Editorial

The currently world-wide available information has reached almost unthinkable dimensions. We currently witness an era in which the internet with its data clouds, its almost unlimited data storage and processing capabilities and its social networks penetrates almost all aspects of society. Traditional ways of knowledge delivery, which have not much changed since the invention of printing in the 15th century, are questioned. Interestingly, the structures of scientific knowledge exchange seem to resist these changes. What has changed is that almost all journals appear as online versions, and that the peer review process is performed via the internet, but the original structure has not changed. Scientific work is submitted to Journals and undergoes a peer-review process before publication. This unidirectional information transfer may ensure quality, but in principle it is contingent upon historical limitations such as limited space and the impossibility to update or improve information once it gets published. Both constraints are not relevant any more, but still the scientific community adheres to this traditional strategy. Alternative ideas of scientific knowledge exchange, e.g. publication that is followed by peer-review of the entire scientific community have been proposed, but did not yet get widely accepted. The "Frontiers"- Journals adopted a compromise by opening the review process to an interactive forum. This is a first step towards the concept that a publication develops by agile interaction of scientists. Within this newsletter the first articles of a special topic in Frontiers in Systems Neuroscience can be found (Ringing ears; the neuroscience of tinnitus). The fast publication time is highly remarkable, but it may be owed to the effort of the guest editors Jos Eggermont and Larry Roberts as much as to the innovative peer review concept.

Clinical management has not yet been significantly influenced by the information era, but it is expected that this will change in the near future. Opportunities, offered by the use of large amounts of data, related challenges and the implication for tinnitus treatment can be found in a comment on the next page.

Also within TRI we aim to improve information exchange and delivery. We initiated a forum for discussing research and clinical questions (TRI Discussion Forum). Already after a short time the forum has been highly accessed and everybody is invited to contribute.

Another innovation on the TRI website is the educational section (Patient’s Corner). Motivated by many mails from patients, who ask about the applicability of recent research results in clinical practice, we aim to provide information about new research developments in order give hope for the many patients suffering from tinnitus, without rising false expectations.

Finally the 6th TRI conference is approaching. It is our belief that meetings, where clinicians and researchers come together and share their results and ideas, and also get to know each other, have the highest relevance for effective collaboration. Internet based communication may complement such meetings, but will never be able to replace them. This year’s meeting is entitled “Tinnitus: the art and science of innovation” and strives to stimulate our creativity by entering into a discussion with artists and historians as in addition to our traditional topics from audiology to neuroscience. We are looking forward to welcome you in June in Bruges (Belgium) (www.tri2012.org).

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

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Big Data: What does it mean for future tinnitus research and treatment?

B. Langguth1, J Gutsche2, M. Landgrebe1,3, B Elgoyhen4, D De Ridder5

1 Department of Psychiatry and Psychotherapy, Interdisciplinary Tinnitus Clinic, University of Regensburg, Germany.
2 Department of Economy, University of Applied Sciences, Merseburg, Germany
3 Department of Psychiatry and Psychotherapy, Bamberg, Germany.
4 Instituto de Investigaciones en Ingeniería Genética y Biología Molecular, Consejo Nacional de Investigaciones Científicas y Técnicas and Tercera Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires, 1428 Buenos Aires, Argentina.
5 TRI, BRAI²N & Department of Neurosurgery, University Hospital Antwerp, 2650 Edegem, Belgium.

“The amount of data in our world has been exploding, and analyzing large data sets - so-called big data - will become a key basis of competition, underpinning new waves of innovation…”, starts a report of the McKinsey Global Institute1. But is this relevant for us as researchers or medical doctors? In general we think that it is sufficient to keep track of new research findings or of new developments in the diagnosis and treatment of patients. We tend to ignore developments in other fields, but if we do “think outside the box” the domains we probably consider less relevant are economy and business. This might be a big mistake, since the era of big data will probably not only revolutionize economy and marketing, but also clinical research and health care. After all, Darwin and Wallace both developed their theory of evolution by means of natural selection based on an essay they both read by Thomas Malthus (an essay on the principle of population), and Malthus was an economist. Furthermore, it has recently been shown, based on big data, that the topology of the financial market and brain are isomorphic2.

The McKinsey report further states that “Leaders in every sector will have to grapple with the implications of big data, not just a few data-oriented managers.” For the health care sector, it is estimated that effective and creative use of data for driving efficacy and quality would reduce the national health expenditures in the US by about 8% and would be more than $300 billion in value every year3.

How can data create value?

There are several ways to leverage big data to create value and offer transformational potential for the design and organization of clinical research and health care.

Creating transparency: Standardized collection of clinical and demographic data of large amounts of tinnitus patients provides transparent information about treatment results, treatment pathways, cost effectiveness and can thus directly improve quality.

Discovering needs: Patient groups or clinical constellations with specific needs can be identified and directly addressed by targeted research.

Improving performance: Collecting and storing patient data enables accurate and detailed analysis of treatment performance both on an individual, institutional, national and/or a global level. Data from each treated patient both in clinical practice and in controlled trials can be collected. Analyzing the pooled data set enables to understand which factors are responsible for the variability in outcome, which in turn will improve clinical management.

Segmenting patient populations: Tinnitus is a heterogeneous condition, but the criteria for subtyping patients are still a matter of debate. Data driven analysis from big data sets can identify subgroups that share important clinical features.

Supporting medical decision making with algorithms: Longitudinal data from large samples will enable the establishment of diagnostic criteria and the recommendation of treatments for the different subgroups.

Customizing treatments: Based on a more and more detailed segmentation, customized treatments can be offered to patients. With large data amounts an expert system could be developed which would provide recommendations for treatment with increased success chances.
Innovating new products and services: Data mining might lead to serendipitous discoveries, unexpected relations and thus generate ideas for innovative treatment.

How can big data drive innovation?

Big data together with sophisticated analysis can substantially improve decision making, minimize risk and lead to valuable insights that would otherwise remain hidden. This might also change the way how innovations emerge. Currently a new treatment is developed and tested before it is offered. Drug development for example requires a R&D program, in which safety and efficacy are tested in several hundred to a thousand patients. Such a program costs about $2 billion for each drug that reaches the market and requires several years, even if only a small dose range and one indication is tested. The experience with this drug after its release is not systematically analyzed any more. Efficacy and safety information from hundreds of thousands of people is lost. Moreover, in spite of investments in research and development of over $60 billion dollar/year this current approach has largely failed to generate real innovations - and has definitively not been successful for the development of a drug against tinnitus. The availability of systematically recorded data from large patient samples could change this situation dramatically. It could enable an ongoing learning with every patient that is treated.

For example it is estimated that alone in western countries about 13 million people seek currently medical help for their tinnitus. If the data of only 10% of these patients were entered in a tinnitus database, an enormous amount of information will become available that is currently still completely lacking: which clinical criteria predict positive outcome, which is the individually best dosage of a drug, which combination of drugs may be beneficial, etc.. In addition to currently available databases such a database could include genetic and imaging data, physiologic data, regular assessments of different aspects of tinnitus over time and socioeconomic data. Systematic assessment of such a dataset may identify patterns that never become obvious in the observation of small samples.

How can big data customize evidence based medicine?

Big data might also change our knowledge level about the efficacy and safety of interventions. Currently meta-analyses of randomized controlled trials are considered as the highest evidence level. This approach assumes that all patients are similar – but they aren’t. We treat individuals and for the individual it is relevant what is beneficial in his situation. Moreover, frequently the patients enrolled in clinical trials are not representative of “real world” patients, e.g. because patients with co-morbidities are in general excluded from participation, and also the treatment within a clinical trial is not representative of the real world treatment. In clinical trials the complexity of the individual case is reduced to a one-dimensional quantification of one symptom. This may work quite well for some diseases (e.g. infectious diseases). However, in brain disorders the complex individual situation is frequently more important than the symptom that is treated. We frequently experience in our clinical practice that results from randomized controlled trials have only limited value for clinical decision making. Therefore, we make clinical decisions by integrating information from pathophysiological models, from controlled trials and from our clinical experience. In practice, this means that for any given patient we chose treatment based on our experience with other comparable cases. Big data may provide the chance for our own clinical experience to become exponentially extended. Big databases could aggregate clinical data from many thousands of patients treated under real world conditions and including detailed information about the individual disposition. Specific algorithms could be developed that extend our current strategy of decision making. Such information will be much more reliable for clinical decision making than data from randomized controlled trials alone and will pave the way towards an evidence-based individualized treatment.
How big data may change the doctor-patient relationship

Similar like people do not buy their books any more from the local book shop but from globally acting internet retailers, online diagnosis and treatment may become more and more usual in the future. Patients have their complete health data stored in data clouds and can receive treatment recommendations by medical doctors world-wide or based on data-driven expert systems of global health institutions. For all forms of diagnostic and therapeutic procedures transparency about quality criteria, success rates, complications and side effects will be demanded by patients. Social media will act as a further control mechanism to identify “black sheep” among medical doctors. Thus the position of the patient will be significantly strengthened and the doctor-patient relationship will change fundamentally.

Big data, the brain and network science

A major challenge is the analysis and the interpretation of the huge amount of data. This is further complicate by all the complex interdependencies within the dataset. The recently developed and still developing field of network science basically already does this. Network science describes large and complex datasets and tries to find structure or patterns in such datasets which permits to better understand the data. Network science can identify how data are related to each other, where in the data-network are the “hubs”, the “masters” and the slaves”. Moreover network science enables also to quantify the stability of the network, and the resistance to changes. Network science has been successfully used for describing all kinds of complex datasets and for predicting their behavior, from the financial markets to brain networks.

What does this mean for TRI?

These are only some examples to illustrate the fact that big data analyses could provide much more appropriate tools to deal with the complexity encountered in clinical medicine, than our currently used methods. The technical basis for big data in medicine is already available. Five billion cell phones are currently used, 12% of them are smart phones and their rate is growing by 20% per year. Thus, it is a matter of short time that questionnaires, rating scales and tinnitus matching or masking procedures will be performed through smart phone apps. This will be complemented by functional neuroimaging, neurophysiological and genetic data and ongoing recordings of physiological data. Recently Nike and Apple have presented a high tech wristband for recording, compiling and sharing physiologic data. Similarly, brain computer interfaces can be created.

Given the enormous gain of relevant clinical information, together with technical feasibility, there is no doubt that large scale data processing will enter the medical field. This will create many new challenges. Importantly data safety and security issues have to be addressed. Beside ethical issues and the development of strategies for data analysis, one of the challenges for the future will be the identification of relevant clinical information to be entered in the databases. The experience with already established databases will speed up this process and increase the steepness of the learning curve. Thus, the experience with the fast growing TRI database will be critical for taking advantage of these new developments in order to increase the care of tinnitus patients. By contributing their patients to the database all clinicians and clinical researchers within TRI can participate in this process.

(1) the full report can be found at: www.mckinsey.com/Insights/MGI/Research/Technology_and_Innovation/Big_data_The_next_frontier_for_innovation
(3) Big data: the next frontier for innovation, competition and productivity, James Manyika et al.; Mc Kinsey Global Institute, May 2011
(4) Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2011


**RESEARCH HIGHLIGHTS**


By demonstrating that sick-leave due to tinnitus is related to a three-fold increased risk of disability pension, the authors highlight the socioeconomic relevance and the need for the development of more effective treatments.


Eggermont JJ. *Hearing loss, hyperacusis, or tinnitus: What is modeled in animal research?* Hear Res. 2012 Feb 7. [Epub ahead of print]. This review summarizes the merit and the limitations of currently used animal models of tinnitus.

Dehmel S, Pradhan S, Koehler S, Bledsoe S, Shore S. *Noise overexposure alters long-term somatosensory-auditory processing in the dorsal cochlear nucleus--possible basis for tinnitus-related hyperactivity?* J Neurosci. 2012 Feb 1;32(5):1660-71. Free article. This study identifies neuroplastic changes in the dorsocochlear nucleus occurring following somatosensory and auditory stimulation. These mechanisms are presumably critical in the pathophysiology of some forms of tinnitus.

Schwartz P, Leyendecker J, Conlon M. *Hyperacusis and misophonia: the lesser-known siblings of tinnitus.* Minn Med. 2011 Nov;94(11):42-3. This review focuses on hyperacusis and misophonia, two conditions which frequently occur in tinnitus patients.

Tass PA, Adamchic I, Freund HJ, von Stackelberg T, Hauptmann C. *Counteracting tinnitus by acoustic coordinated reset neuromodulation.* Restor Neurol Neurosci. 2012 Mar 13. [Epub ahead of print]. In this pilot study coordinated reset, a new form of auditory stimulation has been investigated. This approach is based on the idea that hypersynchronous tinnitus related neuronal activity can be unlearned by presentation of auditory stimuli around the tinnitus frequency.

Newman CW, Sandridge SA. *A Comparison of Benefit and Economic Value between Two Sound Therapy Tinnitus Management Options.* J Am Acad Audiol. 2012 Feb;23(2):126-38. In this study retrospective data from tinnitus patients treated with neuromonics and ear level sound generators were reported and compared.

By ingconfirming earlier studies of alterations of hypothalamus-pituitary adrenal (HPA) axis function in tinnitus patients this study further elucidates the role of stress reactivity in chronic tinnitus.


This functional imaging study highlights the relevance of non-auditory regions for tinnitus related distress. In detail it confirms the relevance of the fronto-parietal attention network and of the unspecific distress network.


Gap-induced prepulse inhibition of acoustic startle (GPIAS) has been proposed for assessing tinnitus behaviourally in animal models. Here GPIAS changes over a time period of 7 months are investigated, which is a necessary precondition for the use of animal models in the investigation of chronic tinnitus.
Extended Abstract Submission Deadline: April 15, 2012
Early Bird Registration until May 1, 2012
http://www.tri2012.org

The 6th Tinnitus Research Initiative (TRI) conference will be organized from June 13th to 16th, 2012 in Bruges, Belgium by the multidisciplinary TRI Tinnitus Unit Antwerp, Belgium, part of Brain Research center Antwerp for Innovative and Interdisciplinary Neuromodulation (BRAI2N), Antwerp University Hospital & Antwerp University and the Tinnitus Research Initiative. TRI 2012 is the premier venue for scientists and clinicians from around the world to discuss cutting-edge research on tinnitus.

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

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

**Exhibits** related to the theory, practice and education of tinnitus and related techniques are invited. Please request our exhibitor package for details.

**More details** can be found at the conference website (http://www.tri2012.org/). Contributors are encouraged to contact the conference coordinator for further information.

**Organizing committee**

Dirk De Ridder, M.D., Ph.D.
Sven Vanneste, Ph.D.
Paul Van de Heyning, M.D., Ph.D.
Berthold Langguth, M.D., Ph.D.
Ana Belén Elgoyhen, Ph.D.

**Conference Coordinators**

Marina Pieters, Brain²n, University Hospital Antwerp, Wilrijkstraat 10, 2650 Edegem
phone: +32 38214538, e-mail: marina.pieters@uza.be

Susanne Staudinger, Sylvia Dorner-Mitschke, Foundation Tinnitus Research Initiative, TRI
Universitaetsstrasse 84, 93053 Regensburg
phone: +49 941 941 2096, fax +49 941 941 2025, e-mail: meetings@tinnitusresearch.org
Upcoming Meetings

XXXI World Congress of Audiology
When: April 29 - May 3, 2012
Where: Moscow, Russia
Detailed information: http://www.wca2012.ru/

The 12th International Conference on Cochlear Implants and other Implantable Auditory Technologies
When: May 3 – 5, 2012
Where: Baltimore, MD, USA
Detailed Information: http://ci-2012.com/

The Acoustics 2012
a joint meeting of the 163rd meeting of the Acoustical Society of America (ASA), the 8th meeting of the acoustical Society of China (ASC), the 11th Western Pacific Acoustics Conference (WESPAC) and the Hong Kong Institute of Acoustics (HKIOA)
When: May 13 - 18, 2012
Where: Hong Kong, China
Detailed information: http://acoustics2012hk.org/

83. Jahresversammlung der Deutschen Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V.
When: May 16 – 20, 2012
Where: Rheingoldhalle Mainz, Germany

Symposium of the International Society of Otoneurology
When: May 17 – 19, 2012
Where: Valais, Switzerland
Detailed Information: www.otoneuro.com
AHS 2012 2nd International Conference on Adult Hearing Screening
When: June 5 - 7 2012
Where: Villa Erba Congress Center Cernobbio, Italy
Detailed Information: http://www.ahs2012.org/

18th Annual Meeting of the Organization for Human Brain Mapping (OHBM2012)
When: June 10 - 14, 2012
Where: China National Convention Center Beijing, China
Detailed Information: www.humanbrainmapping.org/OHBM2012

6th INTERNATIONAL TRI CONFERENCE ON TINNITUS 2012
Tinnitus: the Art and Science of Innovation
When: June 13 – 16, 2012
Where: Bruges, Belgium
Detailed Information: http://www.tri2012.org

EAONO 2012 6th Instructional Workshop and Consensus in Auditory Implants
When: August 30 - September 2, 2012
Where: Bratislawa, Slovakia
Detailed Information: http://www.eaono2012.com/

American Academy of Otolaryngology, Head and Neck Surgery Annual Meeting
When: September 11 - 14, 2012
Where: San Francisco, CA, USA
Detailed Information: http://www.entannualmeeting.org/

Twentieth Annual Conference on Management of the Tinnitus Patient for Patients and Professionals
When: October 5 - 6, 2012
Where: The University of Iowa, Iowa City, IA, USA
Detailed Information: http://www.healthcare.uiowa.edu/otolaryngology/TinnitusCourse/
Tinnitus & Hyperacusis Therapy Masterclass

When: October 8 - 12, 2012
Where: Birbeck College, University of London, UK
Contact: hashir.aazh@nhs.net
Detailed Information: http://tinnitustherapy.org.uk/

EUHA 2012 - 57. International Congress of Hearing Aid Acousticians

When: October 24 - 26 2012
Where: Congress Center Messe Frankfurt
Detailed Information: http://www.euha.org

ASHA 2012 Annual Convention

When: November 15–17, 2012
Where: Atlanta, GA, USA
Detailed Information: http://www.asha.org/Events/convention/Future-Conventions/
I Epidemiology

Occupation and the risk of bothersome tinnitus: results from a prospective cohort study (HUNT).

Engdahl B, Krog NH, Kvestad E, Hoffman HJ, Tambs K.
Norwegian Institute of Public Health, Division of Mental Health, Oslo, Norway.

Objectives: Estimates of occupation-specific tinnitus prevalence may help identify high-risk occupations where interventions are warranted. The authors studied the effect of occupation on prevalence of bothersome tinnitus and estimated the attributable fraction due to occupation. The authors also studied how much of the effect remained after adjusting for noise exposure, education income, hearing thresholds and other risk factors. Design: A prospective cohort study. Setting: A health survey of the Nord-Trøndelag county of Norway. Participants: A sample of the general adult population (n=49 948). Primary outcome measure The primary outcome measure is bothersome tinnitus. Results: Occupation had a marked effect on tinnitus prevalence. The effect of occupation on tinnitus was reduced in men by controlling for self-reported occupational noise exposure and in women by controlling for education and income. Adding hearing loss as a predictor increased the effect of occupation somewhat. In men, age-adjusted prevalence ratios of tinnitus ranged from 1.5 (workshop mechanics) to 2.1 (crane and hoist operators) in the 10 occupations with highest tinnitus prevalence. In women, the most important contribution to the tinnitus prevalence was from the large group of occupationally inactive persons, with a prevalence ratio of 1.5. Conclusion: This study found a moderate association between occupation and bothersome tinnitus.

Sickness absence due to otoaudiological diagnoses and risk of disability pension: a nationwide Swedish prospective cohort study.

Friberg E, Jansson C, Mittendorfer-Rutz E, Rosenhall U, Alexanderson K.
Division of Insurance Medicine, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm,

BACKGROUND: Hearing difficulties are a large public health problem. Knowledge is scarce regarding risk of disability pension among people who have been sickness absent due to these difficulties. METHODS: A cohort including all 4,687,756 individuals living in Sweden in 2005, aged 20-64, and not on disability or old-age pension, was followed through 2009. Incidence rate ratios (RR) of disability pension with 95% confidence intervals (CI) were estimated using Cox proportional hazard models. RESULTS: In multivariable models, individuals who had a sick-leave spell due to otoaudiological diagnoses in 2005 had a 1.52-fold (95% CI: 1.43-1.62) increased risk of being granted a disability pension compared to individuals on sick leave due to other diagnoses. Hearing and tinnitus sick-leave diagnoses were associated with risk of disability pension: RR 3.38, 95% CI: 3.04-3.75, and 3.30, 95% CI: 2.95-3.68, respectively. No association was observed between sick leave due to vertigo diagnoses and disability pension whereas otological diagnoses and no sick leave were inversely associated with risk of disability pension compared to non-otoaudiological sick-leave diagnoses. Sick leave due to otoaudiological diagnoses was positively associated with risk of disability pension due to otoaudiological diagnoses and sick leave due to a tinnitus diagnosis was also associated with risk of disability pension due to mental diagnoses. The risk of disability pension among individuals with hearing or tinnitus sick-leave diagnoses was highest in the age group 35-44. Moreover, men had a slightly higher risk. CONCLUSION: This large cohort study suggests an increased risk of disability pension among those with sickness absence due to otoaudiological diagnoses, particularly hearing and tinnitus diagnoses, compared to those with sickness absence due to non-otoaudiological diagnoses.
The public health effect of financial crises has been emphasized in previous studies. In addition, a series of otorhinolaryngologic disorders and manifestations has been related to psychological factors in the literature. Such conditions include temporomandibular joint disorders, laryngopharyngeal reflux, chronic tinnitus, and vertigo. Focusing on the outpatient database records of a large hospital in Crete, Greece, the objective of this retrospective study was to explore possible occurrence variations within the prementioned otorhinolaryngologic morbidity which may be potentially attributed to increased levels of socioeconomic stress. Results revealed that although the total number of visits between two periods - before and after the beginning of the financial crisis in Greece - was comparable, a significant increase in the diagnosis of two disorders, namely vertigo and tinnitus was found. In addition, a trend toward increased rate of diagnosis for reflux and temporomandibular joint disorders was noted. Potential implications of these findings are discussed. In conclusion, health care providers in this as well as in other countries facing similar socio-economic conditions should be aware of potential changes in the epidemiologic figures regarding specific medical conditions.
II Pathophysiology

Tinnitus severity and its association with cognitive and somatic anxiety: a critical study.
Eur Arch Otorhinolaryngol. 2011 Dec 23. [Epub ahead of print]


Department of Psychoanalysis and Clinical Consulting, Ghent University, H. Dunantlaan 2, 9000, Ghent, Belgium, Els.Ooms@Ugent.be.

Tinnitus has been defined as a phantom auditory perception. Research indicates the necessity to make a distinction between the physical symptom and the subjective severity of the tinnitus symptom, since especially the latter seems to vary among patients. The relationship between tinnitus severity and psychological variables has been well established. Anxiety is considered to be an important variable for understanding the differences in the subjective tinnitus severity. Although many studies confirm the relationship between anxiety and tinnitus severity, most studies do not take the possibility of shared method variance and content overlap between questionnaires into account. Furthermore, anxiety is a broad concept and contains both a cognitive and somatic dimension. Research including both dimensions of anxiety in tinnitus population is rare. According to us two conditions must be fulfilled before theorization on the relation is useful: (1) the presence of clinically relevant cognitive and/or somatic anxiety, (2) evidence of a substantial or “real” relationship. In our sample, almost 60% reported more than average cognitive anxiety and 40.8% reported clinical relevant somatic anxiety. After controlling for content overlap between the questionnaires used, the relation between tinnitus severity and cognitive and somatic anxiety remains significant. Two hypothetical models concerning this relationship that deserve future research attention are described.

Systematic review and meta-analysis of the risk factors for sudden sensorineural hearing loss in adults.

Lin RJ, Krall R, Westerberg BD, Chadha NK, Chau JK.

St. Paul’s Rotary Hearing Clinic, St. Paul’s Hospital, Vancouver, British Columbia.

OBJECTIVES/HYPOTHESIS: To review the medical literature evidence of potential risk factors for sudden sensorineural hearing loss (SSNHL) in the adult general population. STUDY DESIGN: Systematic review of prospective and retrospective studies; meta-analysis of case-controlled studies. METHODS: Three researchers independently reviewed MEDLINE (January 1, 1950-November 30, 2010), Embase (January 1, 1980-November 30, 2010), and Evidence-Based Medicine Reviews databases in addition to conducting a manual reference search. Randomized controlled trials, prospective cohort studies, consecutive/nonconsecutive case series, and retrospective reviews in which a clear definition of SSNHL was stated were included in the study. Researchers individually extracted data regarding patient information and the presumed risk factors. Discrepancies were resolved by mutual consensus. RESULTS: Twenty-two articles met the inclusion criteria. Cardiovascular risk factors (smoking, increased alcohol consumption) appeared to be associated with a higher risk of developing SSNHL. A low level of serum folate may also be implicated as a risk factor. Factor V Leiden and MTHFR gene polymorphisms were found to occur more frequently in patients with SSNHL in several studies, suggesting these inherited prothrombophilic mutations could be independent risk factors of SSNHL. CONCLUSIONS: Acquired and inherited cardiovascular risk factors appeared to be associated with an increased risk of developing SSNHL. Copyright © 2011 The American Laryngological, Rhinological, and Otological Society, Inc.
MTHFR 677T Is a Strong Determinant of the Degree of Hearing Loss Among Polish Males with Postlingual Sensorineural Hearing Impairment.

1 Institute of Physiology and Pathology of Hearing, Warsaw, Poland.

Hearing impairment (HI) is the most common sensory handicap. Congenital HI often has a genetic basis, whereas the etiology of nonsyndromic postlingual HI (npHI) usually remains unidentified. Our purpose was to test whether the MTHFR C677T (rs1801133) polymorphism affecting folate metabolism is associated with the occurrence or severity of npHI. We studied rs1801133 genotypes in 647 npHI patients (age <40, sudden sensorineural loss excluded, HI characterized as mean of better ear hearing thresholds for 0.5-8 kHz) and 3273 adult controls from the background population. Genotype distribution among patients and controls was similar, but among male cases (n=302) we found a dose-dependent correlation of MTHFR 677T with the degree of HI (mean thresholds in dB: 38.8, 44.9, and 53.3, for CC, CT, and TT genotypes, respectively; p=0.0013, p(cor.)=0.017). Among male patients rs1801133 TT significantly increased the risk of severe/profound HI (odds ratio=4.88, p=0.001). Among controls the known effect of MTHFR 677T on plasma total homocysteine was more pronounced in men than in women (p<0.00004 for genotype-sex interaction) suggesting that in Poland folate deficiency is more prevalent in males. In conclusion, we report a novel strong effect of MTHFR 677T among males with npHI. The functional significance of rs1801133 suggests that these patients may benefit from folate supplementation—an intervention which is simple, cheap, and devoid of side effects.

Tracking the expression of excitatory and inhibitory neurotransmission-related proteins and neuroplasticity markers after noise induced hearing loss.

Browne CJ, Morley JW, Parsons CH.

Department of Anatomy and Cell Biology, School of Medicine, The University of Western Sydney, Sydney, New South Wales, Australia.

Excessive exposure to loud noise can damage the cochlea and create a hearing loss. These pathologies coincide with a range of CNS changes including reorganisation of frequency representation, alterations in the pattern of spontaneous activity and changed expression of excitatory and inhibitory neurotransmitters. Moreover, damage to the cochlea is often accompanied by acoustic disorders such as hyperacusis and tinnitus, suggesting that one or more of these neuronal changes may be involved in these disorders, although the mechanisms remain unknown. We tested the hypothesis that excessive noise exposure increases expression of markers of excitation and plasticity, and decreases expression of inhibitory markers over a 32-day recovery period. Adult rats (n = 25) were monaurally exposed to a loud noise (16 kHz, 1/10(th) octave band pass (115 dB SPL)) for 1-hour, or left as non-exposed controls (n=5). Animals were euthanased at either 0, 4, 8, 16 or 32 days following acoustic trauma. We used Western Blots to quantify protein levels of GABA(A) receptor subunit α1 (GABA(A)α1), Glutamic-Acid Decarboxylase-67 (GAD-67), N-Methyl-D-Aspartate receptor subunit 2A (NR2A), Calbindin (Calb1) and Growth Associated Protein 43 (GAP-43) in the Auditory Cortex (AC), Inferior Colliculus (IC) and Dorsal Cochlear Nucleus (DCN). Compared to sham-exposed controls, noise-exposed animals had significantly (p<0.05): lower levels of GABA(A)α1 in the contralateral AC at day-16 and day-32, lower levels of GAD-67 in the ipsilateral DCN at day-4, lower levels of Calb1 in the ipsilateral DCN at day-0, lower levels of GABA(A)α1 in the ipsilateral AC at day-4 and day-32. GAP-43 was reduced in the ipsilateral AC for the duration of the experiment. These complex fluctuations in protein expression suggests that for at least a month following acoustic trauma the auditory system is adapting to a new pattern of sensory input.
Noise overexposure alters long-term somatosensory-auditory processing in the dorsal cochlear nucleus - possible basis for tinnitus-related hyperactivity?
Dehmel S, Pradhan S, Koehler S, Bledsoe S, Shore S.
Kresge Hearing Research Institute, University of Michigan, Ann Arbor, Michigan 48109.
The dorsal cochlear nucleus (DCN) is the first neural site of bimodal auditory-somatosensory integration. Previous studies have shown that stimulation of somatosensory pathways results in immediate suppression or enhancement of subsequent acoustically evoked discharges. In the unimpaired auditory system suppression predominates. However, damage to the auditory input pathway leads to enhancement of excitatory somatosensory inputs to the cochlear nucleus, changing their effects on DCN neurons (Shore et al., 2008; Zeng et al., 2009). Given the well described connection between the somatosensory system and tinnitus in patients we sought to determine whether plastic changes in long-lasting bimodal somatosensory-auditory processing accompany tinnitus. Here we demonstrate for the first time in vivo long-term effects of somatosensory inputs on acoustically evoked discharges of DCN neurons in guinea pigs. The effects of trigeminal nucleus stimulation are compared between normal-hearing animals and animals overexposed with narrow band noise and behaviorally tested for tinnitus. The noise exposure resulted in a temporary threshold shift in auditory brainstem responses but a persistent increase in spontaneous and sound-evoked DCN unit firing rates and increased steepness of rate-level functions. Rate increases were especially prominent in buildup units. The long-term somatosensory enhancement of sound-evoked responses was strengthened while suppressive effects diminished in noise-exposed animals, especially those that developed tinnitus. Damage to the auditory nerve is postulated to trigger compensatory long-term synaptic plasticity of somatosensory inputs that might be an important underlying mechanism for tinnitus generation. Free article.

Spontaneous hyperactivity in the auditory midbrain: Relationship to afferent input.
Hear Res. 2012 Feb 13. [Epub ahead of print]
Robertson D, Bester C, Vogler D, Mulders WH.
The Auditory Laboratory, School of Anatomy, Physiology and Human Biology, M311, The University of Western Australia, 35 Stirling hwy, Crawley, Western Australia 6009, Australia.
Hyperactivity in the form of increased spontaneous firing rates of single neurons develops in the guinea pig inferior colliculus (IC) after unilateral loud sound exposures that result in behavioural signs of tinnitus. The hyperactivity is found in those parts of the topographic frequency map in the IC where neurons possess characteristic frequencies (CFs) closely related to the region in the cochlea where lasting sensitivity changes occur as a result of the loud sound exposure. The observed hyperactivity could be endogenous to the IC, or it could be driven by hyperactivity at lower stages of the auditory pathway. In addition to the dorsal cochlear nucleus (DCN) hyperactivity reported by others, specific cell types in the ventral cochlear nucleus (VCN) also show hyperactivity in this animal model suggesting that increased drive from several regions of the lower brainstem could contribute to the observed hyperactivity in the midbrain. In addition, spontaneous afferent drive from the cochlea itself is necessary for the maintenance of hyperactivity up to about 8 weeks post cochlear trauma. After 8 weeks however, IC hyperactivity becomes less dependent on cochlear input, suggesting that central neurons transition from a state of hyperexcitability to a state in which they generate their own endogenous firing. The results suggest that there might be a “therapeutic window” for early-onset tinnitus, using treatments that reduce cochlear afferent firing. Copyright © 2012. Published by Elsevier B.V.
Reversible Long-Term Changes in Auditory Processing in Mature Auditory Cortex in the Absence of Hearing Loss Induced by Passive, Moderate-Level Sound Exposure.  
Ear Hear. 2012 Feb 16. [Epub ahead of print]

Pienkowski M, Eggermont JJ.

1Departments of Physiology and Pharmacology, University of Calgary, Calgary, Alberta, Canada  
2Departments of Psychology, University of Calgary, Calgary, Alberta, Canada  
3Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta, Canada.

It has become increasingly clear that even occasional exposure to loud sounds in occupational or recreational settings can cause irreversible damage to the hair cells of the cochlea and the auditory nerve fibers, even if the resulting partial loss of hearing sensitivity, usually accompanied by tinnitus, disappears within hours or days of the exposure. Such exposure may explain at least some cases of poor speech intelligibility in noise in the face of a normal or near-normal audiogram. Recent findings from our laboratory suggest that long-term changes to auditory brain function-potentially leading to problems with speech intelligibility-can be effected by persistent, passive exposure to more moderate levels of noise (in the 70 dB SPL range) in the apparent absence of damage to the auditory periphery (as reflected in normal distortion product otoacoustic emissions and auditory brainstem responses). Specifically, passive exposure of adult cats to moderate levels of band-pass-filtered noise, or to band-limited ensembles of dense, random tone pips, can lead to a profound decrease of neural activity in the auditory cortex roughly in the exposure frequency range, and to an increase of activity outside that range. This can progress to an apparent reorganization of the cortical tonotopic map, which is reminiscent of the reorganization resulting from hearing loss restricted to a part of the hearing frequency range, although again, no hearing loss was apparent after our moderate-level sound exposure. Here, we review this work focusing specifically on the potential hearing problems that may arise despite a normally functioning auditory periphery.

Targeting inhibitory neurotransmission in tinnitus.  
Brain Res. 2012 Feb 14. [Epub ahead of print]

Richardson BD, Brozoski TJ, Ling LL, Caspary DM.

Department of Pharmacology, Southern Illinois University School of Medicine, 801 N Rutledge St, Rm. 3234, PO Box 19629, Springfield, IL 62794, USA.

Tinnitus perception depends on the presence of its neural correlates within the auditory neuraxis and associated structures. Targeting specific circuits and receptors within the central nervous system in an effort to relieve the perception of tinnitus and its impact on one’s emotional and mental state has become a focus of tinnitus research. One approach is to upregulate endogenous inhibitory neurotransmitter levels (e.g., glycine and GABA) and selectively target inhibitory receptors in key circuits to normalize tinnitus pathophysiology. Thus, the basic functional and molecular properties of two major ligand-gated inhibitory receptor systems, the GABA(A) receptor (GABA(A)R) and glycine receptor (GlyR) are described. Also reviewed is the rationale for targeting inhibition, which stems from reported tinnitus-related homeostatic plasticity of inhibitory neurotransmitter systems and associated enhanced neuronal excitability throughout most central auditory structures. However, the putative role of the medial geniculate body (MGB) in tinnitus has not been previously addressed, specifically in terms of its inhibitory afferents from inferior colliculus and thalamic reticular nucleus and its GABA(A)R functional heterogeneity. This heterogeneous population of GABA(A)Rs, which may be altered in tinnitus pathology, and its key anatomical position in the auditory CNS make the MGB a compelling structure for tinnitus research. Finally, some selective compounds, which enhance tonic inhibition, have successfully ameliorated tinnitus in animal studies, suggesting that the MGB and, to a lesser degree, the auditory cortex may be their primary locus of action. These pharmacological interventions are examined in terms of their mechanism of action and why these agents may be effective in tinnitus treatment. This article is part of a Special Issue entitled Tinnitus Neuroscience. Copyright Â© 2012 Elsevier B.V. All rights reserved.
Noise exposure enhances auditory cortex responses related to hyperacusis behavior.
Brain Res. 2012 Feb 9. [Epub ahead of print]

Sun W, Deng A, Jayaram A, Gibson B.
Center for Hearing & Deafness, The State University of New York at Buffalo, NY, USA; Department of Communicative Disorders and Sciences, The State University of New York at Buffalo, NY, USA.

Hyperacusis, a marked intolerance to normal environmental sound, is a common symptom in patients with tinnitus, Williams syndrome, autism, and other neurologic diseases. It has been suggested that an imbalance of excitation and inhibition in the central auditory system (CAS) may play an important role in hyperacusis. Recent studies found that noise exposure, one of the most common causes of hearing loss and tinnitus, can increase the auditory cortex (AC) response, presumably by increasing the gain of the AC. However, it is not clear whether the increased cortical response will affect sound sensitivity and induce hyperacusis. In this experiment, we studied the effects of noise exposure (narrow band noise, 12kHz, 120dB SPL, 1hour) on the physiological response of the inferior colliculus (IC) and the AC, and the behavioral sound reaction in conscious Sprague Dawley rats. Noise exposure induced a decrease of sound evoked potential in the IC. However, significant increases of AC response including sound evoked potentials and the spike firing rates of AC neurons were recorded right after the noise exposure. These results suggest that noise exposure induces hyperexcitability of AC presumably by increasing the post-synaptic response of AC neurons. The behavioral consequence of the noise exposure on sound perception was measured by the amplitude of the acoustic startle response before and after noise exposure in a separate group of rats. Although noise exposure caused a moderate hearing loss, the acoustic startle amplitude at the super-threshold level was significantly increased. These results suggest that noise exposure can cause exaggerated the sound reaction which may be related with the enhanced responsiveness of the AC neurons. This phenomenon may be related with noise induced hyperacusis. This article is part of a Special Issue entitled Tinnitus Neuroscience. Published by Elsevier B.V.

Neuroanatomy - Part 2 - Facts and hypotheses on fascia, dura, and brainstem
[Neuroanatomie - Teil 2 - Fakten und Hypothesen zu Faszien, Dura und Hirnstamm]
[Article in German]

von Heymann, W.a, Locher, H.b, Böhni, U.c, Habring, M.d

a Orthopädische Praxis, Schwachhauser Heerstr. 367, Bremen, 28211, Germany
b Zentrum für Schmerztherapie und manuelle Medizin, Tettnang, Germany
c ZeniT Zentrum für interdisziplinäre Therapie des Bewegungsapparates, Schaffhausen, Switzerland
d Praxis für Allgemeinmedizin, Bad Ischl, Austria

In this second part about neuroanatomy as presented at the 3rd Lake Constance Conference, special attention is paid to innervations of the fascia and the dura mater. Although the function is not really clear, the high amount of autonomous nerve fibers in these tissues is described. In particular the innervations of the dorsal fascia seem to have more influence in developing chronic pain than previously estimated. Postoperative sprouting of nerve fibers in the dura is probably an important origin for postnucleotomy syndrome. Nociceptors in the dura are exceptionally dense near arteries. Trigeminal-spinal and similar convergence reactions in the brainstem are important for manual diagnosis and can be explained from the perspective of neuroanatomy. This has an important differential diagnostic impact for an understanding of not only the cervical pathogenesis of headache, dysfunction of swallowing or phonation, dizziness and tinnitus but also for craniomandibular dysfunction as well as disturbances of body statics via pelvic and sacroiliac dysfunctions. Finally the involvement of the vagal system in controlling viscero-somatic and somato-visceral reactions is explained using the example of the solitary tract nucleus. This is a probable explanation for the effects of manual visceral techniques. © 2012 Springer-Verlag.
Vascular compression of the cochlear nerve and tinnitus: a pathophysiological investigation.
TRI Tinnitus Clinic, BRAIN & Department of Neurosurgery, University Hospital Antwerp, Wilrijkstraat 10, 2650, Edegem, Belgium.

De Ridder D, Vanneste S, Adriaensens I, Lee AP, van de Heyning P, Möller A.

OBJECTIVE: Chronic microvascular compressions of the eighth nerve induce a slowing down of signal transmission in the auditory nerve, electrophysiologically characterized by IPL I-III prolongation. METHODS: The authors hypothesize this is compensated by an active slowing down of signal transmission of the contralateral input at the level of the brainstem, characterized by contralateral IPL III-V prolongation. RESULTS: Differences between ipsilateral and contralateral IPL I-III and IPL III-V are analyzed before and after microvascular decompression. ABR diagnostic criteria for microvascular compression are ipsilateral IPL I-III prolongation or ipsilateral peak II decrease + ipsilateral IPL I-III prolongation. With IPL I-III as diagnostic criterion, unlike preoperatively the difference between the ipsi- and contralateral IPL I-III is significant postoperatively. When using the stricter diagnostic criterion of IPL I-III + peak II, there is a preoperative significant difference between ipsi- and contralateral IPL I-III, but postoperatively the difference between the ipsi- and contralateral IPL I-III is not significant. CONCLUSIONS: Preoperatively, there is a marginal significant difference between the ipsi- and contralateral IPL III-V, which disappears postoperatively.

Wavelet analysis demonstrates no abnormality in contralateral suppression of otoacoustic emissions in tinnitus patients.
Hear Res. 2012 Feb 24. [Epub ahead of print]

Geven LI, Wit HP, de Kleine E, van Dijk P.
Department of Otorhinolaryngology/Head and Neck Surgery, University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands; Graduate School of Medical Sciences, Research School of Behavioral and Cognitive Neurosciences, University of Groningen, Groningen, The Netherlands.

The efferent auditory system is thought to play a role in the origin of tinnitus. Part of this system can be tested in humans with contralateral suppression of otoacoustic emissions. Stimulation of the medial olivocochlear efferent system is responsible for this reduction of otoacoustic emissions after contralateral acoustic stimulation. Previous research on patients with tinnitus showed inconclusive results. With wavelet analysis both time and frequency information of the emission can be analysed and compared. Contralateral suppression of otoacoustic emissions was therefore measured in tinnitus patients (n = 26) and normal subjects (n = 37) and analysed using wavelets. No significant difference in suppression was found between the tinnitus patients and the control group. Copyright © 2012. Published by Elsevier B.V.

Gamma-aminobutyric acid and glutamic acid levels in the auditory pathway of rats with chronic tinnitus: a direct determination using high resolution point-resolved proton magnetic resonance spectroscopy (H-MRS).

Brozoski T, Odintsov B, Bauer C.
Division of Otolaryngology, Southern Illinois University School of Medicine, Springfield IL, USA.

Damage to the auditory system following high-level sound exposure reduces afferent input. Homeostatic mechanisms appear to compensate for the loss. Overcompensation may produce the sensation of sound without an objective physical correlate, i.e., tinnitus. Several potential compensatory neural processes have been identified, such as increased spontaneous activity. The cellular mechanisms enabling such compensatory processes may involve down-regulation of inhibitory neurotransmission mediated by...
γ-amino butyric acid (GABA), and/or up-regulation of excitatory neurotransmission, mediated by glutamic acid (Glu). Because central processing systems are integrated and well-regulated, compensatory changes in one system may produce reactive changes in others. Some or all may be relevant to tinnitus. To examine the roles of GABA and Glu in tinnitus, high resolution point-resolved proton magnetic resonance spectroscopy (1H-MRS) was used to quantify their levels in the dorsal cochlear nucleus (DCN), inferior colliculus (IC), medial geniculate body (MGB), and primary auditory cortex (A1) of rats. Chronic tinnitus was produced by a single high-level unilateral exposure to noise, and was measured using a psychophysical procedure sensitive to tinnitus. Decreased GABA levels were evident only in the MGB, with the greatest decrease, relative to unexposed controls, obtained in the contralateral MGB. Small GABA increases may have been present bilaterally in A1 and in the contralateral DCN. Although Glu levels showed considerable variation, Glu was moderately and bilaterally elevated both in the DCN and in A1. In the MGB Glu was increased ipsilaterally but decreased contralaterally. These bidirectional and region-specific alterations in GABA and Glu may reflect large-scale changes in inhibitory and excitatory equilibrium accompanying chronic tinnitus. The present results also suggest that targeting both neurotransmitter systems may be optimal in developing more effective therapeutics.

Nicotinic neuromodulation in auditory cortex requires MAPK activation in thalamocortical and intracortical circuits.
J Neurophysiol. 2012 Feb 22. [Epub ahead of print]
Intskirveli I, Metherate R.

1Univ. of California, Irvine.

Activation of nicotinic acetylcholine receptors (nAChRs) by systemic nicotine enhances sensory-cognitive function and sensory-evoked cortical responses. Although nAChRs mediate fast neurotransmission at many synapses in the nervous system, nicotinic regulation of cortical processing is neuromodulatory. To explore potential mechanisms of nicotinic neuromodulation, we examined whether intracellular signal transduction involving mitogen-activated protein kinase (MAPK) contributes to regulation of tone-evoked responses in primary auditory cortex (A1) in the mouse. Systemic nicotine enhanced characteristic frequency (CF) tone-evoked current-source density (CSD) profiles in A1, including the shortest-latency (presumed thalamocortical) current sink in layer 4 and longer-latency (presumed intracortical) sinks in layers 2-4, by increasing response amplitudes and decreasing response latencies. Microinjection of the MAPK kinase (MEK) inhibitor U0126 into the thalamus, targeting the auditory thalamocortical pathway, blocked the effect of nicotine on the initial (thalamocortical) CSD component, but did not block enhancement of longer-latency (intracortical) responses. Conversely, microinjection of U0126 into supragranular layers of A1 blocked nicotine's effect on intracortical, but not thalamocortical, CSD components. Simultaneously with enhancement of CF-evoked responses, responses to spectrally-distant (nonCF) stimuli were reduced, implying nicotinic “sharpening” of frequency receptive fields, an effect also blocked by MEK inhibition. Consistent with these physiological results, acoustic stimulation with nicotine produced immunolabel for activated MAPK in A1, primarily in layer 2/3 cell bodies. Immunolabel was blocked by intracortical microinjection of the nAChR antagonist dihydro-β-erythroidine, but not methyllycaconitine, implicating α4β2*, but not α7, nAChRs. Thus, activation of MAPK in functionally distinct forebrain circuits-thalamocortical, local intracortical and long-range intracortical-underlies nicotinic neuromodulation of A1.
Unlearning tinnitus-related cerebral synchrony with acoustic coordinated reset stimulation: theoretical concept and modelling.

Tass PA, Popovych OV.

Institute of Neuroscience and Medicine - Neuromodulation (INM-7), Research Center Jülich, 52425, Jülich, Germany, p.tass@fz-juelich.de.

Tinnitus is a deafferentation-induced phantom phenomenon characterized by abnormal cerebral synchrony and connectivity. Computationally, we show that desynchronizing acoustic coordinated reset (CR) stimulation can effectively counteract both up-regulated synchrony and connectivity. CR stimulation has initially been developed for the application to electrical deep brain stimulation. We here adapt this approach to non-invasive, acoustic CR stimulation. For this, we use the tonotopic organization of the central auditory system and replace electrical stimulation bursts applied to different brain sites by acoustically delivered tones of different pitch. Based on our simulations, we propose non-invasive acoustic CR stimulation as a possible novel therapy for tinnitus.

Cortisol suppression and hearing thresholds in tinnitus after low-dose dexamethasone challenge.

Simoens VL, Hebert S.

BACKGROUND: Tinnitus is a frequent, debilitating hearing disorder associated with severe emotional and psychological suffering. Although a link between stress and tinnitus has been widely recognized, the empirical evidence is scant. Our aims were to test for dysregulation of the stress-related hypothalamus-pituitary adrenal (HPA) axis in tinnitus and to examine ear sensitivity variations with cortisol manipulation.

METHODS: Twenty-one tinnitus participants and 21 controls comparable in age, education, and overall health status but without tinnitus underwent basal cortisol assessments on three non-consecutive days and took 0.5 mg of dexamethasone (DEX) at 23:00 on the first day. Cortisol levels were measured hourly the next morning. Detection and discomfort hearing thresholds were measured before and after dexamethasone suppression test. RESULTS: Both groups displayed similar basal cortisol levels, but tinnitus participants showed stronger and longer-lasting cortisol suppression after DEX administration. Suppression was unrelated to hearing loss. Discomfort threshold was lower after cortisol suppression in tinnitus ears. CONCLUSIONS: Our findings suggest heightened glucocorticoid sensitivity in tinnitus in terms of an abnormally strong glucocorticoid receptor (GR)-mediated HPA-axis feedback (despite a normal mineralocorticoid receptor (MR)-mediated tone) and lower tolerance for sound loudness with suppressed cortisol levels. Long-term stress exposure and its deleterious effects therefore constitute an important predisposing factor for, or a significant pathological consequence of, this debilitating hearing disorder. Free article.

Audiometric asymmetry and tinnitus laterality.

Tsai BS, Sweetow RW, Cheung SW.

Department of Otolaryngology-Head and Neck Surgery, Vanderbilt University Medical Center, Vanderbilt University, Nashville, Tennessee.

OBJECTIVES/HYPOTHESIS: To identify an optimal audiometric asymmetry index for predicting tinnitus laterality. STUDY DESIGN: Retrospective medical record review. METHODS: Data from adult tinnitus patients (80 men and 44 women) were extracted for demographic, audiometric, tinnitus laterality, and related information. The main measures were sensitivity, specificity, positive predictive value (PPV), and receiver operating characteristic (ROC) curves. RESULTS: Three audiometric asymmetry indices were constructed using one, two, or three frequency elements to compute the average interaural threshold

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difference (aITD). Tinnitus laterality predictive performance of a particular index was assessed by increasing the cutoff or minimum magnitude of the aITD from 10 to 35 dB in 5-dB steps to determine its ROC curve. Single frequency index performance was inferior to the other two (P < .05). Double and triple frequency indices were indistinguishable (P > .05). Two adjoining frequency elements with aITD ≥ 15 dB performed optimally for predicting tinnitus laterality (sensitivity = 0.59, specificity = 0.71, and PPV = 0.76). Absolute and relative magnitudes of hearing loss in the poorer ear were uncorrelated with tinnitus distress. CONCLUSIONS: An optimal audiometric asymmetry index to predict tinnitus laterality is one whereby 15 dB is the minimum aITD of two adjoining frequencies, inclusive of the maximal ITD. Tinnitus laterality dependency on magnitude of interaural asymmetry may inform design and interpretation of neuroimaging studies. Monaural acoustic tinnitus therapy may be an initial consideration for asymmetric hearing loss meeting the criterion of aITD ≥ 15 dB. Copyright © 2012 The American Laryngological, Rhinological, and Otological Society, Inc.

Self-reported and behavioral sound avoidance in tinnitus and hyperacusis subjects, and association with anxiety ratings.

Blaesing L, Kroener-Herwig B.
Department of Clinical Psychology and Psychotherapy, Georg-August University of Göttingen, Germany.

Objective: The purpose of the study was to analyse the role of sound avoidance and anxiety in tinnitus subjects with hyperacusis, defined as hypersensitivity to low to moderate intensity sounds. Design: A group of tinnitus subjects with hyperacusis was compared to tinnitus subjects without hyperacusis, and healthy controls. For assessing noise avoidance, a questionnaire was developed (noise avoidance questionnaire, NAQ) and the duration of self-exposure to a pure tone was assessed as a behavioral index. Different self-rating instruments concerning tinnitus (STI, TF-12), hyperacusis (GÜF), and anxiety (BAI, STAI-T) were used, as well as a psychoacoustic indicator of hyperacusis (ULL). Study sample: Fifty-six tinnitus subjects with/without hyperacusis and 30 controls without tinnitus and hyperacusis participated in the experiment. Results: The findings indicate that subjects with hyperacusis reported significantly more noise-related avoidance in daily life and show significantly shorter exposure to a pure tone than non-hyperacusic subjects, while discomfort was at the same level for each individual. Self-reported avoidance behavior correlated significantly with distress attributed to hyperacusis (r =0.81), and with anxiety ratings. Conclusions: These results suggest that hyperacusis is associated with noise-related avoidance behavior and anxiety. Systematic exposure to sound could play a significant role in the treatment of hyperacusis.

Time course of tinnitus development following noise exposure in mice.

Turner J, Larsen D, Hughes L, Moechars D, Shore S.
Department of Surgery/Otolaryngology, Southern Illinois University School of Medicine, Springfield, Illinois; Department of Psychology, Illinois College, Jacksonville, Illinois. jturner@siumed.edu.

Gap-induced prepulse inhibition of acoustic startle (GPIAS) has been used in rats and mice to study the problem of tinnitus. The current study demonstrates that similar methods can be used to study the temporal development of tinnitus over time in middle-aged mice. Six-month-old mice on a mixed C57Bl6 × 129 background were anesthetized with isoflurane and exposed to unilateral noise (n = 15), or sham exposure for controls (n = 8), for 1 hr (16-kHz octave band signal, 116-dB SPL). Tinnitus was tested in eight different sound frequency bands before and at postexposure time points of 1, 3-4, 7, 14, 21, and 30 days and monthly thereafter until 7 months postexposure. Noise-exposed mice displayed a number of changes in GPIAS consistent with the presence of hyperacusis and tinnitus. Noise exposure was associated with acute tinnitus measured 1 day later at several frequencies at and above the
exposure frequency center. Consistent, chronic tinnitus then emerged in the 24-kHz range. Several time points following noise exposure suggested evidence of hyperacusis, often followed temporally by the development of deficits in GPIAS (reflecting tinnitus). Temporal development of these changes following noise exposure are discussed in the context of the interactions among aging, noise exposure, and the associated neurochemical changes that occur at early stages of auditory processing. © 2012 Wiley Periodicals, Inc. Copyright © 2012 Wiley Periodicals, Inc.

III Diagnostics

Can Vestibular-Evoked Myogenic Potentials Help Differentiate Meniere Disease from Vestibular Migraine?

Zuniga MG, Janky KL, Schubert MC, Carey JP.

Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.

Objectives. To characterize both cervical and ocular vestibular-evoked myogenic potential (cVEMP, oVEMP) responses to air-conducted sound (ACS) and midline taps in Ménière disease (MD), vestibular migraine (VM), and controls, as well as to determine if cVEMP or oVEMP responses can differentiate MD from VM STUDY DESIGN. Prospective cohort study. SETTING. Tertiary referral center. SUBJECTS AND METHODS. Unilateral definite MD patients (n = 20), VM patients (n = 21) by modified Neuhauser criteria, and age-matched controls (n = 28). cVEMP testing used ACS (clicks), and oVEMP testing used ACS (clicks and 500-Hz tone bursts) and midline tap stimuli (reflex hammer and Mini-Shaker). Outcome parameters were cVEMP peak-to-peak amplitudes and oVEMP n10 amplitudes. RESULTS. Relative to controls, MD and VM groups both showed reduced click-evoked cVEMP (P < .001) and oVEMP (P < .001) amplitudes. Only the MD group showed reduction in tone-evoked amplitudes for oVEMP. Tone-evoked oVEMPs differentiated MD from controls (P = .001) and from VM (P = .007). The oVEMPs in response to the reflex hammer and Mini-Shaker midline taps showed no differences between groups (P > .210). CONCLUSIONS. Using these techniques, VM and MD behaved similarly on most of the VEMP test battery. A link in their pathophysiology may be responsible for these responses. The data suggest a difference in 500-Hz tone burst-evoked oVEMP responses between MD and MV as a group. However, no VEMP test that was investigated segregated individuals with MD from those with VM.

Various levels of plasma brain-derived neurotrophic factor in patients with tinnitus.
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Goto F, Saruta J, Kanzaki S, To M, Tsutsumi T, Tsukinoki K, Ogawa K.

Department of Otolaryngology, Hino Municipal Hospital, Japan; Department of Otolaryngology, Keio University, Japan.

OBJECTIVE: Thus far, no objective measure has been developed to evaluate tinnitus severity. There is a close relationship between tinnitus and depression, in which brain-derived neurotrophic factor (BDNF) has a pathophysiological role. To determine whether BDNF levels could be used to evaluate tinnitus severity, we evaluated plasma BDNF levels in patients with tinnitus. METHODS: Plasma BDNF levels were measured in 43 tinnitus patients and 30 healthy control patients. The severities of tinnitus, depression, and anxiety were measured using the tinnitus handicap inventory (THI) and the hospital anxiety and depression scale (HADS), respectively. Patients with tinnitus were divided into 2 groups depending on their THI scores: mildly handicapped (<36) and severely handicapped (>38). We also divided our subjects into 2 groups depending on the HADS score, which represents patient mood, including depression and anxiety. RESULTS: Plasma BDNF levels were significantly higher in the mildly handicapped group than in the severely handicapped and control groups (P<0.01). Patients with
HADS scores of ≤14 had significantly lower THI scores (P<0.05) and higher BDNF levels (P<0.01).

CONCLUSIONS: Our findings show for the first time that plasma BDNF levels vary with the severity of tinnitus, suggesting that plasma BDNF level is a useful tool for objective evaluation of tinnitus. Copyright © 2012 Elsevier Ireland Ltd. All rights reserved.

A clinical and histopathologic study of jugular bulb abnormalities.

Friedmann DR, Eubig J, Winata LS, Pramanik BK, Merchant SN, Lalwani AK.

Department of Otolaryngology, New York University School of Medicine, 550 First Ave, 7Q, New York, NY 10016. anil.lalwani@nyumc.org.

OBJECTIVE: To further define the spectrum of clinical presentation and explore the histologic sequelae of jugular bulb abnormalities (JBAs). DESIGN: Retrospective review. SETTING: Academic medical center. PATIENTS: Thirty patients with radiologic evidence of inner ear dehiscence by JBA. MAIN OUTCOME MEASURE: Thirty patients with radiologic inner ear dehiscence by JBA and 1579 temporal bone specimens were evaluated for consequences from JBA. RESULTS: We found that JBA-associated inner ear dehiscence could be identified on computed tomography of the temporal bone but not on magnetic resonance imaging scan. Jugular bulb abnormalities eroded the vestibular aqueduct most often (in 25 patients), followed by the facial nerve (5 patients) and the posterior semicircular canal (4 patients). Half of the patients (15) were asymptomatic. Results from vestibular evoked myogenic potential (VEMP) tests were positive in 8 of 12 patients with inner ear dehiscence. Histologically, only 2 of 41 temporal bones with dehiscence of the vestibular aqueduct demonstrated endolymphatic hydrops. CONCLUSIONS: Jugular bulb abnormalities can erode into the vestibular aqueduct, facial nerve, and the posterior semicircular canal. While symptoms may include pulsatile tinnitus, vertigo, or conductive hearing loss, in contrast to earlier reports, half of the patients were asymptomatic. Dehiscence of vestibular aqueduct rarely leads to clinical or histologic hydrops. The VEMP testing was useful in confirming the presence of inner ear dehiscence due to JBAs. Because the natural history of JBAs is unknown, these patients should be followed closely to evaluate for progression of the JBA or development of symptoms.

Tinnitus measurement with conventional audiometer versus high-frequency audiometer
[Medición de acúfenos con audiómetro convencional versus audiómetro de alta frecuencia].
[Article in Spanish]


ª UGC Otorrinolaringología, Hospital Universitario Virgen del Rocío, Sevilla, España
ª Centro Integral de Acúfenos, Sevilla, España

Introduction and objectives: Determinations of the psychoacoustic characteristics of tinnitus (frequency and intensity) are valid for diagnosis, treatment, monitoring and research purposes. The aim of this work is to compare the frequency of the tinnitus measured with a standard audiometer and a high frequency audiometer. Methods: We used a conventional audiometer (frequency range: 125-12 000 Hz) and a high-frequency audiometer (frequency range: 125-18 000 Hz) to measure the frequency and intensity of tinnitus in 47 patients with tinnitus as a continuous ringing. Results: We found statistically-significant differences between the determination of the frequency of tinnitus made with conventional and high-frequency audiometers, as well as a correlation between high-frequency tinnitus and distress expressed by patients. Conclusions: 1) The frequency of tinnitus determined by high-frequency audiometer is greater than the frequency determined by conventional audiometer; 2) the higher the frequency of tinnitus, the more discomfort the patient manifests; and 3) there is no relationship between the intensity and discomfort caused by tinnitus. © 2011 Elsevier España, S.L. All rights reserved.
3-Dimensional reconstruction of the venous system in patients suffering from pulsatile tinnitus. Acta Otolaryngol. 2011 Dec 27. [Epub ahead of print]

Cho IK, Jung JY, Yoo DS, Suh MW.

Department of Otolaryngology-Head & Neck Surgery, Department of Diagnostic Radiology, Medical College Dankook University, Cheonan-si, Korea.

Abstract Conclusions: An abrupt change in the venous caliber, producing turbulent flow, may be a cause of pulsatile tinnitus (PT). The largest area/smallest area (L/S) ratio >4.75 may be a criterion indicating abrupt caliber change and causing PT. Objectives: Contrast-enhanced CT is recommended as an initial work-up modality in PT. But, in the majority of cases, no definite pathology can be found, even after extensive work-up. In these cases, the unilateral dominant venous system may be the cause of PT. The aim of this study was to compare, through 3D-reformatted images of the intracranial venous system, the volume, cross-sectional area, and caliber changes in patients with PT and normal controls. Methods: This was a cross-sectional study set in a tertiary referral center. Eleven patients (11 unilateral PT ears) and 12 normal control ears were enrolled. All the subjects were confirmed with normal CT angiography findings. The intracranial venous structure was three-dimensionally reconstructed. Three areas with the largest and the smallest dimension were selected for further analysis: the transverse sinus (T), isthmus (I), and the jugular bulb (B). The total volume, cross-sectional area, and cross-sectional area ratios of the three areas were compared in the PT group and the normal control group. Results: The L/S ratio was significantly increased in the PT group (5.01), compared with the control group (3.42). When the threshold value of the L/S ratio was assessed by the ROC method, 4.75 seemed to be the significant dissecting point. The sensitivity of this method was 0.64 and the specificity was 0.83.

The Tinnitus Functional Index: Development of a New Clinical Measure for Chronic, Intrusive Tinnitus.


1 Oregon Health & Science University, Portland, Oregon
2 VA National Center for Rehabilitative Auditory Research, Portland, Oregon
3 Bay Pines; VA Healthcare System, Bay Pines, Florida
4 James A. Haley Veterans’, Hospital, Tampa, Florida
5 Cleveland Clinic, Cleveland, Ohio
6 University of Washington, Seattle, Washington
7 Balance and Hearing Center Northwest, Portland, Oregon
8 The House Ear Institute, Los Angeles, California
9 Vanderbilt, University, Nashville, Tennessee
10 Atlanta Medical Consultants, Atlanta, Georgia
11 University of Auckland, Auckland, New Zealand
12 University of California at San Francisco, San Francisco, California.

OBJECTIVES: Chronic subjective tinnitus is a prevalent condition that causes significant distress to millions of Americans. Effective tinnitus treatments are urgently needed, but evaluating them is hampered by the lack of standardized measures that are validated for both intake assessment and evaluation of treatment outcomes. This work was designed to develop a new self-report questionnaire, the Tinnitus Functional Index (TFI), that would have documented validity both for scaling the severity and negative impact of tinnitus for use in intake assessment and for measuring treatment-related changes in tinnitus (responsiveness) and that would provide comprehensive coverage of multiple tinnitus severity domains. DESIGN: To use preexisting knowledge concerning tinnitus-related problems, an Item Selection Panel (17 expert judges) surveyed the content (175 items) of nine widely used tinnitus questionnaires. From
those items, the Panel identified 13 separate domains of tinnitus distress and selected 70 items most likely to be responsive to treatment effects. Eliminating redundant items while retaining good content validity and adding new items to achieve the recommended minimum of 3 to 4 items per domain yielded 43 items, which were then used for constructing TFI Prototype 1. Prototype 1 was tested at five clinics. The 326 participants included consecutive patients receiving tinnitus treatment who provided informed consent—constituting a convenience sample. Construct validity of Prototype 1 as an outcome measure was evaluated by measuring responsiveness of the overall scale and its individual items at 3 and 6 mo follow-up with 65 and 42 participants, respectively. Using a predetermined list of criteria, the 30 best-functioning items were selected for constructing TFI Prototype 2. Prototype 2 was tested at four clinics with 347 participants, including 155 and 86 who provided 3 and 6 mo follow-up data, respectively. Analyses were the same as for Prototype 1. Results were used to select the 25 best-functioning items for the final TFI. Results: Both prototypes and the final TFI displayed strong measurement properties, with few missing data, high validity for scaling of tinnitus severity, and good reliability. All TFI versions exhibited the same eight factors characterizing tinnitus severity and negative impact. Responsiveness, evaluated by computing effect sizes for responses at follow-up, was satisfactory in all TFI versions. In the final TFI, Cronbach’s alpha was 0.97 and test-retest reliability 0.78. Convergent validity (r = 0.86 with Tinnitus Handicap Inventory [THI]; r = 0.75 with Visual Analog Scale [VAS]) and discriminant validity (r = 0.56 with Beck Depression Inventory-Primary Care [BDI-PC]) were good. The final TFI was successful at detecting improvement from the initial clinic visit to 3 mo with moderate to large effect sizes and from initial to 6 mo with large effect sizes. Effect sizes for the TFI were generally larger than those obtained for the VAS and THI. After careful evaluation, a 13-point reduction was considered a preliminary criterion for meaningful reduction in TFI outcome scores. Conclusions: The TFI should be useful in both clinical and research settings because of its responsiveness to treatment-related change, validity for scaling the overall severity of tinnitus, and comprehensive coverage of multiple domains of tinnitus severity.

Pilot study to evaluate ecological momentary assessment of tinnitus.


1VA RR&D National Center for Rehabilitative Auditory Research, VA, Medical Center 2Department of Otolaryngology/Head and Neck Surgery, Oregon Health & Science University (OHSU), Portland, Oregon.

Objectives: Because audiometric evaluation, symptom histories, questionnaires, and similar standard assessment tools may not adequately sample the effects of chronic tinnitus on day-to-day activities, there is a need for alternative methodological approaches to study the impact of tinnitus on day-to-day life. An innovative methodological approach that has shown great promise in the study of chronic health problems characterized by reported temporal and/or situational variability in symptoms and distress is known as ecological momentary assessment (EMA). EMA involves the real-time measurement of states, situational factors, and symptoms by individuals as they go about their day-to-day activities. The objective of this pilot investigation was to explore the feasibility of using EMA methods to examine within- and between-day effects of tinnitus. Design: This study was conducted in three phases: (1) design and development of an EMA methodology that could be used to assess effects of tinnitus; (2) refinement of the methodology through the use of two focus groups; and (3) field-test the methodology with individuals who experienced bothersome tinnitus. For Phase 3, each of the 24 participants wore, throughout their waking hours for 2 weeks, a personal digital assistant that produced alerts four times a day. The alerts prompted participants to respond to 19 questions, including 9 relating to situational and mood factors and 10 comprising the Tinnitus Handicap Inventory-Screening version (THI-S). To evaluate for potential reactive effects of performing the EMA protocol, each participant completed the paper-and-pencil version of the full 25-item THI before and after the 2-week EMA period. Results: Participants responded to the alerts with a 90% compliance rate, providing a total of 1210 completed surveys. At the time of their response, participants indicated that they were in their house or apartment (67.7%), alone (50.2%), happy (50%), and calm (54.5%). Across most responses, participants could hear their tinnitus (97%), and the loudness of their tinnitus averaged 4.7 on a 7-point increasing-loudness scale. The mean THI-S
index score (out of a possible maximum 40 points for greatest tinnitus severity) was 17.0 (moderate self-perceived tinnitus handicap). Repeated THI-S index scores varied considerably both within and between participants. Mean 25-item THI scores were not significantly different before and after the EMA period, suggesting little reactivity of the EMA. CONCLUSIONS: The high compliance rate, positive feedback from participants, lack of reactivity as a result of performing the EMA protocol, and data collected indicate that EMA methodology is feasible with patients who have tinnitus. Outcome data obtained with this methodology cannot be obtained any other way because retrospective questionnaires cannot capture the day-to-day reactions. This methodology has the potential to provide more in-depth and accurate assessments of patients receiving therapy for tinnitus.

Psychological comorbidity in patients with chronic tinnitus: analysis and comparison with chronic pain, asthma or atopic dermatitis patients.
Qual Life Res. 2012 Mar 20. [Epub ahead of print]
Zirke N, Seydel C, Szczepak AJ, Olze H, Haupt H, Mazurek B.
Department of Otorhinolaryngology, Tinnitus Center, Charité - Universitätsmedizin Berlin, Campus Charité Mitte, Berlin, Germany.
PURPOSE: To determine the prevalence and severity of psychological comorbidity in patients with chronic tinnitus in comparison with other chronic illnesses, namely chronic pain, chronic asthma and atopic dermatitis. METHODS: Psychological diagnoses were done according to ICD-10 Chapter V(F). Subjective impairment was evaluated using 5 psychometric questionnaires: tinnitus questionnaire, Berlin mood questionnaire, sense of coherence (SOC-L9) and perceived stress questionnaire. Sleep disturbance was measured by the subdomain 'exhaustion' of the Giessen physical complaints inventory. RESULTS: Somatoform or affective disorders were most frequent in all disease groups. Patients with chronic tinnitus had a stronger SOC and better subjective mood, stronger commitment, and less anger and anxious depression than the patients with chronic pain, chronic asthma or atopic dermatitis. However, in patients with higher tinnitus annoyance, psychological comorbidity was similar to that found in patients with other chronic diseases. CONCLUSIONS: Besides collecting medical and social history, special psychometric instruments should be used for the diagnosis of tinnitus patients. Based on relative high frequency of psychological comorbidity, we recommend interdisciplinary cooperation between otorhinolaryngologists and other specialists (psychosomatic medicine, psychology or psychiatry) during the treatment of tinnitus patients, especially when high degree of tinnitus annoyance is involved.

Localization of sound sources in normal hearing and in hearing impaired people.
Niewiarowicz, M.a, Kaczmarek, T.b
a Department of Otolaryngology, Poznań University of Medical Sciences, Przybyszewskiego 49, 60-355 Poznan, Poland
b Adam Mickiewicz University, Institute of Acoustics, Umultowska 85, 61-614 Poznań, Poland.
This article presents results of investigations of the angle of directional hearing acuity (ADHA) as a measure of the spatial hearing ability with a special emphasis on people with hearing impairments. A modified method proposed by Zakrzewski has been used - ADHA values have been determined for 8 azimuths in the horizontal plane at the height of the listeners' head. The two-alternative-forced-choice method (2AFC), based on a new system of listeners' responses (left - right instead of no difference - difference in location of sound sources) was the procedure used in the experiment. Investigations were carried out for two groups of subjects: normal hearing people (9 persons) and hearing impaired people (sensorineural hearing loss and tinnitus - 9 persons). In the experiment different acoustic signals were used: sinusoidal signals (pure tones), 1/3 octave noise, amplitude modulated 1/3 octave noise, CCITT speech and traffic noises and signals corresponding to personal character of tinnitus for individual subjects. The results obtained in the investigations showed, in general, a better localization of the sound...
source for noise type signals than those for tonal signals. Inessential differences exist in ADHA values for particular signals between the two groups of subjects. On the other hand, significant differences for tinnitus signals and traffic noise signals were stated. A new system of listeners’ responses was used and appeared efficient (less dispersion of results compared to the standard system).

Transtympanic Electrocochleography for the Diagnosis of Ménière's Disease.

Hornibrook J, Kalin C, Lin E, O'Beirne GA, Gourley J.
Department of Otolaryngology and Audiology, Christchurch Hospital, 2 Riccarton Avenue, Christchurch 8011, New Zealand.

This paper evaluated the diagnostic power of electrocochleography (ECochG) in detecting Ménière’s disease (MD) as compared with two subjective assessment methods, including the clinical guidelines provided by the American Academy of Otolaryngology-Head and Neck Surgery Committee on Hearing Equilibrium and the Gibson score. A retrospective study of 250 suspected MD cases was conducted. The agreement between the three assessment methods was found to be relatively high, with a total reliability being higher than 70%. Participants who tested “positive” with ECochG exhibited a higher occurrence rate of asymmetric hearing threshold as well as the four MD symptoms, namely, vertigo, hearing loss, tinnitus, and aural fullness. The “positive” ECochG group also showed a high correlation between the ECochG measures in response to stimuli at adjacent frequency ranges, suggesting that the interfrequency ECochG correspondence may be sensitive to the presence of endolymphatic hydrops and thus may serve as a useful diagnostic marker for MD. Free Full Text.

Validation of the THI-12 questionnaire for international use in assessing tinnitus: A multi-centre, prospective, observational study.

Bankstahl US, Elkin EP, Gebauer A, Görtelmeyer R.
* Merz Pharmaceuticals GmbH Global R&D, Frankfurt, Germany.

Objective: To investigate and confirm the reliability and validity of the tinnitus handicap inventory12 (THI-12) in various countries and languages. Design: Prospective, observational study conducted in seven countries, using linguistically harmonized versions of the THI-12 in six languages. These were evaluated for test-retest reliability, internal consistency reliability, known-groups validity, and construct validity. Basic psychometric properties of supporting instruments were compared. Questionnaires were completed by the subjects at baseline and again after 12-30 days. Study sample: Adults with a clinical diagnosis of subjective tinnitus. Results: An exploratory factor analysis of the THI-12 items for the U.S. study population at baseline revealed a single common factor of high eigenvalue. Confirmatory factor analysis supported this in the separate countries. Test-retest reliability was moderate to high, and the conclusions were supported by a known-groups analysis; correlations with other scales expected to support construct validity were moderate. Conclusions: The THI-12 total score showed acceptable psychometric properties for all countries tested. The relationships between the THI-12 and the one-month and one-week versions of the TRS and TSS were similar and convergent. The THI-12 is thus a promising diagnostic tool for assessing treatment effects in multi-cultural and multi-lingual trials on tinnitus therapy.
Occurrence and suppression effect of Otoacoustic Emissions in normal hearing adults with tinnitus and hyperacusis.
Braz J Otorhinolaryngol. 2012 Feb;78(1):87-94.

Urnau D, Tochetto TM.
Departamento de Fonoaudiologia, UFSM, Santa Maria, RS.

The association between tinnitus and hyperacusis is common according to the literature. AIM: To verify the occurrence and the suppression effect of transient otoacoustic emissions (TEOAE), the existence of association between tinnitus degrees and hyperacusis degrees, and between the suppressive effect of TEOAE and laterality, tinnitus and hyperacusis degrees in normal hearing adults with complaints of tinnitus and hyperacusis. MATERIALS AND METHODS: 25 normal hearing subjects with complaints of hyperacusis and tinnitus were studied in this cross-sectional study. The Tinnitus Handicap Inventory (THI) was used for the classification of tinnitus degrees, and the Loudness Discomfort Level (LDL) for the hyperacusis classification. RESULTS: The occurrence of TEOAE ranged from 33 to 88%. We observed the presence of TEOAE suppression effect on 63.7% in the right ear and 81.7% in the left ear. There was no significant correlation between the degrees of tinnitus and hyperacusis in both ears. No statistically significant associations between the TEOAE suppression effect and laterality, tinnitus degrees and hyperacusis degrees were found. CONCLUSION: The occurrence of TEOAE was lower than that found in normal hearing adults. A higher percentage of the presence of TEOAE suppression effect has been found in both ears. No association between the variables was observed.

Vascular compression of the cochlear nerve and tinnitus: a pathophysiological investigation.
TRI Tinnitus Clinic, BRAI²N & Department of Neurosurgery, University Hospital Antwerp, Wirlijkstraat 10, 2650, Edegem, Belgium.

De Ridder D, Vanneste S, Adriaensens I, Lee AP, van de Heyning P, Möller A.


OBJECTIVE: Chronic microvascular compressions of the eighth nerve induce a slowing down of signal transmission in the auditory nerve, electrophysiologically characterized by IPL I-III prolongation. METHODS: The authors hypothesize this is compensated by an active slowing down of signal transmission of the contralateral input at the level of the brainstem, characterized by contralateral IPL III-V prolongation. RESULTS: Differences between ipsilateral and contralateral IPL I-III and IPL III-V are analyzed before and after microvascular decompression. ABR diagnostic criteria for microvascular compression are ipsilateral IPL I-III prolongation or ipsilateral peak II decrease + ipsilateral IPL I-III prolongation. With IPL I-III as diagnostic criterion, unlike preoperatively the difference between the ipsi- and contralateral IPL I-III is significant postoperatively. When using the stricter diagnostic criterion of IPL I-III + peak II, there is a preoperative significant difference between ipsi- and contralateral IPL I-III, but postoperatively the difference between the ipsi- and contralateral IPL I-III is not significant. CONCLUSIONS: Preoperatively, there is a marginal significant difference between the ipsi- and contralateral IPL III-V, which disappears postoperatively.
Wavelet analysis demonstrates no abnormality in contralateral suppression of otoacoustic emissions in tinnitus patients.
Hear Res. 2012 Feb 24. [Epub ahead of print]

Geven LI, Wit HP, de Kleine E, van Dijk P.
Department of Otorhinolaryngology/Head and Neck Surgery, University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands; Graduate School of Medical Sciences, Research School of Behavioral and Cognitive Neurosciences, University of Groningen, Groningen, The Netherlands.

The efferent auditory system is thought to play a role in the origin of tinnitus. Part of this system can be tested in humans with contralateral suppression of otoacoustic emissions. Stimulation of the medial olivocochlear efferent system is responsible for this reduction of otoacoustic emissions after contralateral acoustic stimulation. Previous research on patients with tinnitus showed inconclusive results. With wavelet analysis both time and frequency information of the emission can be analysed and compared. Contralateral suppression of otoacoustic emissions was therefore measured in tinnitus patients (n = 26) and normal subjects (n = 37) and analysed using wavelets. No significant difference in suppression was found between the tinnitus patients and the control group. Copyright © 2012. Published by Elsevier B.V.

IV Imaging


* Department of Medical Science, Kyungpook National University College of Medicine, Daegu, Korea.

Objective: We report a case study on possible alterations in resting-state functional connectivity between the auditory network and non-auditory brain regions in tinnitus patients. Design: Independent component analyses were performed to evaluate coherent spontaneous activity in distributed brain networks. The resting-state functional connectivity scores between the right and left auditory networks were measured. Direct comparison of resting-state connectivity between tinnitus patients and controls was made using a two-sample t-test. Study sample: Four patients (three male, one female; mean age 45 ± 3.92 years) with chronic tinnitus lateralized to the left ear, and six age-matched controls (four male, two female; mean age 45 ± 2.76 years) participated in this case study. Results: The average resting-state functional connectivity (FC) score between the left and right auditory cortical regions was significantly lower in tinnitus patients than in controls (P < 0.05). Direct comparison between patients and controls showed that increased functional connectivity caused by tinnitus occurred predominantly in the left amygdala and in the dorsomedial prefrontal cortex. Conclusions: Our pilot study suggested that resting state functional magnetic resonance imaging (fMRI) could be useful to investigate possible alterations in resting-state neuronal activity between the auditory and non-auditory networks in tinnitus patients.


Burton H, Wineland A, Bhattacharya M, Nicklaus J, Garcia KS, Piccirillo JF.

BACKGROUND: The objective was to examine functional connectivity linked to the auditory system in patients with bothersome tinnitus. Activity was low frequency (<0.1 Hz), spontaneous blood oxygenation level-dependent (BOLD) responses at rest. The question was whether the experience of chronic bothersome tinnitus induced changes in synaptic efficacy between co-activated components. Functional connectivity for seed regions in auditory, visual, attention, and control networks was computed across all
2mm cubic brain volumes in 17 patients with moderate-severe bothersome tinnitus (Tinnitus Handicap Index: average 53.5 +/- 3.6 (range 38-76)) and 17 age-matched controls. RESULTS: In bothersome tinnitus, negative correlations reciprocally characterized functional connectivity between auditory and occipital/visual cortex. Negative correlations indicate that when BOLD response magnitudes increased in auditory or visual cortex they decreased in the linked visual or auditory cortex, suggesting reciprocally phase reversed activity between functionally connected locations in tinnitus. Both groups showed similar connectivity with positive correlations within the auditory network. Connectivity for primary visual cortex in tinnitus included extensive negative correlations in the ventral attention temporoparietal junction and in the inferior frontal gyrus and rostral insula - executive control network components. Rostral insula and inferior frontal gyrus connectivity in tinnitus also showed greater negative correlations in occipital cortex. CONCLUSIONS: These results imply that in bothersome tinnitus there is dissociation between activity in auditory cortex and visual, attention and control networks. The reciprocal negative correlations in connectivity between these networks might be maladaptive or reflect adaptations to reduce phantom noise salience and conflict with attention to non-auditory tasks.

Prefrontal cortex based sex differences in tinnitus perception: same tinnitus intensity, same tinnitus distress, different mood.

Vanneste S, Joos K, De Ridder D.

Brain, TRI & Department of Neurosurgery, University Hospital Antwerp, Belgium.

BACKGROUND: Tinnitus refers to auditory phantom sensation. It is estimated that for 2% of the population this auditory phantom percept severely affects the quality of life, due to tinnitus related distress. Although the overall distress levels do not differ between sexes in tinnitus, females are more influenced by distress than males. Typically, pain, sleep, and depression are perceived as significantly more severe by female tinnitus patients. Studies on gender differences in emotional regulation indicate that females with high depressive symptoms show greater attention to emotion, and use less anti-rumination emotional repair strategies than males. METHODOLOGY: The objective of this study was to verify whether the activity and connectivity of the resting brain is different for male and female tinnitus patients using resting-state EEG. CONCLUSIONS: Females had a higher mean score than male tinnitus patients on the BDI-II. Female tinnitus patients differ from male tinnitus patients in the orbitofrontal cortex (OFC) extending to the frontopolar cortex in beta1 and beta2. The OFC is important for emotional processing of sounds. Increased functional alpha connectivity is found between the OFC, insula, subgenual anterior cingulate (sgACC), parahippocampal (PHC) areas and the auditory cortex in females. Our data suggest increased functional connectivity that binds tinnitus-related auditory cortex activity to auditory emotion-related areas via the PHC-sgACC connections resulting in a more depressive state even though the tinnitus intensity and tinnitus-related distress are not different from men. Comparing male tinnitus patients to a control group of males significant differences could be found for beta3 in the posterior cingulate cortex (PCC). The PCC might be related to cognitive and memory-related aspects of the tinnitus percept. Our results propose that sex influences in tinnitus research cannot be ignored and should be taken into account in functional imaging studies related to tinnitus.

Tinnitus does not require macroscopic tonotopic map reorganization.

Langers DR, de Kleine E, van Dijk P.

Department of Ototorhinolaryngology/Head and Neck Surgery, University Medical Center Groningen, University of Groningen Groningen, Netherlands.

The pathophysiology underlying tinnitus, a hearing disorder characterized by the chronic perception of phantom sound, has been related to aberrant plastic reorganization of the central auditory system. More specifically, tinnitus is thought to involve changes in the tonotopic representation of sound. In the present
study we used high-resolution functional magnetic resonance imaging to determine tonotopic maps in the auditory cortex of 20 patients with tinnitus but otherwise near-normal hearing, and compared these to equivalent outcomes from 20 healthy controls with matched hearing thresholds. Using a dedicated experimental paradigm and data-driven analysis techniques, multiple tonotopic gradients could be robustly distinguished in both hemispheres, arranged in a pattern consistent with previous findings. Yet, maps were not found to significantly differ between the two groups in any way. In particular, we found no evidence for an overrepresentation of high sound frequencies, matching the tinnitus pitch. A significant difference in evoked response magnitude was found near the low-frequency tonotopic endpoint on the lateral extreme of left Heschl’s gyrus. Our results suggest that macroscopic tonotopic reorganization in the auditory cortex is not required for the emergence of tinnitus, and is not typical for tinnitus that accompanies normal hearing to mild hearing loss.

Cortical Habituation Deficit in Tinnitus Sufferers: Contingent Negative Variation as an Indicator of Duration of the Disease.
Appl Psychophysiol Biofeedback. 2012 Mar 27. [Epub ahead of print]
Medical Faculty, Institute of Medical Psychology and Medical Sociology, University of Rostock, Gehlsheimer Straße 20, 18147, Rostock, Germany, peter.kropp@med.uni-rostock.de.
Cortical attention and habituation parameters are altered in patients suffering from tinnitus. The aim of the study was to quantify cortical attention and habituation parameters in tinnitus patients by recording the contingent negative variation (CNV) response and to correlate amplitudes of different CNV parameters with duration of disease. Twenty patients suffering from tinnitus (median: 44 years) and twenty age- and sex-matched healthy controls (median: 41 years) were tested by a CNV paradigm. We recorded overall CNV, initial CNV, and terminal CNV and calculated habituation slopes. All CNV parameters were Spearman-correlated with individual duration of disease. Highly significant between groups differences emerged in total (tinnitus: -8.4 uV vs. controls: -3.8 uV), initial (-11.2 vs. -6.0 uV), and terminal CNV (-11.9 vs. -6.5 uV) demonstrating higher negative amplitudes in tinnitus patients. Habituation differed in total and terminal CNV, indicating missing habituation in tinnitus patients. Overall CNV (ϱ = -.365) and initial CNV (ϱ = -.529) showed a medium Spearman correlation with duration of disease. We conclude that the correlation between duration of tinnitus and the initial CNV amplitudes indicates an altered state of cortical excitability that can also be observed in more negative CNV-amplitudes in tinnitus patients. We assume that this state indicates a chronicity process in tinnitus disease.

Gray matter in the brain: Differences associated with tinnitus and hearing loss.
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Boyen K, Langers DR, de Kleine E, van Dijk P.
Department of Otorhinolaryngology/Head and Neck Surgery, University of Groningen, University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands; Graduate School of Medical Sciences, Research School of Behavioural and Cognitive Neurosciences, University of Groningen, The Netherlands.
Tinnitus, usually associated with hearing loss, is characterized by the perception of sound without an external sound source. The pathophysiology of tinnitus is poorly understood. In the present study, voxel-based morphometry (VBM) was employed to identify gray matter differences related to hearing loss and tinnitus. VBM was applied to magnetic resonance images of normal-hearing control subjects (n = 24), hearing-impaired subjects without tinnitus (n = 16, HI group) and hearing-impaired subjects with tinnitus (n = 31, HI + T group). This design allowed us to disentangle the gray matter (GM) differences related to hearing loss and tinnitus, respectively. Voxel-based VBM analyses revealed that both HI and
HI + T groups, relative to the controls, had GM increases in the superior and middle temporal gyri, and decreases in the superior frontal gyrus, occipital lobe and hypothalamus. We did not find significant GM differences between both patient groups. Subsequent region-of-interest (ROI) analyses of all Brodmann Areas, the cerebellum and the subcortical auditory nuclei showed a GM increase in the left primary auditory cortex of the tinnitus patients compared to the HI and control groups. Moreover, GM decreases were observed in frontal areas and mainly GM increases in limbic areas, both of which occurred for hearing loss irrespective of tinnitus, relative to the controls. These results suggest a specific role of the left primary auditory cortex and the additional involvement of various non-auditory brain structures in tinnitus. Understanding the causal relation between these GM changes and tinnitus will be an important next step in understanding tinnitus mechanisms. Copyright © 2012. Published by Elsevier B.V.

**Neural correlates of tinnitus related distress: An fMRI-study.**
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**Golm D, Schmidt-Samoa C, Dechent P, Kröner-Herwig B.**
Georg-August-University, Georg-Elias-Mueller-Institute of Psychology, Department of Clinical Psychology and Psychotherapy, Gosslerstrasse 14, 37073 Goettingen, Germany.

Chronic tinnitus affects approximately 5% of the population. Severe distress due to the phantom noise is experienced by 20% of the tinnitus patients. This distress cannot be predicted by psychoacoustic features of the tinnitus. It is commonly assumed that negative cognitive emotional evaluation of the tinnitus and its expected consequences is a major factor that determines the impact of tinnitus-related distress. Models of tinnitus distress and recently conducted research propose differences in limbic, frontal and parietal processing between highly and low distressed tinnitus patients. An experimental paradigm using verbal material to stimulate cognitive emotional processing of tinnitus-related information was conducted. Age and sex matched highly (n = 16) and low (n = 16) distressed tinnitus patients and healthy controls (n = 16) underwent functional magnetic resonance imaging (fMRI) while sentences with neutral, negative or tinnitus-related content were presented. A random effects group analysis was performed on the basis of the general linear model. Tinnitus patients showed stronger activations to tinnitus-related sentences in comparison to neutral sentences than healthy controls in various limbic/emotion processing areas, such as the anterior cingulate cortex, midcingulate cortex, posterior cingulate cortex, retrosplenial cortex and insula and also in frontal areas. Highly and low distressed tinnitus patients differed in terms of activation of the left middle frontal gyrus. A connectivity analysis and correlational analysis between the predictors of the general linear model of relevant contrasts and tinnitus-related distress further supported the idea of a fronto-parietal-cingulate network, which seems to be more active in highly distressed tinnitus patients. This network may present an aspecific distress network. Based on the findings the left middle frontal gyrus and the right medial frontal gyrus are suggested as target regions for neuromodulatory approaches in the treatment of tinnitus. For future studies we recommend the use of idiosyncratic stimulus material. Copyright Â© 2012 Elsevier B.V. All rights reserved.
V Pharmacotherapy

Intratympanic methylprednisolone as first-line therapy in sudden sensorineural hearing loss: preliminary results from a case-control series.

Dallan, I., Fortunato, S., Casani, A.P., Panicucci, E., Berrettini, S., Lenzi, R., Nacci, A.
ENT Unit, Azienda Ospedaliero Universitaria Pisana, Italy.

BACKGROUND: Sudden sensorineural hearing loss is a true audiological emergency, and its management is much discussed. Currently, no single therapy has been proven effective according to evidence criteria. Recently, intratympanic application of steroids has been increasingly used in refractory cases; however, it has only rarely been reported as first-line therapy. MATERIALS AND METHODS: Twenty consecutive patients with sudden sensorineural hearing loss treated between July 2008 and January 2010 were enrolled in this prospective, case-control study. Ten patients were treated with intratympanic steroids and 10 with systemic ‘shotgun’ therapy (including steroids, pentoxifylline, low molecular weight heparin and vitamin E). The two groups were homogeneous in all respects. Pure tone averages were assessed before and after treatment for both groups. RESULTS: There were no statistically significant differences between the two groups. CONCLUSION: Intratympanic steroids seem to offer a valid alternative to systemic therapy, with few risks, in sudden sensorineural hearing loss patients, and we recommend their use as first-line therapy.

L-N-Acetylcysteine treatment is associated with improved hearing outcome in sudden idiopathic sensorineural hearing loss.

Angeli SI, Abi-Hachem RN, Vivero RJ, Telischi FT, Machado JJ.
Department of Otolaryngology-Head and Neck Surgery, University of Miami Miller School of Medicine, Miami, FL, USA.

Abstract Conclusion: Combination therapy corticosteroids plus an oral antioxidant L-N-acetylcysteine (LNAC) was associated with improved hearing over corticosteroids alone, particularly at the 6-month follow-up and at high frequencies (i.e. 4000 Hz). This is the first report of a beneficial effect of LNAC in sudden idiopathic sensorineural hearing loss (SISNHL). Objective: To determine the association between antioxidant treatment and functional outcomes in SISNHL. Methods: This was a case-control study of adult patients with SISNHL, treated with oral prednisone plus intratympanic dexamethasone either alone or in combination with LNAC. The outcome measure was change in pure-tone thresholds at 500-4000 Hz. Hearing recovery was also recorded as the percentage of subjects with final pure-tone threshold average (PTA) within 50% of the difference between the initial value of the affected ear and the value of the unaffected ear. Comparisons were made between combination (corticosteroids plus LNAC) and single (no LNAC use) therapy groups. Results: At 6 months, the mean PTA improvements were 26.1 dB and 15.1 dB for the combination and single therapy groups, respectively (p = 0.046). Higher gains at 4000 Hz were noted with LNAC use. The percentage of patients with at least 50% recovery was 63% and 35% for the combination and single therapy groups, respectively (p = 0.0319).
Effect of Retreatment on the End-stage Sudden Deafness.

Suoqiang Z, Ning Y, Guiliang Z, Yuhua Z, He Q.
Hospital of Otorhinolaryngology Head & Neck Surgery, Institute of Otorhinolaryngology Head & Neck Surgery, Chinese PLA General Hospital, Beijing, 100853, China, zhaisq@plagh.com.cn.

Microcirculatory disturbance of inner ear is probably one of the important etiological factors of sudden deafness. The purpose of this study was to evaluate the effect of retreatment on the end-stage sudden deafness. For this purpose, the patients who met with the criteria for sudden deafness and showed poor response to conventional therapy over 2 months were assigned randomly to the retreatment group. Pure tone audiometry was conducted before and after retreatment among the 103 patients (112 ears). Sodium bicarbonate and dexamethasone were injected by intravenous drip for 2 days and batroxobin 5BU for 6 days. Data were analyzed using analysis of variance and t test to determine the efficacy of retreatment. These data show that the efficacy rate in retreatment group was 46.43% and the difference between before and after retreatment was significant (P < 0.01). It was, therefore, concluded that retreatment of the end-stage sudden deafness could improve the audition of the patients and should be valuable in clinics. In this regard, the combination of sodium bicarbonate and dexamethasone proved a rational therapeutic regimen for the end-stage sudden deafness. However, further large-size multicenter studies will be required for independent validation of these findings.

Evaluation of intratympanic dexamethasone for treatment of refractory sudden sensorineural hearing loss.

Wang YW, Ren JH, Lu YD, Yin TF, Xie DH.
Otolaryngology-Head and Neck Surgery Department, Ningbo First Hospital, Ningbo 315000, China; Otolaryngology-Head and Neck Surgery Department, the Second Xiangya Hospital, Central South University, Changsha 410001, China.

Objective: To observe and compare the efficacy of intratympanic application of dexamethasone (DXM) for the treatment of refractory sudden sensorineural hearing loss (SSNHL), the DXM was given in three different ways: by tympanic membrane injection, by drip through a ventilation tube, and by perfusion through a round window catheter. Methods: We conducted a nonrandomized retrospective clinical trial involving 55 patients with refractory SSNHL. For 21 patients (the perfusion group), DXM (2.5 mg/0.5 ml) was perfused transtympanically through a round window catheter using an infusion pump for 1 h twice a day for 7 d giving a total amount of 35.0 mg. For 23 patients (the injection group), DXM (2.5 mg/time) was injected by tympanic membrane puncture at intervals of 2 d on a total of four occasions giving a total amount of 10.0 mg. For 11 patients (the drip group), DXM (2.5 mg/0.5 ml) was dripped via a ventilation tube placed by myringotomy, once on the first day and twice a day for the remaining 6 d giving a total amount of 32.5 mg. Thirty-two patients with refractory SSNHL who refused to undertake further treatments were defined as the control group. Hearing recovery and complications were compared among the groups. Hearing results were evaluated based on a four-frequency (0.5, 1.0, 2.0, 4.0 kHz) pure tone average (PTA). Results: Post-treatment audiograms were obtained one month after treatments were completed. The improvements in average PTA for the perfusion, injection, and drip groups were 9.0, 8.6, and 1.7 dB, respectively. Hearing improvement was significantly greater in the perfusion and injection groups than in the control group (1.4 dB) (P<0.05). In the perfusion group, 8 out of 21 patients (38.1%) had a PTA improvement of 15-56 dB (mean 29.8 dB); in the injection group, 8 out of 23 patients (34.8%) had a PTA improvement of 16-54 dB (mean 24.9 dB); in the drip group, 1 of 11 patients (9.1%) had a PTA improvement of 26.0 dB; in the control group, 3 out of 32 patients (9.4%) had a PTA improvement of 15-36 dB (mean 14.9 dB). Conclusions: Topical intratympanic application of DXM is a safe and effective method for the treatment of SSNHL cases that are refractory to conventional therapies. Free Article
Corticosteroid Treatment of Idiopathic Sudden Sensorineural Hearing Loss: Randomized Triple-Blind Placebo-Controlled Trial.
Otol Neurotol. 2012 Mar 15. [Epub ahead of print]

Nosrati-Zarenoe R, Hultcrantz E.
Division of Otorhinolaryngology, Department of Clinical and Experimental Medicine, Medical Faculty, Linköping University, Linköping, Sweden.

OBJECTIVE: To compare the effect of Prednisolone and placebo on the recovery of unilateral idiopathic sudden sensorineural hearing loss. STUDY DESIGN: Prospective, randomized, triple-blind, placebo-controlled multicenter trial. SETTING: Four tertiary and 10 secondary referral centers. PATIENTS: Of 103 patients randomly assigned, 93 were included in the modified intention-to-treat analysis. The patients, aged 18 to 80 years, were seeking care within 1 week after onset of acute unilateral sensorineural hearing loss with a mean decrease of 30 dB or greater in the 3 most affected contiguous frequencies. INTERVENTION: Patients were randomly assigned in permuted blocks of 10 to receive Prednisolone or placebo in tapering doses from 60 mg for 3 days and, thereafter, 10 mg less each day until Day 8. If complete recovery, no more medication given, otherwise medication continued at 10 mg per day until Day 30. Final follow-up was after 3 months with audiogram; 47 patients received Prednisolone and 46 placebo. MAIN OUTCOME MEASURE: The primary endpoint was efficacy of treatment on recovery at Day 90. Secondary endpoints were prognostic factors for hearing recovery. Analyses were by modified intention-to-treat and per protocol. RESULTS: Hearing improvement for 47 Prednisolone-treated patients was 25.5 ± 27.1 dB compared to 26.4 ± 26.2 dB for 46 placebo-treated patients at Day 8 and 39 ± 20.1 dB versus 35.1 ± 38.3 dB after 3 months. Vertigo had significant negative effect on hearing improvement and inflammatory signs in the laboratory workup—a positive prognostic effect, irrespective of treatment. CONCLUSION: Prednisolone in customary dosage does not seem to influence recovery of idiopathic sudden sensorineural hearing loss.

Effect of ramelteon (agonist of melatonin) on tinnitus
Practica Oto-Rhino-Laryngologica 105 (2), pp. 167-176

Arao, H.

Arao Internal Medicine and Otolaryngology Clinic, Japan

Ramelteon is a melatonin receptor agonist. Melatonin, a neurohormone secreted by the pineal gland at night, helps regulate the sleep-wake cycle, although tinnitus disturbs sleep. To evaluate ramelteon in treating subjective tinnitus, we administered it internally to 42 subjects not sufficient effectively aided by usual internal treatment. Subjects took 8.0 mg of ramelteon, nightly for 2 weeks or more. We evaluated results, using a visual analog scale (VAS) of the standardized, 1993 Tinnitus Study Group tinnitus test, the tinnitus handicap inventory (THI) for 25 subjects and symptom changes in all 42 subjects. Of the 42 (88.1%), 37 could take ramelteon. Of these 37 (64.9%), 24 improved subjectively, after taking ramelteon. In 7 subjects with Meniere’s disease (MD), 6 improved, possibly from MD melatonin deficiency. Mean VAS and THI decreased significantly between weeks 0 and 4-16 in Wilcoxon’s signed rank test, after taking ramelteon. Ramelteon thus appears to be useful in treating subjective tinnitus, and subjects with MD are most likely to benefit from ramelteon treatment.
Reduction of Tinnitus Severity by the Centrally Acting Muscle Relaxant Cyclobenzaprine: An Open-Label Pilot Study.
Audiol Neurootol. 2012 Jan 31;17(3):179-188. [Epub ahead of print]


Department of Otolaryngology and Head and Neck Surgery, University of Iowa, Iowa City, Iowa, USA.

Tinnitus, the phantom perception of sounds, is a highly prevalent disorder. Although a wide variety of drugs have been investigated off label for the treatment of tinnitus, there is no approved pharmacotherapy. We report an open-label exploratory pilot study to assess the effect of muscle relaxants acting on the central nervous system on tinnitus patients. Cyclobenzaprine at high (30 mg) and low doses (10 mg), orphenadrine (100 mg), tizanidine (24 mg) and eperisone (50 mg) were administered to a maximum of 20 patients per group over a 12-week period. High-dose cyclobenzaprine resulted in a significant reduction in the Tinnitus Handicap Inventory (THI) score between baseline and week 12 in the intention-to-treat sample. On the other hand, other treatments were not effective. These results were confirmed in an explorative analysis where baseline corrected THI and Clinical Global Impression scores at week 12 were compared between groups. The present open trial presents a new promising pharmacotherapy for tinnitus that should be validated in placebo-controlled double-blind trials. Copyright © 2012 S. Karger AG, Basel.

Tinnitus: network pathophysiology - network pharmacology.

Elgoyhen AB, Langguth B, Vanneste S, De Ridder D.

Instituto de Investigaciones en Ingeniería Genética y Biología Molecular, Consejo Nacional de Investigaciones Científicas y Técnicas and Tercera Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires Buenos Aires, Argentina.

Tinnitus, the phantom perception of sound, is a prevalent disorder. One in 10 adults has clinically significant subjective tinnitus, and for one in 100, tinnitus severely affects their quality of life. Despite the significant unmet clinical need for a safe and effective drug targeting tinnitus relief, there is currently not a single Food and Drug Administration (FDA)-approved drug on the market. The search for drugs that target tinnitus is hampered by the lack of a deep knowledge of the underlying neural substrates of this pathology. Recent studies are increasingly demonstrating that, as described for other central nervous system (CNS) disorders, tinnitus is a pathology of brain networks. The application of graph theoretical analysis to brain networks has recently provided new information concerning their topology, their robustness and their vulnerability to attacks. Moreover, the philosophy behind drug design and pharmacotherapy in CNS pathologies is changing from that of “magic bullets” that target individual chemoreceptors or “disease-causing genes" into that of “magic shotguns," “promiscuous" or “dirty drugs" that target “disease-causing networks," also known as network pharmacology. In the present work we provide some insight into how this knowledge could be applied to tinnitus pathophysiology and pharmacotherapy. Free PMC Article.
Noninvasive intratympanic dexamethasone treatment for sudden sensorineural hearing loss.

Zhang Q, Song H, Peng H, Yang X, Zhou J, Huang W.
Department of Otolaryngology, Beijing Hospital, Beijing, China.

Abstract Conclusion: Noninvasive intratympanic dexamethasone perfusion (IDP) through the eustachian tube is an effective and safe therapy in cases of sudden sensorineural hearing loss (SSNHL). Objective: To investigate the effectiveness and safety of noninvasive IDP through the eustachian tube in patients with SSNHL. Methods: In this prospective study, 74 consecutive patients with SSNHL treated between September 2007 and March 2011 were enrolled: 35 patients fitted the criteria for initial treatment in the study (group I), while 39 patients, who had failed systemic therapy, received salvage treatment (group S). IDP through the eustachian tube was applied four times at 2-day intervals. Pure-tone test and tympanometry were performed before starting treatment, and 24 h and 1 week afterwards. Results: All patients tolerated the procedure well. No perforation or infection was noticed in any of the patients at their last visit. With regard to the 74 patients who received intratympanic treatment, 80.0% (28 of 35) of the patients in group I and 64.1% (25 of 39) patients in group S had improvement in their hearing ability. Patients with simultaneous symptoms reported that the symptoms were relieved as follows: tinnitus, 73.3% (44/60); vertigo, 76.2% (16/21); and stuffy ear, 81.1% (30/37).

[Application of antidepressant to treat patients in the department of otolaryngology].
[Article in Japanese].

Goto F, Tsutsumi T, Ogawa K.
Department of Otorhinolaryngology, Hino Municipal Hospital.

There are some patients complaining of somatic symptom who has depression. The use of antidepressant to these patients would be quite useful. Patients with dispersion have a variety sort of physical symptom. The evaluation of depression based on physical complaints may be difficult for otorhinolaryngologists, but it is important to do so where possible to increase the focus on the subject's physical illness. The prevalence of somatic complaints in hospitalized patients whose chief complaint was either dizziness or vertigo was very high. These patients were usually accompanied with depression. Then the effect of paroxetine to the patients with tinnitus was investigated. The paroxetine may be effective in treating distressed tinnitus patients with depression and anxiety by reducing their tinnitus severity as well as their depression and anxiety.

Revisiting baclofen for the treatment of severe chronic tinnitus.

Smith PF, Zheng Y, Darlington CL.
Department of Pharmacology and Toxicology, School of Medical Sciences, University of Otago Medical School, and Brain Health Research Centre, University of Otago Dunedin, New Zealand.

Free PMC article.
Targeting inhibitory neurotransmission in tinnitus.
Brain Res. 2012 Feb 14. [Epub ahead of print]

Richardson BD, Brozoski TJ, Ling LL, Caspary DM.

Department of Pharmacology, Southern Illinois University School of Medicine, 801 N Rutledge St, Rm. 3234, PO Box 19629, Springfield, IL 62794, USA.

Tinnitus perception depends on the presence of its neural correlates within the auditory neuraxis and associated structures. Targeting specific circuits and receptors within the central nervous system in an effort to relieve the perception of tinnitus and its impact on one’s emotional and mental state has become a focus of tinnitus research. One approach is to upregulate endogenous inhibitory neurotransmitter levels (e.g., glycine and GABA) and selectively target inhibitory receptors in key circuits to normalize tinnitus pathophysiology. Thus, the basic functional and molecular properties of two major ligand-gated inhibitory receptor systems, the GABA(A) receptor (GABA(A)R) and glycine receptor (GlyR) are described. Also reviewed is the rationale for targeting inhibition, which stems from reported tinnitus-related homeostatic plasticity of inhibitory neurotransmitter systems and associated enhanced neuronal excitability throughout most central auditory structures. However, the putative role of the medial geniculate body (MGB) in tinnitus has not been previously addressed, specifically in terms of its inhibitory afferents from inferior colliculus and thalamic reticular nucleus and its GABA(A)R functional heterogeneity. This heterogeneous population of GABA(A)Rs, which may be altered in tinnitus pathology, and its key anatomical position in the auditory CNS make the MGB a compelling structure for tinnitus research. Finally, some selective compounds, which enhance tonic inhibition, have successfully ameliorated tinnitus in animal studies, suggesting that the MGB and, to a lesser degree, the auditory cortex may be their primary locus of action. These pharmacological interventions are examined in terms of their mechanism of action and why these agents may be effective in tinnitus treatment. This article is part of a Special Issue entitled Tinnitus Neuroscience. Copyright © 2012 Elsevier B.V. All rights reserved.

Irreversible atorvastatin-associated hearing loss.


The Department of Pharmacy Practice, Arnold and Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Department of Pharmacy Services, Kingsbrook Jewish Medical Center, Brooklyn, New York.

Drug-associated ototoxicity is a potentially irreversible adverse event. Among the several 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) available in the United States, only atorvastatin is associated with tinnitus, but none are associated with any forms of hearing loss. A search of the published literature (1950-August 2011) revealed no published case reports of ototoxicity associated with statins. To our knowledge, we describe the first case of progressive, irreversible hearing loss in a 32-year-old man 18 months after starting atorvastatin therapy. He began taking atorvastatin 20 mg every evening for treatment of hypercholesterolemia. Six months later, he complained of occasional episodes of tinnitus, which resolved spontaneously. An audiogram was obtained and was normal. By 18 months, the tinnitus became continuous. Another audiogram revealed bilateral “cookie-bite” middle-frequency hearing loss. Atorvastatin was immediately discontinued, and the patient was fitted with hearing aids. Four years after drug discontinuation, his hearing loss had neither progressed nor regressed. Use of the Naranjo adverse drug reaction probability scale indicated a possible (score of 2) temporal and causal relationship between the patient's hearing loss and atorvastatin. Causes of “cookie-bite” hearing loss include chronic exposure to loud noises, presbycusis, genetic predisposition, and drugs. The manufacturer of atorvastatin has received three unpublished cases of deafness, but claims that causal relationships were not established. Despite these claims by the manufacturer, based on this case report, we recommend that clinicians and patients be aware of the risk of atorvastatin-associated tinnitus and permanent hearing loss. Further research is needed to better understand the mechanism and frequency of this adverse event. © 2012 Pharmacotherapy Publications, Inc.
Anti-hypertensive effects of shichimotsukokato in 5/6 nephrectomized Wistar rats mediated by the DDAH-ADMA-NO pathway.

Bai F, Makino T, Ono T, Mizukami H.

Department of Pharmacognosy, Graduate School of Pharmaceutical Sciences, Nagoya City University, Nagoya, 467-8603, Japan.

Shichimotsukokato (SKT) is a Kampo formula, comprising astragalus root, phellodendron bark, rehmannia root, peony root, cnidium rhizome, Japanese angelica root, and uncaria hook. It is prescribed to hypertensive patients who complain of a sensation of a rush of blood to the head, shoulder stiffness, tinnitus, and dull headache. We investigated the effects of SKT on renal hypertension in Wistar rats subjected to a 5/6 nephrectomy (Nx). Systolic blood pressure (SBP) increased markedly after surgery and remained high in the Nx rats. Oral treatment of SKT extract at dosages of 0.75 and 1.5 g/kg/day (corresponding to 5- and 10-fold human dosages, respectively) caused a significant suppression of the increase in SBP in Nx rats. Plasma concentrations of nitric oxide (NO) were marginally lower and asymmetric dimethylarginine (ADMA) significantly higher in the Nx rats than in sham-operated rats. SKT administration caused a significant counteraction of these changes. Finally, we evaluated the levels of protein methyltransferase (PRMT), an enzyme that catalyzes the production of ADMA, and the levels of dimethylarginine dimethylaminohydrolase (DDAH), an enzyme involved in the degradation of ADMA, in the remnant kidney. Neither Nx nor SKT treatment affected PRMT-1 or DDAH-1 levels. DDAH-2 levels were reduced significantly in the Nx rats compared with the sham-operated rats. SKT treatment significantly ameliorated this decrease in the DDAH-2 levels. It is considered that SKT reduced blood pressure in the renal hypertension rat model, mediated, at least partially, by the DDAH-ADMA-NO pathway.

Effect of Intravenous Administration of Steroids in the Management of Sudden Sensori-Neural Hearing Loss: Our Experience.

Raghunandhan, S., Agarwal, A.K., Natarajan, K., Murali, S., Anand Kumar, R.S., Kameswaran, M.

Madras ENT Research Foundation, No. 1, 1st Cross Street, Off 2nd Main Road, Raja Annamalai Puram, Chennai, 600028, India

The aim of this study was to investigate the efficacy and outcomes of intravenous high dose steroids in patients diagnosed with sudden sensori-neural hearing loss (SSNHL). The study also looked at the various co-morbidities influencing the outcomes of IV steroid therapy and also evaluated the improvement in associated symptoms like vertigo and tinnitus. This prospective study involved 30 patients treated during the 1 year period from January 2010 to 2011 in the Department of Otolaryngology, Madras ENT Research Foundation, Chennai. Male: female ratio was 1.3:1 and age range was 19-80 years. For all patients, pre treatment pure tone audiometry (PTA) was compared with post treatment PTA at 1 month. Treatment was given in the form of intravenous high dose methyl prednisolone. The patients were divided into two groups. Group 1 (20 pts) included SSNHL with no co-morbidity, group 2 (10 pts) included SSNHL with various co-morbidities. The mean hearing level improved from an average of 79.53 dB (HL) before treatment to 42.33 dB (HL) after treatment. In patients with predominantly low frequency HL (16 pts) PTA improved from 76.01 to 32.6 dB while in high frequency HL PTA improved from 83.55 to 53.43 dB. In our study of 30 patients, complete recovery occurred in 56.66% cases and marked improvement (>30 dB) in 16.66% patients. There was no improvement in 26.66% cases. Patients in group 2 had co-morbid factors like diabetes mellitus, dys-thyroidism and hypertension. A statistically significant improvement in the associated symptoms of tinnitus/vertigo, were also noted after IV steroid treatment. According to our results, emergency administration of high dose of Intra-venous corticosteroids to patients with SSNHL is highly recommended. Patients with high frequency preservation
have better hearing improvement at the end of treatment. The critical time period for commencing IV treatment is less than 6 h from onset of hearing loss in order to restore normal hearing. High dose Intravenous steroids are a safe and effective treatment in sudden sensori-neural hearing loss. © 2012 Association of Otolaryngologists of India.

Microsystems technologies for drug delivery to the inner ear.

Pararas EE, Borkholder DA, Borenstein JT.
Charles Stark Draper Laboratory, 555 Technology Square, Cambridge, MA 02139, USA.

The inner ear represents one of the most technologically challenging targets for local drug delivery, but its clinical significance is rapidly increasing. The prevalence of sensorineural hearing loss and other auditory diseases, along with balance disorders and tinnitus, has spurred broad efforts to develop therapeutic compounds and regenerative approaches to treat these conditions, necessitating advances in systems capable of targeted and sustained drug delivery. The delicate nature of hearing structures combined with the relative inaccessibility of the cochlea by means of conventional delivery routes together necessitate significant advancements in both the precision and miniaturization of delivery systems, and the nature of the molecular and cellular targets for these therapies suggests that multiple compounds may need to be delivered in a time-sequenced fashion over an extended duration. Here we address the various approaches being developed for inner ear drug delivery, including micropump-based devices, reciprocating systems, and cochlear prosthesis-mediated delivery, concluding with an analysis of emerging challenges and opportunities for the first generation of technologies suitable for human clinical use. These developments represent exciting advances that have the potential to repair and regenerate hearing structures in millions of patients for whom no currently available medical treatments exist, a situation that requires them to function with electronic hearing augmentation devices or to live with severely impaired auditory function. These advances also have the potential for broader clinical applications that share similar requirements and challenges with the inner ear, such as drug delivery to the central nervous system. Copyright © 2012. Published by Elsevier B.V.

Role of acamprosate in sensorineural tinnitus.

Sharma DK, Kaur S, Singh J, Kaur I.
Department of ENT, Government Medical College, Amritsar, Punjab, India.

Acamprosate with dual mechanism of action as glutamate antagonist and GABA agonist can be a potential target to decrease the severity of sensorineural tinnitus. OBJECTIVE: (1) To study the effectiveness of acamprosate in providing subjective relief and objective improvement in patients having tinnitus of sensorineural origin. (2) To evaluate the adverse events related to the use of acamprosate and also determine the change in quality of life (QOL) parameters. MATERIALS AND METHODS: The study was randomized double-blind, placebo controlled, crossover. Forty adult subjects (>18 years of age), of either sex with tinnitus of sensorineural origin, were administered either acamprosate 333 mg TDS or matched placebo for a period of six weeks followed by a washout period of one week. Drug therapy was switched for another six weeks in consonance with the crossover design. The effect of acamprosate and placebo on subjective relief and objective improvement was evaluated by using modified tinnitus severity, QOL scores and audiology with tinnitus matching in frequency and loudness. RESULTS: At the end of the study, the drug had shown a statistically significant improvement in reducing the tinnitus score in 92.5% of the patients and placebo with an improvement in 12.5% of the patients. The drug was well tolerated without any serious drug reactions. CONCLUSION: Acamprosate is an effective drug in treating the severity of sensorineural tinnitus without causing much of the side effects. Free PMC Article.
Efficacy of intratympanic steroid administration on idiopathic sudden sensorineural hearing loss in comparison with hyperbaric oxygen therapy.

Department of Otorhinolaryngology, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan. suzuhyde@med.uoeh-u.ac.jp.

OBJECTIVES/HYPOTHESIS: The efficacy of intratympanic steroid administration was examined in comparison with hyperbaric oxygen (HBO) therapy in patients with idiopathic sudden sensorineural hearing loss (ISSNHL). STUDY DESIGN: Retrospective study. METHODS: Two hundred seventy-six consecutive patients with ISSNHL (average hearing levels at 250, 500, 1,000, 2,000, and 4,000 Hz ≥ 40 dB; time from onset to treatment ≤30 days) were enrolled. All the patients were given intravenous hydrocortisone (400 mg/day) followed by tapered doses. In addition, 174 patients underwent HBO therapy (HBO group), and 102 patients received intratympanic dexamethasone injection (IT group). The hearing outcomes were evaluated by six indices; the cure rate, marked-recovery rate (percent of patients with hearing gains ≥30 dB), recovery rate (percent of patients with hearing gains ≥10 dB), hearing gain, hearing level after treatment, and hearing improvement rate compared to the unaffected contralateral ear. RESULTS: There was no significant difference in the cure rate, marked-recovery rate, hearing gain, hearing level after treatment, or hearing improvement rate between the two groups; however, the recovery rate was significantly higher in the IT group than in the HBO group (79.4% vs. 68.4%; P = .048). Multiple logistic regression analysis also showed that patients in the IT group were significantly more likely to recover than those in the HBO group (odds ratio: 2.045; 95% confidence interval: 1.097-3.812; P = .024). CONCLUSIONS: Systemic plus intratympanic steroid administration is more effective than systemic steroids plus HBO therapy, and can be a useful first-choice treatment for ISSNHL.

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VI Auditive Stimulation

Symptom Timeline Preceding Cochlear Implant Failure: An Institutional Experience.

Roby BB, Ferrello M, Huang TC, Rimell FL, Levine SC.
Department of Otolaryngology, University of Minnesota, Minneapolis, Minnesota, USA.

Objective. Review cochlear explants and determine the incidence of device and medical failures and develop a pattern of symptoms indicating probable implant failure. Study Design. Case series with chart review. Setting. Tertiary referral center. Subjects and Methods. Subjects were selected if they underwent cochlear explantation. Data were reviewed to determine initial symptom and symptom timeline preceding implant failure. Results. A total of 847 implants were performed from 1988 to 2008, with 128 devices explanted. Of total implants, 72% were Advanced Bionic devices, and 28% were Cochlear Nucleus devices. Overall failure rate was 128 of 847 (15%), with 51 (6%) medical failures and 77 (9%) device failures. Patients with Advanced Bionic devices underwent 102 explants (16.7% failure rate), with 35% medical failures and 65% device failures. Patients with Nucleus devices underwent 26 explants (11% failure rate), with 58% medical failures and 42% device failures. Medical failures included infected devices and wound dehiscence, with the pattern averaging 4.5 months to explantation. Hard device failures included sudden malfunction and slow decline in function, with pattern of failure over 4.2 months. Soft failures included tinnitus and discomfort, with failure over 8 months. Conclusions. There were common patterns when evaluating both medical and device failures. By recognizing patterns of symptoms that may indicate probable implant failure, otolaryngologists can better counsel patients on what to expect with their implants when they present with certain symptoms.
Tinnitus before and 6 Months after Cochlear Implantation.

Kompis M, Pelizzone M, Dillier N, Allum J, Demin N, Senn P.
Department of ENT, Head and Neck Surgery, Inselspital, University of Bern, Bern, Switzerland.

In this prospective multicenter study, tinnitus loudness and tinnitus-related distress were investigated in 174 cochlear implant (CI) candidates who underwent CI surgery at a Swiss cochlear implant center. All subjects participated in two session, one preoperatively and one 6 months after device activation. In both sessions, tinnitus loudness was assessed using a visual analogue scale and tinnitus distress using a standardized tinnitus questionnaire. The data were compared with unaided pre- and postoperative pure tone thresholds, and postoperative speech reception scores. 71.8% of the subjects reported tinnitus preoperatively. Six months after CI surgery 20.0% of these reported abolition of their tinnitus, 51.2% a subjective improvement, 21.6% no change and 7.2% a deterioration. Of the 49 (28.2%) subjects with no tinnitus preoperatively, 5 developed tinnitus 6 months after CI. These 5 had poorer speech understanding after CI surgery with their device than the group who remained tinnitus free. We found no correlation between tinnitus improvement, age, duration of tinnitus, or change in unaided hearing thresholds between the two sessions. Copyright © 2012 S. Karger AG, Basel.

Sound therapy in sudden deafness [Terapia sonora en sordera súbita].
[Article in Spanish]

a UGC Otorrinolaringología, Hospital Universitario Virgen del Rocío, Sevilla, España
b Centro Integral de Acúfenos, Sevilla, España

Introduction and goals: Idiopathic sudden sensorineural hearing loss is a hearing disorder of unknown cause. The spontaneous recovery rate ranges from 50 to 75% of the patients. Scientific experiments on animals support the present study in patients with sudden deafness treated with sounds. Patients and methods: During the period 2003-2009, patients with idiopathic sudden sensorineural hearing loss were administered steroids, piracetam and antioxidants, together with the addition of sounds by means of music and words. Results: Comparing the results of patients treated with medication (n = 65) and those treated with medication and sounds (n = 67), it was observed that patients treated with medication and sounds had higher recovery. Within the group of patients treated with medication and sounds, 25 (37%) experienced complete recovery, 28 (42%) good recovery, 11 (16%) slight recovery and 3 (5%) poor or no recovery. Conclusion: The patients who recovered more than half of their audition accounted for 54% in the group treated with medication and for 79% in the group of patients receiving medication and sounds. Auditory recuperation showed no alterations, at least up to 12 months after therapy. © 2011 Elsevier España, S.L. All rights reserved.

Effects of tinnitus retraining therapy involving monaural noise generators.
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Oishi N, Shinden S, Kanzaki S, Saito H, Inoue Y, Ogawa K.

Department of Otolaryngology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo, 160-8582, Japan, o-ishi@mub.biglobe.ne.jp.

The aim of this study was to assess how tinnitus retraining therapy (TRT) employing monaural noise generators (NGs) affects tinnitus patients. Ninety-five patients with chronic tinnitus were included in this study. All received directive counseling and monaural NGs without any other combination treatment. Effects were evaluated with the Tinnitus Handicap Inventory (THI) 6, 12, and 24 months after the start of treatment. Multiple regression analysis was used to evaluate factors associated with improvement
of THI scores. We observed a significant improvement in the average THI scores, which ranged from 59 at baseline to 36 after 6 months and were stable up to 24 months. Severely distressed (SD) patients experienced more benefits from the therapy than moderately distressed (MD) patients. Multiple regression analysis revealed that the presence of transient anxiety symptoms, measured by the state section of the State Trait Anxiety Inventory at the beginning of treatment, were associated the most to a decline in THI scores in SD patients. Pure-tone average at three mid frequencies was a negatively contributing factor. Analysis of MD patients did not provide a good model. In conclusion, TRT employing monaural NGs was an effective intervention especially for SD patients, although plateau of the effects after 6 months may be indicative of limitation of applying NGs monaurally. Reducing the patients’ hearing handicap may reinforce the effects of TRT in SD patients. Additional evaluation and interventions for both SD and MD patients might be needed.

**Counteracting tinnitus by acoustic coordinated reset neuromodulation.**

Tass PA, Adamchic I, Freund HJ, von Stackelberg T, Hauptmann C.

Research Center Jülich, Institute for Neuroscience and Medicine - Neuromodulation INM-7, Jülich, Germany Department of Stereotaxic and Functional Neurosurgery, University Hospital, Cologne, Germany.

Purpose: Subjective tinnitus is associated with pathologic enhanced neuronal synchronization. We used a model based desynchronization technique, acoustic coordinated reset (CR) neuromodulation, to specifically counteract tinnitus-related neuronal synchrony thereby inducing an unlearning of pathological synaptic connectivity and neuronal synchrony. Methods: In a prospective, randomized, single blind, placebo-controlled trial in 63 patients with chronic tonal tinnitus and up to 50 dB hearing loss we studied safety and efficacy of different doses of acoustic CR neuromodulation. We measured visual analogue scale and tinnitus questionnaire (TQ) scores and spontaneous EEG. Results: CR treatment was safe, well-tolerated and caused a significant decrease of tinnitus loudness and symptoms. Placebo treatment did not lead to any significant changes. Effects gained in 12 weeks of treatment persisted through a preplanned 4-week therapy pause and showed sustained long-term effects after 10 months of therapy: Response, i.e. a reduction of at least 7 TQ points, was obtained in 75% of patients with a mean TQ reduction of 50% among responders. CR therapy significantly lowered tinnitus frequency and reversed the tinnitus related EEG alterations. Conclusion: The CR-induced reduction of tinnitus and underlying neuronal characteristics indicates a new non-invasive therapy which might also be applicable to other conditions with neuronal hypersynchrony.

**A Comparison of Benefit and Economic Value between Two Sound Therapy Tinnitus Management Options.**

Newman CW, Sandridge SA.

Section of Audiology, Head and Neck Institute, Cleveland Clinic.

Background: Sound therapy coupled with appropriate counseling has gained widespread acceptance in the audiological management of tinnitus. For many years, ear level sound generators (SGs) have been used to provide masking relief and to promote tinnitus habituation. More recently, an alternative treatment device was introduced, the Neuromonics Tinnitus Treatment (NTT), which employs spectrally-modified music in an acoustic desensitization approach in order to help patients overcome the disturbing consequences of tinnitus. It is unknown, however, if one treatment plan is more efficacious and cost-effective in comparison to the other. In today’s economic climate, it has become critical that clinicians justify the value of tinnitus treatment devices in relation to observed benefit. Purpose: To determine perceived benefit from, and economic value associated with, two forms of sound therapy, namely, SGs and NTT. Research Design: Retrospective between-subject clinical study. Study Sample: A sample of
convenience comprised of 56 patients drawn from the Tinnitus Management Clinic at the Cleveland Clinic participated. Twenty-three patients selected SGs, and 33 patients selected NTT as their preferred sound therapy treatment option. Data Collection and Analysis: Sound therapy benefit was quantified using the Tinnitus Handicap Inventory (THI). The questionnaire was administered before and 6 mo after initiation of tinnitus treatment. Prior to device fitting, all patients participated in a 1.5 hr group education session about tinnitus and its management. Economic value comparisons between sound therapy options were made using a cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). Results: THI scores indicated a significant improvement (p < 0.001) in tinnitus reduction for both treatment types between a pre- and 6 mo postfitting interval, yet there were no differences (p > 0.05) between the treatment alternatives at baseline or 6 mo postfitting. The magnitude of improvement for both SGs and NTT was dependent on initial perceived tinnitus handicap. Based on the CEA and CUA economic analyses alone, it appears that the SGs may be the more cost-effective alternative; however, the magnitude of economic value is a function of preexisting perceived tinnitus activity limitation/participation restriction. Conclusions: Both SGs and NTT provide significant reduction in perceived tinnitus handicap, with benefit being more pronounced for those patients having greater tinnitus problems at the beginning of therapy. Although the economic models favored the SGs over the NTT, there are several other critical factors that clinicians must take into account when recommending a specific sound therapy option. These include initial tinnitus severity complaints and a number of patient preference variables such as sound preference, listening acceptability, and lifestyle. American Academy of Audiology.

Unlearning tinnitus-related cerebral synchrony with acoustic coordinated reset stimulation: theoretical concept and modelling.

Tass PA, Popovych OV.

Institute of Neuroscience and Medicine - Neuromodulation (INM-7), Research Center Jülich, 52425, Jülich, Germany, p.tass@fz-juelich.de.

Tinnitus is a deafferentation-induced phantom phenomenon characterized by abnormal cerebral synchrony and connectivity. Computationally, we show that desynchronizing acoustic coordinated reset (CR) stimulation can effectively counteract both up-regulated synchrony and connectivity. CR stimulation has initially been developed for the application to electrical deep brain stimulation. We here adapt this approach to non-invasive, acoustic CR stimulation. For this, we use the tonotopic organization of the central auditory system and replace electrical stimulation bursts applied to different brain sites by acoustically delivered tones of different pitch. Based on our simulations, we propose non-invasive acoustic CR stimulation as a possible novel therapy for tinnitus.

VII Brain Stimulation

Effect of 1 Hz Repetitive Transcranial Magnetic Stimulation Over the Auditory Cortex on Audiometry and Otoacoustic Emissions.
Brain Topogr. 2012 Jan 19. [Epub ahead of print]


Department of Psychiatry and Psychotherapy III, University of Ulm, Leimgrubenweg 12-14, 89075, Ulm, Germany, carlos.schoenfeldt@uni-ulm.de.

Repetitive transcranial magnetic stimulation (rTMS) at low frequencies (≤1 Hz) delivered to the primary motor cortex for 15 min or longer has been shown to reduce motor cortex excitability. Over the visual cortex, 1 Hz rTMS led to increased phosphene thresholds and over the auditory cortex rTMS reduced auditory evoked potentials. rTMS above the auditory or temporo-parietal cortex has also been reported to reduce the severity of auditory hallucinations and the perception of tinnitus. However, possible
unwanted effects on hearing function have not yet been investigated systematically. 12 right-handed normal hearing subjects (5 male, mean age 28.2 ± 4.3) received a single session of 18 min 1 Hz rTMS at 90% resting motor threshold intensity using an established coil positioning method targeting the Heschl’s area of the left superior temporal gyrus. Standard pure tone audiometry and distortion-products otoacoustic emissions (DPOAE) were performed before and immediately after stimulation. The main finding was that one session of 1 Hz rTMS over the temporal cortex modified neither the auditory threshold meaningfully nor the presence of DPOAE in healthy subjects. In conclusion, we found in this pilot approach no obvious indication for auditory dysfunctions due to direct electromagnetic stimulation of the superior temporal gyrus after one session of rTMS in healthy controls that may be interpreted as unwanted side effects. Nevertheless monitoring of auditory functions is strongly recommended in future clinical trials stimulating the auditory cortex, as this has not been done systematically in the past.

A nano power CMOS tinnitus detector for a fully implantable closed-loop neurodevice.

Hiseni, S. a, Sawigun, C. a, Vanneste, S. b c d, Van Der Velden, E. d, De Ridder, D. b c d, Serdijn, W. A. a

a Biomedical Electronics Group, Electronics Research Laboratory, Delft University of Technology, Netherlands
b Brain, University Hospital Antwerp, Belgium
c Tinnitus Research Initiative, University Hospital Antwerp, Belgium
d Department of Neurosurgery, University Hospital Antwerp, Belgium

Analog signal processing offers advantages from a power consumption viewpoint. The real-time tinnitus detection method described in this paper detects tinnitus by comparing ECoG/EEG signal energies from different locations in the brain according to a tinnitus “signature”. First, the proposed strategy selects appropriate ECoG/EEG bands per channel by means of band-pass filters. Next, their extracted energies are compared to their counterparts from a different (healthy) location. Tinnitus is detected only if higher theta and gamma energies associated with lower alpha energy, in comparison to corresponding signal energies from healthy brain region, are present. To verify the detector performance, a tinnitus CMOS detector circuit has been designed to be implemented in AMIS 0.35μm technology (I3T25) and has been verified by means of simulations in Cadence using RF spectre. The final circuit operates from a 1V supply and consumes only 60nA. The applicability of the detector is verified by means of circuit simulations with real neural waveforms and is able to successfully detect tinnitus. © 2011 IEEE.

Electric field and current density distribution in an anatomical head model during transcranial direct current stimulation for tinnitus treatment.

Parazzini M, Fiocchi S, Ravazzani P.

National Research Council, Institute of Biomedical Engineering, ISIB-CNR, Milan, Italy.
marta.parazzini@polimi.it.

Tinnitus is considered an auditory phantom percept. Recently, transcranial direct current stimulation (tDCS) has been proposed as a new approach for tinnitus treatment including, as potential targets of interest, either the temporal and temporoparietal cortex or prefrontal areas. This study investigates and compares the spatial distribution of the magnitude of the electric field and the current density in the brain tissues during tDCS of different brain targets. A numerical method was applied on a realistic human head model to calculate these field distributions in different brain structures, such as the cortex, white matter, cerebellum, hippocampus, medulla oblongata, pons, midbrain, thalamus, and hypothalamus. Moreover, the same distributions were evaluated along the auditory pathways. Results of this study show that tDCS of the left temporoparietal cortex resulted in a widespread diffuse distribution of the magnitude of the electric fields (and also of the current density) on an area of the cortex larger than the target brain region. On the contrary, tDCS of the dorsolateral prefrontal cortex resulted in a stimulation mainly concentrated...
on the target itself. Differences in the magnitude distribution were also found on the structures along the auditory pathways. A sensitivity analysis was also performed, varying the electrode position and the human head models. Accurate estimation of the field distribution during tDCS in different regions of the head could be valuable to better determine and predict efficacy of tDCS for tinnitus suppression. Bioelectromagnetics. © 2012 Wiley Periodicals, Inc. Copyright © 2012 Wiley Periodicals, Inc.


Tringali S, Perrot X, Collet L, Moulin A.

Université de Lyon, Lyon F-69000, France; INSERM U1028, CNRS UMR5292, Lyon Neuroscience Research Center, Brain Dynamics and Cognition Team, Lyon F-69000, France; University Lyon 1, Lyon F-69000, France; Department of ENT, Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre-Bénite F-69495, Cedex, France.

No abstract available.

Predictors for rTMS response in chronic tinnitus.

Lehner A, Schecklmann M, Landgrebe M, Kreuzer PM, Poepppl TB, Frank E, Vielsmeier V, Kleinjung T, Rupprecht R, Langguth B.

Department of Psychiatry and Psychotherapy, University of Regensburg Regensburg, Germany.

Background: Repetitive transcranial magnetic stimulation (rTMS) has been studied as a treatment option for chronic tinnitus for almost 10 years now. Although most of these studies have demonstrated beneficial effects, treatment results show high interindividual variability and yet, little is known about predictors for treatment response. Methods: Data from 538 patients with chronic tinnitus were analyzed. Patients received either low-frequency rTMS over the left temporal cortex (n = 345, 1 Hz, 110% motor threshold, 2000 stimuli/day) or combined temporal and frontal stimulation (n = 193, 110% motor threshold, 2000 stimuli at 20 Hz over left dorsolateral prefrontal cortex plus 2000 stimuli at 1 Hz over temporal cortex). Numerous demographic, clinical, and audiological variables as well as different tinnitus characteristics were analyzed as potential predictors for treatment outcome, which was defined as change in the tinnitus questionnaire (TQ) score. Results: Both stimulation protocols resulted in a significant decrease of TQ scores. Effect sizes were small, however. In the group receiving combined treatment, patients with comorbid temporomandibular complaints benefited more from rTMS than patients without those complaints. In addition, patients with higher TQ scores at baseline had more pronounced TQ reductions than patients with low TQ baseline scores. Also, patients who had already improved from screening to baseline benefited less than patients without initial improvement. Conclusions: The results from this large sample demonstrate that rTMS shows only small but clinically significant effects in the treatment of chronic tinnitus. There are no good demographic or clinical predictors for treatment outcome.
VIII Behavioral Therapy

A randomized controlled trial of internet-delivered cognitive behavior therapy and acceptance and in the treatment of tinnitus.


Objective: Our aim in this randomized controlled trial was to investigate the effects on global tinnitus severity of 2 Internet-delivered psychological treatments, acceptance and commitment therapy (ACT) and cognitive behavior therapy (CBT), in guided self-help format. Method: Ninety-nine participants (mean age = 48.5 years; 43% female) who were significantly distressed by tinnitus were recruited from the community. Participants were randomly assigned to CBT (n = 32), ACT (n = 35), or a control condition (monitored Internet discussion forum; n = 32), and they were assessed with standardized self-report measures (Tinnitus Handicap Inventory; Hospital Anxiety and Depression Scale; Quality of Life Inventory; Perceived Stress Scale; Tinnitus Acceptance Questionnaire) at pre-, posttreatment (8 weeks), and 1-year follow-up. Results: Mixed-effects linear regression analysis of all randomized participants showed significant effects on the primary outcome (Tinnitus Handicap Inventory) for CBT and for ACT compared with control at posttreatment (95% CI [-17.03, -2.94], d = 0.70, and 95% CI [-16.29, -2.53], d = 0.68, respectively). Within-group effects were substantial from pretreatment through 1-year-follow-up for both treatments (95% CI [-44.65, -20.45], d = 1.34), with no significant difference between treatments (95% CI [-14.87, 11.21], d = 0.16). Conclusions: Acceptance-based procedures may be a viable alternative to traditional CBT techniques in the management of tinnitus. The Internet can improve access to psychological interventions for tinnitus. (PsycINFO Database Record (c) 2012 APA, all rights reserved).

Sensorimotor training and its implication on cortical reorganization.

Diers, M., Flor, H.

Department of Clinical and Cognitive Neuroscience, Central Institute of Mental Health, University of Heidelberg, Square J5, D-68159 Mannheim, Germany

Several disorders that involve motor and sensory disturbances such as chronic pain, tinnitus or stroke are also characterized by changes in the sensory and motor maps in the sensorimotor cortices. This article reviews training procedures that target these maladaptive changes in states of chronic pain and the behavioral and cortical changes that accompany them. In addition, we will discuss factors that influence training success and discuss new developments. These procedures include training of perceptual abilities, motor function, and direct cortical stimulation and have been shown to reorganize the altered sensory and motor maps. Treatments that combine several modalities such as imagery or mirror treatment as well as use of prostheses also have beneficial effects. Further research must elucidate the mechanisms of these plastic changes related to the disorders and treatments. © Nova Science Publishers, Inc.
The Efficacy of Minimal Contact Interventions for Acute Tinnitus: A Randomised Controlled Study.
Cogn Behav Ther. 2012 Mar 13. [Epub ahead of print]

Department of Clinical Psychology and Psychotherapy, University of Göttingen, Germany.

Acute tinnitus can lead to substantial distress and eventually result in long-lasting impairment. The aim of this study was to compare the efficacy of a cognitive-behavioural intervention (delivered as Internet self-management, bibliotherapy or group training) to the information-only control condition. Applicants suffered from subjective tinnitus for up to six months, were between 18 and 75 years old and received no other tinnitus-related psychological treatment. A total of 304 participants were randomly assigned to one of the four study arms. Tinnitus distress, depressive symptoms, psychosomatic discomfort and treatment satisfaction were assessed. At the post-assessment tinnitus distress was significantly lower in the Internet and the group training conditions compared to the control condition. Inter-group effect sizes were moderate to large. At follow-up, all active training conditions showed significantly reduced tinnitus distress compared to the control condition (intention-to-treat analysis). An additional completer analysis showed a significant reduction in tinnitus distress only for the group condition. All effect sizes were moderate. There were no differences regarding psychosomatic discomfort, but depressive symptoms were reduced in the group condition at the post-assessment (intention-to-treat analysis). Treatment satisfaction was significantly higher in the training conditions. The dropout rate was 39%. The present study shows that distress can be reduced as early as the acute stadium and that minimal-contact interventions are a promising way to do this. In particular, the Internet and group conditions led to a large, immediate decrease in distress, and the participants were highly satisfied with the training.

IX Somatic Tinnitus

Noise overexposure alters long-term somatosensory-auditory processing in the dorsal cochlear nucleus - possible basis for tinnitus-related hyperactivity?

Dehmel S, Pradhan S, Koehler S, Bledsoe S, Shore S.
Kresge Hearing Research Institute, University of Michigan, Ann Arbor, Michigan 48109.

The dorsal cochlear nucleus (DCN) is the first neural site of bimodal auditory-somatosensory integration. Previous studies have shown that stimulation of somatosensory pathways results in immediate suppression or enhancement of subsequent acoustically evoked discharges. In the unimpaired auditory system suppression predominates. However, damage to the auditory input pathway leads to enhancement of excitatory somatosensory inputs to the cochlear nucleus, changing their effects on DCN neurons (Shore et al., 2008; Zeng et al., 2009). Given the well described connection between the somatosensory system and tinnitus in patients we sought to determine whether plastic changes in long-lasting bimodal somatosensory-auditory processing accompany tinnitus. Here we demonstrate for the first time in vivo long-term effects of somatosensory inputs on acoustically evoked discharges of DCN neurons in guinea pigs. The effects of trigeminal nucleus stimulation are compared between normal-hearing animals and animals overexposed with narrow band noise and behaviorally tested for tinnitus. The noise exposure resulted in a temporary threshold shift in auditory brainstem responses but a persistent increase in spontaneous and sound-evoked DCN unit firing rates and increased steepness of rate-level functions. Rate increases were especially prominent in buildup units. The long-term somatosensory enhancement of sound-evoked responses was strengthened while suppressive effects diminished in noise-exposed animals, especially those that developed tinnitus. Damage to the auditory nerve is postulated to trigger compensatory long-term synaptic plasticity of somatosensory inputs that might be an important underlying mechanism for tinnitus generation. Free article.
Surgical Treatment

Otologic complications of cotton swab use: One institution's experience.

Smith M, Darrat I, Seidman M.

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, Michigan, U.S.A.

OBJECTIVES/HYPOTHESIS: To evaluate the indications for observation versus surgery in the management of cotton swab-induced tympanic membrane perforations (TMP). STUDY DESIGN: Institutional review board-approved retrospective cohort study of 1,540 patients with a diagnosis of TMP from 2001 to 2010. Patients with a cotton swab injury were subdivided into two groups: observation and surgery. METHODS: Data collection included demographics, symptoms, surgery type, and pre- and postintervention audiometry. Successful outcomes were defined as healed TMP; resolution/improvement of vertigo, tinnitus, or facial nerve paralysis; and/or closure of the air-bone gap (ABG). RESULTS: Fifty-four of 1,540 patients presented with a cotton swab-induced TMP. Four of the 54 patients (7.4%) underwent delayed surgical repair with 100% success. Preoperatively, one patient had a facial nerve paralysis and two had vertigo with confirmed perilymphatic fistulae (PLF). Postoperatively, the facial nerve paralysis resolved, and one patient had mild vertigo. Fifty of 54 patients opted to forego surgery with 35 patients available for follow-up. Thirty-four (97%) of the 35 patients had spontaneous healing. The average time to perforation closure was 1.75 months. Twelve of 35 patients had no ABG after healing. CONCLUSIONS: Observation is an appropriate consideration for patients who have a TMP due to a cotton swab injury. Surgical intervention should be offered early when a PLF is suspected, or if facial paralysis, severe vertigo, and/or profound sensorineural hearing loss are present. As otolaryngologists, we should be reluctant to offer surgical intervention of an acute injury without significant symptoms as most patients will heal spontaneously within 2 months. Copyright © 2012 The American Laryngological, Rhinological, and Otological Society, Inc.

Stage II vestibular schwannoma: Predictive factors for postoperative hearing loss and facial palsy.

Milhe de Saint Victor S, Bonnard D, Darrouzet V, Bellec O, Franco-Vidal V.

Service d’otorhinolaryngologie et de chirurgie de la base du crâne, CHU Pellegrin, université Victor-Segalen Bordeaux-2, place Amélie-Raba-Léon, 33076 Bordeaux cedex, France.

OBJECTIVES: To assess predictive factors for deafness and facial palsy after vestibular schwannoma surgery on a translabyrinthine or retrolabyrinthine approach, and to compare sequela results to those for gamma knife radiosurgery. PATIENTS AND METHODS: A retrospective study included 70 patients operated on for stage II vestibular schwannoma (Koos classification). Postoperative hearing was assessed on pure-tone average and speech discrimination score, and facial palsy on the House and Brackmann classification, preoperatively and at 1 year postoperatively. Various predictive factors were assessed for both. Statistical analysis used the Fischer exact test, with a significance threshold of P<0.05. RESULTS: Hearing was conserved in 18.9% of patients operated on with a retrolabyrinthine approach, with 8.1% conserving useful hearing. Facial function was conserved in 91.4%. Predictive factors for hearing conservation did not achieve statistical significance, but showed trends for: preoperative pure-tone average threshold≤30dB and speech discrimination score≥70%, age less than 55 years, tinnitus, nearly normal auditory brainstem response (ABR) latency, and homogeneous tumor on MRI. Predictive factors for conserved facial function likewise did not achieve statistical significance, but showed trends for: age less than 55 years, deafness of progressive onset, absence of cardiovascular risk factors, nearly normal ABR latency and tumor size<13.5mm on MRI. CONCLUSION: Facial nerve risk is largely the same with surgery or gamma knife radiosurgery. Concerning hearing, gamma knife radiosurgery seems to provide better hearing conservation, but only over the short term. Copyright © 2012. Published by Elsevier Masson SAS.
Inner Ear Effects of Canal Wall Down Mastoidectomy.

Leonetti JP, Kircher ML, Jaber JJ, Benscoter BJ, Marmora JJ, Feustel PJ.

Department of Otolaryngology-Head and Neck Surgery, Loyola University Medical Center, Maywood, Illinois, USA.

Objective. To evaluate the inner ear effects of canal wall down (CWD) mastoidectomy without ossiculoplasty in the treatment of chronic otitis media (COM) with regard to sensorineural hearing loss (SNHL) and reported tinnitus and dizziness-related disability. Setting. Tertiary care academic medical center. Subjects and Methods. Prospective study of 86 patients treated by CWD mastoidectomy without ossiculoplasty for COM with or without cholesteatoma. Standard patient workup included preoperative audiogram and completion of 2 surveys: Dizziness Handicap Inventory (DHI) and Tinnitus Handicap Inventory (THI). Patients underwent repeat audiogram, DHI, and THI surveys at 4 to 6 months postoperatively. Preoperative and postoperative data were analyzed. Results. No significant SNHL occurred after CWD mastoidectomy. Thirteen patients (13/34 [38%]) had DHI improvement greater than 18 points, indicating a significant improvement in dizziness-related disability. There were no patients with new-onset postoperative dizziness complaints. Twenty patients (20/43 [46.5%]) had THI improvement greater than 7 points, indicating a significant improvement in tinnitus-related disability. Five patients developed new-onset postoperative tinnitus complaints. The odds ratio for improving DHI and THI scores after surgery was 6.6 (1.8 to 25.0) and 4.2 (95% confidence interval, 1.45% to 12.2%), respectively. Conclusion. In this study, CWD mastoidectomy without ossiculoplasty in the treatment of COM did not cause significant SNHL. In addition, using the DHI and THI measures, patient-perceived disability from dizziness and tinnitus, respectively, was shown to decrease after mastoid surgery.

Tenotomy of the middle ear muscles causes a dramatic reduction in vertigo attacks and improves audiological function in definite Meniere’s disease.
Acta Otolaryngol. 2011 Dec 27. [Epub ahead of print]

Loader B, Beicht D, Hamzavi JS, Franz P.

Department of Otorhinolaryngology Head and Neck Surgery, Medical University of Vienna, Vienna General Hospital, Vienna, Austria.

Conclusions: Because the presented data reveal an immediate and persistent reduction of vertigo and a clear improvement in hearing function and functional scales, we conclude tenotomy to be effective in unilateral, definite Meniere’s disease - laying the foundation for future prospective, randomized controlled trials. Objectives: This study compares the unique long-term results of tenotomy of the stapedius and tensor tympani muscles in definite Meniere’s disease refractory to medical treatment and presents a hypothesis on why tenotomy seems effective. Methods: This was an interventional cohort study. The study sample comprised 30 patients (15 males, 15 females; average age 57 ± 13.1 years) with definite Meniere’s disease (AAO-HNS criteria, 1995). Patients were evaluated pre- and postoperatively using pure tone audiometry, AAO-HNS questionnaires regarding vertigo attacks, functional level scores, and tinnitus, and were followed up for 2-9 years. Postoperative values were calculated for the patient collective as a whole and consequently divided into three equal postoperative terms of 3 years each. Results: A statistically significant improvement of inner ear hearing levels postoperatively (p = 0.041) and a major reduction in vertigo attacks in all groups (p < 0.001) with complete absence of attacks in 26/30 patients was noted. Results remained constant up to 9 years postoperatively. Although tinnitus persisted, the intensity was lower overall (p = 0.013).
**A large vestibular schwannoma that did not grow for 18 years.**


**Timmer, F.C.A., Graamans, K.**

Donders Institute for Brain, Cognition and Behaviour, Department of Otorhinolaryngology, Head and Neck Surgery, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands.

Introduction: Treatment strategies for vestibular schwannoma include microsurgery, stereotactic radiotherapy and conservative management (wait and scan). To avoid neurological complications or even death, surgery is the preferred treatment for large tumours with an extrameatal diameter >3.0 cm. Objective/methods: We present the case history of a man with a large vestibular schwannoma who had refused treatment and was seen again eighteen years later. Results: This patient had not developed symptoms other than the initial hearing loss. Repeated imaging showed that the tumour had not grown and the brainstem compression had not progressed. Conclusion: This case history illustrates the unpredictable growth pattern of vestibular schwannomas. Apparently, even large tumours in close proximity to the brainstem may remain stable for many years. However, there still are no valid arguments to refrain from therapy in patients with a large vestibular schwannoma, since reliable growth predictors are not available.

**The Gruppo Otologico experience of endolymphatic sac tumor.**


**Husseini ST, Piccirillo E, Taibah A, Paties CT, Almutair T, Sanna M.**

Department of Otology and Skull Base Surgery, Gruppo Otologico, Piacenza, Italy.

OBJECTIVE: Endolymphatic sac tumor (ELST) is a rare low grade adenocarcinoma of the skull base. During the past decade the number of the reported cases has increased. This study exposes our experience in the management of ELST with a review of the literature. STUDY DESIGN: Retrospective study of patients with ELST at a quaternary referral otology and skull base center. METHODS: A review of the records from the Gruppo Otologico revealed 7 patients treated for ELST. All papers containing series of three or more cases of ELST published in the English literature were selected for analysis. RESULTS: Hearing loss and tinnitus were present in almost all our cases. All of them were evaluated with audiometric tests, computed tomography and magnetic resonance imaging. All the patients were treated surgically with preservation of the facial nerve and preoperative embolization was performed in 5 patients. Genetic study was performed on all our cases and revealed the presence of von Hippel-Lindau syndrome in one patient who had the tumor as the initial manifestation of his syndrome. None of the patients received postoperative radiotherapy and one of them had recurrence of the tumor 13 years following surgery. CONCLUSIONS: Complete surgical resection with preoperative embolization of large tumors is the mainstay treatment for ELST. The facial nerve should not be sacrificed unless it is totally invaded by the tumor. A long term follow up is recommended and the role of postoperative adjunctive radiotherapy is still controversial. Copyright © 2012 Elsevier Ireland Ltd. All rights reserved.

**Focal defect of mastoid bone shell in the region of the transverse-sigmoid junction: a new cause of pulsatile tinnitus.**

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**Xue J, Li T, Sun X, Liu Y.**

Department of Otolaryngology, Head and Neck Surgery, Peking University First Hospital, Beijing, China.

Objective:Pulsatile tinnitus usually originates from vascular structures, causing an arterial or venous bruit. We report a new cause of pulsatile tinnitus: a focal defect of the mastoid bone shell in the region of the transverse-sigmoid junction, with a normal transverse-sigmoid sinus. Participants and intervention:Three patients complained of unilateral, pulsatile tinnitus present for many years. They
were identified as having a focal defect of the mastoid bone shell in the region of the transverse-sigmoid junction. The patients underwent transmastoid reconstruction of the mastoid bone shell overlying the transverse-sigmoid sinus.

Results: All three patients reported immediate resolution of their symptoms, and were asymptomatic at final follow up. Conclusion: A focal defect of the mastoid bone shell overlying the transverse-sigmoid sinus, with no abnormality of the sinus itself, may be a new cause of pulsatile tinnitus. Surgical reconstruction of the mastoid bone shell overlying the transverse-sigmoid sinus can provide lasting symptom relief for patients with pulsatile tinnitus and computed tomographic evidence of the defect.

XII Review

Psychopathological dimensions of tinnitus and psychopharmacologic approaches in its treatment.
Belli H, Belli S, Oktay MF, Ural C.

Bagcilar Education and Research Hospital Department of Psychiatry, 34400 Istanbul, Turkey.

BACKGROUND: The aim of this review is to investigate the presence of psychopathological states and efficacy of psychopharmacological drugs in the treatment of tinnitus. MATERIALS AND METHODS: An extensive Internet search has been performed for this aim through PubMed using related key words in English. RESULTS: Higher anxiety and depression levels and somatoform disorder clusters are defined in patients with tinnitus. Additionally, impulsivity, hostility, demanding, physical discomfort, anxiety for health, emotionality and suicidal tendency are also defined in these people. Personality characteristics in these patients are depression, hysteria and hypochondriac features. Besides these symptom clusters, more severe psychopathologies like personality disorders may be encountered in these patients. Sertraline, paroxetine and nortriptyline can be considered as the first-line antidepressants in the psychopharmacological treatment of tinnitus. There are studies which have reported the efficacy of sulpiride. Carbamazepine, valproate and gabapentin can be effective as mood stabilizers. Short-acting benzodiazepines like alprazolam and midazolam are effective in signs of anxiety. Clonazepam and diazepam can be evaluated as other options. However, some glutamate receptor antagonists also can be used in the treatment of tinnitus. Disturbed sleep is frequently associated with tinnitus. Sleep disturbance can disrupt the quality of life in the patients with tinnitus. These patients might benefit from cognitive-behavioral therapy, which offers the promise of relief from tinnitus-related distress and insomnia. CONCLUSION: When pathophysiologic reasons are excluded, it should be at least considered that tinnitus is exaggerated by psychopathological symptoms. Life quality of patients can be increased by treating these symptoms. Copyright © 2012 Elsevier Inc. All rights reserved.
Clinical practice guideline: sudden hearing loss.


Department of Otolaryngology, Henry Ford Hospital, Detroit, Michigan, USA.

Objective. Sudden hearing loss (SHL) is a frightening symptom that often prompts an urgent or emergent visit to a physician. This guideline provides evidence-based recommendations for the diagnosis, management, and follow-up of patients who present with SHL. The guideline primarily focuses on sudden sensorineural hearing loss (SSNHL) in adult patients (aged 18 and older). Prompt recognition and management of SSNHL may improve hearing recovery and patient quality of life (QOL). Sudden sensorineural hearing loss affects 5 to 20 per 100,000 population, with about 4000 new cases per year in the United States. This guideline is intended for all clinicians who diagnose or manage adult patients who present with SHL. Purpose. The purpose of this guideline is to provide clinicians with evidence-based recommendations in evaluating patients with SHL, with particular emphasis on managing SSNHL. The panel recognized that patients enter the health care system with SHL as a nonspecific, primary complaint. Therefore, the initial recommendations of the guideline deal with efficiently distinguishing SSNHL from other causes of SHL at the time of presentation. By focusing on opportunities for quality improvement, the guideline should improve diagnostic accuracy, facilitate prompt intervention, decrease variations in management, reduce unnecessary tests and imaging procedures, and improve hearing and rehabilitative outcomes for affected patients. Results. The panel made strong recommendations that clinicians should (1) distinguish sensorineural hearing loss from conductive hearing loss in a patient presenting with SHL; (2) educate patients with idiopathic sudden sensorineural hearing loss (ISSNHL) about the natural history of the condition, the benefits and risks of medical interventions, and the limitations of existing evidence regarding efficacy; and (3) counsel patients with incomplete recovery of hearing about the possible benefits of amplification and hearing-assistive technology and other supportive measures. The panel made recommendations that clinicians should (1) assess patients with presumptive SSNHL for bilateral SHL, recurrent episodes of SHL, or focal neurologic findings; (2) diagnose presumptive ISSNHL if audiometry confirms a 30-dB hearing loss at 3 consecutive frequencies and an underlying condition cannot be identified by history and physical examination; (3) evaluate patients with ISSNHL for retrocochlear pathology by obtaining magnetic resonance imaging, auditory brainstem response, or audiometric follow-up; (4) offer intratympanic steroid perfusion when patients have incomplete recovery from ISSNHL after failure of initial management; and (5) obtain follow-up audiometric evaluation within 6 months of diagnosis for patients with ISSNHL. The panel offered as options that clinicians may offer (1) corticosteroids as initial therapy to patients with ISSNHL and (2) hyperbaric oxygen therapy within 3 months of diagnosis of ISSNHL. The panel made a recommendation against clinicians routinely prescribing antivirals, thrombolytics, vasodilators, vasoactive substances, or antioxidants to patients with ISSNHL. The panel made strong recommendations against clinicians (1) ordering computerized tomography of the head/brain in the initial evaluation of a patient with presumptive SSNHL and (2) obtaining routine laboratory tests in patients with ISSNHL.
Tinnitus.

Savage J, Waddell A.
Southmead Hospital, Bristol, UK.

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 July 2011 (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 29 systematic reviews, RCTs, or observational 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, cinnarizine, electromagnetic stimulation, ginkgo biloba, hearing aids, hypnosis, psychotherapy, tinnitus-masking devices, and tinnitus retraining therapy.

Hearing loss, hyperacusis, or tinnitus: What is modeled in animal research?
Hear Res. 2012 Feb 7. [Epub ahead of print]

Eggermont JJ.
Department of Physiology and Pharmacology, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4; Department of Psychology, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4.

Animal models of tinnitus require a behavioral correlate thereof. Various conditioned response methods and gap-startle reflex methods are in use and the outcomes generally correspond with putative electrophysiological substrates of tinnitus. However, for salicylate-induced tinnitus there is discordance between the behavioral and electrophysiological test results. As a result, it is not clear what the various tests are reflecting. A review of the, mostly sub-cortical, neural circuits that underlie the behavioral responses suggests that cortical electrophysiological correlates do not necessarily have to correspond with behavioral ones. Human objective correlates of tinnitus point heavily into cortical network, but not just auditory cortex, correlates of tinnitus. Furthermore, the synaptic mechanisms underlying spontaneous firing rate changes may be different from those involved in driven neural activity.

Hyperacusis and misophonia: the lesser-known siblings of tinnitus.

Schwartz P, Leyendecker J, Conlon M.
Tinnitus and Hyperacusis Clinic, Twin Cities, USA.

Hyperacusis (decreased sound tolerance) and misophonia (fear of sound) are two conditions about which little is known. Consequently, physicians often struggle when they encounter patients who are affected by them. This article attempts to educate the medical community about hyperacusis and misophonia, both of which can have devastating effects on the lives of patients, and ways to manage them.
Tinnitus: pathology of synaptic plasticity at the cellular and system levels.

Guitton MJ.
Faculty of Medicine, Department of Oto-Rhino-Laryngology and Ophthalmology, Laval University, Quebec City QC, Canada.

Despite being more and more common, and having a high impact on the quality of life of sufferers, tinnitus does not yet have a cure. This has been mostly the result of limited knowledge of the biological mechanisms underlying this adverse pathology. However, the last decade has witnessed tremendous progress in our understanding on the pathophysiology of tinnitus. Animal models have demonstrated that tinnitus is a pathology of neural plasticity, and has two main components: a molecular, peripheral component related to the initiation phase of tinnitus; and a system-level, central component-related to the long-term maintenance of tinnitus. Using the most recent experimental data and the molecular/system dichotomy as a framework, we describe here the biological basis of tinnitus. We then discuss these mechanisms from an evolutionary perspective, highlighting similarities with memory. Finally, we consider how these discoveries can translate into therapies, and we suggest operative strategies to design new and effective combined therapeutic solutions using both pharmacological (local and systemic) and behavioral tools (e.g., using tele-medicine and virtual reality settings). Free PMC Article.

Neuronal connectivity and interactions between the auditory and limbic systems. Effects of noise and tinnitus.
Hear Res. 2012 Mar 7. [Epub ahead of print]

Kraus KS, Canlon B.
Center for Hearing and Deafness, State University of New York at Buffalo, 137 Cary Hall, 3435 Main Street, Buffalo, NY 14214, United States.

Acoustic experience such as sound, noise, or absence of sound induces structural or functional changes in the central auditory system but can also affect limbic regions such as the amygdala and hippocampus. The amygdala is particularly sensitive to sound with valence or meaning, such as vocalizations, crying or music. The amygdala plays a central role in auditory fear conditioning, regulation of the acoustic startle response and can modulate auditory cortex plasticity. A stressful acoustic stimulus, such as noise, causes amygdala-mediated release of stress hormones via the HPA-axis, which may have negative effects on health, as well as the central nervous system. On the contrary, short-term exposure to stress hormones elicits positive effects such as hearing protection. The hippocampus can affect auditory processing by adding a temporal dimension, as well as being able to mediate novelty detection via theta wave phase-locking. Noise exposure affects hippocampal neurogenesis and LTP in a manner that affects structural plasticity, learning and memory. Tinnitus, typically induced by hearing malfunctions, is associated with emotional stress, depression and anatomical changes of the hippocampus. In turn, the limbic system may play a role in the generation as well as the suppression of tinnitus indicating that the limbic system may be essential for tinnitus treatment. A further understanding of auditory-limbic interactions will contribute to future treatment strategies of tinnitus and noise trauma. Copyright © 2012 Elsevier B.V. All rights reserved.
XIII  Others

Strategies and accomplishments of the Tinnitus Research Consortium.
Hear Res. 2012 Jan 8. [Epub ahead of print]

Snow JB Jr.

Tinnitus Research Consortium, 327 Greenbriar Lane, West Grove, PA 19390, USA.

The Tinnitus Research Consortium (TRC) is sponsored by a philanthropist who wants to accelerate progress in basic and clinical research on tinnitus. The TRC consists of 12 distinguished auditory scientists who began meeting in 1998 twice a year for brainstorming for new research approaches to tinnitus, developing requests for applications, judging the scientific merit of the applications received and reviewing the progress of funded projects. Through these efforts, common confounding variables in tinnitus research have been identified, and solutions to these problems have been suggested. TRC grants have been made up to $100,000.00 per year for three years. The sponsor had provided $600,000.00 per year; so two new grants could be made each year. The good news is that the sponsor’s support has been increased by 50% for 2011 so that three grants have been awarded. Some of the landmark studies supported by the TRC over the last 14 years are reviewed as is the changing conceptualization of the pathogenesis of tinnitus and its management. The effect of strategies of the TRC on the applicants, grantees, scientific field, scientific societies and other funding agencies will be discussed. For example, when the TRC was initiated, sessions devoted to tinnitus research at national scientific meetings were rare. Through the efforts of the TRC, the American Tinnitus Association and the American Academy of Audiology, organizations such as the Association for Research in Otolaryngology and the Society for Neuroscience were encouraged to hold special sessions on tinnitus research. Now such organizations have well attended sessions on tinnitus research each year. The size of the TRC grants, large enough to support a substantial research project, has caused several other voluntary agencies to increase the size of their grants toward the TRC standard. The National Institute on Deafness and Other Communication Disorders and other institutes at the National Institutes of Health have devoted far more emphasis on tinnitus. By supporting sound research on tinnitus and recruiting world-class scientists to the field, the TRC has led in making tinnitus research respectable. Copyright © 2012. Published by Elsevier B.V.

Clinical guidelines and practice: a commentary on the complexity of tinnitus management.

Hoare DJ, Hall DA.

1NIHR National Biomedical Research Unit in Hearing, Ropewalk House, Nottingham, United Kingdom.

Subjective tinnitus is an enigmatic and chronic condition that is predominantly managed as symptomatic. Little high-level evidence exists for the efficacy and specificity of the various tinnitus management strategies currently used, and this is reflected in documents that aim to guide clinicians. As a consequence, there are clear gaps in evidence-based practice linking diagnosis to the most effective management strategies as well as a general lack of consensus about which are appropriate strategies for assessment and management. Several guidelines have been produced from research efforts and from expert opinion. All recommend standardization of assessment and a range of management options but do not yet provide a means to link the two. The authors call for clinicians, scientists, and policy makers to work together to address this barrier to good practice.
A commentary on the complexity of tinnitus management: clinical guidelines provide a path through the fog.

Searchfield G.

1 Audiology, School of Population Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand.

There is a desire among many tinnitus researchers and clinicians for greater standardization in the assessment and management of tinnitus. In their commentary on the complexity of tinnitus, Hoare et al. have highlighted the need for strong evidence-based protocols. The authors make many valid and important conclusions as to the current state of clinical guidelines; they identify clear gaps in evidence and limited consensus as to clinical practice. While I agree with the bulk of their commentary there are a few areas where I will offer a counter view. In particular I will address their view that only high-level evidence has a place in forming practice guidelines for tinnitus.

Tinnitus: the complexity of standardization.

Langguth B, Kleinjung T, Landgrebe M.

1 Department of Psychiatry and Psychotherapy, University of Regensburg, Regensburg, Germany.

Tinnitus is a heterogeneous disorder that causes significant impairment in many patients. Treatment is elusive and there is a need for more comprehensive guidelines for diagnosis and management of tinnitus. However, different standardization approaches should be differentiated according to their specific purpose. Standardization of assessment methods and outcome measurements are useful for the performance of clinical trials, for comparison of results across centers, for clinic audits, and for epidemiological studies. In contrast, clinical guidelines are the best approach for the standardization of the clinical management of tinnitus patients. In the development of these clinical guidelines, the heterogeneity of tinnitus should be considered. Tinnitus can be a symptom of a severe underlying disease. Also, there are specific subforms of tinnitus for which curative treatment options are available. Therefore, medical diagnosis is necessarily the first step in tinnitus management. Treatment guidelines should not be restricted to recommendations that are supported by high-level evidence. They should also contain treatment recommendations that have shown clinically highly relevant effects in case series of specific tinnitus subgroups.

[Suction-Generated Noise Levels During Aural Toilet.]
[Article in German]
Laryngorhinootologie. 2012 Jan 4. [Epub ahead of print]

Hansen S, Stupp A, Schwarze S, Schipper J.

Universitätsklinik Düsseldorf, Hals-Nasen-Ohrenklinik, Düsseldorf.

The use of suction for the removal of foreign bodies or cerumen from the external auditory canal is a common procedure in ENT outpatient centers. Patients’ lamentations about high noise levels during microsuction can cause assault charges concerning permanent hearing loss or tinnitus. However, the medical opinion of these cases is difficult because only a small amount of objective data about suction-generated noise is available. In this study, noise levels of different suction devices were measured under standardized conditions in an artificial model head (HEAD acoustics, Germany). In a second set-up water and lard (instead of cerumen) were suctioned from an artificial external auditory canal, which was coupled with a noise mediator (Mediator 2238, Brüel & Kjaer, Denmark). There was a significant influence of the inner diameter of the sucker on the noise level. A sucker with a diameter of 1.4 mm generated a noise level of more than 100 dB(A). The suctioning of water generated a maximum noise level of more
than 130 dB(LAmax), while the suctioning of lard reached nearly 150 dB(LAmax). The time lapse of both noise and frequency level for lard suctioning was characteristic of a bang. This study demonstrates objective and reproducible data for suction-generated noise levels and could help to evaluate patients’ complaints. © Georg Thieme Verlag KG Stuttgart New York.

Changes in audiometry results following laser therapy for tinnitus.
[Tinnitusta lazer tedavi etkinliğinin odyogram ile değerlendirilmesi]

Yildirim, G., Berkiten, G., Uğraş, H., Saltürk, Z.

Okmeydani Education and Research Hospital, ENT Department, Istanbul, Turkey

Aim: To demonstrate the effect of laser therapy in the treatment of tinnitus with changes in audiometric results. Method: This current study included a total of 30 patients (15 females and 15 males). A laser with a 650 nm wave length at 5 mW was applied to the ear with tinnitus complaint on every consecutive week day for 20 minutes with a break on weekends. The process was continued for 8 weeks and a total of 40 sessions were performed. Pure tone audiometric evaluation between 250-20000 Hz frequency ranges was performed prior to the therapy and was repeated right after and two months after the treatment. Tinnitus scoring was performed before and two months after laser therapy. The results, obtained following therapy, were statistically evaluated. Result: 50% of the patients were female, and 50% were male. The patients' ages were between 20 and 74. In 7 of the patients, tinnitus was in the left ear, in 11 patients in the right ear and in 12 it was bilateral. The audiometric values of the patients were evaluated in 3 different conditions which included the values before therapy, values after therapy and values at 2 months following treatment. A greater difference was observed particularly in the frequencies above 8000 Hz. A significant difference was also detected in audiometry results after laser therapy (p<0.001). It was found that the difference between males and females was significant after laser therapy (p<0.001).

Conclusion: The effect of laser therapy is still controversial. In our study, laser therapy seemed to be effective right after therapy. Although the audiometric values returned to pretreatment levels after 2 months, the tinnitus scores have remained lower compared to the pretreatment scores.

Patient preferences and willingness to pay for tinnitus treatments.

Tyler RS.

Departments of Otolaryngology-Head and Neck Surgery and Communication Sciences and Disorders, University of Iowa.

Purpose: There will likely be several different tinnitus treatments necessary, and it is important to understand patient preferences and factors that might contribute to treatment acceptability. This study explores the acceptability of a wide range of different tinnitus treatments, from noninvasive wearable devices to surgically implanted devices in the brain. Understanding how tinnitus sufferers consider and rank such options and how they might be influenced by their own perception of the severity of their tinnitus could help clinicians, researchers, and companies plan future efforts for approaching new treatments. Data Collection and Analysis: 197 tinnitus self-help group attendees rated their acceptance of treatments on a scale from 0 (not acceptable) to 100 (fully acceptable). The treatments included external devices, medications, cochlear implants, an implant on the brain surface, and an implant in the brain. They were also asked how much they would pay for successful treatments. Results: There was a significant correlation between loudness and annoyance (r = .78). To reduce tinnitus by half, an „acceptable“ response between 91 and 100 was reported by 30% of the respondents for devices, by 52% for pills, by 25% for cochlear implants, by 13% for implants on the brain surface, and by 13% for implants in the brain. To reduce tinnitus completely, a 91-100 acceptable response was reported by 42% for devices, by 62% for pills, by 36% for cochlear implants, by 21% for implants on the brain surface, and by 19% for implants in the brain. To reduce tinnitus completely, participants most commonly selected to
pay at least $5000, and 20.3% were willing to pay as much as $25,000. The ratings of tinnitus loudness and annoyance were positively correlated with the likelihood of using any treatment. Surprisingly, there was a weak relationship between annoyance and the amount they were willing to pay. Conclusions: Tinnitus patients are prepared to accept a wide variety of treatments. Medications are the most acceptable. Invasive procedures can also be acceptable to many, particularly if they provide complete relief. American Academy of Audiology.

XIV Case Reports

Extensive Cerebellar Venous Malformation Associated with a Varix and Cavernous Malformations: a Case Report.
Cerebellum. 2012 Jan 27. [Epub ahead of print]

Nakajima R, Uchino A, Saito N, Ishihara S, Kimura F.
Saitama Medical University, International Medical Center, Saitama, Japan, reiko726reiko@gmail.com.

Venous malformations are the most common cerebral vascular malformation, frequently associated with cavernous malformation, and rarely accompanied by a varix. We report the case of a 67-year-old woman with tinnitus, whose cranial magnetic resonance images and selective catheter angiograms showed extensive cerebellar venous malformation with cavernous malformations and varix. Injury of vessel walls by increased blood flow in the draining vein of the malformation may have led to the development of cavernous malformations and a varix. To our knowledge, such association with an extensive cerebellar venous malformation has not been reported.

[A young patient with paraganglioma syndrome type I : An interdisciplinary challenge.]
[Article in German]
HNO. 2012 Jan 28. [Epub ahead of print]

Brase C, Neumann H, Lell M, Schwarz-Furlan S, Rogler K, Hornung J.
Hals-Nasen-Ohren-Klinik, Kopf- und Halschirurgie, Universitätsklinikum Erlangen, Waldstr. 1, 91054, Erlangen, Deutschland, christoph.brase@uk-erlangen.de.

A 33-year old patient presented at our outpatient department with pulse-synchronous tinnitus in the left ear of several years’ standing. Examination of the left ear showed a neoplasm at the base of the meatus in front of the ear drum. In addition, there was paresis of the right hypoglossal nerve and right vocal cord. CT scan showed multiple paraganglioma in the head and neck region. Molecular genetic screening analysis showed a mutation of the SDHD gene and thus the diagnosis of paraganglioma syndrome type 1 was made. In the treatment concept presented here the main goal was preservation of function of the left cranial nerves due to the functional loss of the right cranial nerves X and XII. This goal could be achieved by means of a staged procedure in collaboration with radiotherapists.

Vidian Nerve Neurofibroma Removed via a Transpterygoid Approach.

McLaughlin N, Bresson D, Ditzel Filho LF, Carrau RL, Kelly DF, Prevedello DM, Kassam AB.
Brain Tumor Center, John Wayne Cancer Institute at Saint John’s Health Center, Santa Monica, CA, USA.

Lesions originating in the vidian canal are extremely rare. Most frequently, they are extensions from contiguous carcinomas. We present a rare case of a vidian nerve neurofibroma and discuss its surgical management. A 62-year-old woman with a history of a basal cell skin cancer was evaluated for bilateral tinnitus. Imaging revealed a left-sided lesion at the medial aspect of the pterygoid process base, over the
vidian canal. Under image-guidance, an endonasal endoscopic transpterygoid approach was performed. The histopathological examination supported the diagnosis of neurofibroma. Benign nerve sheath tumors of the vidian nerve should be considered in the differential diagnosis of a vidian canal lesion. Given the propensity of more aggressive tumors, a tissue diagnosis should be warranted in order to coordinate appropriate subsequent treatment. The expanded endonasal transpterygoid approach offers a safe, less invasive, and effective route to perform the excisional biopsy of such a lesion. © Georg Thieme Verlag KG Stuttgart New York.

Susac's Syndrome in a 27-Year-Old Female.

Mohsen Adelpoor, Mohammad Sadegh Farahvash, Masoud Aghsaei Fard, Mojgan Nikdel, Mohammad Yaser Kiarudi.
Department of Ophthalmology, Farabi Eye Research Center, Quazvin Square, Tehran, Iran

A 27-year-old woman was referred by the neurologist for ophthalmic examination. She had a history of headache, visual loss in her right eye, four-limb paresthesia, and behavioral changes over the previous 10 months. The patient complained of tinnitus and hearing loss for two weeks. The patient was initially diagnosed with multiple sclerosis, but auditory and retinal involvement (small branch retinal artery occlusion in fluorescein angiography) raised the possibility of Susac's syndrome.

Spontaneous pneumarthrosis of the atlantoaxial joint: Case report.

Al Felasi, M.a, Venail, F.b, Lonjon, N.a

a Department of Neurosurgery, Centre Hospitalier Universitaire, Gui de Chauliac Hospital, 80 Avenue Augustin Fliche, 34090 Montpellier, France.
b Department of Otolaryngology and Neurotology, Centre Hospitalier Universitaire Gui de Chauliac Hospital, Montpellier, France.

The authors describe the case of a 29-year-old man presenting with left retrooccipital and cervical pain associated with left ear fullness and rhythmic tinnitus. Head rotation movements on the right side and the Valsalva maneuver increased symptoms. A CT scan identified hyperpneumatization of the left temporal bone extending to the occipital bone as well as pneumarthrosis of the atlantoaxial joint. Surgical treatment involving obliteration of the fistula with bone and fat grafts via a computer-aided transmastoid approach was proposed. The surgery resolved all of the patient's symptoms except for the ear fullness. In this case the authors described an original treatment for spontaneous atlantoaxial pneumarthrosis. Long-term follow-up is needed to evaluate the risk of the recurrence of abnormal occipital bone pneumatization and to assess joint function.

Loud clicking sounds associated with rapid soft palate muscle contractions.

Schwartz RH, Bahadori RS, Myseros JS.

From the Departments of *Pediatrics and †Surgery, Section of Pediatric Otolaryngology, Inova Fairfax Hospital for Children, Falls Church, VA; and‡Department of Neurosurgery, Children's National Medical Center, Washington, DC.

An 8-year-old boy was seen by his primary care pediatrician with a chief complaint of “intermittent rapid vibrations of the epiglottis” that began several weeks prior. Intraoral examination revealed rapid, symmetrical bilateral contractions of the soft palate muscles (velum), accompanied by clicking sounds audible to physician (objective tinnitus) and patient. The patient was able to volitionally control the initiation and cessation of the palatal movements. The child’s mother stated that there had been no
clicking noises heard while the boy was sound asleep. Palatal “clonus” was tentatively diagnosed as the cause of the problem. A normal magnetic resonance imaging study with contrast enhancement confirmed that there was no anatomical basis for the localized movement disorder. Palatal myoclonus is an uncommon localized intraoral movement disorder. There are 2 distinct types, and our patient was diagnosed with the essential palatal myoclonus type. This type is characteristically associated with clicking tinnitus, heard by the affected person as well as those in close proximity. The clicking noise is not continuous, ceases during sleep, and is not lifelong.

The post dura puncture headache syndrome. Case report and review.
[Het syndroom van hoofdpijn na durapunctie. Gevvalsbespreking en literatuuroverzicht]
[Article in Dutch]

Scharlaeken, I.ᵃ, Desmet, M.ᵇ, De Keersmaecker, B.ᶜ, Van Belleghem, V.ᵇ

ᵃ K.U.Leuven, Belgium.
b Dienst Anesthesie, AZ Groeninge, Loofstraat 43, 8500 Kortrijk, Belgium.
c Dienst Gynaecologie, AZ Groeninge, Kortrijk, Belgium.

After perforation of the dura mater, loss of cerebrospinal fluid may occur. The excessive loss leads to intracranial hypotension and may result into the post dura puncture headache syndrome. Postural headache and associated symptoms (meningeal signs, visual disturbances, vertigo and tinnitus) occurring after dural perforation are characteristics of the post dura puncture headache syndrome. The risk factors for the development of the PDPH syndrome may be patient dependent or independent. First line therapy consists of bedrest, analgesics and fluid intake. If these measures fail, an epidural blood patch may be performed with a success rate up to 95%.

Post-spinal tinnitus requiring treatment: Efficacy of epidural blood patch: Case report
[Tedavi gerektiren post-spinal tinnitus: Epidural kan yamasi{dotless}ni{dotless}n etkinliği]
Türkiye Klinikleri Journal of Medical Sciences Volume 32, Issue 2, 2012, Pages 515-519

Güngör I., Günaydın B., Taş A., Dayanır H., Altınoy A.

Anesteziyoloji ve Reanimasyon AD, Gazi Üniversitesi, Tip Fakültesi, Ankara, Turkey.

Auditory complications such as frequently seen headache, rarely seen tinnitus and/or sensorineural hearing loss are observed due to cerebrospinal fluid loss following spinal anesthesia. The aim of this case report is to present the efficiency of epidural blood patch in a 33-year-old, multiparous, term pregnant woman with complaints of bilateral tinnitus along with severe headache following spinal anesthesia for Caesarean section. An epidural blood patch was performed in order to treat post-spinal headache and bilateral tinnitus. Although post-spinal headache improved dramatically, improvement of tinnitus completely took a longer time. In conclusion, treating postspinal tinnitus effectively with epidural blood patch is very important in postpartum period because of possible increased risk of morbidity and negative effect on breast-feeding unless it treated completely. Copyright © 2012 by Türkiye Klinikleri.

Isildak H, Albayram S, Isildak H.

Otolaryngology Head and Neck Surgery Department, Cerrahpasa Medical School, Istanbul University, Istanbul, Turkey. mdhuseyin@gmail.com

Hearing loss, tinnitus, and vertigo are very common complaints in otolaryngology practice. Here, we describe spontaneous intracranial hypotension (SIH) as a curable reason of hearing loss, tinnitus, and vertigo. A 29-year-old woman presented to the emergency room with nausea, dizziness, vertigo, instability, hearing loss, tinnitus, and neck and back pain. Cranial computed tomography, magnetic resonance imaging (MRI), and lumbar puncture were performed. The patient stated that the hearing loss and tinnitus became worse after effort or standing for prolonged times. Therefore, we performed audiogram in sitting and standing positions. The tinnitus severity index was used to evaluate tinnitus. Lumbar puncture revealed no cerebrospinal fluid, and cerebrospinal fluid could be obtained by aspiration. Cranial MRI showed dural thickness and venous engorgement in the internal acoustic canals bilaterally. Audiography showed worse hearing capacity in standing position than in sitting position and revealed especially low-frequency hearing loss bilaterally. The patient’s tinnitus severity index was 48 of 60. The patient was diagnosed as having SIH and treated with autologous blood punch. Cranial MRI and audiogram were normal after the treatment. The patient had no tinnitus after the treatment.

Spontaneous intracranial hypotension, which may cause Ménière syndrome-like symptoms, is a curable reason of hearing loss, tinnitus, and vertigo. In addition, the fluctuation of the hearing loss with positional changes supports the use of positional audiometry when evaluating hearing loss-related SIH. Venous engorgement in the internal acoustic canal may be related to the symptoms.


Department of Neurology, Girona Biomedical Research Institute (IDIBGI), Dr. Josep Trueta University Hospital, Avda. França s/n, 17007, Girona, Spain.

Susac’s syndrome is a rare idiopathic microangiopathy affecting the precapillary arterioles of the brain, retina and cochlea leading to the clinical triad of encephalopathy, retinopathy and hearing loss. The objective of this study is to describe a new case of Susac’s syndrome reactivated after a 12-year period with a good response to immunosuppressive therapy. The patient was a 32-year-old woman, complaining of diplopia, right blurred vision, progressive gait disturbance, tinnitus, attention deficit, and slight memory loss. The patient was diagnosed as having Susac’s syndrome and discharged with steroid therapy. After a 12-year period of clinical stability she had a relapse. Immunosuppressive therapy resulted in significant clinical and radiological improvement. Early clinical identification of Susac’s syndrome is crucial for the initiation of immunosuppressive therapy and differential diagnosis. In our case, the combined use of corticosteroids and azathioprine was key in the relapse management.


Department of Medicine, Tokyo Women’s Medical University, Medical Center East, Tokyo, Japan.

No abstract available.
Superficial temporal arteriovenous fistula as a complication of rhytidectomy.

Kominami S, Watanabe A, Akimoto M, Kobayashi S, Teramoto A.

From the Departments of *Neurosurgery and †Plastic Surgery, Chiba-Hokuso Hospital, Nippon Medical School, Chiba, Japan, and ‡Department of Neurosurgery, Nippon Medical School, Tokyo, Japan.

A 67-year-old woman who had undergone rhytidectomy 5 years before her presentation experienced increasing pulsatile tinnitus on the left side that had begun 2 years earlier. Angiography revealed a direct arteriovenous fistula between the superficial temporal artery and superficial temporal vein in front of her left ear. There was a scar from the earlier cosmetic surgery at the site. The fistula was embolized with N-butyl cyanoacrylate, and her tinnitus disappeared. We posit that the fistula was a complication of rhytidectomy and that a small arteriovenous fistula formed at the time of surgery and enlarged over time. This case indicates that arteriovenous fistulae can occur as a delayed complication of cosmetic surgery.

XV Specific Forms of Tinnitus

Audiological signs in pediatric cases with dehiscence of the bony labyrinth caused by a high jugular bulb.

Sone M, Katayama N, Naganawa S, Yoshida T, Teranishi M, Nakashima T.

Department of Otorhinolaryngology, Nagoya University Graduate School of Medicine, Nagoya, Japan.

Clinical findings were assessed in three pediatric cases of dehiscence of the bony labyrinth caused by a high jugular bulb (HJB). Two children had two dehiscent lesions, which included posterior semicircular canal dehiscence (PSCD) and vestibular aqueduct dehiscence (VAD). One child had VAD alone. Two subjects with PSCD, but not with VAD alone, had mixed hearing loss and showed wave motion of the baseline on tympanometry and acoustic reflex testing, and a reduced response on otoacoustic emission. These findings may reflect jugular venous pulsations transmitted through the PSC and represent characteristics of cases with PSCD caused by HJB. Copyright © 2011 Elsevier Ireland Ltd. All rights reserved.

Can Vestibular-Evoked Myogenic Potentials Help Differentiate Meniere Disease from Vestibular Migraine?

Zuniga MG, Janky KL, Schubert MC, Carey JP.

Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.

Objectives. To characterize both cervical and ocular vestibular-evoked myogenic potential (cVEMP, oVEMP) responses to air-conducted sound (ACS) and midline taps in Ménière disease (MD), vestibular migraine (VM), and controls, as well as to determine if cVEMP or oVEMP responses can differentiate MD from VM. Study Design. Prospective cohort study. Setting. Tertiary referral center. Subjects and Methods. Unilateral definite MD patients (n = 20), VM patients (n = 21) by modified Neuhauser criteria, and age-matched controls (n = 28). cVEMP testing used ACS (clicks), and oVEMP testing used ACS (clicks and 500-Hz tone bursts) and midline tap stimuli (reflex hammer and Mini-Shaker). Outcome parameters were cVEMP peak-to-peak amplitudes and oVEMP n10 amplitudes. Results. Relative to controls, MD and VM groups both showed reduced click-evoked cVEMP (P < .001) and oVEMP (P < .001) amplitudes. Only the MD group showed reduction in tone-evoked amplitudes for oVEMP. Tone-evoked oVEMPs differentiated MD from controls (P = .001) and from VM (P = .007). The oVEMPs in response to the reflex hammer and Mini-Shaker midline taps showed no differences between groups (P > .210). Conclusions.
Using these techniques, VM and MD behaved similarly on most of the VEMP test battery. A link in their pathophysiology may be responsible for these responses. The data suggest a difference in 500-Hz tone burst-evoked oVEMP responses between MD and MV as a group. However, no VEMP test that was investigated segregated individuals with MD from those with VM.

**Impact of long-term serum platinum concentrations on neuro- and ototoxicity in Cisplatin-treated survivors of testicular cancer.**


Sprauten M, Darrah TH, Peterson DR, Campbell ME, Hannigan RE, Cvancarova M, Beard C, Haugnes HS, Fossà SD, Oldenburg J, Travis LB.

Department of Clinical Cancer Research, Norwegian Radium Hospital, Postboks 4953 Nydalen, N-0424 Oslo, Norway; s.d.fossa@medisin.uio.no.

**PURPOSE** Cisplatin-induced neurotoxicity and ototoxicity (NTX) are important adverse effects after chemotherapy for testicular cancer (TC). Although serum platinum is measurable years after therapy, its impact on NTX has not been evaluated. PATIENTS AND METHODS In all, 169 cisplatin-treated survivors of TC provided blood samples at Survey I and reported NTX during Survey I (1998-2002) and Survey II (2007-2008). Serum platinum was quantified by inductively coupled plasma mass spectrometry. Patient-reported outcomes were evaluated with the Scale for Chemotherapy-Induced Neurotoxicity (SCIN), regarding the extent of symptom bother as 0, “not at all”; 1, “a little”; 2, “quite a bit”; or 3, “very much.” Summing the six symptom scores yielded a total SCIN score of 0 to 18. Categorizing total SCIN scores into quartiles yielded similar-sized groups with increasing symptoms. Multivariate ordinal logistic regression analyses evaluated associations between NTX and long-term serum platinum levels, adjusting for cisplatin dose, dosing schedule, and age. Results At Survey I, a significant four- to five-fold association with total SCIN score emerged for the highest serum platinum quartile (odds ratio [OR], 4.69; 95% CI, 1.82 to 12.08). Paresthesias and Raynaud’s syndrome (hands and feet) showed significant two- to four-fold increased risks with the highest platinum quartile. At Survey II, total SCIN score remained significantly associated with the highest platinum quartile (OR, 4.28; 95% CI, 1.36 to 13.48). Paresthesias (hands and feet) and tinnitus showed significant three- to four-fold increased risks for the highest platinum quartile. Cumulative cisplatin dose was not associated with total SCIN score or individual SCIN symptoms in multivariate analyses. CONCLUSION Here we document a significant relationship between increasing levels of residual serum platinum and NTX severity after adjusting for initial cisplatin dose.

**A clinical and histopathologic study of jugular bulb abnormalities.**


Friedmann DR, Eubig J, Winata LS, Pramanik BK, Merchant SN, Lalwani AK.

Department of Otolaryngology, New York University School of Medicine, 550 First Ave, 7Q, New York, NY 10016. anil.lalwani@nyumc.org.

**OBJECTIVE:** To further define the spectrum of clinical presentation and explore the histologic sequelae of jugular bulb abnormalities (JBAs). DESIGN: Retrospective review. SETTING: Academic medical center. PATIENTS: Thirty patients with radiologic evidence of inner ear dehiscence by JBA. MAIN OUTCOME MEASURE: Thirty patients with radiologic inner ear dehiscence by JBA and 1579 temporal bone specimens were evaluated for consequences from JBA. RESULTS: We found that JBA-associated inner ear dehiscence could be identified on computed tomography of the temporal bone but not on magnetic resonance imaging scan. Jugular bulb abnormalities eroded the vestibular aqueduct most often (in 25 patients), followed by the facial nerve (5 patients) and the posterior semicircular canal (4 patients). Half of the patients (15) were asymptomatic. Results from vestibular evoked myogenic potential (VEMP) tests were positive in 8 of 12 patients with inner ear dehiscence. Histologically, only 2 of 41 temporal bones with dehiscence of the vestibular aqueduct demonstrated endolymphatic
CONCLUSIONS: Jugular bulb abnormalities can erode into the vestibular aqueduct, facial nerve, and the posterior semicircular canal. While symptoms may include pulsatile tinnitus, vertigo, or conductive hearing loss, in contrast to earlier reports, half of the patients were asymptomatic. Dehiscence of vestibular aqueduct rarely leads to clinical or histologic hydrops. The VEMP testing was useful in confirming the presence of inner ear dehiscence due to JBAs. Because the natural history of JBAs is unknown, these patients should be followed closely to evaluate for progression of the JBA or development of symptoms.

*Ménière's disease in children aged 4-7 years.*  
**Brantberg K, Duan M, Falahat B.**  
Department of Audiology and Neurotology, Karolinska University Hospital.  
This is a retrospective review of clinical data and audiovestibular test results from four children in whom symptoms suggesting Ménière's disease started at 4-7 years of age. The four patients all had spontaneous recurrent attacks of (spinning) vertigo and fluctuating low frequency sensorineural hearing loss from an early age, suggesting a diagnosis of definite Ménière’s disease. Presumably, due to age-related inability to communicate auditory symptoms, the children did not initially meet requirements for a diagnosis of Ménière's disease. However, by 8 years of age, all four children reported tinnitus and/or fullness in the affected ear and, thus, met the AAO criteria for Ménière's disease. Even if information on subjective auditory symptoms is missing, it is reasonable to consider young children with idiopathic spontaneous recurrent attacks of vertigo in whom audiograms reveals fluctuating low frequency hearing loss to have Ménière’s disease. This report is a reminder that Ménière’s disease may also occur in young children.

*Idiopathic Tinnitus Concomitant With Eye Closure.*  
Otol Neurotol. 2011 Dec 30. [Epub ahead of print]  
**Ohki M, Kato H.**  
Department of Otolaryngology, Saitama Medical Center, Saitama, Japan. m-ohki@umin.ac.jp.  
OBJECTIVE: To describe 2 patients presenting with idiopathic tinnitus concomitant with eye closure.  
STUDY DESIGN: Clinical capsule report. SETTING: University hospital. PATIENTS: Two patients presented with intermittent tinnitus synchronous with eye closing or blinking. Otoscopic examination revealed inward movement of tympanic membranes concomitantly with eye blinking or eye closure in 1 patient. Neither patient had facial nerve disease or myoclonus. INTERVENTIONS: Compliance in impedance audiometry was recorded. RESULTS: Compliance in impedance audiometry was reduced during eye blinking and eye closure in both cases. The tinnitus was attributed to muscular tinnitus via stapedial muscle contraction during eye closure. CONCLUSION: These are the rare 2 reported patients presenting with idiopathic muscular tinnitus concomitant with eye closure. The reductive change of compliance in impedance audiometry during tinnitus coincident with eye closure is a feature of this form of tinnitus. We suggest evaluation of compliance change in impedance audiometry to be a key examination in patients with stapedial muscular tinnitus concomitant with eye closure.
Inferior vestibular neuritis.
J Neurol. 2012 Jan 4. [Epub ahead of print]

Kim JS, Kim HJ.

Department of Neurology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 300 Gumi-dong, Bundang-gu, Seongnam-si, Gyeonggi-do, 463-707, South Korea, jisookim@snu.ac.kr.

Vestibular neuritis (VN) mostly involves the superior portion of the vestibular nerve and labyrinth. This study aimed to describe the clinical features of VN involving the inferior vestibular labyrinth and its afferents only. Of the 703 patients with a diagnosis of VN or labyrinthitis at Seoul National University Bundang Hospital from 2004 to 2010, we retrospectively recruited 9 patients (6 women, age range 15-75) with a diagnosis of isolated inferior VN. Diagnosis of isolated inferior VN was based on torsional downbeating spontaneous nystagmus, abnormal head-impulse test (HIT) for the posterior semicircular canal (PC), and abnormal cervical vestibular-evoked myogenic potentials (VEMP) in the presence of normally functioning horizontal and anterior semicircular canals, as determined by normal HIT and bithermal caloric tests. All patients presented with acute vertigo with nausea, vomiting, and imbalance. Three patients also had tinnitus and hearing loss in the involved side. The rotation axis of torsional downbeating spontaneous nystagmus was best aligned with that of the involved PC. HIT was also positive only for the involved PC. Cervical VEMP was abnormal in seven patients, and ocular VEMP was normal in all four patients tested. Ocular torsion and subjective visual vertical tests were mostly within the normal range. Since isolated inferior VN lacks the typical findings of much more prevalent superior VN, it may be mistaken for a central vestibular disorder. Recognition of this rare disorder may help avoid unnecessary workups in patients with acute vestibulopathy.

Tenotomy of the middle ear muscles causes a dramatic reduction in vertigo attacks and improves audiological function in definite Meniere’s disease.
Acta Otolaryngol. 2011 Dec 27. [Epub ahead of print]

Loader B, Beicht D, Hamzavi JS, Franz P.

Department of Otorhinolaryngology Head and Neck Surgery, Medical University of Vienna, Vienna General Hospital, Vienna, Austria.

Conclusions: Because the presented data reveal an immediate and persistent reduction of vertigo and a clear improvement in hearing function and functional scales, we conclude tenotomy to be effective in unilateral, definite Meniere’s disease - laying the foundation for future prospective, randomized controlled trials. Objectives: This study compares the unique long-term results of tenotomy of the stapedius and tensor tympani muscles in definite Meniere’s disease refractory to medical treatment and presents a hypothesis on why tenotomy seems effective. Methods: This was an interventional cohort study. The study sample comprised 30 patients (15 males, 15 females; average age 57 ± 13.1 years) with definite Meniere’s disease (AAO-HNS criteria, 1995). Patients were evaluated pre- and postoperatively using pure tone audiometry, AAO-HNS questionnaires regarding vertigo attacks, functional level scores, and tinnitus, and were followed up for 2-9 years. Postoperative values were calculated for the patient collective as a whole and consequently divided into three equal postoperative terms of 3 years each. Results: A statistically significant improvement of inner ear hearing levels postoperatively (p = 0.041) and a major reduction in vertigo attacks in all groups (p < 0.001) with complete absence of attacks in 26/30 patients was noted. Results remained constant up to 9 years postoperatively. Although tinnitus persisted, the intensity was lower overall (p = 0.013).
Three cases of adult mumps deafness with acute vestibular symptoms.
Practica Oto-Rhino-Laryngologica 105 (2), pp. 99-104.

Tsubota, M., Nakagawa, H., Watanabe, Y.
Joetsu General Hospital, University of Toyama, Japan.

We report three cases of adult mumps deafness with acute vestibular symptoms. Case 1: A 61 year-old woman whose mumps infection was initially diagnosed elsewhere was seen by us 1 week later for vertigo and nausea. Neurootological examination showed positional left-beating nystagmus and spontaneous right-beating nystagmus changed the next day. Caloric testing showed left canal paresis and audiogram tracing showed severe sensorineural left ear hearing loss. Two weeks after drip infusion, she had recovered from vertigo and nausea but not from hearing loss. Case 2: A 27 year-old woman seen initially for left tinnitus and hearing impairment was found in audiogram tracing to have mild sensorineural left ear hearing loss. Several days later, she had left parotid gland swelling and hearing deterioration. Based on a diagnosis of mumps deafness, we treated her with drip infusion. Four days after admission, she felt vertigo and nausea. Neurootological examination showed spontaneous right-beating nystagmus. She recovered from vertigo and nausea 1 week later but not from hearing loss. Case 3: A 29 year-old man with mumps initially diagnosed elsewhere and experiencing right hearing impairment 2 days after diagnosis, reported vertigo and nausea 2 days after admission. Neurootological examination showed spontaneous left-beating nystagmus. 1 week later, he had recovered from vertigo and nausea but not from hearing loss. Adult mumps deafness with vestibular symptoms occurs at a high rate compared to that in children. We strongly suggest inviting subjects to undergo mumps vaccination to prevent such cases.

Histopathology of the temporal bone in a case of superior canal dehiscence syndrome.

Teixido M, Kung B, Rosowski JJ, Merchant SN.
Department of Otolaryngology, Christiana Care Health System, Wilmington, Delaware, USA.

OBJECTIVES: We describe the histopathologic findings in the temporal bones of a patient who had, during life, received a diagnosis of superior canal dehiscence (SCD) syndrome. METHODS: The patient was found to have SCD syndrome at 59 years of age. She became a temporal bone donor, and died of unrelated causes at 62 years of age. Both temporal bones were prepared in celloidin and examined by light microscopy. RESULTS: The patient developed bilateral aural fullness, pulsatile tinnitus, and difficulty tolerating loud noises after minor head trauma at 53 years of age. The symptoms were worse on the right. She also had Valsalva-induced dizziness and eye movements, as well as sound-induced dizziness (more prominent on the right). Audiometry showed a small air-bone gap of 10 dB in the right ear. Vestibular evoked myogenic potential testing showed an abnormally low threshold of 66 dB on the right, and a computed tomography scan showed dehiscence of the superior canal on the right. Histopathologic examination of the right ear showed a 1.4 x 0.6-mm dehiscence of bone covering the superior canal. Dura was in direct contact with the endosteum and the membranous duct at the level of the dehiscence. No osteoclastic process was evident within the otic capsule bone surrounding the dehiscence. The left ear showed thin but intact bone over the superior canal. Both ears showed focal microdehiscences of the tegmen tympani and tegmen mastoideum. The auditory and vestibular sense organs on both sides appeared normal. No endolymphatic hydrops was observed. CONCLUSIONS: The findings were consistent with the hypothesis put forth by Carey and colleagues that SCD may arise from a failure of postnatal bone development, and that minor trauma may disrupt thin bone or stable dura over the superior canal.
Prevalence of Musical Hallucinations in Patients Referred for Audiometric Testing.

Teunisse RJ, Rikkert MG.

From the Department of Geriatric Psychiatry (RJT), Dimence, Deventer, and Department of Geriatric Medicine (MGMOR), Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.

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

Transtympanic Electrocochleography for the Diagnosis of Ménière's Disease.

Hornibrook J, Kalin C, Lin E, O'Beirne GA, Gourley J.

Department of Otolaryngology and Audiology, Christchurch Hospital, 2 Riccarton Avenue, Christchurch 8011, New Zealand.

This paper evaluated the diagnostic power of electrocochleography (ECochG) in detecting Ménière's disease (MD) as compared with two subjective assessment methods, including the clinical guidelines provided by the American Academy of Otolaryngology-Head and Neck Surgery Committee on Hearing Equilibrium and the Gibson score. A retrospective study of 250 suspected MD cases was conducted. The agreement between the three assessment methods was found to be relatively high, with a total reliability being higher than 70%. Participants who tested „positive” with ECochG exhibited a higher occurrence rate of asymmetric hearing threshold as well as the four MD symptoms, namely, vertigo, hearing loss, tinnitus, and aural fullness. The „positive” ECochG group also showed a high correlation between the ECochG measures in response to stimuli at adjacent frequency ranges, suggesting that the interfrequency ECochG correspondence may be sensitive to the presence of endolymphatic hydrops and thus may serve as a useful diagnostic marker for MD. Free Full Text.

Meniere's disease might be an autoimmune condition?

Greco A, Gallo A, Fusconi M, Marinelli C, Macri GF, de Vincentiis M.

OBJECTIVES: To review our current knowledge of the pathogenesis of Meniere's disease, including viral infection and immune system-mediated mechanisms, and to discuss the pathogenesis as it relates to pharmacotherapy. SYSTEMATIC REVIEW. METHODOLOGY: Relevant publications on the aetio-pathogenesis, molecular biology, genetics and histopathology of Meniere's disease from 1861 to 2011 were analysed. RESULTS AND CONCLUSIONS: Meniere’s disease is characterised by intermittent episodes of vertigo, fluctuating sensorineural hearing loss, tinnitus, and aural pressure. The aetiology and pathogenesis remain unknown. Proposed theories of causation include viral infections and immune system-mediated mechanisms. The immune response in Meniere’s disease is focused on inner ear antigens. Approximately one-third of Meniere’s disease cases seem to be of an autoimmune origin although the immunological mechanisms involved are not clear. The diagnosis of autoimmune inner ear disease is based either on clinical criteria or on a positive response to steroids. The antiviral approach has virtually eliminated the use of various surgical methods used in the past. Steroid responsiveness is high, and with prompt treatment, inner ear damage may be reversible. The administration of etanercept improves or stabilises symptoms in treated patients. Treatment of antiphospholipid syndrome can be
directed toward preventing thromboembolic events by using antithrombotic medications. Only warfarin has been shown to be effective. Gene therapy can be used to transfer genetic material into inner ear cells using viral vectors and to protect, rescue, and even regenerate hair cells of the inner ear.

Sporadic endolymphatic sac tumor: Its clinical, radiological, and histological features, management, and follow-up.


Department of Otorhinolaryngology, Istituto Clinico Humanitas IRCCS, Rozzano, Milan, Italy. arturo.poletti@humanitas.it.

BACKGROUND: Sporadic endolymphatic sac tumor (ELST) is rare. We described the clinical, radiological, and histological features, treatment, and follow-up of ELST. METHOD: This was a retrospective analysis of 7 cases of sporadic ELST that were managed between 1993 and 2010. RESULTS: Twenty-five to 75 years was the age range of the patients. Subjective hearing loss and tinnitus were the most common presenting features. Five patients had total deafness and 2 had severe sensorineural hearing loss. The most common radiological feature was temporal bone destruction with tumor extension to cerebellopontine angle and posterior cranial fossa. Cholesterol or hemosiderin cysts around the tumor could be a characteristic feature. Major skull base procedures were performed in all 7 cases, and complete tumor excision was achieved in 6 of them. One patient needed a second surgery after she was referred to us after an incomplete first surgery. Recurrences were detected in 2 patients during follow-up; 1 of them received irradiation without minimal change to the tumor size and the second refused any treatment for the recurrence. Both of them are alive with disease. CONCLUSION: Early detection and radical surgical excision at first attempt give best results. Radiotherapy could be considered only in unresectable recurrences. © 2012 Wiley Periodicals, Inc. Head Neck, 2012.

Is Allergy Related to Meniere's Disease?


Banks C, McGinness S, Harvey R, Sacks R.

Department of Otolaryngology, Sydney Hospital, 8 Macquarie Street, Sydney, New South Wales, 2000, Australia, catherine.banks@sesiahhs.health.nsw.gov.au.

Meniere's disease (MD) is characterized by episodic rotational vertigo, fluctuating sensorineural hearing loss, aural pressure, and tinnitus. The cause of MD is thought to be multifactorial, with anatomic and genetic contributions. Allergy is thought to be one of the possible extrinsic factors that, when combined with underlying intrinsic factors, may lead to MD. We review the epidemiologic associations of MD and allergy and review the recent literature on the association of allergy and MD.
Clinical Trials
Source: www.clinicaltrials.gov (31th March 2012)

A Double-Blind, Randomized, Placebo-Controlled, Single-Dose, Crossover Study Of The Safety And Efficacy Of Two Fixed Doses Of PF-04958242 In Subjects With Age-Related Sensorineural Hearing Loss.

This study is currently recruiting participants.
Study NCT01518920.
Information provided by Pfizer.
First Received on January 23, 2012.

The objective of this study is to examine the safety, tolerability, and effects on hearing thresholds of two single doses of PF-04958242 and placebo in subjects with age-related hearing loss.

Treatment of Hearing Fluctuation in Unilateral Meniere's Disease: A Randomized, Placebo-controlled Clinical Trial of Famciclovir.

This study is ongoing, but not recruiting participants.
Study NCT01526408.
Information provided by House Research Institute.
First Received on January 31, 2012.

The specific aim of this study is to determine the efficacy of treatment with famciclovir in unilateral Meniere's Disease patients, specifically whether hearing can be improved. The investigators will determine the percentage of unilateral Meniere's Disease patients experiencing an absence of hearing fluctuation after 3 months of treatment with famciclovir as compared to the placebo arm.


This study is not yet open for participant recruitment.
Study NCT01541969.
Information provided by Nottingham University Hospitals NHS Trust.
First Received on February 24, 2012.

The purpose of this study is to determine whether a new device delivering a sound-based intervention (termed acoustic coordinated reset neuromodulation) has significant clinical benefit for people with intrusive tinnitus. It is hypothesised that the particular pattern of sound stimulation delivered by the device acts to break up patterns of synchronous nerve firing in the brain that may be responsible for the sensation of tinnitus. We will also measure brain activity in a subset of participants to determine if the intervention results in changes in brainwave activity.

Treatment of Chronic Bothersome Tinnitus Using Cognitive Training and D-cycloserine.

This study is currently recruiting participants.
Study NCT01550796.
Information provided by Washington University School of Medicine.
First Received on January 25, 2012.

The purpose of this research study is to determine if a medication along with a computer program designed to improve memory and other mental processes can help people like yourself with tinnitus. The medication that will be investigated, d-cycloserine, was developed as an antibiotic. However, more recently, research in other studies has shown that this medication may enhance learning and memory. The investigators would like to determine if computer programs designed to improve memory and
attention are enhanced by this medication. In addition, the investigators hope to learn if the use of these programs can help participants with their tinnitus as well as their ability to remember and focus. All research participants will receive therapy with a computer-based program designed to improve memory and attention. Half of participants will also receive d-cycloserine while the other half of participants will receive placebo. The placebo is a sugar pill without active medication.

**Neuro-Music Therapy for Recent Onset Tinnitus: Evaluation of a Therapy Concept.**

This study is currently recruiting participants.
Study NCT01566708.
Information provided by German Center for Music Therapy Research
First Received on March 23, 2012.

To date, the pharmacological treatment options for tinnitus are unsatisfactory. For acute tinnitus drug treatments are only rated as being successful in approximately half of all cases. Therefore, the purpose of this study is to evaluate a neuro-music therapeutic approach (the „Heidelberg Model of Music Therapy“) as a new treatment option for patients with recent onset tinnitus after initial medical treatment has failed.