorder. Hippokratia 2014; 18 (2):168-171. Free PMC Article.

Autoimmunity as a Candidate for the Etiopathogenesis of Meniere's Disease: Detection of Autoimmune Reactions and Diagnostic Biomarker Candidate.

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Meniere's disease is an inner ear disorder that can manifest as fluctuating vertigo, sensorineural hearing loss, tinnitus, and aural fullness. However, the pathologic mechanism of Meniere's disease is still unclear. In this study, we evaluated autoimmunity as a potential cause of Meniere's disease. In addition we tried to find useful biomarker candidates for diagnosis. We investigated the protein composition of human inner ear fluid using liquid column mass spectrometry, the autoimmune reaction between circulating autoantibodies in patient serum and multiple antigens using the Protoarray system, the immune reaction between patient serum and mouse inner ear tissues using western blot analysis. Nine proteins, including immunoglobulin and its variants and interferon regulatory factor 7, were found only in the inner ear fluid of patients with Meniere's disease. Enhanced immune reactions with 18 candidate antigens were detected in patients with Meniere's disease in Protoarray analysis; levels of 8 of these antigens were more than 10-fold higher in patients than in controls. Antigen-antibody reactions between mouse inner ear proteins with molecular weights of 23-48 kDa and 63-75 kDa and patient sera were detected in 8 patients. These findings suggest that autoimmunity could be one of the pathologic mechanisms behind Meniere's disease. Multiple autoantibodies and antigens may be involved in the autoimmune reaction. Specific antigens that caused immune reactions with patient's serum in Protoarray analysis can be candidates for the diagnostic biomarkers of Meniere's disease. Free PMC Article.
Intradiploic Epidermoid of Temporal Bone Presenting as Pulsatile Tinnitus.

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No abstract available.

Evidence of Multidomain Mild Cognitive Impairment in Idiopathic Intracranial Hypertension.
J Neuroophthalmol. 2014 Nov 7. [Epub ahead of print]

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BACKGROUND: Idiopathic intracranial hypertension (IIH), a disorder of unknown etiology, may occur in all age groups, but is most common in young obese women. Goals of treatment are to preserve vision and alleviate symptoms, including intractable headache, pulsatile tinnitus, and nausea. Cognitive function is not addressed routinely during clinical evaluation of IIH patients. The aim of our study was to test whether there is cognitive impairment in IIH patients and to evaluate the nature and characteristics of cognitive functions. METHODS: Design-Prospective cross-sectional observational study; Setting-Institutional; Study population-Thirty consecutive IIH patients (3 men and 27 women), mean age at time of testing was 34.4 years; Procedures-All participants completed a cognitive test battery; Outcome measures-Impairment of non-verbal memory, executive function, visual spatial processing, attention, motor skills, problem solving, and information processing speed in IIH patients. RESULTS: Mean scores for all domain index scores were below average for age and education. The global cognitive score, attention, and visual spatial indices had the lowest scores. CONCLUSIONS: Our results indicate that patients with IIH have mild cognitive impairment. All domain measures apart from memory showed a statistically significant difference from normal individuals, indicating that there is a form of multidomain cognitive impairment in IIH. The relationship between cognitive impairment and chronically elevated intracranial pressures and its role in contributing to patient morbidity requires further study.

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The ability to reproducibly match tinnitus loudness and pitch is important to research and clinical management. Here we examine agreement and reliability of tinnitus loudness matching and pitch likeness ratings when using a computer-based method to measure the tinnitus spectrum and estimate a dominant tinnitus pitch, using tonal or narrowband sounds. Group level data indicated a significant effect of time between test session 1 and 2 for loudness matching, likely procedural or perceptual learning, which needs to be accounted in study design. Pitch likeness rating across multiple frequencies appeared inherently more variable and with no systematic effect of time. Dominant pitch estimates reached a level of clinical acceptability when sessions were spaced two weeks apart. However when dominant tinnitus pitch assessments were separated by three months, acceptable agreement was achieved only for group mean data, not for individual estimates. This has implications for prescription of some sound-based interventions that rely on accurate measures of individual dominant tinnitus pitch. Free Article.

Relationship between tinnitus pitch and edge of hearing loss in individuals with a narrow tinnitus bandwidth.

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Objective: Psychoacoustic measures of tinnitus, in particular dominant tinnitus pitch and its relationship to the shape of the audiogram, are important in determining and verifying pathophysiological mechanisms of the condition. Our previous study postulated that this relationship might vary between different groups of people with tinnitus. For a small subset of participants with narrow tinnitus bandwidth, pitch was associated with the audiometric edge, consistent with the tonotopic reorganization theory. The current study objective was to establish this relationship in an independent sample. Design: This was a retrospective design using data from five studies conducted between 2008 and 2013. Study sample: From a cohort of 380 participants, a subgroup group of 129 with narrow tinnitus bandwidth were selected. Results: Tinnitus pitch generally fell within the area of hearing loss. There was a statistically significant correlation between dominant tinnitus pitch and edge frequency; higher edge frequency being associated with higher dominant tinnitus pitch. However, similar to our previous study, for the majority of participants pitch was more than an octave above the edge frequency. Conclusions: The findings did not support our prediction and are therefore not consistent with the reorganization theory postulating tinnitus pitch to correspond to the audiometric edge.
IV Imaging


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Objective. Several neuroscience tools showed the involvement of auditory cortex in chronic tinnitus. In this proof-of-principle study we probed the capability of functional near-infrared spectroscopy (fNIRS) for the measurement of brain oxygenation in auditory cortex in dependence from chronic tinnitus and from intervention with transcranial magnetic stimulation.

Methods. Twenty-three patients received continuous theta burst stimulation over the left primary auditory cortex in a randomized sham-controlled neuronavigated trial (verum = 12; placebo = 11). Before and after treatment, sound-evoked brain oxygenation in temporal areas was measured with fNIRS. Brain oxygenation was measured once in healthy controls (n = 12).

Results. Sound-evoked activity in right temporal areas was increased in the patients in contrast to healthy controls. Left-sided temporal activity under the stimulated area changed over the course of the trial; high baseline oxygenation was reduced and vice versa.

Conclusions. By demonstrating that rTMS interacts with auditory evoked brain activity, our results confirm earlier electrophysiological findings and indicate the sensitivity of fNIRS for detecting rTMS induced changes in brain activity. Moreover, our findings of trait- and state-related oxygenation changes indicate the potential of fNIRS for the investigation of tinnitus pathophysiology and treatment response. Free Article.

Inhibition-induced plasticity in tinnitus patients after repetitive exposure to tailor-made notched music.

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OBJECTIVE: Notch-filtered music has been shown to induce frequency-specific inhibition. Here, we investigated which cortical structures are affected by tailor-made notched music (TMNM) in tinnitus patients and how this inhibition-induced plasticity develops over time.

METHODS: Nine subjects suffering from chronic tonal tinnitus listened to music passing through a notch-filter centered at the patient’s individual tinnitus frequency (TMNM) for three hours on three consecutive days. Before and after each listening session, a tone at the tinnitus frequency and a control tone of 500Hz were presented in the magnetoencephalograph. Subjective tinnitus loudness was measured via visual analog scales.

RESULTS: TMNM exposure reduced subjective tinnitus loudness and neural activity evoked by the tinnitus tone in temporal, parietal and frontal regions within the N1m time interval. Reduction of temporal and frontal activation correlated significantly with tinnitus loudness decline. Reduction of tinnitus related neural activity persisted and accumulated over three days.

CONCLUSIONS: Inhibition-induced plasticity occurs in a cortical network, known to be crucial for tinnitus perception. This cortical reorganization evolves fast and accumulates across sessions.

SIGNIFICANCE: This study extends previous work on inhibition-induced plasticity, as it demonstrates the involvement of parietal and frontal areas and discovers a cumulative effect of cortical reorganization in tinnitus patients. Copyright © 2014 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.
The Application of Electro- and Magneto-Encephalography in Tinnitus Research - Methods and Interpretations.
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In recent years, there has been a significant increase in the use of electroencephalography (EEG) and magnetoencephalography (MEG) to investigate changes in oscillatory brain activity associated with tinnitus with many conflicting results. Current view of the underlying mechanism of tinnitus is that it results from changes in brain activity in various structures of the brain as a consequence of sensory deprivation. This in turn gives rise to increased spontaneous activity and/or synchrony in the auditory centers but also involves modulation from non-auditory processes from structures of the limbic and paralimbic system. Some of the neural changes associated with tinnitus may be assessed non-invasively in human beings with MEG and EEG (M/EEG) in ways, which are superior to animal studies and other non-invasive imaging techniques. However, both MEG and EEG have their limitations and research results can be misinterpreted without appropriate consideration of these limitations. In this article, I intend to provide a brief review of these techniques, describe what the recorded signals reflect in terms of the underlying neural activity, and their strengths and limitations. I also discuss some pertinent methodological issues involved in tinnitus-related studies and conclude with suggestions to minimize possible discrepancies between results. The overall message is that while MEG and EEG are extremely useful techniques, the interpretation of results from tinnitus studies requires much caution given the individual variability in oscillatory activity and the limits of these techniques. Free Article.

CT characteristics of dehiscent sigmoid plates presenting as pulsatile tinnitus: a study of 23 patients.
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BACKGROUND: Although some features of dehiscent sigmoid plates as a cause of pulsatile tinnitus (PT) have been reported, detailed imaging findings have not been evaluated. PURPOSE: To retrospectively evaluate the computed tomography (CT) features of dehiscent sigmoid plates associated with PT. MATERIAL AND METHODS: The CT images of 23 PT patients were assessed to evaluate the features of the dehiscent sigmoid plates, lateral sinuses, and temporal bone pneumatization. RESULTS: A total of 31 defects were found on the PT side. Twenty-five defects involved the superior curve or the descending segment, four involved above both sites, and only two involved the inferior curve. Twenty-six defects involved the anterior border or the anterolateral border, and only five involved the lateral border of the sigmoid sinus. The dehiscent sigmoid plate was on the dominant side in all 18 patients with a unilateral dominant lateral sinus, and on the right side in two patients and on the left side in three patients with co-dominant lateral sinuses. Fourteen patients had hyperpneumatization and nine had good pneumatization of temporal bone. Fifteen of the 17 patients with resolution of PT after surgery had a single defect. Four of the six patients with persistence of PT after surgery had more than one defect. CONCLUSION: Sigmoid plate dehiscence often involves the anterior or anterolateral border of the superior curve or the descending segment of the sigmoid sinus on the side of the dominant lateral sinus, which often coexists with extensive pneumatization of the temporal bone. © The Foundation Acta Radiologica 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav.
Cost-Effective Analysis of Unilateral Vestibular Weakness Investigation.

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OBJECTIVES: To evaluate the cost-effectiveness of obtaining a magnetic resonance imaging (MRI) in patients with abnormal electronystagmography (ENG) or videonystagmography (VNG) results. STUDY DESIGN: Retrospective chart review. SETTINGS: Academic specialty center. PATIENTS: Patients presenting with vertigo between January 1, 2010, and August 30, 2013. METHODS: Patients who fit the following abnormal criteria were included in the study: unilateral caloric weakness (≥20%), abnormal ocular motor testing, and nystagmus on positional testing. Patients with abnormal findings who then underwent MRI with gadolinium were evaluated. RESULTS: Of the 1,996 charts reviewed, there were 1,358 patients who met the inclusion criteria. The average age of these patients was 62 years (12-94 yr). The male:female ratio was approximately 1:2. Of the 1,358 patients, 253 received an MRI with the following pathologies: four vestibular schwannomas, three subcortical/periventricular white matter changes suspicious for demyelinating disease, four acute cerebellar/posterior circulation infarct, two vertebral artery narrowing, one pseudomeningocele of internal auditory canal, and two white matter changes indicative of migraines. The positive detection rate on MRI was 5.5% based on MRI findings of treatable pathologies causing vertigo. Average cost of an MRI is $1,200, thereby making the average cost of identifying a patient with a positive MRI finding $15,180. CONCLUSION: In our study, those patients with a positive MRI had a constellation of symptoms and findings (asymmetric sensorineural hearing loss, tinnitus, vertigo, and abnormal ENG/VNG). Cost-effectiveness can be improved by ordering an MRI only when clinical examination and VNG point toward a central pathology. Clinical examination and appropriate testing should be factored when considering the cost-effectiveness of obtaining an MRI in patients with abnormal ENG/VNG findings.

CT arteriography and venography in the evaluation of Pulsatile tinnitus with normal otoscopic examination.

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OBJECTIVES/HYPOTHESIS: Our retrospective study aims to assess the ability of computed tomography arteriography and venography (CT A/V) to detect various findings that suggest a potential cause of pulsatile tinnitus and to examine the association between these findings and the side of pulsatile tinnitus. STUDY DESIGN: A retrospective review of CT arteriography and venography of 32 patients with established pulsatile tinnitus and normal otoscopic examination was performed. The scans were performed using a 64-slice multidetector scanner and were reviewed to look for findings that are known to cause pulsatile tinnitus. RESULTS: One or more findings that are known to cause pulsatile tinnitus were detected on the symptomatic side in 30 patients; on the asymptomatic side in 3 patients, one patient with bilateral pulsatile tinnitus showed a potential cause of symptoms only on one side, and in one patient no potential cause could be identified. There is a significant association seen between the side of pulsatile tinnitus and various potential causes of pulsatile tinnitus detected (P<0.001), between the side of pulsatile tinnitus and various potential venous cause detected (P<0.001), and between the side of pulsatile tinnitus and the side of dominant venous system (P=0.02). CONCLUSION: CT arteriography and venography is a useful tool in detecting many described potential causes of pulsatile tinnitus. Significant association is demonstrated between the side of pulsatile tinnitus and the potential causes of pulsatile tinnitus detected by CT arteriography and venography when the otoscopic examination is normal. LEVEL OF EVIDENCE: 4. Laryngoscope, 2014. © 2014 The American Laryngological, Rhinological and Otological Society, Inc.
Aberrant spontaneous brain activity in chronic tinnitus patients revealed by resting-state functional MRI.


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OBJECTIVE: The neural mechanisms that give rise to the phantom sound of tinnitus are poorly understood. This study aims to investigate whether aberrant spontaneous brain activity exists in chronic tinnitus patients using resting-state functional magnetic resonance imaging (fMRI) technique. MATERIALS AND METHODS: A total of 31 patients with chronic tinnitus patients and 32 healthy age-, sex-, and education-matched healthy controls were prospectively examined. Both groups had normal hearing thresholds. We calculated the amplitude of low-frequency fluctuations (ALFFs) of fMRI signals to measure spontaneous neuronal activity and detect the relationship between fMRI information and clinical data of tinnitus. RESULTS: Compared with healthy controls, we observed significant increased ALFF within several selected regions including the right middle temporal gyrus (MTG), right superior frontal gyrus (SFG), and right angular gyrus; decreased ALFF was detected in the left cuneus, right middle occipital gyrus and bilateral thalamus. Moreover, tinnitus distress correlated positively with increased ALFF in right MTG and right SFG; tinnitus duration correlated positively with higher ALFF values in right SFG. CONCLUSIONS: The present study confirms that chronic tinnitus patients have aberrant ALFF in many brain regions, which is associated with specific clinical tinnitus characteristics. ALFF disturbance in specific brain regions might be used to identify the neuro-pathophysiological mechanisms in chronic tinnitus patients. Free PMC Article.

Unilateral Tinnitus: Changes in Connectivity and Response Lateralization Measured with fMRI.


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Tinnitus is a percept of sound that is not related to an acoustic source outside the body. For many forms of tinnitus, mechanisms in the central nervous system are believed to play a role in the pathology. In this work we specifically assessed possible neural correlates of unilateral tinnitus. Functional magnetic resonance imaging (fMRI) was used to investigate differences in sound-evoked neural activity between controls, subjects with left-sided tinnitus, and subjects with right-sided tinnitus. We assessed connectivity patterns between auditory nuclei and the lateralization of the sound-evoked responses. Interestingly, these response characteristics did not relate to the laterality of tinnitus. The lateralization for left- or right ear stimuli, as expressed in a lateralization index, was considerably smaller in subjects with tinnitus compared to that in controls, reaching significance in the right primary auditory cortex (PAC) and the right inferior colliculus (IC). Reduced functional connectivity between the brainstem and the cortex was observed in subjects with tinnitus. These differences are consistent with two existing models that relate tinnitus to i) changes in the corticothalamic feedback loops or ii) reduced inhibitory effectiveness between the limbic system and the thalamus. The vermis of the cerebellum also responded to monaural sound in subjects with unilateral tinnitus. In contrast, no cerebellar response was observed in control subjects. This suggests the involvement of the vermis of the cerebellum in unilateral tinnitus. Free PMC Article.
V Pharmacotherapy

Cochlear Damage Affects Neurotransmitter Chemistry in the Central Auditory System.
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Tinnitus, the perception of a monotonous sound not actually present in the environment, affects nearly 20% of the population of the United States. Although there has been great progress in tinnitus research over the past 25 years, the neurochemical basis of tinnitus is still poorly understood. We review current research about the effects of various types of cochlear damage on the neurotransmitter chemistry in the central auditory system and document evidence that different changes in this chemistry can underlie similar behaviorally measured tinnitus symptoms. Most available data have been obtained from rodents following cochlear damage produced by cochlear ablation, intense sound, or ototoxic drugs. Effects on neurotransmitter systems have been measured as changes in neurotransmitter level, synthesis, release, uptake, and receptors. In this review, magnitudes of changes are presented for neurotransmitter-related amino acids, acetylcholine, and serotonin. A variety of effects have been found in these studies that may be related to animal model, survival time, type and/or magnitude of cochlear damage, or methodology. The overall impression from the evidence presented is that any imbalance of neurotransmitter-related chemistry could disrupt auditory processing in such a way as to produce tinnitus. Free Article.

Evaluation of the efficacy of combined treatment with sulodexide and melatonin in patients with tinnitus: a retrospective study.
Ferrari G1, Agnese A, Cavallero A, Delehaye E, Rocchetti O, Rossi W, Tombolini A.
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Tinnitus is the perception of sound in the absence of an apparent acoustic stimulus. A widespread and highly debilitating disease difficult to cure. Several treatments have been advocated for tinnitus in the last years, including surgery, pharmacotherapy, counselling, cognitive behavioural therapy, sound therapy, but unfortunately without definitive conclusions. The surgery treatments could represent an important therapeutic choice on specific subgroups of tinnitus with defined causes but obviously this approach represent an invasive treatment and it should be considered with extreme caution and then, alternative pharmacological options should be investigated. In this retrospective study 30 patients with tinnitus were treated with sulodexide (250 mg bid, in the morning and in the evening) and melatonin (3 mg in the evening before going to sleep) for 80 days. The evaluations were performed comparing different parameters at basal (T0) and after 40 days (T1) and 80 days (T2) of treatment. The results of Tinnitus Handicap Inventory (THI) and acufenometry showed a significative improvement of tinnitus after treatment with sulodexide and melatonin. In particular, THI total score was reduced from 37±20 to 27±18 (p<0.001) and 21±19 (p<0.001) at T1 and T2, respectively. The percentage of patients with improved symptoms (i.e. reduced score at THI) was 76.7% at T1 and 90.0% at T2. Finally a significant improvement was also detected in the tone audiometry test. No side effects were observed during the treatment period. In conclusion, the combined use of sulodexide, a natural glycosaminoglycan with antithrombotic, pro-fibrinolytic and vascular anti-inflammatory properties used in the treatment of many vascular diseases, included the vertigo of vascular origin and melatonin, a neurohormone produced by the pineal gland and related to multiple physiological functions, confirms to an important and promising therapeutically option in the tinnitus management.
Long term outcome of patients with clinical stage I high-risk nonseminomatous germ cell tumors 15 years after one adjuvant cycle of Bleomycin, Etoposide and Cisplatin chemotherapy.

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BACKGROUND: To report the long-term results of adjuvant treatment with 1 cycle of modified bleomycin, etoposide, and cisplatin (BEP) in patients with clinical stage I (CS I) nonseminomatous germ cell tumors (NSGCT) at high risk of relapse. PATIENTS AND METHODS: In a single-arm, phase II clinical trial, 40 patients with CS I NSGCT with vascular invasion and/or >50% embryonal cell carcinoma in the orchiectomy specimen received one cycle of adjuvant BEP (20 mg/m2 bleomycin as a continuous infusion over 24 hours, 120 mg/m2 etoposide and 40 mg/m2 cisplatin each on days 1-3). Primary endpoint was the relapse rate. RESULTS: Median follow-up was 186 months. One patient (2.5%) had a pulmonary relapse 13 months after 1 BEP and died after 3 additional cycles of BEP chemotherapy. Three patients (7.5%) presented with a contralateral metachronous testicular tumor, and 3 (7.5%) developed a secondary malignancy. 3 patients (7.5%) reported intermittent tinnitus and 1 had grade 2 peripheral polyneuropathy (2.5%). CONCLUSIONS: Adjuvant chemotherapy with 1 cycle of modified BEP is a feasible and safe treatment for patients with CS I NSGCT at high risk of relapse. In these patients it appears to be an alternative to 2 cycles of BEP and to have a lower relapse rate than retroperitoneal lymph node dissection (RPLND). If confirmed by other centers, 1 cycle of adjuvant BEP chemotherapy should become a first line treatment option for this group of patients. © The Author 2014. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com.

Treatment of the Patulous Eustachian Tube With Soft-Tissue Bulking Agent Injections.
Otol Neurotol. 2014 Oct 29. [Epub ahead of print]

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OBJECTIVE: A patulous Eustachian tube ([ET] tuba aperta) may cause symptoms as autophony, breath synchronous tinnitus, pressure sensation, and conductive hearing loss and thus lead to an enormous cutback in quality of life. In combination with “snifffing,” it can trigger the development of cholesteatoma. Because of the ambiguous symptoms, the diagnosis can be challenging. A patulous ET can only be diagnosed through a well-structured examination, including patient history, physical examination with thorough observation of the movements of the tympanic membrane, and tympanometry with reflex-decay. STUDY DESIGN AND METHODS: Transnasal endoscopic injection of injectable soft-tissue bulking agent into the torus tubarius was performed in 20 patients as a new treatment option for patulous ET. All patients were followed up 6 weeks and 6 and 12 months after treatment. For each intervention, 0.8 to 2 mL of injectable soft-tissue bulking agent was used. RESULTS: In nine patients, more than one procedure was necessary. On follow-up, 10 out of 15 patients were satisfied with the result. Only three out of 15 patients reported no improvement of their symptoms. The procedure was minimally invasive, fast, and easy to perform. CONCLUSION: There is no gold standard for the therapy of patulous ET. The injection of soft-tissue bulking agent in the torus tubarius is a new minimally invasive therapeutic approach, but much more clinical experience is needed. LEVEL OF EVIDENCE: IV.
A Novel Treatment for Tinnitus and Tinnitus-Related Cognitive Difficulties Using Computer-Based Cognitive Training and D-Cycloserine.

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Importance: Tinnitus affects more than 40 million people in the United States, and cognitive difficulties are among the most commonly associated symptoms. Objective: To test the feasibility and preliminarily the effectiveness of using a putative neuroplasticity-enhancing drug, D-cycloserine, to facilitate a computer-assisted CT program for improving tinnitus bother and related cognitive difficulties. Design, Setting, and Participants: Double-blind, randomized clinical trial at an outpatient academic medical center of 34 participants aged 35 to 65 years with subjective, unilateral or bilateral, nonpulsatile tinnitus of at least 6 months’ duration. Interventions: Five weeks of twice-weekly computer-based CT with either 250 mg D-cycloserine or placebo orally prior to computer CT sessions. Main Outcomes and Measures: Difference in the change in Tinnitus Functional Index (TFI) score between the 2 groups. Results: After excluding 1 participant lost to follow-up, 1 who withdrew, 1 who did not complete 90% of sessions, and 1 outlier, 30 participants were included in the analysis. The D-cycloserine plus CT group showed a significant improvement in median TFI score (-5.8 [95% CI, -9.4 to -1.1]) and self-reported cognitive deficits (-4.5 [95% CI, -11.5 to -1.0]), but the placebo group did not (-1.0 [95% CI, -11.7 to 4.9] and -2.0 [95% CI, -5.1 to -2.0], respectively). After controlling for age and duration of tinnitus, there was no significant difference in TFI score change between the 2 groups (P = .41). After confounders were controlled for, the D-cycloserine group demonstrated a significantly greater improvement in self-reported cognitive deficits as compared with the placebo group (P = .03). No serious adverse events were reported. Conclusions and Relevance: Use of a computer-based CT program with a putative neuroplasticity-sensitizing drug, D-cycloserine, was feasible and well tolerated. With the limited sample size, the adjuvant use of D-cycloserine was no more effective than placebo at improving tinnitus bother. The finding that D-cycloserine use was more effective than placebo at improving self-reported cognitive difficulties could be important given the high rate of concern for cognitive deficits in patients with tinnitus. D-cycloserine and other putative neuroplasticity-facilitating agents could be investigated in the future as a strategy to enhance neuroplasticity-based tinnitus treatments. Trial Registration: clinicaltrials.gov Identifier: NCT01550796.

Cervical Epidural Steroid Injection for Refractory Somatic Tinnitus.

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Somatic tinnitus is a common disorder, yet few treatments described in the literature have demonstrated strong efficacy. We report a case of a 61-year-old male with refractory somatic tinnitus, temporally related to a prior bacterial otitis media, wherein auditory symptoms were successfully treated with cervical epidural injections of long-acting corticosteroid. We discuss the proposed mechanism of somatic tinnitus and the means by which neuraxial steroids may inhibit somatic tinnitus symptoms. © 2014 World Institute of Pain.
A Nationwide Retrospective Study of Perioperative Chemotherapy for Gastroesophageal Adenocarcinoma: Tolerability, Outcome, and Prognostic Factors.


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BACKGROUND: Recent clinical trials have demonstrated the benefit and feasibility of perioperative chemotherapy for treatment of gastroesophageal adenocarcinoma (GEA). Despite convincing results, patients entering such trials usually represent only a fraction of those who are candidates for treatment. Confirmation of trial-reported effects and tolerability in unselected cohorts is therefore required. The aims of this study were to confirm the safety and efficacy of perioperative chemotherapy for resectable GEA and to delineate risks of treatment failure. METHODS: We conducted a national retrospective cohort analysis of patients admitted for perioperative chemotherapy for resectable GEA. Regimens were epirubicin and capecitabine combined with oxaliplatin or cisplatin. RESULTS: The intention-to-treat analysis included 271 patients. Eighty-seven percent of patients completed preoperative chemotherapy, and 63 % received radical resection. Age >70 years (odds ratio 2.58) and hypoalbuminemia (odds ratio 4.10) were independent predictors of not undergoing scheduled surgery (P = 0.033). Grade 3 or higher febrile neutropenia, fatigue, and diarrhea were common in the oxaliplatin group (n = 128), but hypomagnesaemia and tinnitus/hearing loss were more common in the cisplatin group (n = 135). The median overall survival was 26.4 months, and the 1- and 2-year survival rates were 76 and 53 %, respectively. Performance status >0 (hazard ratio 1.64) and elevated serum lactate dehydrogenase (hazard ratio 3.03) were independent predictors of poor prognosis (P ≤ 0.05). CONCLUSIONS: Perioperative chemotherapy is feasible and well tolerated in patients with good performance status and low incidence of comorbidities.

VI Auditive Stimulation

Non-penetrating round window electrode stimulation for tinnitus therapy followed by cochlear implantation.
Eur Arch Otorhinolaryngol. 2014 Dec 6. [Epub ahead of print]


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One main theory behind the origin of tinnitus is based on the idea that alterations of the spontaneous electrical activity within the auditory system lead to abnormal firing patterns in the affected nervous structures [1]. A possible therapeutic option is the use of electrical stimulation of the auditory nerve for the recovery or at least limitation of the abnormal firing pattern to a level that can be easily tolerated by the patient. The Tinnelec Implant consists of a single non-penetrating stimulation electrode connected to a Neurelec cochlear implant system. As a first feasibility study, before starting implantations in hearing patients, we thought to assess the potential of the Tinnelec stimulation to treat tinnitus in unilateral deaf patients, analysing hereby its effectivity and risks. Three patients suffering from unilateral tinnitus resistant to pharmacological treatment and ipsilateral severe to profound sensorineural hearing loss/deafness were implanted with a Tinnelec system between September 2007 and July 2008, at the ENT Department of Hannover Medical School. The stimulation strategy was chosen to induce alleviation of the tinnitus through suppression, masking and/or habituation and the response of each patient on the treatment was monitored using a visual analogue scale (VAS) on loudness and annoyance of tinnitus, mood of the patient, as well as the tinnitus handicap inventory (THI). All patients had a benefit from the electrical stimulation for their tinnitus (THI-score improvement of 20-70), however, not all participants profited from the Tinnelec system in same way and degree. In one patient, despite good results, the device had to be replaced.
with a conventional cochlear implant because of Tinnelec-independent increase in hearing loss on the contralateral ear. Additionally, due to the extension of cochlear implant indications, the devices of the other two patients have been meanwhile replaced with a conventional cochlear implant to benefit additionally from hearing improvement. As demonstrated in the present study, sensorineural tinnitus in humans may be suppressed/masked/habituated by electrical stimulation. The main advantage of the Tinnelec implant would be the option to treat patients with normal and usable hearing, stimulating the affected ear with the cochlear non-penetrating stimulation electrode of the device, and extend the treatment in cases of progressive hearing loss by explanation and reimplantation with a penetrating electrode addressing tinnitus as well as the hearing impairment. The present study is the first report on a long-term follow-up on tinnitus patients implanted with Tinnelec. Further clinical studies to implant tinnitus patients with residual or normal hearing on the affected ear are on the way.

[Research on fractal tones generating method for tinnitus rehabilitation based on musical instrument digital interface technology].
[Article in Chinese]
Wang L, He P, Pan F.
Tinnitus is a subjective sensation of sound without external stimulation. It has become ubiquitous and has therefore aroused much attention in recent years. According to the survey, ameliorating tinnitus based on special music and reducing pressure have good effects on the treatment of it. Meantime, vicious cycle chains between tinnitus and bad feelings have been broken. However, tinnitus therapy has been restricted by using looping music. Therefore, a method of generating fractal tones based on musical instrument digital interface (MIDI) technology and pink noise has been proposed in this paper. The experimental results showed that the fractal fragments were self-similar, incompletely reduplicate, and no sudden changes in pitches and would have a referential significance for tinnitus therapy.

[A modified speech enhancement algorithm for electronic cochlear implant and its digital signal processing realization].
[Article in Chinese]
Wang Y, Tian X.
In order to improve the speech quality and auditory perceptiveness of electronic cochlear implant under strong noise background, a speech enhancement system used for electronic cochlear implant front-end was constructed. Taking digital signal processing (DSP) as the core, the system combines its multi-channel buffered serial port (McBSP) data transmission channel with extended audio interface chip TLV320AIC10, so speech signal acquisition and output with high speed are realized. Meanwhile, due to the traditional speech enhancement method which has the problems as bad adaptability, slow convergence speed and big steady-state error, versiera function and de-correlation principle were used to improve the existing adaptive filtering algorithm, which effectively enhanced the quality of voice communications. Test results verified the stability of the system and the de-noising performance of the algorithm, and it also proved that they could provide clearer speech signals for the deaf or tinnitus patients.
Auditory Cortex Stimulation Might be Efficacious in a Subgroup of Tinnitus Patients.

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No abstract available

Hearing Performance in Single-Sided Deaf Cochlear Implant Users After Upgrade to a Single-Unit Speech Processor.
Otol Neurotol. 2014 Nov 18. [Epub ahead of print]

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INTRODUCTION: Single-sided deaf (SSD) patients report multiple benefits after cochlear implantation (CI), such as tinnitus suppression, speech perception, and sound localization. The first single-unit speech processor, the RONDO, was launched recently. Both the RONDO and the well-known behind-the-ear (BTE) speech processor work on the same audio processor platform. However, in contrast to the BTE, the microphone placement on the RONDO is different. The aim of this study was to evaluate the hearing performances using the BTE speech processor versus using the single-unit speech processor. Subjective and objective outcomes in SSD CI patients with a BTE speech processor and a single-unit speech processor, with particular focus on spatial hearing, were compared. METHODOLOGY: Ten adults with unilateral incapacitating tinnitus resulting from ipsilateral sensorineural deafness were enrolled in the study. The mean age at enrollment in the study was 56 (standard deviation, 13) years. The subjects were cochlear implanted at a mean age of 48 (standard deviation, 14) years and had on average 8 years' experience with their CI (range, 4-11 yr). At the first test interval (T0), testing was conducted using the subject's BTE speech processor, with which they were already familiar. Aided free-field audiometry, speech reception in noise, and sound localization testing were performed. Self-administered questionnaires on subjective evaluation consisted of HISQUI-NL, SSQ5, SHQ, and a Visual Analogue Scale to assess tinnitus loudness and disturbance. All 10 subjects were upgraded to the single-unit processor and retested after 28 days (T28) with the same fitting map. At T28, an additional single-unit questionnaire was administered to determine qualitative experiences and the effect of the position of the microphone on the new speech processor. RESULTS: Equal hearing outcomes were found between the single-unit speech processor: median PTAsingle-unit (0.5, 1, 2 kHz) = 40 (range, 33-48) dB HL; median Speech Reception Threshold in noise = -1.00 (range, -8.50 to +1.00) dB SNR; median Root Mean Square Error of sound localization = 45 (range, 19-139) degrees; HISQUI = 128 (range, 106-180); SHQ = 68 (range, 45-83); SSQ5 = 6 (range, 3-9) and the BTE speech processor: median PTABTE (0.5, 1, 2 kHz) = 41 (range, 30-53) dB HL; median Speech Reception Threshold in noise = -0.25 (range, -7.00 to +4.00) dB SNR; median Root Mean Square Error of sound localization = 38 (range, 26-164) degrees; HISQUI = 144 (range, 120-183); SHQ = 56 (range, 47-85); SSQ5 = 6 (range, 3-9). The results in the condition with the single-unit speech processor were not significantly influenced by the position of the microphone. CONCLUSION: The study showed that long-term BTE speech processor SSD users are able to be upgraded to a single-unit speech processor without compromising their speech performance, aided hearing thresholds, sound localization, objective speech quality, hearing abilities, sound localization, and tinnitus reduction. Microphone position on the single-unit speech processor did not influence the outcomes measures. Moreover, after a short time of experience, 80% of the users preferred the single-unit processor.
An Initial Experience of Cochlear Implantation for Patients With Single-Sided Deafness After Prior Osseointegrated Hearing Device.
Otol Neurotol. 2014 Nov 18. [Epub ahead of print]

**Erbele ID**, **Bernstein JG**, **Schuchman GI**, **Brungart DS**, **Rivera A.**

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**OBJECTIVE:** To compare preoperative and postoperative sound localization and surgical outcomes in patients with a history of osseointegrated hearing device (OHD) placement who underwent cochlear implantation for severe to profound sensorineural hearing loss in one ear and normal cochlear function in the contralateral ear (single-sided deafness [SSD]).

**STUDY DESIGN:** Case series. **STUDY SETTING:** Tertiary care center, cochlear implant (CI) program. **PATIENTS:** Five patients with a previously placed OHD, implanted at our institution between late 2012 and late 2013, who were undergoing cochlear implantation to address SSD. Causes of their initial SSD included iatrogenic sudden sensorineural hearing loss, and perilymphatic fistula. Indications for cochlear implantation included a desire for binaural hearing, surgical treatment for tinnitus, and staging for treatment of contralateral conductive hearing loss.

**INTERVENTIONS:** Cochlear implantation; intraoperative and postoperative antibiotics. **MAIN OUTCOME MEASURES:** Accuracy of sound localization for environmental sounds presented in a mixture for three device conditions: monaurally with the acoustic hearing ear only, OHD in addition to the acoustic hearing ear, and CI in addition to the acoustic hearing ear. Complications. Continued use of CI.

**RESULTS:** Modestly improved sound localization with CI compared with monaural listening or listening with an OHD (p < 0.0001). Wound dehiscence and infection with our first two patients; none with the use of perioperative and postoperative antibiotics (three patients). Four patients continued to use their CI for at least 4 months after activation (mean, 13 mo) and expressed satisfaction with the device; one was lost to follow-up.

**CONCLUSION:** Cochlear implantation for this population of patients produced modestly improved localization accuracy, and most patients expressed satisfaction with this intervention. In this series of cochlear implantation after OHD, our first two patients had wound infection and dehiscence. We recommend perioperative and postoperative antibiotics to prevent this complication.

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A Novel Treatment for Tinnitus and Tinnitus-Related Cognitive Difficulties Using Computer-Based Cognitive Training and D-Cycloserine.


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**Importance:** Tinnitus affects more than 40 million people in the United States, and cognitive difficulties are among the most commonly associated symptoms. **Objective:** To test the feasibility and preliminarily the effectiveness of using a putative neuroplasticity-enhancing drug, D-cycloserine, to facilitate a computer-assisted CT program for improving tinnitus bother and related cognitive difficulties.

**Design, Setting, and Participants:** Double-blind, randomized clinical trial at an outpatient academic medical center of 34 participants aged 35 to 65 years with subjective, unilateral or bilateral, nonpulsatile tinnitus of at least 6 months' duration. Interventions: Five weeks of twice-weekly computer-based CT with either 250 mg D-cycloserine or placebo orally prior to computer CT sessions. **Main Outcomes and Measures:** Difference in the change in Tinnitus Functional Index (TFI) score between the 2 groups.

**Results:** After excluding 1 participant lost to follow-up, 1 who withdrew, 1 who did not complete 90% of sessions, and 1 outlier, 30 participants were included in the analysis. The D-cycloserine plus CT group showed a significant improvement in median TFI score (-5.8 [95% CI, -9.4 to -1.1]) and self-reported cognitive deficits (-4.5 [95% CI, -11.5 to -1.1]), but the placebo group did not (-1.0 [95% CI, -11.7 to 4.9] and -2.0 [95% CI, -5.1 to 2.0], respectively). After controlling for age and duration of tinnitus, there was no significant difference in TFI score change between the 2 groups (P = .41). After confounders were controlled for, the D-cycloserine...
group demonstrated a significantly greater improvement in self-reported cognitive deficits as compared with the placebo group (P = .03). No serious adverse events were reported. Conclusions and Relevance: Use of a computer-based CT program with a putative neuroplasticity-sensitizing drug, D-cycloserine, was feasible and well tolerated. With the limited sample size, the adjuvant use of D-cycloserine was no more effective than placebo at improving tinnitus bother. The finding that D-cycloserine use was more effective than placebo at improving self-reported cognitive difficulties could be important given the high rate of concern for cognitive deficits in patients with tinnitus. D-cycloserine and other putative neuroplasticity-facilitating agents could be investigated in the future as a strategy to enhance neuroplasticity-based tinnitus treatments. Trial Registration: clinicaltrials.gov Identifier: NCT01550796. Free full text.

Inhibition-induced plasticity in tinnitus patients after repetitive exposure to tailor-made notched music.

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OBJECTIVE: Notch-filtered music has been shown to induce frequency-specific inhibition. Here, we investigated which cortical structures are affected by tailor-made notched music (TMNM) in tinnitus patients and how this inhibition-induced plasticity develops over time. METHODS: Nine subjects suffering from chronic tonal tinnitus listened to music passing through a notch-filter centered at the patient's individual tinnitus frequency (TMNM) for three hours on three consecutive days. Before and after each listening session, a tone at the tinnitus frequency and a control tone of 500Hz were presented in the magnetoencephalograph. Subjective tinnitus loudness was measured via visual analog scales. RESULTS: TMNM exposure reduced subjective tinnitus loudness and neural activity evoked by the tinnitus tone in temporal, parietal and frontal regions within the N1m time interval. Reduction of temporal and frontal activation correlated significantly with tinnitus loudness decline. Reduction of tinnitus related neural activity persisted and accumulated over three days. CONCLUSIONS: Inhibition-induced plasticity occurs in a cortical network, known to be crucial for tinnitus perception. This cortical reorganization evolves fast and accumulates across sessions. SIGNIFICANCE: This study extends previous work on inhibition-induced plasticity, as it demonstrates the involvement of parietal and frontal areas and discovers a cumulative effect of cortical reorganization in tinnitus patients. Copyright © 2014 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.
VII Brain Stimulation

**Transcutaneous Vagus Nerve Stimulation Modulates Tinnitus-Related Beta- and Gamma-Band Activity.**
Ear Hear. 2014 Nov 26. [Epub ahead of print]

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OBJECTIVES: The ability of a treatment method to interfere with tinnitus-related neural activity patterns, such as cortical gamma rhythms, has been suggested to indicate its potential in relieving tinnitus. Therapeutic modulation of gamma-band oscillations with vagus nerve stimulation has been recently reported in epileptic patients. The aim of this study was to investigate the effects of transcutaneous vagus nerve stimulation (tVNS) on neural oscillatory patterns. DESIGN: We calculated the power spectral density and synchrony of magnetoencephalography recordings during auditory stimulation in seven tinnitus patients and eight normal-hearing control subjects. Comparisons between subject groups were performed to reveal electrophysiological markers of tinnitus. tVNS-specific effects within each group were studied by comparing recording blocks with and without tVNS. We also investigated the correlation of each measure with individual ratings of tinnitus distress, as measured by the tinnitus handicap inventory questionnaire. RESULTS: Tinnitus patients differed from controls in the baseline condition (no tVNS applied), measured by both cortical oscillatory power and synchronization, particularly at beta and gamma frequencies. Importantly, we found tVNS-induced changes in synchrony, correlating strongly with tinnitus handicap inventory scores, at whole-head beta-band (r = -0.857, p = 0.007), whole-head gamma-band (r = -0.952, p = 0.0003), and frontal gamma-band (r = -0.952, p = 0.0003). CONCLUSIONS: We conclude that tVNS was successful in modulating tinnitus-related beta- and gamma-band activity and thus could have potential as a treatment method for tinnitus.
VIII Behavioral Therapy

Formative evaluation of a multimedia self-administered computerized hearing loss prevention program.

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Objective: To determine which features make a computer-based hearing health education intervention effective, easy to use, and enjoyable. The study examined which features of a multimedia self-administered computerized hearing loss prevention program, developed by the National Center for Rehabilitative Auditory Research (referred to as the NCRAR-HLPP), users liked and disliked, and the reasons why.

Design: A formative evaluation was conducted in which participants completed a questionnaire to assess knowledge and attitudes towards hearing and hearing loss prevention, used the NCRAR-HLPP, completed the questionnaire for a second time, and were interviewed to learn their opinions about the NCRAR-HLPP.

Study sample: Twenty-five male and four female Veterans recruited from the Portland VA Medical Center who were aged between 25 and 65 years.

Results: Participants reported that using the NCRAR-HLPP was a positive experience. Ease of use, multimedia content, personal relevance, and use of emotion were positive features of the program. The questionnaire showed increased knowledge and improved attitude scores following use of the program.

Conclusion: This formative evaluation showed changes designed to target user preferences and improve user instructions will be made in future versions of the program.

Three Years Later: Report on the State of Well-Being of Patients with Chronic Tinnitus Who Underwent Modified Tinnitus Retraining Therapy.

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Successful management of patients with chronic tinnitus is an important health issue. One of the tinnitus management strategies used at our Tinnitus Center is a combination of tinnitus retraining therapy (TRT) with physiotherapy and psychological management [called modified TRT (MTRT)]. We have used this type of management for over a decade and have described the protocol in detail elsewhere. In the present study, we wanted to determine the effect of MTRT on the well-being of tinnitus patients 3 years after treatment onset. One hundred and thirty patients with chronic tinnitus were assessed using psychometric instruments immediately before 7-day MTRT, immediately after the therapy and 3 years later. Patients with very severe tinnitus-related distress associated with major depression and a risk of suicide were excluded from this study. MTRT resulted in a sustained reduction of tinnitus-related distress. Moreover, the quality of life of patients had increased, as assessed by a separate questionnaire. The effect of MTRT was influenced by the degree of tinnitus-related distress and by the patients' age, the latter being gender dependent. Hearing loss and tinnitus duration had only a minor influence on the therapeutic effect. Taken together, we report a positive change in the state of well-being of patients with chronic tinnitus measurable with various psychometric instruments 3 years after the onset of MTRT. © 2014 S. Karger AG, Basel.

Theodoroff SM1, Schuette A2, Griest S1, Henry JA1.

1 Veterans Affairs (VA) Rehabilitation Research and Development Service, National Center for Rehabilitative Auditory Research, VA Medical Center, Portland, OR; Department of Otolaryngology/Head and Neck Surgery, Oregon Health & Science University, Portland, OR.

BACKGROUND: Little is known about patient factors that might influence outcomes of tinnitus interventions. Determining such factors would offer insights into why some individuals benefit from tinnitus intervention whereas others do not. PURPOSE: The purpose of this study was to evaluate selected patient factors that may be associated with outcomes of tinnitus intervention. Factors studied include demographics, tinnitus characteristics, psychoacoustic tinnitus measures, audiometric data, and overall physical/emotional health status. RESEARCH DESIGN: A retrospective analysis was performed on data obtained from a controlled clinical study that compared factors associated with tinnitus relief after tinnitus masking and tinnitus retraining therapy. STUDY SAMPLE: A total of 126 military veterans participated in this controlled clinical study. Of these, 89 completed outcome measures at both baseline and 12 mo and were included in the present analysis. DATA COLLECTION AND ANALYSIS: A "responder" to intervention was identified as having a decrease (improvement) of 20 or more points on the Tinnitus Handicap Inventory between baseline and 12 mo. A "nonresponder" did not achieve a 20-point improvement on the Tinnitus Handicap Inventory. Individual patient factors were examined using independent t-tests or χ² analysis. A logistic regression model was used to determine how well each factor predicted treatment outcome (responder or nonresponder) while controlling for each of the other factors. RESULTS: Five patient factors were significantly different (p ≤ 0.05) between responders and nonresponders. Responders tended to (1) be younger in age; (2) have better low-frequency hearing sensitivity; (3) have greater problems with overall hearing; (4) be more likely to have tinnitus for shorter durations; and (5) perceive their tinnitus to be located "in the head" versus "in the ears." A logistic regression was then performed to determine how well each factor predicted the treatment outcome (responder versus nonresponder) while controlling for each of the other factors. RESULTS from the logistic regression revealed two of the five factors, localization of tinnitus and self-report of hearing problems, to be statistically significant. CONCLUSIONS: Examining the association of individual patient factors to a specific tinnitus intervention yielded several significant findings. Although these findings are not definitive, they reveal the capability that exists to perform these kinds of analyses to investigate relationships between individual patient characteristics and outcomes of intervention for tinnitus. Prospective research using systematic approaches is needed to identify these relationships that would contribute toward the ability to differentially predict outcomes of various tinnitus interventions. Obtaining this information would lead to more targeted therapy and ultimately more effective intervention. American Academy of Audiology.
Clinical efficacy of tinnitus retraining therapy and cognitive behavioural therapy in the treatment of subjective tinnitus: a systematic review.
J Laryngol Otol. 2014 Nov 24;1-6. [Epub ahead of print]

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Objective: This study aimed to compare the outcomes of two frequently employed interventions for the management of tinnitus: tinnitus retraining therapy and cognitive behavioural therapy. Method: A systematic review of literature published up to and including February 2013 was performed. Only randomised control trials and studies involving only human participants were included. Results: Nine high-quality studies evaluating the efficacy of tinnitus retraining therapy and cognitive behavioural therapy were identified. Of these, eight assessed cognitive behavioural therapy relative to a no-treatment control and one compared tinnitus retraining therapy to tinnitus masking therapy. Each study used a variety of standardised and validated questionnaires. Outcome measures were heterogeneous, but both therapies resulted in significant improvements in quality of life scores. Depression scores improved with cognitive behavioural therapy. Conclusion: Both cognitive behavioural therapy and tinnitus retraining therapy are effective for tinnitus, with neither therapy being demonstrably superior. Further research using standardised, validated questionnaires is needed so that objective comparisons can be made.

The Tinnitus Retraining Therapy Trial (TRTT): study protocol for a randomized controlled trial.


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BACKGROUND: Subjective tinnitus is the perception of sound in the absence of a corresponding external sound for which there is no known medical etiology. For a minority of individuals with tinnitus, the condition impacts their ability to lead a normal lifestyle and is severely debilitating. There is no known cure for tinnitus, so current therapy focuses on reducing the effect of tinnitus on the patient's quality of life. Tinnitus retraining therapy (TRT) uses non-psychiatric tinnitus-specific educational counseling and sound therapy in a habituation-based protocol to reduce the patient's tinnitus-evoked negative reaction to, and awareness of, the tinnitus, with the ultimate goal of reducing the tinnitus impact on the patient's quality of life. Some studies support the efficacy of TRT, but no trial to date has compared TRT with the current standard of care or evaluated the separate contributions of TRT counseling and sound therapy. The Tinnitus Retraining Therapy Trial (TRTT) is a randomized, double-blind, placebo-controlled, multicenter trial for individuals with intolerable tinnitus. METHODS/DESIGN: The TRTT is enrolling active-duty and retired military personnel and their dependents with functionally adequate hearing sensitivity and severe tinnitus at US Air Force, Navy, and Army medical centers. Eligible study participants are randomized to TRT, partial TRT, or standard care to determine the efficacy of TRT and its components (TRT counseling and sound therapy). The primary outcome is change in score on the Tinnitus Questionnaire assessed longitudinally between baseline and follow-up (3, 6, 12, and 18 months following treatment). Secondary outcomes include subscale score changes in the Tinnitus Questionnaire, overall and subscale score changes in the Tinnitus Functional Index and Tinnitus Handicap Inventory, and change in the visual analog scale of the TRT Interview Form. Audiological outcomes include tinnitus pitch and loudness match and measures of loudness discomfort levels. The incidence of depression as a safety measure is assessed at each visit using the Beck Depression Inventory Fast Screen. TRIAL REGISTRATION: Clinicaltrials.gov NCT01177137. Free Article.
IX Somatic Tinnitus

Cervical Spine Dysfunctions in Patients with Chronic Subjective Tinnitus.
Otol Neurotol. 2014 Nov 20. [Epub ahead of print]

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OBJECTIVE: To assess, characterize, and quantify cervical spine dysfunction in patients with cervicogenic somatic tinnitus (CST) compared to patients suffering from other forms of chronic subjective non-pulsatile tinnitus. STUDY DESIGN: Cross-sectional study. SETTING: Tertiary referral center. PATIENTS: Consecutive adult patients suffering from chronic subjective non-pulsatile tinnitus were included. Exclusion criteria: Ménière’s disease, middle ear pathology, intracranial pathology, cervical spine surgery, whiplash trauma, temporomandibular dysfunction. INTERVENTION: Assessment comprises medical history, ENT examination with micro-otoscopy, audiometry, tinnitus assessment, temporomandibular and cervical spine investigation, and brain MRI. Patients were classified into CST and non-CST population. Cervical spine dysfunction was investigated using the Neck Bournemouth Questionnaire (NBQ) and clinical tests of the cervical spine, containing range of motion, pain provocation (adapted Spurling test, AST), and muscle tests (tenderness via trigger points, strength and endurance of deep neck flexors). MAIN OUTCOME MEASURES: Between-group analysis was performed. The prevalence of cervical spine dysfunction was described for the total group and for CST and non-CST groups. RESULTS: In total, 87 patients were included, of which 37 (43%) were diagnosed with CST. In comparison with the non-CST group, the CST group demonstrated a significantly higher prevalence of cervical spine dysfunction. In the CST group, 68% had a positive manual rotation test, 47% a positive AST, 49% a positive score on both, and 81% had positive trigger points. In the non-CST group, these percentages were 36, 18, 10, and 50%, respectively. Furthermore, 79% of the CST group had a positive NBQ versus 40% in the non-CST group. Significant differences between the both groups were found for all the aforementioned variables (all p <0.005). CONCLUSIONS: Although a higher prevalence of neck dysfunction was found in the CST group, neck dysfunction is often in non-CST patients.

Cervical Epidural Steroid Injection for Refractory Somatic Tinnitus.

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Somatic tinnitus is a common disorder, yet few treatments described in the literature have demonstrated strong efficacy. We report a case of a 61-year-old male with refractory somatic tinnitus, temporally related to a prior bacterial otitis media, wherein auditory symptoms were successfully treated with cervical epidural injections of long-acting corticosteroid. We discuss the proposed mechanism of somatic tinnitus and the means by which neuraxial steroids may inhibit somatic tinnitus symptoms. © 2014 World Institute of Pain.
Chronic neck pain: making the connection between capsular ligament laxity and cervical instability.

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The use of conventional modalities for chronic neck pain remains debatable, primarily because most treatments have had limited success. We conducted a review of the literature published up to December 2013 on the diagnostic and treatment modalities of disorders related to chronic neck pain and concluded that, despite providing temporary relief of symptoms, these treatments do not address the specific problems of healing and are not likely to offer long-term cures. The objectives of this narrative review are to provide an overview of chronic neck pain as it relates to cervical instability, to describe the anatomical features of the cervical spine and the impact of capsular ligament laxity, to discuss the disorders causing chronic neck pain and their current treatments, and lastly, to present prolotherapy as a viable treatment option that heals injured ligaments, restores stability to the spine, and resolves chronic neck pain. The capsular ligaments are the main stabilizing structures of the facet joints in the cervical spine and have been implicated as a major source of chronic neck pain. Chronic neck pain often reflects a state of instability in the cervical spine and is a symptom common to a number of conditions described herein, including disc herniation, cervical spondylosis, whiplash injury and whiplash associated disorder, postconcussion syndrome, vertebrobasilar insufficiency, and Barré-Liéou syndrome. When the capsular ligaments are injured, they become elongated and exhibit laxity, which causes excessive movement of the cervical vertebrae. In the upper cervical spine (C0-C2), this can cause a number of other symptoms including, but not limited to, nerve irritation and vertebrobasilar insufficiency with associated vertigo, tinnitus, dizziness, facial pain, arm pain, and migraine headaches. In the lower cervical spine (C3-C7), this can cause muscle spasms, crepitation, and/or paresthesia in addition to chronic neck pain. In either case, the presence of excessive motion between two adjacent cervical vertebrae and these associated symptoms is described as cervical instability. Therefore, we propose that in many cases of chronic neck pain, the cause may be underlying joint instability due to capsular ligament laxity. Currently, curative treatment options for this type of cervical instability are inconclusive and inadequate. Based on clinical studies and experience with patients who have visited our chronic pain clinic with complaints of chronic neck pain, we contend that prolotherapy offers a potentially curative treatment option for chronic neck pain related to capsular ligament laxity and underlying cervical instability. Free PMC Article.

X Surgical Treatment

Endovascular treatment of symptomatic vestibular aqueduct dehiscence as a result of jugular bulb abnormalities.

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A new endovascular treatment consisting of stent-assisted coil implantation is described for jugular bulb abnormalities causing symptomatic vestibular aqueduct dehiscence. Three patients presenting with vertigo associated with pulsatile tinnitus or hearing loss were treated. This technique cured the vertigo and pulsatile tinnitus in all patients and preserved normal cerebral venous drainage with no side effects. Copyright © 2014 SIR. Published by Elsevier Inc. All rights reserved.
Greater occipital nerve block for postdural puncture headache (PDPH): A prospective audit of a modified guideline for the management of PDPH and review of the literature.

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STUDY OBJECTIVE: To perform a prospective audit of the modified guideline for the management postdural puncture headache (PDPH) and present the results at 6 months. DESIGN: Prospective single-center audit. SETTING: University hospital. PATIENTS: 24 adult, ASA physical status 1, 2, and 3 patients presenting with PDPH in both the obstetric and nonobstetric setting. INTERVENTIONS: Epidural blood patch (EBP) and bilateral greater occipital nerve blocks (GONB) were administered. MEASUREMENTS: Headache scores, nausea scores, presence and severity of neck stiffness, tinnitus, photophobia, and any complications with either technique. RESULTS: 24 patients were audited. Nineteen patients failed conservative management and were offered both GONB and EBP. One patient chose the EBP and was successfully treated. Of the 18 patients who received the GONB, headache resolved in 12 patients (66%). Six patients had a partial response to nerve block and were treated with an EBP. CONCLUSION: Greater occipital nerve block with dexamethasone may have a role in the management of patients presenting with PDPH, who have failed conservative management. We present the results of our prospective audit and review the literature on GONB in the management of PDPH. Copyright © 2014 Elsevier Inc. All rights reserved.

Gamma Knife radiosurgery for vestibular schwannoma: clinical results at long-term follow-up in a series of 379 patients.

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Object Since the 1990s, Gamma Knife radiosurgery (GKRS) has become the first-line treatment option for small- to medium-size vestibular schwannomas (VSs), especially in patients without mass effect-related symptoms and with functional hearing. The aim of this study was to assess the safety and efficacy of GKRS, in terms of tumor control, hearing preservation, and complications, in a series of 379 consecutive patients treated for VS. Methods Of 523 patients treated at the authors’ institution for VS between 2001 and 2010, the authors included 379 who underwent GKRS as the primary treatment. These patients were not affected by Type 2 neurofibromatosis and had clinical follow-up of at least 36 months. Clinical follow-up (mean and median 75.7 and 69.5 months, respectively) was performed for all patients, whereas audiometric and quantitative radiological follow-up examinations were obtained for only 153 and 219 patients, respectively. The patients’ ages ranged from 23 to 85 years (mean 59 years). The mean tumor volume was 1.94 ± 2.2 cm(3) (median 1.2 cm(3), range 0.013-14.3 cm(3)), and the median margin dose was 13 Gy (range 11-15 Gy). Parameters considered as determinants of the clinical outcome were long-term tumor control, hearing preservation, and complications. A statistical analysis was performed to correlate clinical outcomes with the radiological features of the tumor, dose-planning parameters, and patient characteristics. Results Control of the tumor with GKRS was achieved in 97.1% of the patients. In 82.7% of the patients, the tumor volume had decreased at the last follow-up, with a mean relative reduction of 34.1%. The rate of complications was very low, with most consisting of a transient worsening of preexisting symptoms. Patients who had vertigo, balance disorders, or facial or trigeminal impairment usually experienced a complete or at least significant symptom relief after treatment. However, no significant improvement was observed in patients previously reporting tinnitus. The overall rate of preservation of functional hearing at the long-term follow-up was 49%; in patients with hearing classified as Gardner-Robertson (GR) Class I, this value was 71% and reached 93% among cases of GR Class I hearing in patients younger than 55 years. Conclusions Gamma Knife radiosurgery is a safe and effective treatment for VS, achieving tumor control in 97.1% of cases and
resulting in a very low morbidity rate. Younger GR Class I patients had a significantly higher probability of retaining functional hearing even at the 10-year follow-up; for this reason, the time between symptom onset, diagnosis, and treatment should be shortened to achieve better outcomes in functional hearing preservation.

**Gamma Knife surgery for facial nerve schwannomas.**


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Object The aim of this study was to evaluate the tumor control rate and functional outcomes after Gamma Knife surgery (GKS) among patients with a facial nerve schwannoma. Methods The authors reviewed the radiological data and clinical records for 14 patients who had consecutively undergone GKS for a facial nerve schwannoma. Before GKS, 12 patients had facial palsy, 7 patients had hearing disturbance, and 5 patients had undergone partial or subtotal tumor resection. The mean and median tumor volumes were 3707 mm(3) and 3000 mm(3), respectively (range 117-10,100 mm(3)). The mean tumor margin dose was 13.2 Gy (range 12-15 Gy), and the mean maximum tumor dose was 26.4 Gy (range 24-30 Gy). The mean follow-up period was 80.7 months (range 2-170 months). Results Control of tumor growth was achieved in all 12 (100%) patients who were followed up for longer than 2 years. After GKS, facial nerve function improved in 2 patients, remained unchanged in 9 patients, and worsened in 3 patients. All patients who had had serviceable hearing at the preliminary examination maintained their hearing at a useful level after GKS. Other than mild tinnitus reported by 3 patients, no other major complications developed. Conclusions GKS for facial nerve schwannomas resulted in excellent tumor control rates and functional outcomes. GKS might be a good primary treatment option for patients with a small- to medium-sized facial nerve schwannoma when facial nerve function and hearing are relatively preserved.

**Endolymphatic Duct Blockage: A Randomized Controlled Trial of a Novel Surgical Technique for Ménière’s Disease Treatment.**


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OBJECTIVES: To compare the effectiveness of the endolymphatic duct blockage (EDB) and the endolymphatic sac decompression (ESD) to control Ménière’s disease symptoms and to evaluate their effect on hearing level. STUDY DESIGN: Prospective nonblinded randomized study. SETTING: Tertiary medical center. SUBJECTS AND METHODS: Fifty-seven patients affected by a refractory Ménière’s disease were included out of which 22 underwent an ESD and 35 underwent an EDB. Five periods of follow-up were considered: 0 to 1 week, 1 week to 6 months, 6 to 12 months, 12 to 18 months, and 18 to 24 months. Mean outcome measurements consisted of vertigo control, tinnitus, aural fullness, instability, and hearing level. Hearing level was evaluated using pure-tone average (PTA) and speech discrimination score (SDS). RESULTS: There was no significant difference between the 2 groups in the number of vertigo spells per months preoperatively (P = .153). Twenty-four months postoperatively, 96.5% of the EDB group had achieved a complete control of vertigo spells against 37.5% of the ESD group with a statistically significant difference (P = .002). There was a better control of tinnitus and aural fullness with EDB (P = .021 and P = .014, respectively). There was not statistically significant difference in hearing level preoperatively (P = .976) and 24 months postoperatively (P = .287) between the 2 groups. Hearing level was preserved in each group with no significant difference between the preoperative and the postoperative levels (P > .05). CONCLUSION: EDB is more effective than the traditional ESD in controlling the symptoms of Ménière’s disease. It is a novel surgical technique with promising results for a complete treatment of Ménière’s disease. There are no significant complications or adverse effect. © American Academy of Otolaryngology—Head and Neck Surgery Foundation 2014.
Hearing Status in Pediatric Renal Transplant Recipients.

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OBJECTIVES: Renal transplant provides a long-term survival. Hearing impairment is a major factor in subjective health status. Status of hearing and the cause of hearing impairment in the pediatric renal transplant group have not been evaluated. Here, we studied to evaluate hearing status in pediatric renal transplant patients and to determine the factors that cause hearing impairment. MATERIALS and METHODS: Twenty-seven pediatric renal transplant recipients were investigated. All patients underwent audiologic assessment by means of pure-tone audiometry. The factors on hearing impairment were performed. RESULTS: Sensorineural hearing impairment was found in 17 patients. There was marked hearing impairment for the higher frequencies between 4000 and 8000 Hz. Sudden hearing loss developed in 2 patients, 1 of them had tinnitus. Decrease of speech understanding was found in 8 patients. The cyclosporine level was significantly high in patients with hearing impairment compared with group without hearing impairment. Cyclosporine levels also were found to be statistically significantly high when compared with the group with decrease of speech understanding and the group without decrease of speech understanding. Similar relations cannot be found between tacrolimus levels and hearing impairment and speech understanding. CONCLUSIONS: Sensorineural hearing impairment prevalence was high in pediatric renal transplant recipients when compared with the general population of children. Cyclosporine may be responsible for causing hearing impairment after renal transplant. We suggest that this effect is a dose-dependent toxicity.

Efficacy and Safety of Semicircular Canal Occlusion for Intractable Horizontal Semicircular Benign Paroxysmal Positional Vertigo.


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BACKGROUND: Some studies have suggested that semicircular canal occlusion is effective and safe for treating intractable posterior semicircular benign paroxysmal positional vertigo (PSC-BPPV), and adverse effects of canal occlusions for intractable horizontal semicircular BPPV (HSC-BPPV) were rarely reported. The aim of this study was to retrospectively discuss the efficacy of semicircular canal occlusion for intractable HSC-BPPV with at least 2 years of follow-up. METHODS: From 2000 to 2011, 3 female patients (average age = 60 ± 6.9 years), with a diagnosis of HSC-BPPV refractory to head-shake and barbecue roll maneuver, underwent semicircular canal occlusion treatment in our hospital. The supine roll test was performed to diagnose HSC-BPPV and evaluate the treatment efficacy. RESULTS: All patients with intractable HSC-BPPV had complete resolution of their positional vertigo after semicircular canal occlusion with a negative supine roll test. All patients reported transient postoperative disequilibrium, nausea, and vomiting, which resolved within 2 weeks. In addition, 1 patient (33.3%) had transient tinnitus, which resolved after 4 months. There were no other significant long-term complications. CONCLUSION: Semicircular canal occlusion appears to be a safe and well-tolerated treatment modality for intractable HSC-BPPV. However, further studies with large sample sizes are needed to confirm our conclusion. © The Author(s) 2014.
XI Holistic

No publications this time.

XII Review

The Application of Electro- and Magneto-Encephalography in Tinnitus Research - Methods and Interpretations.

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In recent years, there has been a significant increase in the use of electroencephalography (EEG) and magnetoencephalography (MEG) to investigate changes in oscillatory brain activity associated with tinnitus with many conflicting results. Current view of the underlying mechanism of tinnitus is that it results from changes in brain activity in various structures of the brain as a consequence of sensory deprivation. This in turn gives rise to increased spontaneous activity and/or synchrony in the auditory centers but also involves modulation from non-auditory processes from structures of the limbic and paralimbic system. Some of the neural changes associated with tinnitus may be assessed non-invasively in human beings with MEG and EEG (M/EEG) in ways, which are superior to animal studies and other non-invasive imaging techniques. However, both MEG and EEG have their limitations and research results can be misinterpreted without appropriate consideration of these limitations. In this article, I intend to provide a brief review of these techniques, describe what the recorded signals reflect in terms of the underlying neural activity, and their strengths and limitations. I also discuss some pertinent methodological issues involved in tinnitus-related studies and conclude with suggestions to minimize possible discrepancies between results. The overall message is that while MEG and EEG are extremely useful techniques, the interpretation of results from tinnitus studies requires much caution given the individual variability in oscillatory activity and the limits of these techniques. Free Article.

Clinical efficacy of tinnitus retraining therapy and cognitive behavioural therapy in the treatment of subjective tinnitus: a systematic review.

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Objective: This study aimed to compare the outcomes of two frequently employed interventions for the management of tinnitus: tinnitus retraining therapy and cognitive behavioural therapy. Method: A systematic review of literature published up to and including February 2013 was performed. Only randomised control trials and studies involving only human participants were included. Results: Nine high-quality studies evaluating the efficacy of tinnitus retraining therapy and cognitive behavioural therapy were identified. Of these, eight assessed cognitive behavioural therapy relative to a no-treatment control and one compared tinnitus retraining therapy to tinnitus masking therapy. Each study used a variety of standardised and validated questionnaires. Outcome measures were heterogeneous, but both therapies resulted in significant improvements in quality of life scores. Depression scores improved with cognitive behavioural therapy. Conclusion: Both cognitive behavioural therapy and tinnitus retraining therapy are effective for tinnitus, with neither therapy being demonstrably superior. Further research using standardised, validated questionnaires is needed so that objective comparisons can be made.
Dural arteriovenous fistulas of the hypoglossal canal: systematic review on imaging anatomy, clinical findings, and endovascular management.

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Dural arteriovenous fistulas (DAVFs) of the hypoglossal canal (HCDAVFs) are rare and display a complex angiographic anatomy. Hitherto, they have been referred to as various entities (for example, "marginal sinus DAVFs") solely described in case reports or small series. In this in-depth review of HCDAVF, the authors describe clinical and imaging findings, as well as treatment strategies and subsequent outcomes, based on a systematic literature review supplemented by their own cases (120 cases total). Further, the involved craniocervical venous anatomy with variable venous anastomoses is summarized. Hypoglossal canal DAVFs consist of a fistulous pouch involving the anterior condylar confluence and/or anterior condylar vein with a variable intraosseous component. Three major types of venous drainage are associated with distinct clinical patterns: Type 1, with anterograde drainage (62.5%), mostly presents with pulsatile tinnitus; Type 2, with retrograde drainage to the cavernous sinus and/or orbital veins (23.3%), is associated with ocular symptoms and may mimic cavernous sinus DAVF; and Type 3, with cortical and/or perimedullary drainage (14.2%), presents with either hemorrhage or cervical myelopathy. For Types 1 and 2 HCDAVF, transvenous embolization demonstrates high safety and efficacy (2.9% morbidity, 92.7% total occlusion). Understanding the complex venous anatomy is crucial for planning alternative approaches if standard transjugular access is impossible. Transarterial embolization or surgical disconnection (morbidity 13.3%-16.7%) should be reserved for Type 3 HCDAVFs or lesions with poor venous access. A conservative strategy could be appropriate in Type 1 HCDAVF for which spontaneous regression (5.8%) may be observed. KEYWORDS: ACC = anterior condylar confluence; ACV = anterior condylar vein; AIVVP = anterior internal vertebral venous plexus; CTA = CT angiography; DAVF = dural arteriovenous fistula; DSA = digital subtraction angiography; EVT = endovascular treatment; HCDAVF = hypoglossal canal DAVF; ICAVP = internal carotid artery venous plexus (of Rektorzik); IJV = internal jugular vein; IPS = inferior petrosal sinus; LCV = lateral condylar vein; MEV = mastoid emissary vein; MRA = magnetic resonance angiography; NBCA = N-butyl cyanoacrylate; PCV = posterior condylar vein; PT = pulse-synchronous tinnitus; PVA = polyvinyl alcohol; SOV = superior ophthalmic vein; TAE = transarterial embolization; TOF = time-of-flight; TVE = transvenous embolization; VA = vertebral artery; VAVP = vertebral artery venous plexus; VVP = vertebral venous plexus; anterior condylar confluence; anterior condylar vein; dural arteriovenous fistula; endovascular therapy; hypoglossal canal; skull base vein; transvenous embolization; vascular disorders
Central gain control in tinnitus and hyperacusis.

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Sensorineural hearing loss induced by noise or ototoxic drug exposure reduces the neural activity transmitted from the cochlea to the central auditory system. Despite a reduced cochlear output, neural activity from more central auditory structures is paradoxically enhanced at suprathreshold intensities. This compensatory increase in the central auditory activity in response to the loss of sensory input is referred to as central gain enhancement. Enhanced central gain is hypothesized to be a potential mechanism that gives rise to hyperacusis and tinnitus, two debilitating auditory perceptual disorders that afflict millions of individuals. This review will examine the evidence for gain enhancement in the central auditory system in response to cochlear damage. Further, it will address the potential cellular and molecular mechanisms underlying this enhancement and discuss the contribution of central gain enhancement to tinnitus and hyperacusis. Current evidence suggests that multiple mechanisms with distinct temporal and spectral profiles are likely to contribute to central gain enhancement. Dissecting the contributions of these different mechanisms at different levels of the central auditory system is essential for elucidating the role of central gain enhancement in tinnitus and hyperacusis and, most importantly, the development of novel treatments for these disorders. Free PMC Article.

Acupuncture in the treatment of tinnitus: a systematic review and meta-analysis.
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This study aimed at a systematic review and meta-analysis of all available randomized controlled trials (RCTs) using acupuncture to treat tinnitus. Five electronic databases, in both English and Chinese, were searched. All studies in our review and meta-analysis included parallel RCTs of tinnitus patients which compared subjects receiving acupuncture (or its other forms, such as electroacupuncture) to subjects receiving no treatment, sham treatment, drugs or basic medical therapy. Data from the articles were validated and extracted using a predefined data extraction form. Nearly all of Chinese studies reported positive results, while most of English studies reported negative results. Analysis of the combined data found that the acupuncture treatments seemed to provide some advantages over conventional therapies for tinnitus. It had difference in acupuncture points and sessions between Chinese studies and English studies. Methodological flaws were also found in many of the RCTs, especially in Chinese studies. The results of this review suggest that acupuncture therapy may offer subjective benefit to some tinnitus patients. Acupuncture points and sessions used in Chinese studies may be more appropriate, whereas these studies have many methodological flaws and risk bias, which prevents us making a definitive conclusion.
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INTRODUCTION: Up to 18% of people in industrialised societies are mildly affected by chronic tinnitus, and 0.5% report tinnitus having a severe effect on their daily life. Tinnitus can be associated with hearing loss, acoustic neuromas, drug toxicity, ear diseases, and depression. Tinnitus can last for many years, and can interfere with sleep and concentration. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments for chronic tinnitus? We searched: Medline, Embase, The Cochrane Library, and other important databases up to November 2013 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 33 studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: acamprosate, acupuncture, antidepressant drugs, benzodiazepines, carbamazepine, electromagnetic stimulation, ginkgo biloba, hearing aids, hypnosis, psychotherapy, tinnitus-masking devices, and cognitive behavioural therapy plus tinnitus-masking device (tinnitus retraining therapy).

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Ten years ago, animal models of noise-induced hearing loss predicted three cortical neural correlates of tinnitus resulting from noise-induced hearing loss: increased spontaneous firing rates, increased neural synchrony, and reorganization of tonotopic maps. Salicylate also induces tinnitus, however, the cortical correlates were reduced spontaneous firing rates, unchanged neural synchrony but some change to the tonotopic map. In both conditions increased central gain, potentially a correlate of hyperacusis, was found. Behavioral animal models suggested that tinnitus occurred, albeit not in all cases. The study of the neural substrates of tinnitus in humans is currently strongly based on network connectivity using either spontaneous EEG or MEG. Brain imaging combined with powerful analyses is now able to provide in excellent detail the lay out of tonotopic maps, and has shown that in people with tinnitus (and clinical normal hearing up to 8 kHz) no changes in tonotopic maps need to occur, dispensing therefore of one of the postulated neural correlates. Patients with hyperacusis and tinnitus showed increased gain, as measured using fMRI, from brainstem to cortex, whereas patients with tinnitus without hyperacusis only showed this in auditory cortex. This suggested that top down mechanisms are also needed. The open problems can be formulated by the following questions. 1) Are the neural substrates of tinnitus etiology dependent? 2) Can animal results based on single unit and local field potentials be validated in humans? 3) Can sufficient vs. necessary neural substrates for tinnitus be established. 4) What is the role of attention and stress in engraining tinnitus in memory? Copyright © 2014. Published by Elsevier B.V.
In this study literature search was performed on tinnitus guidelines and treatment. Tinnitus can be described as the perception of sound in the absence of external acoustic stimulation, and validated questionnaires, oto-neurological examination, audiometry tests, MRI and angiography are necessary as diagnostic tools. Antidepressants, melatonin and cognitive behavioural therapy have no effect on tinnitus, whereas sound generators, hearing aids and tinnitus retraining therapy show some but limited improvement. National recommendations are required to ensure a homogenous and optimum offer for all patients.

Plasticity of neural systems in tinnitus.

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Health Effects Related to Wind Turbine Noise Exposure: A Systematic Review.

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BACKGROUND: Wind turbine noise exposure and suspected health-related effects thereof have attracted substantial attention. Various symptoms such as sleep-related problems, headache, tinnitus and vertigo have been described by subjects suspected of having been exposed to wind turbine noise. OBJECTIVE: This review was conducted systematically with the purpose of identifying any reported associations between wind turbine noise exposure and suspected health-related effects. DATA SOURCES: A search of the scientific literature concerning the health-related effects of wind turbine noise was conducted on PubMed, Web of Science, Google Scholar and various other Internet sources. STUDY ELIGIBILITY CRITERIA: All studies investigating suspected health-related outcomes associated with wind turbine noise exposure were included. RESULTS: Wind turbines emit noise, including low-frequency noise, which decreases incrementally with increases in distance from the wind turbines. Likewise, evidence of a dose-response relationship between wind turbine noise linked to noise annoyance, sleep disturbance and possibly even psychological distress was present in the literature. Currently, there is no further existing statistically-significant evidence indicating any association between wind turbine noise exposure and tinnitus, hearing loss, vertigo or headache. LIMITATIONS: Selection bias and information bias of differing
magnitudes were found to be present in all current studies investigating wind turbine noise exposure and adverse health effects. Only articles published in English, German or Scandinavian languages were reviewed. CONCLUSIONS: Exposure to wind turbines does seem to increase the risk of annoyance and self-reported sleep disturbance in a dose-response relationship. There appears, though, to be a tolerable level of around LAeq of 35 dB. Of the many other claimed health effects of wind turbine noise exposure reported in the literature, however, no conclusive evidence could be found. Future studies should focus on investigations aimed at objectively demonstrating whether or not measureable health-related outcomes can be proven to fluctuate depending on exposure to wind turbines.

**Primary acquired nasolacrimal duct obstruction: is it really related to paranasal abnormalities?**


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PURPOSE: To investigate whether there is an association between primary acquired nasolacrimal duct obstruction and paranasal computed tomography (CT) findings. MATERIALS AND METHODS: The study cohort consisted of paranasal CT images from 40 patients being treated for unilateral primary nasolacrimal duct obstruction (PANDO) and the reformatted coronal temporal CT images of 71 control subjects who attended the ENT clinic with the complaint of vertigo and tinnitus. A radiologist masked to the clinical situation of participants, investigated the paranasal CT findings of the PANDO and control patients retrospectively. The side, localization, and angle of the septal deviation as well as the thickness and lateralization angle of the inferior turbinate's were recorded. Additionally maxillary and ethmoid sinusitis, concha bullosa, Agger nasi cell formation, and osteomeatal complex status were evaluated. RESULTS: No significant difference was found between the paranasal abnormality incidence in the PANDO and non-PANDO sides of the patients or the control group. Only the side of the septal deviation correlated with the side of the PANDO (p = 0.008). CONCLUSIONS: The incidence of PANDO may not be directly related to paranasal abnormalities. Further large-scale studies should be performed to clarify the relationship between paranasal abnormalities and PANDO.

**Effectiveness of De Qi during acupuncture for the treatment of tinnitus: study protocol for a randomized controlled trial.**


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BACKGROUND: Acupuncture has been used in China to treat tinnitus for a long time. There is debate as to whether or not De Qi is a key factor in achieving the efficacy of acupuncture. However, there is no sufficient evidence obtained from randomized controlled trials to confirm the role of De Qi in the treatment of acupuncture for tinnitus. This study aims to identify the effect of De Qi for patients who receive acupuncture to alleviate tinnitus by a prospective, double-blind, randomized, sham-controlled trial. METHODS AND DESIGN: This study compares two acupuncture groups (with or without manipulation) in 292 patients with a history of subjective tinnitus. The trial will be conducted in the Teaching Hospital of Chengdu University of Traditional Chinese Medicine. In the study, the patients will be randomly assigned into two groups according to a computer-generated randomization list and assessed prior to treatment. Then, they will receive 5 daily sessions of 30 minutes each time for 4 consecutive weeks and undergo a 12-week follow-up phase. The administration of acupuncture follows the guidelines for clinical research on acupuncture (WHO Regional Publication, Western Pacific Series Number 15, 1995), and is performed double-blind by physicians well-trained in acupuncture. The measures of outcome include the subjective symptoms scores
and quantitative sensations of De Qi evaluated by Visual Analog Scales (VAS) and the Chinese version of the 'modified' Massachusetts General Hospital Acupuncture Sensation Scale (C-MMASS). Furthermore, adverse events are recorded and analyzed. If any subjects are withdrawn from the trial, intention-to-treat analysis (ITT) and per-protocol (PP) analysis will be performed. DISCUSSION: The key features of this trial include the randomization procedures, large sample and the standardized protocol to evaluate De Qi qualitatively and quantitatively in the treatment of acupuncture for tinnitus. The trial will be the first study with a high evidence level in China to assess the efficacy of De Qi in the treatment of tinnitus in a randomized, double-blind, sham-controlled manner. TRIAL REGISTRATION: Chinese Clinical Trial Registry: ChiCTR-TRC-14004720 (6 May 2014). Free Article.

Cost-Effective Analysis of Unilateral Vestibular Weakness Investigation.

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OBJECTIVES: To evaluate the cost-effectiveness of obtaining a magnetic resonance imaging (MRI) in patients with abnormal electronystagmography (ENG) or videonystagmography (VNG) results. STUDY DESIGN: Retrospective chart review. SETTINGS: Academic specialty center. PATIENTS: Patients presenting with vertigo between January 1, 2010, and August 30, 2013. METHODS: Patients who fit the following abnormal criteria were included in the study: unilateral caloric weakness (≥20%), abnormal ocular motor testing, and nystagmus on positional testing. Patients with abnormal findings who then underwent MRI with gadolinium were evaluated. RESULTS: Of the 1,996 charts reviewed, there were 1,358 patients who met the inclusion criteria. The average age of these patients was 62 years (12-94 yr). The male:female ratio was approximately 1:2. Of the 1,358 patients, 253 received an MRI with the following pathologies: four vestibular schwannomas, three subcortical/periventricular white matter changes suspicious for demyelinating disease, four acute cerebellar/posterior circulation infarct, two vertebral artery narrowing, one pseudomeningocele of internal auditory canal, and two white matter changes indicative of migraines. The positive detection rate on MRI was 5.5% based on MRI findings of treatable pathologies causing vertigo. Average cost of an MRI is $1,200, thereby making the average cost of identifying a patient with a positive MRI finding $15,180. CONCLUSION: In our study, those patients with a positive MRI had a constellation of symptoms and findings (asymmetric sensorineural hearing loss, tinnitus, vertigo, and abnormal ENG/VNG). Cost-effectiveness can be improved by ordering an MRI only when clinical examination and VNG point toward a central pathology. Clinical examination and appropriate testing should be factored when considering the cost-effectiveness of obtaining an MRI in patients with abnormal ENG/VNG findings.
Bilateral muscular tinnitus due to myoclonus of extrinsic auricular muscles.

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The muscular tinnitus due to an extrinsic auricular myoclonus is an extremely rare disorder which demonstrates a semirhythmic involuntary movement of the ear. We report a 33-year-old man with clicking tinnitus caused by focal myoclonic jerks of bilateral posterior auricularis muscle and bilateral temporalis muscle. This muscular tinnitus persisted except for when he was sleeping or breath holding. His symptom responded poorly to medical therapy but was controlled by botulinum toxin type A injection under electromyography monitoring with favorable outcome. Previous reports of this condition and possible therapeutic approaches are discussed. Copyright © 2014 Elsevier Ireland Ltd. All rights reserved.

A Unique Case of Adolescent Neuroborreliosis Presenting With Multiple Cranial Neuritis and Cochlear Inflammation on Magnetic Resonance Imaging.

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BACKGROUND: Lyme disease is the most common vector-borne disease in the United States and is caused by infection with the spirochete Borrelia burgdorferi. In children, neuroborreliosis usually presents as peripheral facial nerve palsy and lymphocytic meningitis and only rarely is associated with cranial polyneuritis. PATIENT DESCRIPTION: We present a 15-year-old with tinnitus, hearing loss, and facial nerve palsy in the setting of acute, severe right arm pain and a several week history of malaise and headache. Lumbar puncture was notable for lymphocytic pleocytosis. Serologic testing demonstrated positive Lyme antibody and a positive immunoglobulin M Western blot. Immunofluorescent assay of cerebrospinal fluid was also positive for anti-Lyme immunoglobulin M. Audiologic testing revealed mixed, right-sided hearing loss. Neuroimaging demonstrated cranial polyneuritis and right-sided cochlear inflammation. The patient was treated with parenteral ceftriaxone with resolution of his symptoms at close follow-up. DISCUSSION: Neuroborreliosis with radiculopathy, lymphocytic meningitis, and cranial polyneuritis is a rare presentation of pediatric Lyme disease. Additionally, cochlear inflammation along with cranial nerve VIII inflammation may contribute to hearing loss in patients with neuroborreliosis. Copyright © 2014 Elsevier Inc. All rights reserved.
Hearing loss in a pediatric patient following cisplatin chemotherapy and subsequent exposure to excessive noise.

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Cisplatin is a commonly-used chemotherapeutic agent that is highly-effective against a variety of pediatric cancers. Unfortunately, it may lead to ototoxicity, with serious consequences on the quality of life of survivors. Patients remain at risk of progression of ototoxicity even after completion of treatment. We report the case of a medulloblastoma survivor with previously documented normal hearing, who developed significant hearing loss and tinnitus following exposure to excessive noise at a nightclub three years after completion of treatment. We highlight the importance of long-term audiological follow up and education about the increased risk of hearing loss in this population. Copyright © 2014 Elsevier Ireland Ltd. All rights reserved.

Long-term progressive deterioration of visual function after papilledema improved by embolization of a dural arteriovenous fistula in the sigmoid sinus: a case report.

Zako M, Murata K, Inukai T, Yasuda M, Iwaki M.

INTRODUCTION: It is generally believed that people affected by papilledema will not have progressive damage to their eyesight if they receive adequate medical care to treat the underlying cause of the papilledema. We present a case that appears to contradict this widely accepted belief. CASE PRESENTATION: A 53-year-old Japanese man with tinnitus visited our hospital. His initial best-corrected visual acuity in either eye was not impaired, although they both exhibited papilledema. Magnetic resonance imaging did not reveal a mass or hemorrhagic lesion in our patient's brain. Nevertheless, his best-corrected visual acuity gradually deteriorated over the following three months. Angiography demonstrated a dural arteriovenous fistula in his sigmoid sinus. After embolization therapy, the papilledema improved in both eyes. However, over the subsequent four years, his best-corrected visual acuity progressively deteriorated due to an unknown cause, despite the successful embolization of the dural arteriovenous fistula. CONCLUSION: There may be delayed onset of an unknown pathophysiology in the visual system after treatment for the underlying cause of papilledema, implying an uncertain visual prognosis for patients with this condition. Free Article.

Sudden sensorineural hearing loss as the first manifestation of chronic myeloid leukaemia: case report.

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BACKGROUND: Sudden sensorineural hearing loss rarely occurs in patients with chronic myeloid leukaemia.

CASE REPORT: We present a case report of a patient who presented with sudden sensorineural hearing loss as the first manifestation of chronic myeloid leukaemia, and review the mechanisms responsible for sudden sensorineural hearing loss in leukaemic patients. RESULTS: A 31-year-old female presented to our clinic with unilateral sudden sensorineural hearing loss and tinnitus. Pure tone audiometry revealed profound sensorineural hearing loss in the left ear at all frequencies. During an investigation into her hearing loss, the patient was found to have chronic myeloid leukaemia. CONCLUSION: Every case of sudden sensorineural hearing loss must be carefully evaluated, and haematological disorders must be considered in the differential diagnosis of sudden hearing loss.
A case of intractable suspected perilymph fistula with severe depression.

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A 68-year-old woman presented dizziness whenever she put her finger into the right ear and also complained of water-streaming tinnitus, which indicated she would have been suffering from perilymph fistula. An exploratory tympanotomy was conducted. Leakage of perilymph from the round window was suspected, although the cochlin-tomoprotein (CTP) results were negative. After the procedure, the patient's finger-induced dizziness, tinnitus, and vertigo spells disappeared completely. However, her dizzy symptom did not improve. The patient also complained of general fatigue, weight loss, and insomnia, which led us to suspect comorbid depression. Antidepressants and vestibular rehabilitation treatment resulted in a significant improvement in her dizziness. Although it is not apparent whether the patient had a perilymph fistula, this case demonstrates the importance of evaluating not only physical symptoms but also psychological comorbidity, especially when the physical symptoms are intractable despite treatment. Free PMC Article.

Bilateral Internal Auditory Canal Metastasis of Non-small Cell Lung Cancer.

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We report on a patient with brain metastasis involving bilateral internal auditory canal from non-small cell lung cancer (NSCLC). A 49-year-old woman who had been diagnosed with NSCLC (T2aN1M0) complained of persistent vertigo and bilateral tinnitus for three months. The patient had refused all treatments, including surgery and chemotherapy; however, she sought alternative medicine. The patient's hearing loss showed rapid progression bilaterally, and rotatory vertigo with peripheral-type nystagmus developed. Magnetic resonance imaging of the brain showed irregular nodular enhancement within both internal auditory canals with leptomeningeal enhancement and multiple intracranial metastasis. The patient was treated with epidermal growth factor receptor-tyrosine kinase inhibitor, and the tumor showed partial response. This was a rare case of multiple brain metastases involving bilateral internal auditory canal from known NSCLC presenting with vertigo and hearing loss.
Endovascular treatment of symptomatic high-flow vertebral arteriovenous fistula as a complication after C1 screw insertion.


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High-flow vertebral arteriovenous fistulas (VAVF) are rare complications of cervical spine surgery and characterized by iatrogenic direct-communication of the extracranial vertebral artery (VA) to the surrounding venous plexuses. The authors describe two patients with VAVF presenting with ischemic presentation after C1 pedicle screw insertion for a treatment of C2 fracture and nontraumatic atlantoaxial subluxation. The first patient presented with drowsy consciousness with blurred vision. The diffusion MRI showed an acute infarction on bilateral cerebellum and occipital lobes. The second patient presented with pulsatile tinnitus, dysarthria and a subjective weakness and numbness of extremities. In both cases, digital subtraction angiography demonstrated high-flow direct VAVFs adjacent to C1 screws. The VAVF of the second case occurred near the left posterior inferior cerebellar artery originated from the persistent first intersegmental artery of the left VA. Both cases were successfully treated by complete occlusion of the fistulous portion and the involved segment of the left VA using endovascular coil embolization. The authors reviewed the VAVFs after the upper-cervical spine surgery including C1 screw insertion and the feasibility with the attention notes of its endovascular treatment. Ned Tijdschr Geneeskd. 2014;158:A7995.

Predicting who will benefit from tinnitus therapies.


Jacobson GP.

Editor-in-Chief.

No abstract available.

[Take the time: primary healthcare for people with intellectual disabilities].
[Article in Dutch]


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People with intellectual disabilities (ID) have a higher prevalence of health problems than the general population and their health needs are often unrecognized and unmet. In this article we present three cases of patients with ID to illustrate some specific problems. A 22-year-old man, severely intellectually disabled, presented with an unsteady gait. He had recently been diagnosed with Cohen Syndrome. Since he was unable to express himself, it took some time to discover that he had additional symptoms, e.g. frequent infections. Eventually, all his complaints fit with his syndrome. A 54-year-old woman, severely to moderately intellectually disabled, presented with new behaviour, i.e. loss of appetite, weakness in her legs and excessive thirst. Although she was able to speak, she was unable to explain what was wrong with her. Since we were aware of the etiology of her disability, Prader Willi syndrome, we were more aware of the possibility of diabetes mellitus. A 56-year-old man, mildly intellectually disabled, presented with hearing voices for which he received antipsychotic medication. After a conversation in simple language, we discovered that he heard humming sounds rather than voices. He was ultimately diagnosed with tinnitus rather than psychosis. It takes time to discover the health issues that affect patients with ID. This is due to communication problems, the inability to understand bodily functions, symptoms and diseases, multi-morbidity, the atypical presentation of disease at times and the different prevalence rates for certain diseases when compared with the general population.
Facial nerve schwannoma: A case report and review of the literature. 

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A vestibular schwannoma, often termed an acoustic neuroma, is a type of benign primary intracranial tumor of the myelin-forming cells of the vestibulocochlear nerve. The typical clinical presentation often includes ipsilateral sensorineural hearing loss/deafness, vertigo and tinnitus. In the present study, the case of a young male patient who presented with recurrent unilateral facial palsy without hearing impairment is presented. The patient was diagnosed with vestibular schwannoma and received steroidal treatment with prednisolone for two weeks. The patient's facial weakness recovered three weeks following treatment, however, the tumor subsequently grew. The patient then underwent Gamma Knife radiosurgery with a margin dose of 13 Gy. Six months after the radiosurgery, the tumor was stable without progression, and the patient's facial nerve function and hearing remained intact.

XV Specific Forms of Tinnitus


Lamech F.

Context • In 2006, the government in the state of Victoria, Australia, mandated the rollout of smart meters in Victoria, which effectively removed a whole population's ability to avoid exposure to human-made high-frequency nonionizing radiation. This issue appears to constitute an unprecedented public health challenge for Victoria. By August 2013, 142 people had reported adverse health effects from wireless smart meters by submitting information on an Australian public Web site using its health and legal registers. Objective • The study evaluated the information in the registers to determine the types of symptoms that Victorian residents were developing from exposure to wireless smart meters. Design • In this case series, the registers' managers eliminated those cases that did not clearly identify the people providing information by name, surname, postal address, and/or e-mail to make sure that they were genuine registrants. Then they obtained consent from participants to have their deidentified data used to compile the data for the case series. The author later removed any individual from outside of Victoria. Participants • The study included 92 residents of Victoria, Australia. Outcome Measures • The author used her medical experience and judgment to group symptoms into clinically relevant clusters (eg, pain in the head was grouped with headache, tinnitus was grouped with ringing in the ears). The author stayed quite close to the wording used in the original entries. She then calculated total numbers and percentages for each symptom cluster. Percentages were rounded to the nearest whole number. Results • The most frequently reported symptoms from exposure to smart meters were (1) insomnia, (2) headaches, (3) tinnitus, (4) fatigue, (5) cognitive disturbances, (6) dysesthesias (abnormal sensation), and (7) dizziness. The effects of these symptoms on people's lives were significant. Conclusions • Review of some key studies, both recent and old (1971), reveals that the participants' symptoms were the same as those reported by people exposed to radiofrequency fields emitted by devices other than smart meters. Interestingly, the vast majority of Victorian cases did not state that they had been sufferers of electromagnetic hypersensitivity syndrome (EHS) prior to exposure to the wireless meters, which points to the possibility that smart meters may have unique characteristics that lower people's threshold for symptom development.
Sodium salicylate (SS) is a widely used medication with side effects on hearing. In order to understand these side effects, we recorded sound-driven local-field potentials in a neural structure, the dorsal cortex of the inferior colliculus (ICd). Using a microiontophoretic technique, we applied SS at sites of recording and studied how auditory responses were affected by the drug. Furthermore, we studied how the responses were affected by combined local application of SS and an agonists/antagonist of the type-A or type-B γ-aminobutyric acid receptor (GABAA or GABAB receptor). Results revealed that SS applied alone enhanced auditory responses in the ICd, indicating that the drug had local targets in the structure. Simultaneous application of the drug and a GABAergic receptor antagonist synergistically enhanced amplitudes of responses. The synergistic interaction between SS and a GABAA receptor antagonist had a relatively early start in reference to the onset of acoustic stimulation and the duration of this interaction was independent of sound intensity. The interaction between SS and a GABAB receptor antagonist had a relatively late start, and the duration of this interaction was dependent on sound intensity. Simultaneous application of the drug and a GABAergic receptor agonist produced an effect different from the sum of effects produced by the two drugs released individually. Differences between simultaneous and individual drug applications suggest that SS modified GABAergic inhibition in the ICd. Our results indicate that SS can affect sound-driven activity in the ICd by modulating local GABAergic inhibition.

Stimulus-timing dependent modifications of rate-level functions in animals with and without tinnitus.

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Tinnitus has been associated with enhanced central gain manifested by increased spontaneous activity and sound evoked firing rates of principal neurons at various stations of the auditory pathway. Yet, the mechanisms leading to these modifications are not well understood. In a recent in vivo study, we demonstrated that stimulus-timing dependent bimodal plasticity mediates modifications of spontaneous and tone-evoked responses of fusiform cells in the dorsal cochlear nucleus (DCN) of the guinea pig. Fusiform cells from sham animals showed primarily Hebbian learning rules while noise exposed animals showed primarily anti-Hebbian rules, with broadened profiles for the animals with behaviorally verified tinnitus (Koehler and Shore, 2013a). In the present study we show that well-timed bimodal stimulation induces alterations in the rate level functions (RLFs) of fusiform cells. The RLF gains and maximum amplitudes show Hebbian modifications in sham and no-tinnitus animals, but anti-Hebbian modifications in noise exposed animals with evidence for tinnitus. These findings suggest that stimulus-timing bimodal plasticity produced by the DCN circuitry is a contributing mechanism to enhanced central gain associated with tinnitus. Copyright © 2014, Journal of Neurophysiology.
Spontaneous behavior in noise and silence: a possible new measure to assess tinnitus in Guinea pigs.

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This study describes two experiments that were conducted in search for a behavioral paradigm to test for tinnitus in guinea pigs. Conditioning paradigms are available to determine the presence of tinnitus in animals and are based on the assumption that tinnitus impairs their ability to detect silent intervals in continuous noise. Guinea pigs have not been subjected to these paradigms yet; therefore, we investigated whether guinea pigs could be conditioned in the two-way shuttle-box paradigm to respond to silent intervals in noise. Even though guinea pigs could be trained relatively easy to respond to the presence of a noise interval, training guinea pigs to silent intervals in noise was unsuccessful. Instead, it appeared that they became immobile when the continuous stimulus was suddenly stopped. This was confirmed by the next experiment, in which we subjected guinea pigs to alternating intervals of noise and silence with a random duration between 30 and 120 s. Indeed, guinea pigs were significantly longer immobile during silence compared to during noise. By interpreting immobility as a signature of perceiving silence, we hypothesized that the presence of tinnitus would reduce immobility in silence. Therefore, we unilaterally exposed one group of guinea pigs to an 11-kHz tone of 124 dB sound pressure level for 1 h. A subset of the exposed animals was significantly more active in silence, but also more active in noise, as compared to the control group. The increased mobility during silent intervals might represent tinnitus. However, the increased mobility in noise of this group implies that the observed behavior could have derived from, e.g., an overall increase in activity. Therefore, conducting validation experiments is very important before implementing this method as a new screening tool for tinnitus. Follow-up experiments are discussed to further elucidate the origin of the increased mobility in both silence and noise. Free full text.

Modulation of gene expression in guinea pig paraflocculus after induction of hearing loss.

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Hearing loss often results in plastic changes in the central auditory pathways, which may be involved in the generation of tinnitus, a phantom auditory sensation. However, although animal studies have consistently shown increased neural activity in auditory structures after hearing loss, tinnitus does not always develop. It has therefore been suggested that non-auditory structures perform a gating or regulatory role that determines whether the increased activity in auditory structures leads to conscious perception. Recent evidence points to the paraflocculus of the cerebellum as having such a role. Therefore, we investigated the early effects of hearing loss on gene expression in guinea pig paraflocculus. Gene expression was investigated after two weeks recovery from either acoustic or mechanical cochlear trauma. The genes investigated in our study were associated with inhibitory neurotransmission (GABA-A receptor subunit alpha 1; glutamate decarboxylase 1), excitatory neurotransmission (glutamate receptor NMDA subunit 1), and regulation of transmitter release (member of RAB family of small GTPase). Our results show increased mRNA levels of glutamate decarboxylase 1 in ipsilateral paraflocculus with no difference between the different methods of cochlear trauma. Early modulation of gene expression in the paraflocculus suggests that an early effect of hearing loss may affect the influence of this structure on auditory processing. Free PMC Article.
Changes in the response properties of inferior colliculus neurons relating to tinnitus.

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Tinnitus is often identified in animal models by using the gap prepulse inhibition of acoustic startle. Impaired gap detection following acoustic over-exposure (AOE) is thought to be caused by tinnitus "filling in" the gap, thus, reducing its salience. This presumably involves altered perception, and could conceivably be caused by changes at the level of the neocortex, i.e., cortical reorganization. Alternatively, reduced gap detection ability might reflect poorer temporal processing in the brainstem, caused by AOE; in which case, impaired gap detection would not be a reliable indicator of tinnitus. We tested the latter hypothesis by examining gap detection in inferior colliculus (IC) neurons following AOE. Seven of nine unilaterally noise-exposed guinea pigs exhibited behavioral evidence of tinnitus. In these tinnitus animals, neural gap detection thresholds (GDTs) in the IC significantly increased in response to broadband noise stimuli, but not to pure tones or narrow-band noise. In addition, when IC neurons were sub-divided according to temporal response profile (onset vs. sustained firing patterns), we found a significant increase in the proportion of onset-type responses after AOE. Importantly, however, GDTs were still considerably shorter than gap durations commonly used in objective behavioral tests for tinnitus. These data indicate that the neural changes observed in the IC are insufficient to explain deficits in behavioral gap detection that are commonly attributed to tinnitus. The subtle changes in IC neuron response profiles following AOE warrant further investigation. Free Article.

XVII Psychological Factors

Altered top-down cognitive control and auditory processing in tinnitus: evidences from auditory and visual spatial stroop.
Restor Neurol Neurosci. 2014 Nov 24. [Epub ahead of print]

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Purpose: Tinnitus is the perception of a sound in the absence of external stimulus. Currently, the pathophysiology of tinnitus is not fully understood, but recent studies indicate that alterations in the brain involve non-auditory areas, including the prefrontal cortex. Here, we hypothesize that these brain alterations affect top-down cognitive control mechanisms that play a role in the regulation of sensations, emotions and attention resources. Methods: The efficiency of the executive control as well as simple reaction speed and processing speed were evaluated in tinnitus participants (TP) and matched control subjects (CS) in both the auditory and the visual modalities using a spatial Stroop paradigm. Results: TP were slower and less accurate than CS during both the auditory and the visual spatial Stroop tasks, while simple reaction speed and stimulus processing speed were affected in TP in the auditory modality only. Conclusions: Tinnitus is associated both with modality-specific deficits along the auditory processing system and an impairment of cognitive control mechanisms that are involved both in vision and audition (i.e. that are supra-modal). We postulate that this deficit in the top-down cognitive control is a key-factor in the development and maintenance of tinnitus and may also explain some of the cognitive difficulties reported by tinnitus sufferers.
Severe to profound hearing impairment: quality of life, psychosocial consequences and audiological rehabilitation.

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Purpose: To study the quality of life (QoL) and psychosocial consequences in terms of sick leave and audiological rehabilitation given to patients with severe to profound hearing impairment. Method: A retrospective study of data on 2319 patients with severe to profound hearing impairment in The Swedish Quality Register of Otorhinolaryngology, followed by a posted questionnaire including The Hospital Anxiety and Depression Scale (HADS). Results: The results indicate greater levels of anxiety and depression among patients with severe or profound hearing impairment than in the general population, and annoying tinnitus and vertigo had strong negative effects on QoL. The proportion of sick leave differed between the studied dimensions in the study. The proportion of patients who received extended audiological rehabilitation was 38% in the present study. Conclusions: Treatment focused on anxiety, depression, tinnitus and vertigo must be given early in the rehabilitation process in patients with severe or profound hearing impairment. Because sick leave differs greatly within this group of patients, collaboration with the regional Social Insurance Agency is crucial part of the rehabilitation. The study also shows that presently, only a small proportion of patients in Sweden with severe to profound hearing impairment receive extended audiological rehabilitation. Implications for Rehabilitation Greater levels of anxiety and depression have been found among patients with severe or profound hearing impairment than in the general population, and annoying tinnitus and vertigo have strong negative effects on QoL in this group of patients. Only a small proportion of patients with severe to profound hearing impairment receive extended audiological rehabilitation today, including medical, technical and psychosocial efforts. Extended audiological rehabilitation focused on anxiety, depression, tinnitus and vertigo must be given, together with technical rehabilitation, early in the rehabilitation process in patients with severe or profound hearing impairment.

Evidence of Multidomain Mild Cognitive Impairment in Idiopathic Intracranial Hypertension.
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BACKGROUND: Idiopathic intracranial hypertension (IIH), a disorder of unknown etiology, may occur in all age groups, but is most common in young obese women. Goals of treatment are to preserve vision and alleviate symptoms, including intractable headache, pulsatile tinnitus, and nausea. Cognitive function is not addressed routinely during clinical evaluation of IIH patients. The aim of our study was to test whether there is cognitive impairment in IIH patients and to evaluate the nature and characteristics of cognitive functions. METHODS: Design-Prospective cross-sectional observational study; Setting-Institutional; Study population-Thirty consecutive IIH patients (3 men and 27 women), mean age at time of testing was 34.4 years; Procedures-All participants completed a cognitive test battery; Outcome measures-Impairment of non-verbal memory, executive function, visual spatial processing, attention, motor skills, problem solving, and information processing speed in IIH patients. RESULTS: Mean scores for all domain index scores were below average for age and education. The global cognitive score, attention, and visual spatial indices had the lowest scores. CONCLUSIONS: Our results indicate that patients with IIH have mild cognitive impairment. All domain measures apart from memory showed a statistically significant difference from normal individuals, indicating that there is a form of multidomain cognitive impairment in IIH. The relationship between cognitive impairment and chronically elevated intracranial pressures and its role in contributing to patient morbidity requires further study.
A scientific cognitive-behavioral model of tinnitus: novel conceptualizations of tinnitus distress.

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The importance of psychological factors in tinnitus distress has been formally recognized for almost three decades. The psychological understanding of why tinnitus can be a distressing condition posits that it becomes problematic when it acquires an emotive significance through cognitive processes. Principle therapeutic efforts are directed at reducing or removing the cognitive (and behavioral) obstacles to habituation. Here, the evidence relevant to a new psychological model of tinnitus is critically reviewed. The model posits that patients’ interpretations of tinnitus and the changes in behavior that result are given a central role in creating and maintaining distress. The importance of selective attention and the possibility that this leads to distorted perception of tinnitus is highlighted. From this body of evidence, we propose a coherent cognitive-behavioral model of tinnitus distress that is more in keeping with contemporary psychological theories of clinical problems (particularly that of insomnia) and which postulates a number of behavioral processes that are seen as cognitively mediated. This new model provides testable hypotheses to guide future research to unravel the complex mechanisms underpinning tinnitus distress. It is also well suited to define individual symptomatology and to provide a framework for the delivery of cognitive-behavioral therapy. Free PMC Article.

XVIII Hyperacusis

No publications this time.

XIX Heterogeneity of Tinnitus

Auditory Cortex Stimulation Might be Efficacious in a Subgroup of Tinnitus Patients.

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No abstract available

Chronic Neck Pain and Episodic Vertigo and Tinnitus.

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No abstract available.
A Comparison of CBT and CET Interventions for Veterans With Tinnitus

This study is not yet open for participant recruitment.
ClinicalTrials.gov Identifier: NCT02293512
Sponsor: Department of Veterans Affairs
Information provided by (Responsible Party): Department of Veterans Affairs
Study start: January 2015
First received: November 5, 2014

Tinnitus (i.e., ringing in the ears) is currently the most prevalent disability in the VA system. Numerous clinical interventions have been created to systematically address the range of issues caused by tinnitus. Only a few tinnitus interventions have focused on coping strategies. Coping strategies are cognitive, affective, and behavioral attempts to master new events, such as the onset of a disability or an impairment like tinnitus, that are overwhelming to an individual, and that because of their newness, an individual does not necessarily have automatic, adaptive responses (Inglehart, 1991; Lazarus & Folkman, 1984; Livneh, 2000).

The present study proposes a development of a Coping Effectiveness Training (CET) protocol for Veterans with tinnitus and a pilot study that assesses the effectiveness of a CET intervention compared to the current clinical practice of a cognitive-behavioral therapy (CBT) intervention. Evidence suggests that CET is effective in facilitating adaptive coping strategies among individuals with several types of impairments or disabilities (Chesney et al., 2003; Chesney, Folkman, & Chambers, 1996; Kennedy, Duff, Evans, & Beedie, 2003; King, & Kennedy, 1999). The proposed study will be the first application of CET to a tinnitus population.

The primary goal of this study is to develop a CET protocol and materials for tinnitus. The second goal of this pilot study will be to compare CET to the standard practice of CBT in the context of the Progressive Tinnitus Management (PTM) program for Veterans. The overarching goal of the proposed pilot study is to gain information that can be used to provide Veterans with the best care for helping them to more successfully cope with tinnitus.

The aims of this research are to: 1) develop a CET protocol for Veterans with tinnitus by means of information gathered from two focus groups and from CET consultants; 2) to examine whether a 3-session CET group intervention is more effective than a 3-session CBT group intervention or waitlist control in increasing coping strategies among Veterans with tinnitus.
Effectiveness of Acupuncture as a Treatment for Tinnitus: a Randomized Controlled Trial Using 99mTc-ECD SPECT

This study is completed.
ClinicalTrials.gov Identifier: NCT02290015
Sponsor: Federal University of São Paulo
Information provided by (Responsible Party): Maura Regina Laureano, Federal University of São Paulo
Study start: August 2010
First received: October 28, 2014

Acupuncture (ACP) is frequently used to treat tinnitus, the condition defined as the perception of sound in the absence of an external auditory stimulus. However, no information is available regarding the consequences of ACP on the neural architecture and functionality of the brain in tinnitus patients. The aim of this study was to investigate changes in brain activity using ethylcysteine dimer single-photon emission computer tomography (99mTc-ECD SPECT) in patients with tinnitus and normal hearing who underwent ACP treatment. Methods and Findings: This was a randomized, single-blinded, sham-controlled study. The participants were adults (18-60 years old) with either normal hearing or chronic, idiopathic and continuous (+ 3 months) tinnitus. Fifty-seven (57) subjects were randomized to receive true (n=30) or sham (n=27) ACP, and 99mTc-ECD SPECT exams were performed seven days before (baseline) and seven days after twelve ACP sessions (up to six weeks), which were performed twice a week. Secondary outcomes included changes in the Tinnitus Handicap Inventory (THI), the Visual Analog Scale (VAS), the Hamilton Anxiety Scale (HAS) and the Beck Depression Inventory (BDI). Data regarding imaging outcomes were analyzed with Statistical Parametric Mapping (SPM8) software using a factorial design. For secondary outcomes, regression models were built considering two different analytical paradigms: intention-to-treat (ITT; where multiple imputations were conducted due to loss to follow-up) and complete cases. No significant differences in brain perfusion were observed between patients who underwent true versus sham ACP treatment. However, a significant improvement in THI scores at the end of true ACP treatment was observed for all domains (all p < 0.001), with the exception of the catastrophic field. For the other outcome measurements (VAS, BDI and HAS), no significant differences were observed between groups. The small sample size represents a potential limitation of this study. Conclusions: These findings suggest that ACP may improve the impact of tinnitus on daily life, although additional studies are needed to verify the consequences of ACP on the neural architecture and functionality of the brain in tinnitus patients.
Acoustic Stimulation Paired With Body and Cortical Stimulation for Modulating Tinnitus

This study is not yet open for participant recruitment.
ClinicalTrials.gov Identifier: NCT02283216
Sponsor: University of Minnesota - Clinical and Translational Science Institute
Information provided by (Responsible Party): Hubert H Lim, PhD, University of Minnesota - Clinical and Translational Science Institute
Study start: January 2015
First received: October 26, 2014

The purpose of the study is to investigate different stimulation parameters for a new noninvasive approach for modulating the brain that could potentially be beneficial for decreasing tinnitus perception. The new approach is called Multimodal Synchronization Therapy (mSync). mSync uses a combination of acoustic stimulation played through headphones and low levels of electrical current delivered via electrodes placed on the surface of different body regions. The timing interval between the acoustic and body stimulation is varied in order to cause different types of changes in the brain. In addition to acoustic and body stimulation, noninvasive cortical stimulation will also be presented as part of mSync to attempt to further modulate or decrease the tinnitus percept. Cortical stimulation will be performed by placing a magnetic coil over a spot on the head and sending a brief magnetic pulse that can travel through the skin and bone to create electrical current inside the head. For this study, different body locations as well as specific timing intervals among acoustic, body, and cortical stimulation will be investigated to identify appropriate parameters that can modulate and potentially decrease tinnitus perception. Different mSync parameters will be investigated across multiple testing sessions (up to 16 weekly sessions) and the tinnitus percept will be closely monitored throughout the study.

Combined Transcranial and Peripheral Muscle Magnetic Stimulation in Chronic Tinnitus

This study is currently recruiting participants.
ClinicalTrials.gov Identifier: NCT02306447
Sponsor: University of Regensburg
Information provided by (Responsible Party): Berthold Langguth, MD, Ph.D., University of Regensburg
Study start: August 2014
First received: Dec 1, 2014

Chronic tinnitus is characterized by several comorbid disorders. One of them is neck and back pain. Here, we investigate the feasibility, safety and clinical efficacy of the combination of repetitive transcranial magnetic stimulation (rTMS) and peripheral muscle stimulation (rPMS) in chronic tinnitus in a pilot study. rTMS is considered to interact with neural tinnitus networks. rPMS is suggested to bring relief to muscle tension. This is an one arm study where explorative analyses will be done with special consideration on patients suffering from neck pain in the analysis.
A Balanced Randomised Placebo Controlled Double-blind Phase IIa Study to Investigate the Efficacy and Safety of AUT00063 Versus Placebo in Subjective Tinnitus

This study is currently recruiting participants.
ClinicalTrials.gov Identifier: NCT02315508
Sponsor: Autifony Therapeutics Limited
Information provided by (Responsible Party): Autifony Therapeutics Limited
Study start: October 2014
First received: December 9, 2014

Reduced activity at certain sites in the brain (called "voltage-gated potassium channels") has been linked to hearing problems, like age-related loss of hearing or tinnitus (a 'ringing' or buzzing noise in the ears). AUT00063 is an experimental new medicine that has been developed to improve the action of these specific channels and so treat the brain component of these hearing problems.

The main purpose of this study is to try to demonstrate an improvement in the severity of tinnitus after 4 weeks of treatment with the study medicine or the placebo (dummy drug which does not contain the medication). Subjects will undergo a safety follow-up after the treatment period. Safety and efficacy will be determined by looking at a number of assessments (physical examinations, blood sampling, hearing assessments, questionnaires, etc.) and in case of any serious medical event during the study. The amount of drug in the blood will also be measured.

It is expected that up to 152 people with tinnitus may take part in the study. The study participants will be recruited at around 12 Hospital sites in the UK.

The Effect of Physiotherapy on Cervicogenic Somatic Tinnitus

This study is completed.
ClinicalTrials.gov Identifier: NCT02016313
Sponsor: Universiteit Antwerpen
Information provided by (Responsible Party): Sarah Michiels, Universiteit Antwerpen
Study start: May 2014
Study Completion: December 2014
First received: December 09, 2013

The purpose of this study is to determine whether physiotherapy is effective in the treatment of a group of tinnitus patients with neck complaints.

Publications:
The Effect of Transcranial Direct Current Stimulation (tDCS) in Addition to Tinnitus Retraining Therapy (TRT) for Treatment of Chronic Tinnitus Patients

This study is currently recruiting participants.
ClinicalTrials.gov Identifier: NCT02285803
Sponsor: University Hospital, Antwerp
Information provided by (Responsible Party): Ethisch Comité UZ Antwerpen, University Hospital, Antwerp
Study start: November 2014
First received: October 31, 2014

The aim of this study is to evaluate the added effect of tDCS to TRT within patients with chronic, non-pulsatile tinnitus. Patients were randomised in two groups namely, TRT and real tDCS and the second one is TRT with sham tDCS. Evaluations took place at the start of therapy, at the end of the counselling and at last a follow-up visit will be planned after 84 days of the start of the therapy. Subjective outcome measurements such as Tinnitus Functional Index and Visual Analogue Scales of loudness are the primary outcome measurement. Secondary outcome measurements are the Hospital Anxiety and Depression Scale, hyperacusis questionnaire and psychoacoustic measurements.