Dear friends and colleagues,

In the last years the tinnitus field has seen a large increase in the amount of articles that have been published. This is of course wonderful but also creates the need to integrate this increasing amount of information. One way to do so is by summarizing the newly available knowledge in a book. This requires the editorial capacities of a person who can deal with both basic neuroscience, basic hearing research and clinical research. Luckily the tinnitus field knows such a person: Aage Moller. And it was also clear that it would happen, after Aage Moller agreed enthusiastically to take care of this endeavour. During the many months of editing almost 100 chapters, Aage may have regretted his commitment. However, there was never any doubt that he would finish the book.

It is on purpose that the book has been named “Textbook of Tinnitus”, in analogy to the well established “Textbook of Pain”.

The goal of the book is to provide a multidisciplinary comprehensive coverage of the diagnosis and treatments of the different forms of tinnitus. A general introduction provides an overview of subjective tinnitus, emphasizing that tinnitus is not one disease but a group of rather diverse disorders with different pathophysiology, different causes and consequently, different treatments. In the second part, the multidisciplinary aspect of tinnitus management is stressed by describing the approach to Tinnitus from the perspective of many specialties ranging from audiology, via psychology, to the different disciplines of medicine and surgery. The following parts cover diagnosis and therapy. Diagnosis of tinnitus is a challenge, because there are so many different forms of tinnitus and few objective signs. Treatment is equally challenging because of the difficulties to identify the cause and the anatomical location of the pathology. Thus, the new book provides a wide-ranging coverage of up-to-date knowledge about tinnitus, its diagnosis and treatment.

In order to provide an overlook, the forewords and the content of the book can be found on the following pages. In addition, a special order form with a 25% prepublication discount is included (page 15). Finally we want to invite you all to the book presentation Symposium on December 11th in Regensburg (page 16).

Berthold Langguth Ana Belén Elgoyhen Dirk de Ridder Susanne Staudinger
Foreword
(to the „Textbook of Tinnitus“ by Matteo de Nora)

Reflections on a 1000-day adventure in a research project

October is a very nice month in the Egyptian desert. It is also when the “Rally of the Pharaons” takes place; an intensive ride in the sand where the main objective is not to get stuck or lost and to arrive at the right place before most of the others.

In 2004, like other times, I was participating and enjoying the concentration, the scenery, and the short nights in a camp, preparing the mind and the equipment for the next day. The next day, half an hour before the end of the stage, I passed the wheel to an impatient navigator who wanted his moment of piloting glory.

A few minutes later, the car went the wrong side of the hill, “rolled over” several times, and landed upside down at the bottom of the hill.

Whiplash, stressful emotion, and lack of oxygen to the ear (dissection of the carotid artery); I had just landed at the perfect scenario for developing something that was totally unknown to me until then: TINNITUS!!

After 6 months of panic and useless wondering to find a cure, I was left with two choices: live with it or try to do something about it. Although accepting to live with it was probably the best cure at that moment, I chose to try to do something about it.

Not out of generosity or because I thought I was called upon the task by higher duties but because

-- Unlike other pathologies, time was on my side: I was not going to die or get worse over time
-- I had experience in organizing research
-- I had the motivation to walk in other people’s life and ask them into a project I believed in
-- I had the time, having sold my main business believing I could not lead as well anymore
-- I had the money, and
-- I did not want to regret that I had not tried

The “program” turned out to be a venture in frustration and hope, a balancing act between logic and instinct, and maybe a little but important milestone for successful therapies in the future. Also, and not surprisingly, it was a human adventure about people and their beliefs, their weaknesses, and their strengths. Here is how I remember it and what I would consider if it started again.

As an independent entrepreneur, I wanted to give some structure to my program, but without losing flexibility and making sure I would not “play doctor.” The main immediate points were
-- How to finance it and through what entity
-- How to choose the people
-- How to choose and coordinate the research program, and my role in it, and
-- How and when to end it, the businessman’s “exit strategy”

How to Finance it and Through What Entity

(a) An existing pharmaceutical company would seem the most immediate choice. However, their managers are guided by long-term survival of their companies and consequently by considerations such as short-term cash flow, risk, time to market of a product, and reimbursement by health care, and are often not open to innovation if it overlaps existing businesses (like in the case of new hearing aids).

(b) Co-investing with government funding was not really an option. Tinnitus not being a life-threatening disease would not get a lot of attention. Moreover, government projects have a long bureaucratic approval process and once funded, they lack the flexibility to change directions during the research if the interim results so suggest.

(c) An existing association was another obvious choice. Scott Mitchell, member of the board of ATA, has written many interesting articles and believes that public non-profit organizations appear to be the best vehicle for funding tinnitus research. Although I agree with him to some extent, it is normal that every time you are managing other people's money, you are somewhat restricted by present logic and paradigms, and have to allocate a lot of time and resources for explanations and accounting to “shareholders,” in addition to public awareness, prevention, support to patients, etc.

(d) Direct funding to individuals by an individual

As more individuals live long and achieve financial success, they reach a point where they feel they can use their money and their experience to make a difference in a field other than their own – and make it their “legacy.”

Teaming up with one of them would be risky because these are in all likelihood strong personalities who bring into a program their style, their objectives, and their people, and since it is their “legacy” after all, often want a lot of exposure.

In addition, I wanted to try to bring together cross-border and interdisciplinary knowledge in a field where not enough was yet known to make it interesting to future participants (industry, governments, and associations) and had my own ideas on what was important – and what was going to make this possible.

Chances of improving were higher because we started from zero.

My program would be based on the idea that tinnitus research was still in a phase where to get to the next step it was better to stay away from too many “models,” and that some of it had to be done by somebody who was willing to fail, make mistakes, change his mind, not understand, and ultimately not base his decisions on risk/reward but on people who were willing to work on a project for the right reasons and with the right attitude.

“Life is like a game of chess; the first moves are very important, but until the game is over you still have some good moves to play.”

Anna Frank
How to Choose the People

I have always been involved in science – and yet know very little. My father was a brilliant scientist, with many researchers around him. I never tried to compete directly, but learned a lot from “back stage” and over the years. He had a sign in his office that said: “if you want to lose money spend it on boats, women and research.” Even if we have not spent a lot of time together, I must have taken that part from him!

The process of choosing the scientists whom I would have liked to meet each other and work together was very intuitive, but I can try to list a few characteristics that I think are common to successful scientists – they:

--- Are optimistic but realistic
--- Do not promise more than what they can deliver
--- Are capable of giving bad news
--- Take pleasure and attention in the growth of people around them
--- Simplify and explain complicated things in a simple way
--- See a problem and turn it into an opportunity
--- Do not have what is called the “not invented here syndrome”: they listen with an open mind to other people’s ideas
--- Recognize today’s assumptions and question them
--- Look beyond the obvious
--- Find a way to look at something new without rejecting the current concept
--- Don’t look at an idea only to see what is wrong with it and how they can reject it
--- Think and work a lot – genius ideas are a result of it
--- Have a high sense of responsibility
--- Always want to do things better and
--- Try to do the best they can.

Some of these characteristics usually surface even in a short interview and I always saw some of them in the people who have at some stage participated in the TRI research program. I am naturally honored that they have accepted to work with TRI as I never took it for granted.

“The scientific mind does not so much provide the right answers as ask the right questions.”
Claude Levi Strauss

How to Choose and Coordinate the Research Program, and My Role in it

A traditional program would have three main components.

Leadership, to clearly identify the objectives so as to produce the results.
Organization, to identify the different functions and to allocate them to the best people.
Administration, to allocate the resources where and when necessary.

One difference in this case was that none of the participants was directly employed and that the relationship was based more on attitude and trust than otherwise. Each had their own existing activity.
The main objective was not to organize an effective research program but to encourage multidisciplinary, interdisciplinary exchange in the belief that the right people would seize the opportunity.

Personal interaction coupled with the exposure to different therapeutic areas would combine the knowledge without setting boundaries of research, and ultimately, individuals would choose their partners in the program.

Their partners would possibly be from different areas, different levels, and different countries and cultures, and that combination would increase understanding, innovation, and the feeling that the “mission” was doable.

Over time strategic groups and their performance obligations would form. Diversification would increase the effort of coordinating their work but would naturally identify specific areas of research.

Workgroups in pharmacology, neurostimulation, auditory stimulation, somatosensory modulation, and eventually tinnitus clinics (when the need for integrating research and clinical medicine became more evident) were formed, but these were based more on the individuals who chose to work together than on an imposed structure or organization.

Somehow the dynamics were quite different than those of a company.

Later I would have worked more closely to improve the connection between innovation and actual therapy. I knew that existing commercial compounds generated less problems. I also had learned that successful players design the most incisive clinical trials and were not necessarily hung up on publishing a lot.

The dynamics were a strange mix of what I had lived in the past, and my role was going to shape accordingly.

Rod Davis, coach of Team New Zealand sailing team, wrote an interesting article to explain coaching and support: The invisible hand. He says coaching is a weird combination of teaching, mentoring, being the hatchet man (at times), and being a nanny, throw it all in a blender and make something good out of it. Coaching, Rod writes, is not rocket science. In fact, it is not a science at all, it is art. Coaches provide the environment for driven talent to become champions. The ones with talent who take full advantage of the opportunities presented became champions.

Environment means unloading distractions – It means create a belief in the ability to perform in tasks that are the most important to them. He adds that a big part of self-confidence is self-responsibility: if someone knows that it is up to him to be in control of his own destiny and knows he has done all that is needed to be ready, how can he not be self-confident?

This improves the chances of success, but there are no guarantees – there are thousands of pieces to the puzzle – but if the environment is right, the end result is certainly more likely to be positive.

Interestingly enough, two successive research coordinators failed in their mission, probably because they did not see the program the same way.

I was going to try and follow Rod’s “art,” keeping in mind that it was also my role – at least at the beginning, to add strong leadership and sense of the mission, just like Grant Dalton does with the very successful Team New Zealand.
How and When to End it

Basic research delivers the technology platform, the ideas, and concepts but they are often not at first accepted by industry or peers. This is the innovation gap and it needs to be bridged by the public hand. At a certain point, there needs to be an investment of the government to share the risk: political will is not only the weakest link in the chain, but also the hardest to fix. ¹

Governments, whose biggest expense is becoming health care, have a difficult task in choosing priorities. As an example, a very small percentage of cancer research spending would make a huge difference in other areas, including tinnitus.

Maybe a better way to look at it would be to present the issue in a more global way. Now that the majority of researchers agree that tinnitus is a malfunction or reorganization that takes place with the neurons in the brain, its research implications go together with the understanding of other pathologies such as Alzheimer’s or Parkinson's that are more easily understood as terribly detrimental.

Public nonprofit organizations should help bridge the gap to government involvement in addition to encouraging awareness and prevention.

Contrary to many, I believe that it is important that at a certain point the individual sponsor disappears. A more structured and long-term mechanism has to take place. People and programs should not depend solely on the sponsor.

In this specific case, the objective was to install new energy toward an "undervalued" problem and contribute to make it a stand-alone research area for medicine.

Only time will tell how much has been achieved toward that end.

“You can have a dialogue about solving future problems all you like, but if you do not behave any differently when you go out of here, it won’t make any difference.”

Dennis Meadows

“Limits to growth”

Conclusions

Strategy is about the future and then making decisions based on that. The worst thing you can do is not to have an opinion, and not make decisions. ²

More than ever, success depends on our ability to learn and to create value from what we learn.

In these times of uncertainty, scientists and physicians have to be agents of change in the right direction, accelerate science, advance medicine, and also direct it in a more integrated and patient-driven experience that is comprehensive to all.

Individuals still play an important role in sponsoring and discovery: it is everybody’s task to create the environment and attitude for positive change.

Whether we made a change and the change was meaningful we will not know for years and maybe never. But I believe it would be a mistake to lose the momentum and coordination that TRI has created.

¹Peter Gruss, president Max-Planck-Society
²Alan Mulally, president Ford Motor Company
On a personal note, I have met some extraordinary people and scientists: although my tinnitus is still there, I believe that we have cured people who otherwise would still be suffering. I believe I will be cured in the next 3–5 years and that I will have that cure available before it enters the global market.

Is that enough?

It is one of the best things I ever did!

Matteo de Nora
Tinnitus (ringing in the ears) has many forms, and the severity of tinnitus ranges widely from being a slight nuisance to affecting a person’s daily life. How loud the tinnitus is perceived does not directly relate to how much it distresses the patient. Thus even tinnitus very close to the hearing threshold can be a disabling symptom that amounts to a major burden; it can reduce the quality of life by generating anxiety and concentration problems impairing the ability to do intellectual work, making it difficult to sleep; causing depression and tinnitus can ultimately lead to suicide. Tinnitus can already occur at young age, but its prevalence steadily increases with the degree of age-related hearing loss and can reach 12-15% for people aged 65 and over. Moreover, tinnitus incidence is increasing dramatically with increased leisure noise, more work-related noise trauma and longer lifespan.

The different forms of tinnitus have similarities with different kinds of pain; many forms of pain and tinnitus are phantom sensations. Another important commonality is that pain and tinnitus lack detectable signs; imaging tests (structural MRI, CT, etc.) and common electrophysiological test results are the same whether or not a person has tinnitus.

For a long time it was believed that the anatomical location of the physiological abnormalities that caused the tinnitus was the ear. However, it was later understood that most forms of tinnitus are caused by abnormalities in the central nervous system and that these abnormalities are often caused by expression of neural plasticity.

Many structures of the body, such as the ear, the auditory nervous system, the somatosensory system, other parts of the brain, and muscles of the head and the neck are directly or indirectly involved in different forms of tinnitus. To treat and understand the pathology of tinnitus therefore requires involvement of many specialties of medicine, surgery, psychology, and neuroscience.

Tinnitus may occur after noise exposure and administration of pharmacological agents, but the cause of subjective tinnitus is often unknown. Severe tinnitus is often accompanied by symptoms such as hyperacusis (lowered tolerance to sound) and distortion of sounds. Affective disorders such as phonophobia (fear of sound) and depression often occur in individuals with severe tinnitus. With such differences in attributes, it is not reasonable to expect that a single cause can be responsible for severe tinnitus, again a factor that makes managing the tinnitus patient a challenge for health care professionals.

Realizing the complexity of tinnitus has highlighted the importance of interdisciplinary research, and the fact that most forms of tinnitus are disorders of the nervous system has put emphasis on neuroscience, both in studies and in treatment of tinnitus. However, few clinicians are specifically trained in tinnitus treatment, and there is a lack of suitable books that describe how to diagnose and treat each of these many forms of tinnitus most effectively.

Each of the authors contributing to the “Textbook of Tinnitus” were therefore chosen from many specialties of medicine, surgery, psychology, and neuroscience, and came from diverse areas of expertise such as Neurology, Neurosurgery, Audiology, Otolaryngology, Psychiatry, Clinical- and Experimental Psychology, Pharmacology, Dentistry and Neuroscience.

Unlike pain, which has considerable literature including a book with the title “Textbook of Pain” now in its fifths edition, there is no comprehensive book that covers many aspects of tinnitus. This book, therefore, fills a void by providing relevant information about tinnitus as a disease and how to treat it effectively. The “Textbook of tinnitus” is directed towards the clinician and gives detailed information about diagnosis of the many different forms of tinnitus and their treatment. The book also provides an overview of what is known about the pathophysiology of different kinds of tinnitus.
It has become more and more evident that neural plasticity plays an important role, not only in adapting the nervous system to changes in demand and after injuries, but also as a cause of symptoms and signs of disease. Such diseases have been called “plasticity disorders”. The role of neural plasticity in creating symptoms of disease such as many forms of tinnitus has only been described in a few books directed to neurologists and researchers in neuroscience. This means the medical community in general is often unaware that functional changes in the nervous system can be the cause of a patient’s complaints, and that hampers the diagnosis of disorders such as tinnitus. Therefore, effective treatment of tinnitus also requires knowledge about neural plasticity as a cause of diseases. This is one of the aspects of tinnitus that is covered in the “Textbook of Tinnitus”.

The fact that tinnitus is not a single disease but a group of diseases means tinnitus cannot be effectively treated by a single approach, and several disciplines of health care must be involved in managing the patient with tinnitus. Treatment of the patient with severe tinnitus requires collaborations between clinicians in many different fields of medicine, audiology, and psychology. Accordingly, tinnitus research and treatment have been performed by a variety of disciplines, viewing the problem from various perspectives, focusing on different targets, and using diverse approaches. New developments regarding treatment have prompted involvement of neurosurgeons, neurologists, psychiatrists and dentists. Therefore, an important challenge for the future consists in improving cooperation between different disciplines involved in tinnitus research and treatment.

It is a challenge to translate the results from basic research into clinical practice. The “Textbook of Tinnitus” provides the basis for multidisciplinary management of the tinnitus patient using the most modern methods of treatment. The book represents a new and broad interdisciplinary approach to tinnitus by bringing together in a single book, contributions from many different areas of basic science, and clinical research and health care to guide the management of the tinnitus patient. This is the first time that such broad efforts have been made regarding treatment of tinnitus.

The 95 chapters in this book express the independent views of the authors, some of which may diverge and some may complement one and another. The editors have made no attempts to modify individual authors views, only attempts have been made to achieve a similar style of writing in the different chapters.

The book describes both the theoretical background of the different forms of tinnitus and detailed knowledge of state of the art treatment of tinnitus written for clinicians by clinicians and researchers in tinnitus. It provides up-to-date information in forms that are suitable for those who diagnose and treat patients with tinnitus in their clinical praxis as otolaryngologists, neurologists, psychiatrists, neurosurgeons, clinical audiologists, dentists and psychologists. The book can also serve as a reference for clinicians who do not treat tinnitus patients routinely because of its organization and extensive subject index.

The book has five sections, I Basics about tinnitus, II Causes of Tinnitus, III Differential diagnosis of tinnitus, IV Clinical characteristics of different forms of tinnitus, and V Management of Tinnitus.

The first section describes the basic aspects of tinnitus and the symptoms that often accompany the disorder, such as hyperacusis and misophonia. The section includes chapters on the epidemiology of tinnitus in children as well as adults and discusses the role of genetics in tinnitus. The anatomy and physiology of the normal auditory system and the pathologic system are the topics of other chapters; chapters on pain and similarities between tinnitus and pain are also included, as are chapters that discuss the use of special forms of neuroimaging for studies of tinnitus. Modeling of the pathologies of tinnitus is the topic of two chapters, and one chapter discusses how clinical trials are performed. The last part of the section concerns how tinnitus is
perceived and approached by members of different specialties in research and treatment of tinnitus, including a chapter about how tinnitus is viewed by the patients themselves.

Section II has chapters about different causes of tinnitus, such as the role of disorders of the ear, age, and exposure to noise and ototoxic substances. Diseases associated with tinnitus such as vestibular schwannoma and Ménière’s disease are the topic of other chapters in this section. Yet another chapter covers the cause of somatosensory tinnitus. Other chapters concern the role of different disorders of the central nervous system. The role of disorders of the masticatory system, including that of the temporomandibular joint, is the topic of the last chapter in the section.

Section III discusses diagnosis of tinnitus and a chapter presents a diagnostic algorithm for tinnitus, followed by chapters how the different diagnostic methods are performed. Chapters covering otologic, audiologic and neuro-otologic assessment and examination follow a chapter about history and questionnaires. A chapter describes the diagnosis of somatosensory tinnitus, and another the assessment of temporomandibular disorders. The last chapter in the section covers psychological and psychiatric assessments.

The chapters of Section IV cover the clinical characteristics of the different forms of tinnitus. In order to better meet the need of clinicians, the section is organized according to symptoms and syndromes as presented by the patients. The chapters describe the management of tinnitus with sudden hearing loss, hyperacusis and phonophobia, intermittent tinnitus, and pulsatile tinnitus. Tinnitus that occurs together with other symptoms such as Ménière’s disease, headache, and psychiatric disorders (depression, anxiety, and insomnia) are also covered in separate chapters. Finally posttraumatic tinnitus and tinnitus caused by blast injuries that occur in wars are described.

The chapters of Section V concern management of the various forms of tinnitus. The chapters provide an extensive coverage of the available treatments. Chapters review treatments such as counseling, cognitive behavioral treatment, and auditory training which includes various forms of sound stimulation. Specific treatment programs such as the Tinnitus Retraining Therapy (TRT) and the Neuromonics program are described. Chapters also discuss different kinds of pharmacologic treatment. Treatment using botulinum toxin and different forms of surgical treatment are covered in separate chapters. Other chapters describe different forms of neuromodulation, and one chapter discusses complimentary treatments. The two final chapters include treatment of tinnitus and pain and strategies for TMJ disorders as their topics.

Many of the contributors to “Textbook of Tinnitus” are involved in research sponsored by the international research organization, “The Tinnitus Research Initiative” (TRI). The goal of the TRI is to improve treatment for tinnitus through advances in the understanding of the pathophysiology of tinnitus. This organization has promoted collaborative interdisciplinary research on tinnitus during the past 5 years. It has now been converted into an international research foundation, The Tinnitus Research Initiative Foundation.

TRI’s goal is to provide a basis for collaborations between researchers and clinicians from different fields to achieve an integrated approach to studies of the pathophysiology of tinnitus and develop and test treatments of different forms of tinnitus.

The Editors thank Mr. Matteo de Nora for his support to research on tinnitus through the TRI and for his support in the preparation of this book.
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CHAPTER 95. Treatment strategies of temporomandibular joint and masticatory muscle disorders in patients with tinnitus by Ralf Bürgers, Michael Behr and Martin Gosau
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Samstag, den 11. Dezember 2010
09:00 - 15:00 Uhr

Klinikum der Universität Regensburg
Großer Horsaal, Bauteil A0, 1. OG
Franz-Josef-Strauß Allee 11, 93053 Regensburg

Eine Veranstaltung des Tinnituszentrums Regensburg und der Tinnitus Research Initiative

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5 Fortbildungspunkte - Die Teilnahme ist kostenfrei

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We would like to draw your attention to the next International TRI Tinnitus Meeting, 2011 in Buffalo. More detailed information will be available soon on www.tinnitusresearch.org
Upcoming Meetings

Cochlear Implants 2010: The State of the Art
When: November 5, 2010
Where: The Ear Foundation, Marjorie Sherman House, NOTTINGHAM, UK
Phone: +44 (0)115 942 1985
Fax: +44 (0)115 924 9054
Detailed information: http://www.earfoundation.org.uk/education/articles/603

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

ARO (The Association for Research in Otolaryngology) 34th MidWinter Meeting
When: February 19 – 23, 2011
Where: Baltimore, MD, USA
E-Mail: aspringer@talley.com
Detailed Information: http://www.aro.org/mwm/mwm.html

12th Asia-Oceania Otolaryngology Conference
When: March 1 – 4, 2011
Where: Auckland, New Zealand
Contact: The Conference Company
PO Box 90-040, Auckland, New Zealand
Phone: +64 9 360 1240
Fax: +64 9 360 1242
E-mail: asia-oceania@tcc.co.nz

American Auditory Society Annual Meeting
When: March 3 – 5, 2011
Where: Scottsdale, AZ, United States
Detailed Information: http://www.amauditorysoc.org/annual-meeting/reginfo.htm
14. Jahrestagung der Deutschen Gesellschaft für Audiologie (DGA e.V.)
When: March 10 – 13, 2011
Where: Jena, Germany

X International Tinnitus Seminar - ITS 2011
When: March 16 – 19, 2011
Where: Florianopolis, Santa Catarina, Brazil
Detailed Information: http://www.its2011brazil.com.br

55. Jahrestagung der Deutschen Gesellschaft für Klinische Neurophysiologie und Funktionelle Bildgebung
When: March 16 – 19, 2011
Where: Münster, Germany
Detailed Information: http://www.congrex.de/dgkn2011

37. Jahrestagung der Deutschen Gesellschaft für Akustik DEGA (DAGA 2011)
When: March 21 – 24, 2011
Where: Düsseldorf, Germany
Detailed Information: http://www.dega-akustik.de/

9th Göttingen Meeting of the German Neuroscience Society
When: March 23 – 27, 2011
Where: Göttingen, Germany
Contact: German Neuroscience Society (Neurowissenschaftliche Gesellschaft e.V. /NWG) MDC
Robert-Rössle-Str. 10, 13125 Berlin
Phone: +49 (0)30 9406 3336
Fax: +49 (0)30 9406 2813
E-Mail: gibson@mdc-berlin.de
Detailed Information: http://www.nwg-goettingen.de/2011/

Academy Research Conference - Current Trends in the Evaluation of Tinnitus
(a day-long conference coinciding with the first day of AudiologyNOW! 2011)
When: April 6, 2011
Where: Chicago, IL, United States
Detailed Information: www.AcademyResearchConference.org

AudiologyNOW!® 2011
When: April 6 – 9, 2011
Where: Mc Cormick Place Convention Center Chicago, IL, United States
Detailed Information: www.AudiologyNOW.org
International Conference on Theoretical & Computational Acoustics (ICTCA) 2011

When: April 25 – 28, 2011
Where: Taipei, Taiwan
Contact: Miss Pichun Wu
Department of Engineering Science and Ocean Engineering, National Taiwan University
Phone: +886-2-3366-5735
Fax: +886-2-3366-5781
E-mail: secretary.ictca2011@gmail.com
Detailed Information: http://www.esoe.ntu.edu.tw/ictca2011/

161st Meeting of the Acoustical Society of America

When: May 23 – 27, 2011
Where: Seattle, Washington
E-Mail: asa@aip.org
Detailed Information: http://asa.aip.org/meetings.html

82. Jahresversammlung der Deutschen Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V.

When: June 1 – 5, 2011
Where: Freiburg, Germany
Contact: Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie, Hittorffstr. 7, 53129 Bonn
Phone: +49 (0)2 28/23 17 70
Fax: +49 (0)2 28/23 93 85
E-Mail: info@hno.org
Detailed Information: http://www.hno.org/veranstaltungen/ankuendigungen.html

10th EFAS Congress

When: June 22 – 25, 2011
Where: Warsaw, Poland
E-Mail: efas2011@ifps.org
Detailed Information: http://www.efas2011.org/

Human Brain Mapping Annual Meeting

When: June 26 – 30, 2011
Where: Quebec City, Canada
Detailed Information: www.humanbrainmapping.org

XXII IERASG Biennial Symposium

When: June 26 – 30, 2011
Where: Moscow, Russia
Detailed Information: http://www.ierasg2011.ru/
1st Congress of the Confederation of the European ORL-HNS
When: July 2 – 4, 2011
Where: Barcelona, Spain
Detailed Information: http://www.ceorlhnsbarcelona2011.org/

5th International TRI Tinnitus Conference. The Neuroscience of Tinnitus.
When: August 19 – 21, 2011
Where: Buffalo, NY, USA
E-Mail: meetings@tinnitusresearch.org
Detailed Information: http://www.tinnitusresearch.org/

American Academy of Otolaryngology, Head and Neck Surgery Annual Meeting
When: September 11 – 14, 2011
Where: San Francisco, CA, USA
Detailed Information: http://www.entnet.org

28. Politzer Society Meeting
When: September 29 – October 1, 2011
Where: Zappeion Exhibition Hall, Athens, Greece
Contact: GOLDAIR Congress,
15 Panepistimiou Avenue, 10564 Athens, Greece
Phone: +30 210 3274570
Fax: +30 210 3311021
E-Mail: info@politzer-athens2011.gr
and/or congress@goldair.gr
56th International Congress of Hearing Aid Acousticians
When: October 19 – 21, 2011
Where: CongressCenter Nürnberg, CCN East, Germany
Detailed Information: http://www.euha.org

Asia Pacific symposium on Cochlear Implant and Related Science
When: October 26 – 28, 2011
Where: Korea
Detailed Information: http://knuh.knu.ac.kr

162nd Meeting of the Acoustical Society of America
When: October 31 – November 4, 2011
Where: San Diego, California, United States
E-Mail: asa@aip.org
Detailed Information: http://asa.aip.org/meetings.html

8th Meeting of the British Society of Neuro-Otology
When: November 2011
Where: National Hospital for Neurology and Neurosurgery, Queen Square, London
Contact: Miss J. Mills
        Neuro-Otology Group, Imperial College London, Charing Cross Hospital
        Fulham Palace Road London W6 8RF
        Phone: +44 (0)208 846 7285
        Fax: +44 (0)208 846 7577
        E-Mail: neuro-otology@imperial.ac.uk
Detailed Information: http://www.bsno.org.uk/8th%20meeting.html
Recently published literature (articles of authors who are funded by TRI are marked in blue)

I Epidemiology

Impact of tinnitus as measured by the Tinnitus Handicap Inventory among tinnitus sufferers in Singapore.

Lim JJ, Lu PK, Koh DS, Eng SP.
Department of Otolaryngology, Changi General Hospital, 2 Simei Street 3, Singapore 529889. joyce_ lim@cgh.com.sg

INTRODUCTION: The effects of tinnitus on quality of life (QOL) have never been extensively studied in Singapore. We describe the characteristics of tinnitus and its impact on QOL as measured by the Tinnitus Handicap Inventory (THI) in a series of ear, nose and throat clinic patients. METHODS: A total of 327 patients who attended a tinnitus counselling clinic completed the THI questionnaire, a self-report measure with 25 items grouped into functional, emotional and catastrophic subscales. RESULTS: The mean age of the 134 female and 193 male patients was 48.9 years. 36.7 percent of these patients had bilateral tinnitus and 64.6 percent had symptoms for less than one year. 270 patients had hearing loss, 74 percent of whom presented with bilateral high frequency hearing loss. Most patients (84.1 percent) perceived only one type of sound. The total THI score distribution was: 107 (33 percent) patients had THI less than 16, 100 (31 percent) had THI 18 to 36, 59 (18 percent) had THI 38 to 56, and 61 (19 percent) had THI more than 58. There were no differences in the overall THI and subscale scores between the patients’ gender, those with or without hearing loss, and those with unilateral or bilateral tinnitus. However, significantly higher total THI and all subscale scores were found among patients who were hearing more than one type of tinnitus sound. The areas of concern that were commonly reported by the patients in this series were a lack of control over tinnitus, frustration and stress. CONCLUSION: Tinnitus patients who hear multiple sounds tend to have a higher THI and subscale scores. The management of tinnitus should address common areas of concern, and may include counselling. The THI is a potential screening tool to determine if patients require counselling. A series of THI assessments can be used to chart the progress of treatment.


Amini R, Haghani H, Masoumi M.
Janbazan Medical and Engineering Research Center, Tehran, Iran. amini@jmerc.ac.ir.

BACKGROUND: Quality of Life measurements are necessary tools for effectively evaluating health services. In the population of patients afflicted with war-related blindness in Iran, such measurements have yet to be documented and utilized. „The design and implementation of this study involved the determination of a baseline score for QOL in a population of Iranian blinded in the Iraq-Iran war in order to facilitate the design of interventions intended to improve the population’s QOL. “

METHODS: This was a cross-sectional study of a representative population of 250 war victims blind in both eyes at a 14-day recreational conference.

RESULTS: Participants had a mean age of 43.20(SD8.34) and their composition was 96.5% male and 3.5% female with a mean SF-36 QOL score of 59.20(SD22.80). An increasing level of education among the participants correlated with a higher QOL score (p = 0.006). The QOL also has a significant correlation to number of injuries (p < 0.0001). High systolic and diastolic blood pressure, hearing loss, and tinnitus had negative individual correlations to QOL (p = 0.016, 0.016, 0.005, p < 0.0001). The male sexual disorders of erectile dysfunction and premature ejaculation both had significant correlations to QOL (p = 0.026, p < 0.0001). Hypercholesterolemia showed significant correlation to QOL (p = 0.021).
CONCLUSIONS: As blind war survivors' age, they will present with a greater set of burdens despite their relatively better QOL in the physical component scale when compared with lower limb amputees. Risk factors of cardiovascular attack such as high blood pressure and hypercholesterolemia were present and need future interventions. KEY WORDS: Quality of life, blindness, SF36, health

The association between tinnitus and mental health in a general population sample: results from the HUNT Study.
Krog NH, Engdahl B, Tambs K.
Division of Mental Health, Norwegian Institute of Public Health, Oslo, Norway.

OBJECTIVES: Clinical studies indicate a strong association between tinnitus and mental health, but results from general population data are missing. The purpose of the study was to examine the association between tinnitus, mental health, and well-being in the general adult population and to identify factors that might mediate and moderate this association.

METHODS: Data from 51,574 adults participating in the Nord-Trøndelag Hearing Loss Study (1995-1997), part of the Nord-Trøndelag Health Study (HUNT-2), were analyzed. The association between tinnitus symptom intensity and symptoms of depression, anxiety, self-esteem, and subjective well-being was examined by multivariate ANOVA, stratified by age group and sex. Explanatory variables were age, marital status, education, hearing, dizziness, vision, physical disability, and somatic illness. In a subsample of participants with tinnitus, the effects of "time since onset," "predictability of tinnitus episodes," and "noise sensitivity" were tested.

RESULTS: Participants with tinnitus scored significantly higher on anxiety and depression and lower on self-esteem and well-being than people without tinnitus. The effect sizes were small and quite similar across levels of tinnitus symptom intensity. No significant effect of time since onset was found. A significant effect of predictability of tinnitus episodes and noise sensitivity was found in some groups.

CONCLUSION: A weak association between tinnitus and mental health was found in this general population study.

Studying tinnitus in the ICF framework.
Ramkumar V, Rangasayee R.
Department of Speech, Language, and Hearing Sciences, Sri Ramachandra University, Chennai, Tamil Nadu, India. vidya.ramkumar@gmail.com

Activity limitation and participation restriction (AL/PR) on account of tinnitus was studied in the ICF framework in order to understand how tinnitus restricts individuals from fulfilling social and economic obligations. The objective of the study was to study the impact of tinnitus in the framework of ICF. Twenty-one adults in the age range of 20-60 years with chronic tinnitus (>3 months) and with normal hearing sensitivity were included in the study. THI was mapped to the framework of ICF. Twenty out of twenty-five items belonged to the domains under body function and five items addressed AL/PR. Five more AL/PR items applicable to tinnitus were added to THI. The THI+ICF questionnaire tested well on test reliability (0.987) and internal consistency (0.873). Body function was significantly more affected than AL/PR (P = 0.0005). These results suggest that tinnitus does not result in significant AL/PR from the ICF perspective. Further, psycho-acoustic characteristics such as intensity, frequency of tinnitus, and time since onset of tinnitus have only minimal if any impact on AL/PR.
Tinnitus onset rates from chemotherapeutic agents and ototoxic antibiotics: results of a large prospective study.

Dille MF, Konrad-Martin D, Gallun F, Helt WJ, Gordon JS, Reavis KM, Bratt GW, Fausti SA.
VA RR & D National Center for Rehabilitative Auditory Research, Portland VA Medical Center, Portland, OR 97239, USA. marilyn.dille@va.gov

BACKGROUND AND PURPOSE: To report on the incidence and relative risk of tinnitus onset from a variety of drug therapies known to be ototoxic. Two main questions were asked: (1) What is the prevalence and incidence of tinnitus among patients treated with cisplatin, carboplatin, or ototoxic antibiotic therapies? (2) Do commonly reported treatment or subject factors confound or modify the incidence of tinnitus onset?

DATA COLLECTION AND ANALYSIS: A prospective observational study design was used to evaluate occurrence of significant otologic changes in 488 veterans (962 ears) receiving chemotherapeutic agents (cisplatin, carboplatin), ototoxic antibiotics (primarily aminoglycoside), or nonototoxic drugs (control medications). A subset of 260 veterans lacking tinnitus prior to drug exposure was used to compare rates of tinnitus onset. Subjects were tested prior to, during, and following their treatment. Planned comparisons using logistic regression, analysis of variance (ANOVA), and chi(2) statistics were made among groups by the type of medication taken, age, presence of preexisting hearing loss, days on drug, and cumulative dose of drug.

RESULTS: Baseline tinnitus rates were high (nearly 47%) relative to the general population of a similar age. Subjects with exposure to ototoxic medications had significantly increased risk for developing tinnitus. Those on chemotherapeutic agents were found to have the greatest risk. Cisplatin elevated the risk by 5.53 times while carboplatin increased the risk by 3.75 over nonototoxic control medications. Ototoxic antibiotics resulted in borderline risk (2.81) for new tinnitus. Contrary to other reports, we did not find that subject factors (increased age or pre-existing hearing loss) or treatment factors (days on drug or cumulative dose) contributed to rates of tinnitus onset during treatment.

CONCLUSIONS: This large prospective study confirms that new tinnitus during treatment is associated with chemotherapy and with certain ototoxic antibiotic treatment. Cisplatin and carboplatin were found to be the most potent ototoxic agents causing tinnitus at much greater numbers than the other drugs studied. Implications for counseling and audiological resource allocation are discussed.

Prevalence and characteristics of tinnitus among US adults.

Shargorodsky J, Curhan GC, Farwell WR.
Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Boston, Mass, USA.

BACKGROUND: Tinnitus is common; however, few risk factors for tinnitus are known.
METHODS: We examined cross-sectional relations between several potential risk factors and self-reported tinnitus in 14,178 participants in the 1999-2004 National Health and Nutrition Examination Surveys, a nationally representative database. We calculated the prevalence of any and frequent (at least daily) tinnitus in the overall US population and among subgroups. Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI) after adjusting for multiple potential confounders.

RESULTS: Approximately 50 million US adults reported having any tinnitus, and 16 million US adults reported having frequent tinnitus in the past year. The prevalence of frequent tinnitus increased with increasing age, peaking at 14.3% between 60 and 69 years of age. Non-Hispanic whites had higher odds of frequent tinnitus compared with other racial/ethnic groups. Hypertension and former smoking were associated with an increase in odds of frequent tinnitus. Loud leisure-time, firearm, and occupational noise exposure also were associated with increased odds of frequent tinnitus. Among participants who had an audiogram, frequent tinnitus was associated with low-mid frequency
(OR 2.37; 95% CI, 1.76-3.21) and high frequency (OR 3.00; 95% CI, 1.78-5.04) hearing impairment. Among participants who were tested for mental health conditions, frequent tinnitus was associated with generalized anxiety disorder (OR 6.07; 95% CI, 2.33-15.78) but not major depressive disorder (OR 1.58; 95% CI, 0.54-4.62).

CONCLUSIONS: The prevalence of frequent tinnitus is highest among older adults, non-Hispanic whites, former smokers, and adults with hypertension, hearing impairment, loud noise exposure, or generalized anxiety disorder. Prospective studies of risk factors for tinnitus are needed.

Investigation of tinnitus patients in Italy: clinical and audiological characteristics.

Martines F, Bentivegna D, Di Piazza F, Martines E, Sciacca V, Martinciglio G.

Dipartimento di Neuroscienze Cliniche (DINEC), Sezione di Otorinolaringoiatria, Università degli Studi di Palermo, Via del Vespro, 129-90127 Palermo, Italy.

Objective. 312 tinnitus sufferers were studied in order to analyze: the clinical characteristics of tinnitus; the presence of tinnitus-age correlation and tinnitus-hearing loss correlation; the impact of tinnitus on subjects' life and where possible the etiological/predisposing factors of tinnitus. Results. There is a slight predominance of males. The highest percentage of tinnitus results in the decades 61-70. Of the tinnitus sufferers, 197 (63.14%) have a hearing deficit (light hearing loss in 37.18% of cases). The hearing impairment results of sensorineural type in 74.62% and limited to the high frequencies in 58.50%. The tinnitus is referred as unilateral in 59.93%, a pure tone in 66.99% and 10 dB above the hearing threshold in 37.7%. It is limited to high frequencies in 72.10% of the patients with sensorineural hearing loss (SNHL) while the 88.37% of the patients with high-frequency SNHL have a high-pitched tinnitus (chi(2) = 66.26;P < .005). Conclusion. Hearing status and age represent the principal tinnitus related factors; there is a statistically significant association between high-pitched tinnitus and high-frequency SNHL. There is no significant correlation between tinnitus severity and tinnitus loudness confirming the possibility that neural connection involved in evoking tinnitus-related negative reactions are governed by conditioned reflexes.

II Pathophysiology

[Cortical plasticity and changes in tinnitus : Treatment options.]
HNO. 2010 Sep 8. [Epub ahead of print]
[Article in German]

Weisz N, Langguth B.

Fachbereich Psychologie, Universität Konstanz, D23, 78457, Konstanz, Deutschland, nathan.weisz@uni-konstanz.de.

A growing consensus in current tinnitus research suggests central nervous changes as the cause of tinnitus. Several animal and human experimental studies were able to show altered tonotopic representations as well as spontaneous activity in the auditory cortex. However, a causal relationship between altered neurophysiological processes and aspects of tinnitus are still missing. Furthermore, it is likely that the importance of diverse processes changes with continuing duration of tinnitus. These open questions complicate the development of effective treatments. Nevertheless, today several neuroscientifically motivated treatments are available, or treatments that can be integrated into a neuroscientific framework. This article gives an overview of current neuroscientific developments in tinnitus research and discusses their implications for the treatment of tinnitus.
Peripheral and central structures are involved in the onset of tinnitus. Neuronal plasticity is of special importance for the occurrence of central tinnitus and its persistent form. Neuronal plasticity is the ability of the brain to adapt its own structure (synapses, nerve cells, or even whole areas of the brain) and its organization to modified biological requirements. Neuroplasticity is an ongoing dynamic process. Generally speaking, there are two types of plasticity: synaptic and cortical. Cortical plasticity involves activity-dependent changes in size, connectivity, or in the activation pattern of cortical networks. Synaptic plasticity refers to the activity-dependent change in the strength of synaptic transmission and can affect both the morphology and physiology of the synapse. The stimulation of afferent fibers leads to long-lasting changes in synaptic transmission. This phenomenon is called long-term potentiation (LTP) or long-term depression (LTD). From the perspective of molecular biology, synaptic plasticity is of particular importance for the development of tinnitus and its persistence. Ultimately, the damage to the hair cells, auditory nerve, and excitotoxicity results in an imbalance between LTP and LTD and thus in changes of synaptic plasticity. After excessive acoustic stimulation, LTP can be induced by the increase of afferent inputs, whereas decreased afferent inputs generate LTD. The imbalance between LTP and LTD leads to changes in gene expression and involves changes in neurotransmission, in the expression of the receptors, ion channels, regulatory enzymes, and in direct changes on the synapses. This causes an increase of activity on the cellular level. As a result, the imbalance can lead to hyperactivity in the dorsal cochlear nucleus, inferior colliculus, and in the auditory cortex and, later on, to changes in cortical plasticity leading to tinnitus.

**Round window perfusion dynamics: implications for intracochlear therapy.**


**Bowe SN, Jacob A.**

Department of Otolaryngology-Head and Neck Surgery, The Ohio State University Medical Center, Columbus, Ohio 43212, USA.

PURPOSE OF REVIEW: The treatments for inner ear diseases are evolving as the systemic administration of medication is replaced by novel intratympanic and intracochlear drug delivery. The current review explores the background and recent developments in this field.

RECENT FINDINGS: Although still in various stages of clinical development, novel drug delivery techniques such as the Silverstein MicroWick, the round window microcatheter, biodegradable hydrogels, biopolymers, nanoparticles, newly designed cochlear implant arrays, osmotic mini/micro pumps, and reciprocating perfusion systems hold significant promise. Animal data suggest that sustained delivery systems have more reliable inner ear pharmacokinetics than both systemic administration and intratympanic injections.

SUMMARY: As research scientists advance technologies for treating inner ear diseases, drug delivery techniques must keep pace. Viable treatment options for sensorineural hearing loss, tinnitus, and vestibular disorders are on the horizon and may usher in a new golden age for otology.
**Effect of tacrolimus on the excitatory synaptic transmission between the parallel fibers and pyramidal cells in the rat dorsal cochlear nucleus.**  

Szabó L, Rusznák Z, Szucs G, Asztalos L, Pál B.

Institute of Surgery, Medical and Health Science Center, University of Debrecen, Debrecen, Hungary.  
drszabolaszlo@gmail.com

AIM: The immunosuppressive drug tacrolimus has several effects on the central nervous system. Besides its protective effect in hearing deficiencies, it is also considered to be able to cause tinnitus. In the present work, we attempted to describe its effects on a characteristic synapse of the auditory system that may be involved in the pathogenesis of tinnitus.

METHODS/MATERIALS: Slices of the dorsal cochlear nucleus (200 microm thick) were prepared from 9- to 14-day-old Wistar rats. In response to stimulation targeting the superficial layer of the nucleus, we recorded excitatory postsynaptic currents (EPSCs) developing in the cell bodies of the pyramidal neurons using whole-cell voltage clamps. Inhibitory synaptic activity was inhibited by the application of bicuculline and strychnine. Short-term plasticity was investigated using high-frequency stimulation (50 Hz). Unambiguous identification of the investigated neurons was ensured by employing biocytin in the pipette solution, which allowed the confocal reconstruction of the cells after the functional measurements. A concentration of 1 micromol/L tacrolimus was applied extracellularly.

RESULTS: Tacrolimus effectively and reversibly inhibited glutamatergic neurotransmission in the investigated synapse from -145 +/- 26 pA to -55 +/- 15 pA (n = 7; P = .00928). In contrast, EPSC amplitudes without failures were not significantly reduced (from -153 +/- 26 pA to -131 +/- 23 pA) in the presence of tacrolimus, but there were increased failure numbers of synaptic transmission. These data suggested that application of tacrolimus produced a combined pre- and postsynaptic inhibition.

CONCLUSION: Tacrolimus affected short-term synaptic plasticity in the rat dorsal cochlear nucleus. It was also capable of inhibiting the glutamatergic neurotransmission. These effects suggested that tacrolimus may have neuroprotective effects in this structure.
Efferent pathways modulate hyperactivity in inferior colliculus.

Mulders WH, Seluakumaran K, Robertson D.

The Auditory Laboratory, Discipline of Physiology, School of Biomedical, Biomolecular, and Chemical Sciences, The University of Western Australia, Crawley, Western Australia, Australia. hmulders@cyllene.uwa.edu.au

Animal models have demonstrated that mild hearing loss caused by acoustic trauma results in spontaneous hyperactivity in the central auditory pathways. This hyperactivity has been hypothesized to be involved in the generation of tinnitus, a phantom auditory sensation. We have recently shown that such hyperactivity, recorded in the inferior colliculus, is still dependent on cochlear neural output for some time after recovery (up to 6 weeks). We have now studied the capacity of an intrinsic efferent system, i.e., the olivocochlear system, to alter hyperactivity. This system is known to modulate cochlear neural output. Anesthetized guinea pigs were exposed to a loud sound and after 2 or 3 weeks of recovery, single-neuron recordings in inferior colliculus were made to confirm hyperactivity. Olivocochlear axons were electrically stimulated and effects on cochlear neural output and on highly spontaneous neurons in inferior colliculus were assessed. Olivocochlear stimulation suppressed spontaneous hyperactivity in the inferior colliculus. This result is in agreement with our earlier finding that hyperactivity can be modulated by altering cochlear neural output. Interestingly, the central suppression was generally much larger and longer lasting than reported previously for primary afferents. Blockade of the intracochlear effects of olivocochlear system activation eliminated some but not all of the effects observed on spontaneous activity, suggesting also a central component to the effects of stimulation. More research is needed to investigate whether these central effects of olivocochlear efferent stimulation are due to central intrinsic circuitry or to coactivation of central efferent collaterals to the cochlear nucleus.

Can homeostatic plasticity in deafferented primary auditory cortex lead to travelling waves of excitation?

Chrostowski M, Yang L, Wilson HR, Bruce IC, Becker S.

McMaster Integrative Neuroscience Discovery & Study, McMaster University, 1280 Main Street West, Hamilton, ON, Canada, L8S 4K1, chrostm@mcmaster.ca.

Travelling waves of activity in neural circuits have been proposed as a mechanism underlying a variety of neurological disorders, including epileptic seizures, migraine auras and brain injury. The highly influential Wilson-Cowan cortical model describes the dynamics of a network of excitatory and inhibitory neurons. The Wilson-Cowan equations predict travelling waves of activity in rate-based models that have sufficiently reduced levels of lateral inhibition. Travelling waves of excitation may play a role in functional changes in the auditory cortex after hearing loss. We propose that down-regulation of lateral inhibition may be induced in deafferented cortex via homeostatic plasticity mechanisms. We use the Wilson-Cowan equations to construct a spiking model of the primary auditory cortex that includes a novel, mathematically formalized description of homeostatic plasticity. In our model, the homeostatic mechanisms respond to hearing loss by reducing inhibition and increasing excitation, producing conditions under which travelling waves of excitation can emerge. However, our model predicts that the presence of spontaneous activity prevents the development of long-range travelling waves of excitation. Rather, our simulations show short-duration excitatory waves that cancel each other out. We also describe changes in spontaneous firing, synchrony and tuning after simulated hearing loss. With the exception of shifts in characteristic frequency, changes after hearing loss were qualitatively the same as empirical findings. Finally, we discuss possible applications to tinnitus, the perception of sound without an external stimulus.
Ill Diagnostics

Correlation analysis of hearing thresholds, validated questionnaires and psychoacoustic measurements in tinnitus patients.
[Article in English, Portuguese]

Figueiredo RR, Rates MA, Azevedo AA, Oliveira PM, Navarro PB.
Federal University of Rio de Janeiro, Medical School of Valença, RJ.

One of the most criticized points in tinnitus clinical studies arise from the lack of consensus about measurement methods.
AIM: To evaluate the correlation between audiometric thresholds, pitch matching (PM), minimum masking level (MML), Tinnitus Handicap Inventory (THI) and the Beck Depression Inventory (BDI) in tinnitus patients.
STUDY DESIGN: Prospective, cross-sectional.
MATERIALS AND METHODS: Subjects were submitted to tonal audiometry, PM and MML for tinnitus. They also filled out the THI and BDI. Data was statistically compared for correlation purposes between audiometric thresholds, psycho-acoustic measures and questionnaires.
RESULTS: There was no statistically significant correlation between THI and MML, both in patients with BDI scores under and over 14 points. There was no statistically significant correlation between the worst hearing frequency and PM, as well as between the cut-off frequency and the PM in patients with descending hearing curves in their audiograms.
CONCLUSIONS: There is no statistically significant correlation between psycho-acoustic measures (PM and MML), audiometric thresholds, THI and BDI. Tinnitus is a very complex symptom and isolated measures by psycho-acoustic methods; tinnitus and depression questionnaires are not satisfactory.

Internal carotid artery agenesis: diagnosis, clinical spectrum, associated conditions and its importance in the era of stroke interventions.
Neurol Res. 2010 Aug 16. [Epub ahead of print]

Cohen JE, Gomori JM, Leker RR.

BACKGROUND: Internal carotid artery (ICA) agenesis has been usually reported as an asymptomatic condition in association with other congenital anomalies. However, it is less well described in the context of clinical neurological syndromes.
METHOD: Five cases of ICA agenesis are reviewed. The diagnosis of ICA agenesis was based on the absence of bony carotid canal on computed tomography. Brain CT and magnetic resonance image (MRI) scans were done in all the patients and four vessels digital angiograms were obtained in two. Clinical presentation, coexistent radiological findings and associated abnormalities are reviewed.
FINDINGS: The initial presentations were pulsatile tinnitus, ischemic stroke, migraine, Horner’s syndrome, and subarachnoid hemorrhage. Collateral circulation was supplied via the posterior communicating artery and the anterior communicating artery. Ophthalmic artery was supplied by meningeal arteries. On CT, all cases demonstrated agenesis of the bony carotid canal. Smaller cavernous sinus were detected in all cases, enlargement of the foramen spinosum was found in three patients and hyper-pneumatization of the petrous apex was detected in two cases. In one patient a cerebral aneurysms was detected and treated with an endovascular approach. Other associated vascular abnormalities were aortic origin of the vertebral artery in two patients, ICA coiling in two cases and fenestration of basilar artery in one case.
CONCLUSION: ICA agenesis is usually asymptomatic but occasionally may be associated with ischemic stroke. Collateral supply is usually effective in preventing stroke but may become inefficient leading to ischemia. Associated anomalies such as cerebral aneurysms are commonly depicted on the same side as the ICA agenesis and may represent a potential life-threatening condition.
MRI performed after intratympanic gadolinium administration in patients with Ménière’s disease: correlation with symptoms and signs.
Eur Arch Otorhinolaryngol. 2010 Aug 10. [Epub ahead of print]

Fiorino F, Pizzini FB, Beltramello A, Barbieri F.

Department of Otolaryngology, Ospedale Civile Maggiore, Azienda Ospedaliera Universitaria Integrata, Verona, Italy, franco.fiorino@virgilio.it.

The objective of the study was to compare the outcomes of a series of diagnostic parameters in Ménière’s disease (MD) patients with the extent of endolymphatic hydrops (EH) as shown by magnetic resonance imaging (MRI) performed after intra-tympanic gadolinium administration using 18 patients (13 males and 5 females, age 25-78 years, median age 54.3 years) with definite MD. A 0.6-ml solution of Gadobutrol (1 mmol/ml) diluted 1:7 in saline was injected through the inferior-posterior quadrant of the tympanic membrane, using a 22-gauge spinal needle. The patient was kept with the head rotated 45 degrees contralaterally for 30 min after the injection. Twenty-four hours later, three-dimensional fluid-attenuated inversion recovery MRI, using a 3-Tesla unit, was performed. Prevalence and extension of EH in MD patients was evaluated and correlated with age, duration and stage of the disease, frequency of attacks, time interval from the last attack, functional level scale, tinnitus, aural fullness, caloric stimulation, electrocochleography, and vestibular evoked myogenic potentials. All patients showed impaired enhancement of the inner ear of variable degree with the vestibular portion of the labyrinth more frequently involved than the cochlea. Abnormal vestibular evoked myogenic potentials, duration, and stage of the disease were significantly correlated to the number of inner ear sites involved. Modern imaging makes possible the identification of the endolymphatic hydrops in MD patients, improving diagnostic accuracy. The role of hydrops in the clinical manifestations and its correlation with most of the diagnostic parameters remain, however, not completely clear.

Measuring disease-specific health-related quality of life to evaluate treatment outcomes in tinnitus patients: a systematic review.

Kamalski DM, Hoekstra CE, van Zanten BG, Grolman W, Rovers MM.

Department of Otolaryngology, University Medical Center Utrecht, Utrecht, The Netherlands.
d.m.a.kamalski@umcutrecht.nl

OBJECTIVE: To identify all disease-specific health-related quality-of-life (HR-QoL) instruments used to assess tinnitus in clinical trials and detail their psychometric properties.

DATA SOURCES: A literature search was performed in the bibliographical databases of PubMed and Embase to identify all articles using specific HR-QoL instruments in tinnitus trials.

REVIEW METHODS: The HR-QoL instruments used in these articles were investigated in more detail, focusing on characteristics and psychometric values by two independent reviewers.

RESULTS: Seventeen studies were identified by the systematic search. The most used HR-QoL questionnaire was the Tinnitus Questionnaire, followed by the Tinnitus Handicap Inventory, the Tinnitus Reaction Questionnaire, and the Tinnitus Handicap Questionnaire. Internal consistency (Cronbach’s alpha > 0.9) and reproducibility (> 0.8) were high for all questionnaires, and there was heterogeneity in responses between patients, endorsing the use of these questionnaires for discriminative purposes. However, the responsiveness, i.e., the usefulness of these questionnaires in evaluating treatment effects, is not known yet.

CONCLUSION: The HR-QoL instruments used in tinnitus trials appear not to be validated to measure effectiveness of interventions. Using tests or instruments that are valid and reliable is a crucial component of research quality, and both should therefore be studied before final conclusions can be drawn from the questionnaires in upcoming clinical trials.
IV Imaging

**The difference between uni- and bilateral auditory phantom percept.**

**Vaneste S, Plazier M, van der Loo E, Van de Heyning P, De Ridder D**

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

**OBJECTIVE:** Tinnitus can be considered an auditory phantom percept, in which patients hear an internal sound in the absence of any external sound source, mimicking tonal memory. Tinnitus however can be perceived exclusively uni- or bilaterally.

**METHODS:** The neurophysiological differences were investigated between unilateral and bilateral tinnitus using LORETA source localized resting state EEG recordings.

**RESULTS:** The difference between unilateral and bilateral tinnitus is reflected by high frequency activity (beta and gamma) in the superior prefrontal gyrus, right parahippocampus, right angular gyrus and right auditory cortex. Unilateral tinnitus is characterized by contralateral beta2 in the superior prefrontal gyrus in comparison to bilateral tinnitus, but gamma in comparison to non-tinnitus subjects. Bilateral tinnitus has delta activity in the ventrolateral prefrontal cortex in comparison to unilateral tinnitus, and bilateral beta1 in comparison to non-tinnitus subjects. Bilateral tinnitus is also characterized by bilateral frontopolar beta1 activity.

**CONCLUSIONS:** Unilateral and bilateral tinnitus can be differentiated based on their resting state oscillation patterns: beta3 and gamma-band activity in the superior premotor cortex, parahippocampal area and angular gyrus seem to form the core of a spatial localization network involved in tinnitus.

**SIGNIFICANCE:** These differences should be taken into account when evaluating functional neuroimaging data relating to tinnitus.

V Pharmacotherapy

[Pharmacotherapy of acute and chronic hearing loss.]
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[Article in German]

**Hesse G, Laubert A.**

Tinnitus-Klinik, Krankenhaus Bad Arolsen, Grosse Allee 50, 34454, Bad Arolsen, Deutschland, ghesse@tinnitus-klinik.net.

The aetiology of acute hearing loss is mostly idiopathic like sudden sensorineural hearing loss and rarely infectious or vascular. Several studies and meta-analyses of pharmacotherapy are reviewed: In chronic tinnitus there is no indication for pharmacotherapy; sometimes a possible psychosomatic comorbidity has to be treated with psychopharmaceutical agents. Despite a low level of evidence treatment with steroids and initially plasma expanding infusions is recommended for acute tinnitus if there is no spontaneous remission. Intratympanic steroid therapy can be used as an alternative if there is severe hearing loss together with tinnitus.
The effects of the synthetic cannabinoid receptor agonists, WIN55,212-2 and CP55,940, on salicylate-induced tinnitus in rats.
Zheng Y, Stiles L, Hamilton E, Smith PF, Darlington CL.

Department of Pharmacology and Toxicology, School of Medical Sciences, University of Otago Medical School, PO Box 913, Dunedin, New Zealand. yiwen.zheng@stonebow.otago.ac.nz

Previous studies in animals and humans have shown that, in some cases at least, anti-epileptic drugs can reduce the severity of tinnitus. Given that cannabinoid receptor agonists have been shown to exert anti-epileptic effects in some circumstances, we investigated whether two synthetic CB(1)/CB(2) receptor agonists, WIN55,212-2, and CP55,940, could inhibit the behavioural manifestations of salicylate-induced tinnitus in rats in a conditioned suppression task. We found that neither WIN55,212-2 (3.0 mg/kg s.c) nor CP55,940 (0.1 or 0.3 mg/kg s.c), significantly reduced conditioned behaviour associated with tinnitus. However, both 3 mg/kg WIN55,212-2 and 0.3 mg/kg CP55,940 did significantly increase tinnitus-related behaviour compared to the vehicle control groups. These results suggest that cannabinoid receptor agonists may not be useful in the treatment of salicylate-induced tinnitus and that at certain doses, they could actually exacerbate the condition.

Tinnitus psychopharmacology: A comprehensive review of its pathomechanisms and management.
Fornaro M, Martino M.

Department of Neuroscience, Section of Psychiatry, University of Genova, Genova, Italy.

BACKGROUND: Subjective tinnitus is a frequent, impairing condition, which may also cause neurotransmitter imbalance at the cochlea. Psychopharmacologic agents, although not being the first-line treatment for tinnitus, may modulate cochlear neurotransmission, thereby influencing the subjective tinnitus experience.

METHOD: A comprehensive review of MEDLINE literature (from January 1990-January 2010) was performed searching for: „tinnitus“, major classes of psychopharmacological agents, and psychiatric disorders. The most relevant clinical evidence is reported briefly along with a concise description of the main neurotransmitters purported to be involved in tinnitus, in order to provide the reader with a rational evaluation of tinnitus therapy with psychopharmacological agents.

RESULTS: Although strong methodological issues limit the reliability of the current results, a broad number of psychopharmacological agents have already been considered for tinnitus, both as candidate triggers or potential therapies.

CONCLUSIONS: Selected psychopharmacological drugs may play a role in the clinical management of this disorder. While the rational use of these agents for the treatment of tinnitus should not be overlooked, research should be undertaken on their neuromodulating actions at the cochlea.
VI Auditive Stimulation

[Hearing aids, implantable hearing aids and cochlear implants in chronic tinnitus therapy.]
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[Article in German]

Olze H, Zahnert T, Hesse G.
HNO-Klinik, Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum, Augustenburger Platz 1, 13353, Berlin, Deutschland, heidi.olze@charite.de.

Chronic tinnitus can be influenced positively by plastic cortical changes of tinnitus assignment and auditory perception. Acoustic stimulation plays an important role, either through active hearing therapy or through a hearing device. The positive effect of hearing aids regarding tinnitus loudness and severity has been shown in many studies with large numbers of patients and amounts to up to 70%. Implantable hearing systems and their effect on tinnitus have not been examined sufficiently yet; there are reports about positive as well as negative effects on tinnitus perception. There is a strong indication, however, when pathological processes in the middle ear need direct coupling of the implantable hearing aid with the stapes or the round window and there is no possibility of providing a conventional hearing aid due to high-grade combined hearing loss. Cochlear implants (CI) for profoundly deaf patients influence tinnitus loudness and severity in 34-93% of the patients; the large deviation is due to inhomogeneous parameters in the studies that are not always based on validated questionnaires. Existing tinnitus, however, influences the outcome of CI patients. There are studies and discussions about the effect of CI for unilateral deafness with tinnitus.

[Music therapy for noisiform tinnitus : Concept development and evaluation.]
HNO. 2010 Sep 1. [Epub ahead of print]
[Article in German]

Argstatter H, Krick C, Plinkert P, Bolay HV.
Deutsches Zentrum für Musiktherapieforschung (Viktor Dulger Institut), Heidelberg, Deutschland, heike.argstatter@fh-heidelberg.de.

BACKGROUND: Music therapy in chronic tonal tinnitus according to the “Heidelberger model” presents an effective treatment, which is substantiated by neuroscientific and psychological evaluation.
METHOD: The music therapy approach was specifically extended to include noisiform tinnitus, taking sound quality and cardiovascular influences into consideration. Outcome criteria were psychological tinnitus load, psychophysiological parameters and brain imaging procedures.
RESULTS: Psychological outcomes of the pilot study indicate that 21 of the 23 patients (i.e. more than 90%) achieved a reliable reduction of symptoms (TQ scores: pre: 40.1+/-11.4; post: 27.9+/-12.8; at 3-month-follow-up: 24.0+/-12.2). Results of the imaging examinations demonstrated neuroplastic changes in the putamen and insula. Psychophysiological measurements indicate cardiovascular influences on noisiform tinnitus.
DISCUSSION: Therapy success depends on the sound quality of the tinnitus; therefore, any treatment should take this into consideration. Cardiovascular influences were important insofar as active control of the heart rate was an important predictor of long-term therapy outcome. Overall, brain imaging data confirm the top-down-model of tinnitus generation.
Effects of acoustical stimuli delivered through hearing aids on tinnitus.

Sweetow RW, Sabes JH.

University of California, San Francisco, CA 94115, USA. Robert.Sweetow@ucsfmedctr.org

BACKGROUND: The use of acoustic signals to mask, mix with, or ease the distress associated with tinnitus has been clinically employed for decades. It has been proposed that expanding acoustic options for tinnitus sufferers due to personal preferences is desirable. Fractal tones incorporate many useful characteristics of music while avoiding certain features that could be distracting to some individuals.

PURPOSE: To assess the effects on relaxation, tinnitus annoyance, tinnitus handicap, and tinnitus reaction from the use of a hearing aid that incorporates combinations of amplification, fractal tones, and white noise.

RESEARCH DESIGN: Participants listened to experimental hearing aids containing several acoustic options and were asked to rate the signals in terms of their effect on relaxation and tinnitus annoyance. They subsequently wore the hearing aids for 6 mo and completed tinnitus handicap and reaction scales.

STUDY SAMPLE: Fourteen hearing-impaired adults with primary complaints of subjective tinnitus.

INTERVENTION: Participants were tested wearing hearing aids containing several programs including amplification only, fractal tones only, and a combination of amplification, noise, and/or fractal tones. The fractal tones (now commercially available as the „Zen“ feature) were generated by the Widex Mind hearing aid. Rating procedures were conducted in the laboratory, and tinnitus reaction and handicap were assessed during and following a 6 mo field trial.

DATA COLLECTION AND ANALYSIS: Data were collected at the initial visit, one week, 1 mo, 3 mo, and 6 mo. Nonparametric statistics included Wilcoxon matched-pairs signed-rank, chi(2), and repeated-measures analyses of variance.

RESULTS: Thirteen of 14 participants reported that their tinnitus annoyance, as measured by the Tinnitus Annoyance Scale, was reduced for at least one of the amplified conditions (with or without fractal tones or noise), relative to the unaided condition. Nine assigned a lower tinnitus annoyance rating when listening to fractal tones alone versus the amplification-alone condition. There was a range of preferences observed for fractal settings, with most participants preferring fractals with a slow or medium tempo and restricted dynamic range. The majority (86%) indicated that it was easier to relax while listening to fractal signals. Participants had preferences for certain programs and fractal characteristics. Although seven participants rated the noise-only condition as providing the least tinnitus annoyance, only two opted to have noise only as a program during the field trial, and none selected the noise-only condition as the preferred setting. Furthermore, while all four of the experienced hearing aid users selected noise as producing the least annoying tinnitus in the laboratory, only one selected it for field wear. Tinnitus Handicap Inventory and Tinnitus Reaction Questionnaire scores were improved over the course of the 6 mo trial, with clinically significant improvements occurring for over half of the participants on at least one of the measures.

CONCLUSIONS: The results suggest that use of acoustic stimuli, particularly fractal tones, delivered through hearing aids can provide amplification while allowing for relief for some tinnitus sufferers. It is important to recognize, however, that tinnitus management procedures need to be supplemented with appropriate counseling.
Cochlear Implantation in Unilateral Deaf Subjects Associated With Ipsilateral Tinnitus.
Otol Neurotol. 2010 Aug 20. [Epub ahead of print]


*Medical University of Hannover, Department of Otolaryngology, Hannover, Germany; daggerAdvanced Bionics European Research Center GmbH, Hannover, Germany; and double daggerMedical University of Hannover, Department of Psychosomatic, Hannover, Germany.

OBJECTIVE: In subjects who are deaf and who also have tinnitus in the affected ear, tinnitus treatments based on acoustic input are impossible. On the other hand, tinnitus suppression using electric stimulation has been reported to be successful. Therefore, a study was initiated to investigate the potential of cochlear implantation (CI) in unilateral deaf subjects regarding tinnitus suppression, device acceptance, and restoration of spatial hearing.

METHOD: Five subjects with severe to profound unilateral deafness having also ipsilateral tinnitus were enrolled. In monthly visits, the speech processor program was optimized, and the hearing performance as well as tinnitus were monitored. In addition, it was investigated whether the CI improves hearing in adverse listening situations when combined with the normal hearing side.

RESULTS: In 3 participants, the tinnitus was significantly suppressed while wearing the device. In the other 2 participants, the tinnitus could be reduced in certain situations. Speech perception tests revealed a significant benefit with the CI in combination with the normal-hearing side for 3 participants. All participants accepted the device in a clinical setting; adaptation of the frequency allocation was not required.

CONCLUSION: Improvements were found regarding the hearing and the tinnitus. Not all participants benefit from the CI to the same degree and in the same situations. The results indicate that cochlear implantation in subjects with unilateral severe to profound hearing loss and ipsilateral tinnitus may be beneficial on a case-to-case basis. Further work needs to be performed to define the appropriate indication criteria.

Customized notched music training reduces tinnitus loudness.

Stracke H, Okamoto H, Pantev C.

Institute for Biomagnetism & Biosignalanalysis; University Hospital; Westfalian Wilhelms-University; Münster, Germany.

Chronic tinnitus is a symptom with high prevalence. There is evidence that the tinnitus perception is related to unfavorable cortical plastic changes. In our recent study we have developed and evaluated a customized music training strategy that appears capable of both reducing cortical tinnitus related neuronal activity and alleviating subjective tinnitus perception. We hypothesize that the regular and enjoyable music training reverses unprofitable cortical reorganization to a certain degree by means of the focused strengthening of auditory inhibitory neuronal networks.

[Analysis and comparison of the masking and TRT for patients with subjective tinnitus]
Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2010 May;24(10):442-6.
[Article in Chinese]


Department of Otolaryngology, the Second Hospital, Sun Yat-sen University, The Institute of Hearing and Speech-Language Science of Sun Yet-Sen University, Guangzhou, 510120, China.

OBJECTIVE: To compare the effect of tinnitus masking and tinnitus retraining therapy (TRT) in patients with subjective tinnitus, and to analyze the effect of TRT within the positive or negative group of tinnitus masking test.
METHOD: The 217 patients from January, 2006 to April, 2008 in our hospital, were performed with the
determination of tinnitus including pitch matching, intensity matching, Feldmann masking curve and
residual inhibition test with TinniTest. Of which 143 cases were positive and 74 were negative in tinnitus
masking. The follow-up was 6 months and 10 cases were lost. 207 patients were divided into two groups
for prospective study: 69 cases in tinnitus masking group and 138 cases in TRT group, The curative
effect was evaluated according to tinnitus handicap inventory (THI) and Subjective Visual Tinnitus Scale
(SVTS).

RESULT: Both masking treatment and TRT were effective for cases with tinnitus, there was significan
difference of the score of THI and SVTS of tinnitus between pretherapy and posttherapy (P < 0.01).
TRT therapy was more effective than masking therapy, there was significant difference of the THI score
between TRT and masking group, but there was no significant difference of of the SVTS between them.
TRT therapy was suitable for the patients with both positive effect and negative effect of masking test,
and there was no significant difference between them.

CONCLUSION: Both TRT and masking therapy are the most important therapy for tinnitus patients, but
TRT is much more effective than masking therapy in some aspects.

The Efficacy of Auditory Perceptual Training for Tinnitus: A Systematic Review.
Ann Behav Med. 2010 Jul 29. [Epub ahead of print]

Hoare DJ, Stacey PC, Hall DA.

National Biomedical Research Unit in Hearing, Ropewalk House, 113 The Ropewalk, Nottingham, NG1
5DU, UK, derek.hoare@nottingham.ac.uk.

Auditory perceptual training affects neural plasticity and so represents a potential strategy for tinnitus
management. We assessed the effects of auditory perceptual training on tinnitus perception and/or its
intrusiveness via a systematic review of published literature. An electronic database search using the
keywords ‘tinnitus and learning’ or ‘tinnitus and training’ was conducted, updated by a hand search.
The ten studies identified were reviewed independently by two reviewers, data were extracted, study
quality was assessed according to a number of specific criteria and the information was synthesised
using a narrative approach. Nine out of the ten studies reported some significant change in either self-
reported or psychoacoustic outcome measures after auditory training. However, all studies were quality
rated as providing low or moderate levels of evidence for an effect. We identify a need for appropriately
randomised and controlled studies that will generate high-quality unbiased and generalisable evidence to
ascertain whether or not auditory perceptual training has a clinically relevant effect on tinnitus.

VII Brain Stimulation

Surgical treatment by electrical stimulation of the auditory cortex for intractable tinnitus.

Littré CF, Theret E, Tran H, Lévêque M, Portefaix C, Gierski F, Emeriau S, Peruzzi P.

Department of Neurosurgery, Pr Rousseaux CHU Maison Blanche, 45 Rue Cognacq Jay, Reims,
France. fabien.litre@mac.com

Tinnitus is a public health issue in France. Around 1% of the population is affected and 30,000 people
are handicapped in their daily life. The treatments available for disabling tinnitus have until now been
disappointing. We are reporting on the surgical treatment by electrical stimulation of the auditory cortex
of a female patient affected by disabling tinnitus that resisted classical treatments. The tinnitus appeared
suddenly 10 years ago after a left ear tympanoplasty. The acouphenometry measures revealed a
bilateral tinnitus, predominant on the right side, constant, with high frequency (6000 Hz). Transcranial
magnetic stimulation (TMS) was performed at first with several supraliminal and infraliminal protocols.
This showed promising results. Anatomic and functional magnetic resonance imaging (fMRI) of the
auditory cortex before and after repetitive TMS (rTMS) demonstrated a modification of the cortical
activity and where the ideal location for a cortical electrode might be, to straddle primary and secondary auditory cortex. After these investigations, two quadra polar electrodes (Resume, Medtronic Ltd, Hertfordshire, UK), connected to a stimulating device implanted under the skin (Synergy, Medtronic Ltd), were extradurally implanted. The surgical procedure was similar to the one performed for analgesic cortical stimulation. No surgical complications were reported. The activation of the stimulator provided a reduction of 65% of the tinnitus impact, with a persistent effect on the right side. The feasibility of the cortical stimulation in symptomatic treatment of tinnitus was proven by this preparatory work. The middle- and long-term therapeutic effects remain to be evaluated.

Brain Stimulation: New Vistas for the Exploration and Treatment of Tinnitus.
CNS Neurosci Ther. 2010 Jul 8. [Epub ahead of print]

Plewnia C.

Department of Psychiatry and Psychotherapy, Neurophysiology and Interventional Psychiatry, University of Tübingen Medical School, Osianderstrasse 24, D-72076 Tübingen, Germany.

SUMMARY Aims: Tinnitus, the perception of sounds or noise in the absence of auditory stimuli, is a frequent and often severely disabling symptom of different disorders of the auditory system. Attempts to develop evidence-based therapies have been thwarted by a poor understanding of the underlying pathophysiology. However, recent work points toward a pivotal role of maladaptive cortical reorganization in the generation and perpetuation of tinnitus. Changes in the representation of sounds, abnormalities of oscillatory activity, and hyperactivity in higher order areas of auditory processing have been linked with the perception of tinnitus. Brain stimulation techniques have entered the field and have opened exciting new perspectives for the modulation of dysfunctional brain activity. In this review, a comprehensive overview on the use of brain-stimulation techniques in the exploration and experimental treatment of tinnitus is provided. Discussions: Noninvasive and invasive brain stimulation techniques, for example, transcranial magnetic stimulation (TMS), direct current stimulation (tDCS), and direct electrical cortical stimulation gave rise to a new line of investigation in tinnitus research. First, it has been shown that focal interference with presumably pathological cortical function can reduce tinnitus at least transiently. Second, the reduction of tinnitus-associated enhancement of cortical activity by neuronavigated TMS has been demonstrated to ameliorate tinnitus. Third, preliminary data suggest that repeated application of TMS or continuous cortical stimulation may lead to a longer lasting suppression of tinnitus. Conclusions: These proof of principle studies point toward a new option for the investigation and neurophysiology based treatment of tinnitus. Based on these findings, larger scale randomized clinical trials are needed to explore the efficacy of different brain stimulation techniques and parameters as well as the optimal target sites and treatment schedules. Particularly, a careful evaluation of clinical relevance under consideration of an adequate sham control and attention to possible unwanted side effects of these new interventions are indispensable.
VIII Behavioral Therapy

Cognitive behavioural therapy for tinnitus.
Cochrane Database Syst Rev. 2010 Sep 8;9:CD005233.

Martinez-Devesa P, Perera R, Theodoulou M, Waddell A.

ENT Department, John Radcliffe Hospital - West Wing, Headley Way, Oxford, UK, OX3 9DU.

Update of:


BACKGROUND: This is an update of a Cochrane Review originally published in Issue 1, 2007 of The Cochrane Library. Tinnitus is an auditory perception that can be described as the experience of sound, in the ear or in the head, in the absence of external acoustic stimulation. Cognitive behavioural therapy (CBT) uses relaxation, cognitive restructuring of the thoughts and exposure to exacerbating situations in order to promote habituation and may benefit tinnitus patients, as may the treatment of associated psychological conditions.

OBJECTIVES: To assess whether CBT is effective in the management of patients suffering from tinnitus.

SEARCH STRATEGY: We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; PsycINFO; ISRCTN and additional sources for published and unpublished trials. The date of the most recent search was 6 May 2010.

SELECTION CRITERIA: Randomised controlled trials in which patients with unilateral or bilateral tinnitus as their main symptom received cognitive behavioural treatment.

DATA COLLECTION AND ANALYSIS: One review author (PMD) assessed every report identified by the search strategy. Three authors (PMD, AW and MT) assessed the methodological quality and applied inclusion/exclusion criteria. Two authors (PMD and RP) extracted data and conducted the meta-analysis. The four authors contributed to the final text of the review.

MAIN RESULTS: Eight trials comprising 468 participants were included. For the primary outcome of subjective tinnitus loudness we found no evidence of a difference between CBT and no treatment or another intervention (yoga, education and ‘minimal contact - education’). In the secondary outcomes we found evidence that quality of life scores were improved in participants who had tinnitus when comparing CBT to no treatment or another intervention (education and ‘minimal contact education’). We also found evidence that depression scores improved when comparing CBT to no treatment. We found no evidence of benefit in depression scores when comparing CBT to other treatments (yoga, education and ‘minimal contact - education’). There were no adverse/side effects reported in any trial.

AUTHORS’ CONCLUSIONS: In six studies we found no evidence of a significant difference in the subjective loudness of tinnitus. However, we found a significant improvement in depression score (in six studies) and quality of life (decrease of global tinnitus severity) in another five studies, suggesting that CBT has a positive effect on the management of tinnitus.

[TRT and psychotherapy in the treatment of tinnitus.]
HNO. 2010 Sep 3. [Epub ahead of print]
[Article in German]

Schaaf H, Gieler U.

Tinnitus-Klinik Dr. Hesse im Krankenhaus Arolsen, Grosse Allee 50, 34454, Bad Arolsen, Deutschland, hschaaf@tinnitus-klinik.net.

Basic requirements and results of tinnitus retraining therapy (TRT) as well as other habituation therapies with psychotherapeutic approaches in the treatment of tinnitus are examined closely in this literature review. In German-speaking countries experts generally aim for involvement of psychotherapists
beyond the classic TRT developed by Jastreboff and Hazell. On the basis of a validated diagnostic test such as the Tinnitus Questionnaire according to Hiller and Goebel (1998), such a therapy regime is more effective than the „classic“ procedure. Under different treatment approaches, cognitive behavioural therapy elements have been proven to be effective—even as a component of the TRT—as well as integrated variants in psychodynamic therapies. We have to give consideration to the fact that in all studies about the selection and inclusion criteria selective test conditions were established which suggest that in each case diverse patient groups were studied. In the overall picture it becomes apparent that depending on the severity of the tinnitus and accompanying hearing problems a dysfunction-oriented and staged approach makes sense.

Qigong for the treatment of tinnitus: a prospective randomized controlled study.

Biesinger E, Kipman U, Schätz S, Langguth B.
ENT-Clinic and Otolaryngology Department, Klinikum Traunstein, Traunstein, Germany.

Comment in:

OBJECTIVE: Tinnitus is a frequent disorder which is very difficult to treat. Qigong is a mindful exercise and an important constituent of traditional Chinese medical practice. Here we performed a randomized controlled trial to evaluate the effect of a Qigong intervention on patients with tinnitus. We hypothesized that especially tinnitus patients with somatosensoric components may benefit from the mind-body technique of Qigong.

METHODS: Eighty patients with tinnitus of at least 3 months duration were randomly assigned to an intervention group (n=40) consisting of 10 Qigong training sessions in 5 weeks or a waiting-list control group (n=40). Tinnitus severity was assessed with a visual analogue scale (VAS) and with a tinnitus questionnaire (TBF-12) before treatment, immediately after treatment, and 1 and 3 months after treatment.

RESULTS: Qigong did not cause any side effects and was completed by 80% of the assigned patients. Compared with the control group, Qigong participants experienced improvement in tinnitus severity, as reflected by a significant reduction in both the VAS and the TBF-12. In the subgroup of patients with somatosensoric tinnitus, Qigong effects were more pronounced, resulting in a highly significant improvement in both scales compared to the waiting-list group.

CONCLUSION: These findings suggest that Qigong interventions could be a useful complement to the therapeutic management of patients with tinnitus and especially for those with somatosensoric components. Satisfaction with the intervention, a high degree of completion, and stability of the effects for at least 3 months after the intervention further underscore the potential of Qigong in the treatment of tinnitus.
IX Somatic Tinnitus

Aural Symptoms in Patients With Temporomandibular Joint Disorders: Multiple Frequency Tympanometry Provides Objective Evidence of Changes in Middle Ear Impedance.
Otol Neurotol. 2010 Jul 31. [Epub ahead of print]

Riga M, Xenellis J, Peraki E, Ferekidou E, Korres S.

*ENT Department, University Hospital of Alexandroupolis, Demokritos University of Thrace, Alexandroupolis; and daggerENT Department, Hippokration Hospital of Athens, National University of Athens, Athens, Greece.

OBJECTIVE: The association of temporomandibular joint (TMJ) disorders with aural symptoms, such as tinnitus, otic fullness, and subjective decrease of hearing acuity, is a well-established clinical observation. Although several hypotheses have been made about the otic-conductive origin of these complaints, conventional 226-Hz tympanometry has failed to demonstrate any middle ear abnormalities. The aim of this study was to evaluate patients with TMJ disorders with multiple frequency tympanometry (MFT).

STUDY DESIGN: Prospective clinical study.

SETTING: Outpatient clinic.

PATIENTS: The population of this study consisted of 40 patients with unilateral TMJ disorders diagnosed for longer than 1 month.

INTERVENTIONS: After verifying that there were no abnormal otoscopic findings, 226-Hz tympanometry, conventional pure-tone audiometry, brainstem auditory evoked potentials, and MFT were performed.

MAIN OUTCOME MEASURE: Resonant frequency (RF) values.

RESULTS: With the exception of MFT, no abnormal audiologic findings were revealed. The ear ipsilateral to the lesion demonstrated significantly higher (p = 0.002) RF values in comparison to the contralateral ear. The difference in RF values was more obvious in patients aged 45 years or younger.

CONCLUSION: The results of this study imply an increase in the stiffness of the middle ear, which has not been detected by conventional tympanometry. This represents the first concrete documentation of minor alterations in the conductive properties of the middle ear and seems to support the various hypotheses on the middle-ear origin of aural complaints in patients with TMJ disorders. Further studies are needed before a clear insight on the presumably multifactorial pathophysiology of these complaints can finally be reached.

Central crosstalk for somatic tinnitus: abnormal vergence eye movements.


Group IRIS, CNRS, Service d’Ophtalmologie-ORL-Stomatologie, Hôpital Européen Georges Pompidou, Paris, France. qing.yang@egp.aphp.fr

BACKGROUND: Frequent oculomotoric problems with orthoptic testing were reported in patients with tinnitus. This study examines with objective recordings vergence eye movements in patients with somatic tinnitus patients with ability to modify their subjective tinnitus percept by various movements, such as jaw, neck, eye movements or skin pressure.

METHODS: Vergence eye movements were recorded with the Eyelink II video system in 15 (23-63 years) control adults and 19 (36-62 years) subjects with somatic tinnitus.

FINDINGS: 1) Accuracy of divergence but not of convergence was lower in subjects with somatic tinnitus than in control subjects. 2) Vergence duration was longer and peak velocity was lower in subjects with somatic tinnitus than in control subjects. 3) The number of embedded saccades and the amplitude of saccades coinciding with the peak velocity of vergence were higher for tinnitus subjects. Yet, saccades did not increase peak velocity of vergence for tinnitus subjects, but they did so for controls. 4) In contrast, there was no significant difference of vergence latency between these two groups.
INTERPRETATION: The results suggest dysfunction of vergence areas involving cortical-brainstem-cerebellar circuits. We hypothesize that central auditory dysfunction related to tinnitus percept could trigger mild cerebellar-brainstem dysfunction or that tinnitus and vergence dysfunction could both be manifestations of mild cortical-brainstem-cerebellar syndrome reflecting abnormal cross-modality interactions between vergence eye movements and auditory signals.

X Surgical Treatment

XI Holistics

XII Review

Cognitive behavioural therapy for tinnitus.
Cochrane Database Syst Rev. 2010 Sep 8;9:CD005233.

Martinez-Devesa P, Perera R, Theodoulou M, Waddell A.
ENT Department, John Radcliffe Hospital - West Wing, Headley Way, Oxford, UK, OX3 9DU.

Update of:


BACKGROUND: This is an update of a Cochrane Review originally published in Issue 1, 2007 of The Cochrane Library. Tinnitus is an auditory perception that can be described as the experience of sound, in the ear or in the head, in the absence of external acoustic stimulation. Cognitive behavioural therapy (CBT) uses relaxation, cognitive restructuring of the thoughts and exposure to exacerbating situations in order to promote habituation and may benefit tinnitus patients, as may the treatment of associated psychological conditions.

OBJECTIVES: To assess whether CBT is effective in the management of patients suffering from tinnitus.

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DATA COLLECTION AND ANALYSIS: One review author (PMD) assessed every report identified by the search strategy. Three authors (PMD, AW and MT) assessed the methodological quality and applied inclusion/exclusion criteria. Two authors (PMD and RP) extracted data and conducted the meta-analysis. The four authors contributed to the final text of the review.

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AUTHORS’ CONCLUSIONS: In six studies we found no evidence of a significant difference in the subjective loudness of tinnitus. However, we found a significant improvement in depression score (in six studies) and quality of life (decrease of global tinnitus severity) in another five studies, suggesting that CBT has a positive effect on the management of tinnitus.
The Efficacy of Auditory Perceptual Training for Tinnitus: A Systematic Review.
Ann Behav Med. 2010 Jul 29. [Epub ahead of print]

Hoare DJ, Stacey PC, Hall DA.
National Biomedical Research Unit in Hearing, Ropewalk House, 113 The Ropewalk, Nottingham, NG1 5DU, UK, derek.hoare@nottingham.ac.uk.

Auditory perceptual training affects neural plasticity and so represents a potential strategy for tinnitus management. We assessed the effects of auditory perceptual training on tinnitus perception and/or its intrusiveness via a systematic review of published literature. An electronic database search using the keywords 'tinnitus and learning' or 'tinnitus and training' was conducted, updated by a hand search. The ten studies identified were reviewed independently by two reviewers, data were extracted, study quality was assessed according to a number of specific criteria and the information was synthesised using a narrative approach. Nine out of the ten studies reported some significant change in either self-reported or psychoacoustic outcome measures after auditory training. However, all studies were quality rated as providing low or moderate levels of evidence for an effect. We identify a need for appropriately randomised and controlled studies that will generate high-quality unbiased and generalisable evidence to ascertain whether or not auditory perceptual training has a clinically relevant effect on tinnitus.

Tinnitus psychopharmacology: A comprehensive review of its pathomechanisms and management.

Fornaro M, Martino M.
Department of Neuroscience, Section of Psychiatry, University of Genova, Genova, Italy.

BACKGROUND: Subjective tinnitus is a frequent, impairing condition, which may also cause neurotransmitter imbalance at the cochlea. Psychopharmacologic agents, although not being the first-line treatment for tinnitus, may modulate cochlear neurotransmission, thereby influencing the subjective tinnitus experience.

METHOD: A comprehensive review of MEDLINE literature (from January 1990-January 2010) was performed searching for: "tinnitus", major classes of psychopharmacological agents, and psychiatric disorders. The most relevant clinical evidence is reported briefly along with a concise description of the main neurotransmitters purported to be involved in tinnitus, in order to provide the reader with a rational evaluation of tinnitus therapy with psychopharmacological agents.

RESULTS: Although strong methodological issues limit the reliability of the current results, a broad number of psychopharmacological agents have already been considered for tinnitus, both as candidate triggers or potential therapies.

CONCLUSIONS: Selected psychopharmacological drugs may play a role in the clinical management of this disorder. While the rational use of these agents for the treatment of tinnitus should not be overlooked, research should be undertaken on their neuromodulating actions at the cochlea.

Tinnitus: current understanding and contemporary management.

Seidman MD, Standring RT, Dornhoff JL.
Henry Ford Health System, Director Division Otologic/Neurotologic Surgery, Medical Director Center for Integrative Medicine, Detroit, MI 48202, USA. mseidma1@hfhs.org

PURPOSE OF REVIEW: Tinnitus is a debilitating condition that affects a broad range of patients. Despite thorough and extensive research, the cause of tinnitus has yet to be determined. Also, there has never been a single intervention identified that can consistently eliminate the symptoms of tinnitus. However, despite our inability to ‘cure’ tinnitus, there are many medical and behavioral strategies that
may result in symptomatic relief. The purpose of this article is to review some of the previous information on tinnitus and to examine the recent research on the etiology and management of this condition.

RECENT FINDINGS: Recent research into the etiology of tinnitus has demonstrated that genetics plays less of a role than previously thought. Although many medications can cause some relief of tinnitus, a number of well designed studies have failed to identify a single cure. For patients with severe tinnitus who have failed other treatments, such as dietary modification, herbs and nutrients, sound therapies (tinnitus retraining, Neuromonics, masking, and others), or centrally acting medications, transcranial magnetic stimulation has emerged as a viable treatment option.

SUMMARY: Tinnitus is a common medical complaint and debilitating problem for some patients. It has a broad range of etiologies and even more potential treatments. This review is meant to inform the reader on the current options available to treat this condition.

**XIII Others**

**Pop-rock musicians: assessment of their satisfaction provided by hearing protectors.**
[Article in English, Portuguese]

**Santoni CB, Fiorini AC.**

Pontifical Catholic University, Sao Paulo.

Pop-rock musicians are at risk of developing hearing loss and other symptoms related to amplified music.

AIM: The aim of the present study was to assess the satisfaction provided by the use of hearing protection in pop-rock musicians. Study design: Contemporary cohort study.

MATERIALS AND METHODS: A study of 23 male pop-rock musicians, aged between 25 to 45 years. After audiological evaluation (pure tone audiometry, middle ear analysis, TEOAE and DPOAE) hearing protective devices were provided to be used for three months. After that musicians answered a satisfaction assessment questionnaire.

RESULTS: The prevalence of hearing loss was of 21.7%. The most common complaints about the hearing protectors were: autophonia, pressure in the ears, interference in high frequencies perception and full time use of the hearing protector during concerts. There was a positive correlation between a reduction in tinnitus after the use of the HPD with the following complaints: tinnitus after the beginning of the career (p= 0.044), discomfort with the sound intensity in the workplace (p= 0.009) and intolerance to loud sound (p= 0.029).

CONCLUSIONS: There was a high prevalence of hearing loss and a positive tendency towards the use of the ear protector device among the sample population.

**MP3 player listening habits of 17 to 23 year old university students.**

**McNeill K, Keith SE, Feder K, Konkle AT, Michaud DS.**

Faculty of Social Sciences, School of Psychology, University of Ottawa, Ottawa, Ontario K1N 6N5, Canada.

This study evaluated the potential risk to hearing associated with the use of portable digital audio players. Twenty-eight university students (12 males, 16 females; aged 17-23) completed a 49-item questionnaire assessing user listening habits and subjective measures of hearing health. Sound level measurements of participants' self-identified typical and 'worst case' volume levels were taken in different classrooms with background sound levels between 43 and 52 dBA. The median frequency and duration of use was 2 h per day, 6.5 days a week. The median sound levels and interquartile ranges (IQR) at typical and 'worst case' volume settings were 71 dBA (IQR=12) and 79 dBA (IQR=9),
respectively. When typical sound levels were considered with self-reported duration of daily use, none of the participants surpassed Leq(8) 85 dBA. On the questionnaire, 19 students reported experiencing at least one symptom of possible noise-induced hearing loss. Significant differences in MP3 user listening patterns were found between respondents who had experienced tinnitus and those who had not. The findings add to a growing body of literature that collectively supports a need for further research investigating MP3 player user listening habits in order to assess their potential risk to hearing health.


Department of Psychiatry, University of Regensburg, Universitaetsstrasse 84, 93053 Regensburg, Germany. michael.landgrebe@medbo.de

Tinnitus, the phantom perception of sound, is a frequent disorder that causes significant morbidity and treatment is elusive. A large variety of different treatment options have been proposed and from most of them some patients benefit. However, a particular treatment that helps one patient may fail for others. This suggests that there are different forms of tinnitus which differ in their pathophysiology and their response to specific treatments. Therefore, it is a major challenge for tinnitus treatment to identify the most promising therapy for a specific patient. However, most published clinical treatment studies have enrolled only relatively small patient samples, making it difficult to identify predictors of treatment response for specific approaches. Furthermore, inter-study comparability is limited because of varying methods of tinnitus assessment and different outcome parameters. Performing clinical trials according to standardized methodology and pooling the data in a database should facilitate both clinical subtypisation of different forms of tinnitus, and identification of promising treatments for different types of tinnitus. This would be an important step towards the goal of individualized treatment of tinnitus. For these reasons, an international database of tinnitus patients, who undergo specific treatments, and are assessed during the course of this treatment with standardized instruments (e.g., psychoacoustic measures, questionnaires) has been established. The primary objectives of this database are (1) collecting a standardized set of data on patient characteristics, treatments, and outcomes from tinnitus patients consulting specialized tinnitus clinics all over the world (at present 13 centers in 8 countries), (2) delineating different subtypes of tinnitus based on data that has been systematically collected and (3) identifying predictors for individual treatment response based on the clinical profile. Starting in 2008, the database currently contains data from more than 400 patients. It is expected that more centers will join the project and that the patient numbers will rapidly grow, so that this international database will further facilitate future research and contribute to the development of evidence based on individualized treatment.
XIV Case Reports

Botox transient treatment of tinnitus due to stapedius myoclonus: Case report.
Clin Neurol Neurosurg. 2010 Aug 25. [Epub ahead of print]

Liu HB, Fan JP, Lin SZ, Zhao SW, Lin Z.
Department of Otolaryngology-Head & Neck Surgery, ChangZheng Hospital, Second Military Medical University, Fengyang Road 415, Huangpu District, Shanghai, China.

OBJECT: To explore the feasibility of using botulinum toxin type A (BTXA) to treat tinnitus due to stapedius myoclonus.

METHOD: A piece of gelfoam containing BTXA (25U/ml) was placed, through a perforation in tympanic membrane, into the middle ear cavity of a patient suffering from tinnitus due to stapedius myoclonus.

RESULTS: The tinnitus disappeared on the second day after the BTXA treatment. The patient was free of symptoms during a 3-month follow-up period. Tinnitus reappeared at 4 months, and disappeared after second BTXA local treatment.

CONCLUSION: Local BTXA treatment may be considered as a treatment for tinnitus caused by stapedius myoclonus.

Myiasis of the external and middle ear.

Hatten K, Gulleth Y, Meyer T, Eisenman DJ.
Department of Otorhinolaryngology-Head and Neck Surgery, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA.

Aural myiasis is a rare otolaryngological disease typically seen in poor hygienic conditions and medically disabled patients. We present a case of aural myiasis in a healthy woman who had no apparent risk factors for infestation and required extensive surgical intervention. We also discuss the literature of documented otolaryngological cases of myiasis and effective therapies. In our patient, symptoms of otalgia, otorrhea, and tinnitus resolved after multiple attempts at extraction resulted in successful eradication of larvae. The patient required tympanoplasty to reconstruct the damaged external and middle ear. Physicians should have a clinical suspicion of aural myiasis in patients with a travel history and an atypical presentation of acute otalgia and otorrhea.

Sudden (reversible) sensorineural hearing loss in pregnancy.

Kenny R, Patil N, Considine N.
Department of Audiology, Sligo General Hospital, Sligo, Ireland, rsmith1968@yahoo.com.

BACKGROUND: Sudden hearing loss directly associated with pregnancy or birth is a little known and rare occurrence. The temporary, unilateral, low-frequency sensorineural hearing loss in this case was reported after the birth of the patient's first child, and again during the third trimester of her second pregnancy.

AIMS: This paper discusses the different explanations as to why hearing losses occur due to physical changes within the body during pregnancy and birth. It is probable that this patient had significant anatomical asymmetry with one patent and one non-patient cochlear aqueduct, allowing increased pressure unilaterally. The mechanical restriction of the inner ear hair cells caused the hearing loss that returned to normal, when the pressure returned to normal.

CONCLUSIONS: Our case demonstrates that pregnancy can lead to hearing loss in two sequential pregnancies. Mechanisms are discussed in detail. Clinically it appears that the hearing loss and tinnitus associated with pregnancy can spontaneously recover.
Irreversible sensorineural hearing loss: an unusual side effect of non-steroidal anti-inflammatory drugs.

Ahmad S, Bhanji A, Pal S, Karim M.

Department of Renal Medicine, Norfolk and Norwich University Hospital, Norwich, UK.

OBJECTIVE: Non-steroidal anti-inflammatory drugs are known to have a number of potential side effects. Here we report a case demonstrating an uncommon complication, irreversible sensorineural deafness.

CASE HISTORY: A 41-year-old man with pre-existing cardiac and renal dysfunction (for which his regular medications included furosemide) presumed secondary to a viral myocarditis developed acute sensorineural hearing loss 5 days after commencing treatment with indomethacin 25 mg tds for acute gout. His hearing loss was preceded by the development of tinnitus and failed to recover.

CONCLUSION: Permanent deafness is a rare but serious side effect of NSAIDs. Tinnitus developing in patients on these agents should be regarded as a potential warning sign of impending irreversible ototoxicity.

Aneurysm of the petrous portion of the internal carotid artery at the foramen lacerum: anatomic, imaging, and otologic findings.
Ear Nose Throat J. 2010 Jul;89(7):303-5.

Palacios E, Gómez J, Alvernia JE, Jacob C.

Department of Radiology, Tulane University Hospital and Clinic, 1514 Tulane Ave., New Orleans, LA 70112, USA. drpalacios@aol.com

Aneurysms of the petrous portion of the internal carotid artery (ICA) are rare. Their etiology is usually congenital, traumatic, or mycotic. Depending on the size and location of the aneurysm, the direction of its growth, and the specific adjacent structures involved, patients may or may not present with signs and symptoms. When signs and symptoms do manifest, they may include headaches, epistaxis, a vascular retrotympanic mass with hemotympanum and/or otorrhagia, pulsatile tinnitus, hearing loss, vertigo, and Horner syndrome or Raeder paratrigeminal neuralgia. We describe the imaging aspects of the case of a 27-year-old man who presented with a 5-day history of unilateral symptoms secondary to a lesion located in the area of the right foramen lacerum. The lesion proved to be an aneurysm of the petrous portion of the ICA. We discuss the anatomic, imaging, and otologic aspects of ICA aneurysms in this location.

Inflammatory pseudotumor (plasma cell granuloma) of the temporal bone.

Ajibade DV, Tanaka IK, Paghda KV, Mirani N, Lee HJ, Jyung RW.

Division of Otolaryngology, Department of Surgery, New Jersey Medical School, University of Medicine and Dentistry of New Jersey, Newark, NJ, USA.

We report the case of a 41-year-old man who presented with progressive right-sided ear pressure, otalgia, hearing loss, tinnitus, and intermittent otorrhea. Computed tomography and magnetic resonance imaging detected a soft-tissue mass in the right mastoid with intracranial invasion and erosion through the tegmen tympani and mastoid cortex. Histopathologic examination was consistent with an inflammatory pseudotumor (plasma cell granuloma). These lesions rarely occur in the temporal bone. When they do, they are locally destructive and can erode bone and soft tissues. Aggressive surgery is recommended as a first-line treatment, with adjunctive steroid or radiotherapy reserved for residual or refractory disease. Our patient subsequently experienced multiple recurrences, and his treatment required all of these modalities. At the most recent follow-up, he was disease-free and doing well.
**XV Specific Forms of Tinnitus**

**Disease activity in idiopathic intracranial hypertension: a 3-month follow-up study.**
J Neurol. 2010 Sep 19. [Epub ahead of print]

Skau M, Sander B, Milea D, Jensen R.

Department of Neurology, Danish Headache Center, Glostrup Hospital, University of Copenhagen, Nordre Ringvej 57, 2600, Glostrup, Denmark.

Idiopathic intracranial hypertension (IIH) is a disorder of raised intracranial pressure (ICP) in the absence of identifiable pathology. The purpose of this study was to evaluate the clinical presentation and monitor a 3-month course using frequent optical coherence tomography (OCT) evaluations, visual field testing and lumbar opening pressure measurements. A longitudinal study of 17 patients with newly diagnosed IIH and 20 healthy overweight controls were included in the study. Peripapillary retinal nerve fiber layer thickness (RNFLT) and retinal thickness (RT) measurements (Stratus OCT-3, fast RNFL 3.4 protocol), and Humphrey visual field testing were evaluated at regular intervals. Repeat lumbar puncture was performed at final visit (n = 13). The diagnostic delay was 3 months and initial symptoms were headache (94%), visual blurring (82%) and pulsatile tinnitus (65%). Complete clinical remission was achieved in 65%, partial in 29% and unchanged symptoms in 6%. Total average RNFLT and RT decreased significantly during the follow-up period (p < 0.0001 and p < 0.0001, respectively). Changes in RNFLT and RT correlated with improvements in visual field mean deviation (MD) (RNFLT: p = 0.006; RT: p = 0.03) and pattern standard deviation (PSD) (RNFLT: p = 0.002; RT: p = 0.003). In patients with weight-loss >3.5% of BMI, ICP decreased significantly (p = 0.0003). In patients with weight-loss <3.5% of BMI, changes in ICP were insignificant (p = 0.6). OCT combined with visual field testing may be a valuable objective tool to monitor IIH patients and the short term IIH outcome is positive. Weight-loss is the main predictor of a favorable outcome with respect to CSF pressure.

**Multimodality treatment of intracranial dural arteriovenous fistulas in the onyx era: a single center experience.**

Natarajan SK, Ghodke B, Kim LJ, Hallam DK, Britz GW, Sekhar LN.

Department of Neurological Surgery, Harborview Medical Center, University of Washington, Seattle, Washington, USA.

BACKGROUND: The results of treatment of intracranial dural arteriovenous fistulas (DAVFs) since Onyx became available as an embolic agent at our institution is reported. An algorithm is presented for treatment of DAVFs with Onyx, and the role of endovascular transvenous, surgical, and radiosurgical approaches are presented.

METHODS: Thirty-two patients with DAVFs treated between November 2005 and November 2008 by endovascular embolization, surgery, or radiosurgery were identified by a retrospective chart review. Treatment strategies were based on the location or complexity of the fistula and the patient’s clinical status. Data collected included DAVF characteristics, obliteration rates, complications, and outcomes. The results were analyzed and correlated with the treatment modality.

RESULTS: Presenting symptoms were as follows: hemorrhage (n = 12 patients), headaches (n = 12), tinnitus (n = 5), orbital symptoms (n = 7), and seizures (n = 1). Thirty patients were treated by endovascular embolization (transarterial only with Onyx-21, transvenous only with platinum coils-6, transarterial [Onyx] and transvenous [coils]-3). Five patients (4 after incomplete/failed embolization) had surgical excision of the fistula. Three patients were treated with Gamma Knife radiosurgery (primary-1, 2 after incomplete/failed embolization). The locations of the fistulas were transverse sigmoid (10 patients), petrotenorial (7 patients), indirect carotid cavernous fistula (7 patients), parasagittal/falcine (3 patients), middle fossa dura (3 patients), torcula (1 patient), and anterior fossa dura (1 patient).
The distribution of patients according to Borden classification was I-6, II-13, and III-13. Complete obliteration of the fistula was achieved in 26/32 (81%) patients after multimodal treatment. All surgical cases had complete obliteration. In the high-risk group with cortical venous reflux, 23/26 (89%) patients were cured. Endovascular complications included a stuck microcatheter tip with fracture of the tip in two patients and cranial nerves V and VII palsies in one patient. At last follow-up (range 1-36 months), 24 patients had modified Rankin score of 0-2, 5 patients had modified Rankin score of 3-5, and 3 patients were dead. Two patients died during admission due to the insult of the hemorrhage, and one died after an accidental fall with subsequent traumatic subdural hematoma.

CONCLUSIONS: Multimodality treatment of DAVFs has high success rates for cure at our center. Transarterial embolization with Onyx has become the primary treatment for intracranial DAVFs at our center and is associated with high safety profile and efficacy. Transvenous coil embolization is still preferred in DAVFs with supply from arterial branches supplying cranial nerves, predominant internal carotid artery feeders and potential extracranial-intracranial collateral anastomosis. In our series, patients with incompletely treated DAVFs were treated with surgery and those with partially treated type I fistulas had radiosurgery for palliation.
METHODS: Twenty-one patients presented consecutively with pulsating tinnitus as leading symptom and with angiographically proven dAVF at the transverse or sigmoid sinus (Borden I). Nine patients underwent different types of endovascular embolisation, and 12 patients were not treated. After a median follow-up period of 2.3 years, outcome was evaluated by assessing the patients' symptoms and scores on the mRS, EQ-5D, SF-36 and HIT-6 scales.

RESULTS: Complete long-term closure of the dAVF was achieved in two out of nine cases; subtotal occlusion was found in seven patients. Pulsating tinnitus persisted less frequently in treated than in untreated patients. Neurologic symptoms occurred in both groups. Neither these findings nor the clinical outcome and scores on the quality-of-life scales varied substantially between the two groups.

CONCLUSION: Partial treatment did not resolve the clinical symptoms of patients with „benign“ dural AVF in the follow-up and was not clearly superior to conservative management. These results suggest that embolisation should be offered only if there is a possibility of a complete cure without major perinterventional risks. Further studies should be performed to assess the risk-benefit ratio of pursuing more aggressive treatment strategies in patients with unbearable symptoms.

Otol Neurotol. 2010 Aug 20. [Epub ahead of print]


Depts of *Neurosurgery, and Otolaryngology, Uppsala University Hospital, Uppsala, Sweden.

OBJECTIVE: To analyze surgical treatment and outcome in patients with facial neuromas at a tertiary referral hospital.

STUDY DESIGN: A chart review of 26 patients treated between 1971 and 2006, with questionnaire follow-up ranging from 2 to 19 years. All patients except one were operated with radical tumor removal approaches.

RESULTS: Approximately 54% of the patients presented with symptoms related to the VIIth cranial nerve (facial palsy and facial spasm), 58% with symptoms related to the VIIIth cranial nerve (hearing deficit, tinnitus, and vertigo), and 8% related to the Vth cranial nerve (facial pain and facial sensory deficit). Approximately 39% presented with no facial symptoms. Twenty-one patients received a facial nerve graft from the greater auricular nerve or the sural nerve; 1 patient had an accessory-facial anastomosis. One patient had a subtotal tumor removal preserving the facial nerve. Three patients were not grafted. Most tumors (88%) affect the geniculate ganglion. Approximately 82% of the grafted patients regained a House-Brackmann facial nerve function (HB) grade III; 14% regained HB grades IV to V. No serious morbidity or mortality was reported. No recurrences have been reported where a total tumor removal was performed.

CONCLUSION: Surgical removal of facial neuroma is a safe procedure with a low complication rate and a low recurrence rate. First symptoms are diverse and are predominantly derived from the facial and vestibulocochlear nerve. Facial nerve grafting is reliable, giving the patient an acceptable facial nerve function (HB III).

Expression and Translocation of Aquaporin-2 in the Endolymphatic Sac in Patients with Meniere's Disease.


From the Dept of Otolaryngology, Osaka University, School of Medicine and The Dept of Neuroanatomy, Osaka City University, School of Medicine, Osaka, Japan.

Meniere's disease characterized by episodic vertigo, fluctuating hearing loss and tinnitus, can occur under conditions of stress. Its pathology was first revealed to be inner ear hydrops through temporal bone studies in 1938.
Although its pathogenesis has been proposed to be a disorder of water transport in the inner ear since then, it remains unsolved until now. The recent study revealed that both plasma stress hormone, vasopressin (pAVP) and its receptor, V2 (V2R) expression in the inner ear endolymphatic sac were significantly higher in Meniere's patients. In the present study, to link V2R-related molecules and inner ear hydrops, we examined V2R-linked water channel molecule, aquaporin-2 (AQP2) expression and translocation in human endolymphatic sac. AQP2 mRNA expression in the endolymphatic sac was significantly higher in Meniere’s patients by using real-time PCR, further confirmed by western blotting. AQP2-like immunoreactivity (-LIR) was translocated from luminal to basolateral side with endosomal trapping in the endolymphatic sac at the time of AVP exposure in human endolymphatic sac tissue culture. The similar AQP2-LIR translocation was also demonstrated by forskolin and blocked by vasopressin/V2R specific antagonist, OPC31260 and protein kinase A (PKA) specific antagonists, H-89 and KT-5720. We concluded that in the pathogenesis of inner ear hydrops resulting in Meniere's attacks, pAVP elevation due to stress and subsequent V2R-cyclic AMP-PKA-AQP2 activation and endosomal trapping of AQP2 in the endolymphatic sac might be important as a basis of this disease. Further experimental and clinical studies will be needed to better clarify the neuroscientific relationship between stress and Meniere’s disease.

Early vestibular physical therapy rehabilitation for Meniere's disease.

Gottshall KR, Topp SG, Hoffer ME.
Department of Otolaryngology, Naval Medical Center San Diego, Spatial Orientation Center, 34520 Bob Wilson Drive, Suite 200, San Diego, CA 92134, USA.

Meniere disease includes symptoms of fluctuating hearing loss, tinnitus, and subjective ear fullness accompanied by episodic vertigo. Along with these symptoms, patients with chronic Meniere often develop symptoms of disequilibrium and unsteadiness that extend beyond the episodic attacks and contribute to the total disability and reduced quality of life attributed to the disease. Vestibular rehabilitation physical therapy has been used only after vestibular ablation has stabilized the vestibular loss, and for patients stably managed on medical therapy who exhibit no fluctuation in symptoms. This article reviews the data substantiating current applications of vestibular therapy, including improvements in subjective and objective balance outcome measures, and explores the possible extension of vestibular rehabilitation to treatment of patients exhibiting continued fluctuating vestibular loss.

Endolymphatic sac shunt, labyrinthectomy, and vestibular nerve section in Meniere’s disease.

Teufert KB, Doherty J.
House Ear Institute, Los Angeles, CA, USA. KTeufert@hei.org

Medical treatment for Meniere's disease is effective in controlling vertigo for approximately 85% of patients. However, when disabling vertigo continues, surgical therapy is indicated. Several surgical approaches are performed to control the symptoms of peripheral vestibular disorders refractory to medical measures, each procedure having many technical variations. Surgery is usually reserved for patients with disabling vertigo. Here, the authors discuss surgical options for vertigo control in Meniere’s disease and review the literature on outcomes of these management options. The authors discuss endolymphatic sac shunt (ie, endolymphatic mastoid shunt), vestibular nerve section, cochleosacculotomy, and labyrinthectomy. When looking at data based on patient ratings, the authors find that surgery improves vertigo in endolymphatic sac shunt, vestibular nerve section, and labyrinthectomy groups and improves imbalance for the endolymphatic sac shunt and vestibular nerve section groups. Labyrinthectomy and translabyrinthine vestibular nerve section both offer excellent control of intractable vertigo. However, patients undergoing translabyrinthine vestibular nerve section are more likely to show improvement in imbalance and functional disability. This outcome is more likely for diagnoses other than Meniere’s disease. There are potential prognostic factors that can be helpful in
the preoperative or postoperative counseling of patients undergoing surgical treatment of vertigo. Patients who rate themselves as more disabled before surgery are less likely to achieve the best outcomes. Several other factors, such as duration of disease, contralateral tinnitus, eye disease, and allergy, may play a role.

**Physiologic effects on the vestibular system in Meniere’s disease.**

**Agrawal Y, Minor LB.**

Department of Otolaryngology-Head and Neck Surgery, The Johns Hopkins University School of Medicine, 601 North Caroline Street, Baltimore, MD 21287, USA. yagrawa1@jhmi.edu

Ménière syndrome is an inner ear disorder characterized by spontaneous attacks of vertigo, fluctuating low-frequency sensorineural hearing loss, aural fullness and tinnitus. When the syndrome is idiopathic and cannot be attributed to any other cause (eg, syphilis, immune-mediated inner ear disease, surgical trauma), it is referred to as Ménière disease. This article reviews the physiologic effects of Ménière disease on vestibular function, as measured by caloric, head impulse, and vestibular-evoked myogenic potential testing.

**Audiovestibular factors influencing quality of life in patients with conservatively managed sporadic vestibular schwannoma.**

**Lloyd SK, Kasbekar AV, Baguley DM, Moffat DA.**

University Department of Otolaryngology-Head and Neck Surgery, Central Manchester NHS Foundation Trust, Manchester Royal Infirmary, Manchester, UK. sklloyd@me.com

OBJECTIVES: To measure the health-related quality of life (QoL) of patients undergoing conservative management of a vestibular schwannoma and to identify audiovestibular factors that influence health-related QoL.

STUDY DESIGN: Cross-sectional case-control study.

INTERVENTION: Adult patients undergoing conservative management of a sporadic vestibular schwannoma were identified from a prospectively updated database. Each patient was asked to complete a series of questionnaires, including the Short Form 36 health-related QoL instrument, the Hearing Handicap Inventory, the Tinnitus Handicap Inventory, and the Dizziness Handicap Inventory. The QoL data obtained were compared with UK normal data. Multiple linear regression was performed to identify audiovestibular factors influencing QoL.

PATIENTS: Of 241 patients still undergoing conservative management, 165 completed the questionnaires. The mean age was 66.6 years. Mean duration of follow-up was 5.7 years.

RESULTS: Physical component summary scores were significantly lower than those of the normal population. Mental component summary scores were significantly above the normal population. Regression analysis showed that dizziness handicap score and age were strong predictors of physical component summary (both \( p < 0.0001 \)). Dizziness handicap score and tinnitus handicap score were significant predictors of mental component summary (\( p = 0.0004 \) and \( p = 0.027 \) respectively). However, the model only explained a small amount of the data, suggesting that there may be other factors influencing QoL.

CONCLUSION: Dizziness is the most significant audiovestibular predictor of QoL in patients with vestibular schwannomas. Tinnitus also has an impact on mental QoL. Hearing loss does not seem to influence QoL. Other factors such as illness perception may have an important role to play in determining QoL.
Meniere's disease: update of etiopathogenetic theories and proposal of a possible model of explanation.

Pirodda A, Brandolini C, Chiara Raimondi M, Gaetano Ferri G, Modugno GC, Borghi C.

Department of Specialistic Surgical & Anaesthesiological Sciences, ENT Section, S. Orsola Malpighi University Hospital, Bologna, Italy. antonio.pirodda@unibo.it

Meniere's Disease (MD) is an affection consisting of an association of sensorineural hearing loss, tinnitus and vertigo initially presenting by crises. A review of the most considered possible causative factors and pathophysiologic interpretations allows us to underline the uncertainties which still exist about the genesis of this illness. We propose a mechanistic model based on the effect of a haemodynamic imbalance leading to transient ischaemia which could have an effect on the pH of the inner ear as well as on the work of the inner ear proton pumps. It is hypothesized that under ischaemic conditions and consequent metabolic acidity a preserved proton pump activity can generate an overload of anions in the endolymphatic partition, which is a closed system, thus resulting in an enhancement of osmolarity and consequently in the formation of a hydrops resulting in the development of fluctuating hearing loss, tinnitus and vertigo which characterize Meniere’s Disease.

The impact of tinnitus and vertigo on patient-perceived quality of life after cerebellopontine angle surgery.
Neurosurgery. 2010 Sep;67(3):601-9; discussion 609-10.

Grauvogel J, Kaminsky J, Rosahl SK.

Dept of Neurosurgery, Albert-Ludwigs University, Freiburg, Germany. juergen.grauvogel@uniklinik-freiburg.de

BACKGROUND: Quality of life (QOL) has come into focus after treatment for cerebellopontine angle (CPA) lesions.
OBJECTIVE: This study compared subjective (tinnitus, vertigo) and objective (hearing loss, facial palsy) results of CPA surgery with patient-perceived impairment of QOL.
METHODS: A retrospective analysis of a consecutive series of 48 patients operated on for either a vestibular schwannoma or a meningioma in the CPA was performed. Patient's subjective impairment of QOL by tinnitus, vertigo, hearing loss, and facial nerve palsy was assessed by a visual analog scale (VAS). Objective facial nerve and hearing function were determined using House-Brackmann and Gardner-Robertson classification systems, respectively.
RESULTS: The return rate of questionnaires was 64.4%, with mean follow-up time of 417.2 (+/- 46.4) days. Mean preoperative tinnitus score was 2.5 (+/- 0.5) and increased to 4.6 (+/- 0.7) postoperatively (P < .01). The vertigo score increased from 2.0 (+/- 0.3) to 5.8 (+/- 0.6) (P < .001). Pre- and postoperative values for hearing loss were 3.4 (+/- 0.6) and 5.9 (+/- 0.7), respectively (P < .01), and for facial nerve palsy 0.7 (+/- 0.4) compared with 3.1 (+/- 0.6) postoperatively (P < .01). House-Brackmann grade 1 or 2 was determined in 87.1% of patients before and in 80.6% after surgery. Serviceable hearing (Gardner-Robertson classes I-III) was found in 75% before and in 64.3% after surgery.
CONCLUSION: Preservation of facial nerve and hearing function are not the only important criteria defining QOL after CPA surgery. Tinnitus and vertigo may have a significant underestimated impact on the patient's postoperative course and QOL.

Contemporary perspectives on the pathophysiology of Meniere's disease: implications for treatment.

Semaan MT, Megerian CA

Dept of Otolaryngology-Head and Neck Surgery, Univ Hospitals Case Medical Center, Cleveland, Ohio, USA.

PURPOSE OF REVIEW: Meniere's disease is characterized by episodic vertigo, fluctuating hearing loss, aural fullness and tinnitus. Endolymphatic hydrops, found on post-mortem examination, is the histologic
hallmark. Recent research suggests that endolymphatic hydrops results from cytochemical perturbations of unknown etiology that lead to disturbance of the normal endolymphatic fluid homeostasis. This consequent hydropic state or the associated cytochemical perturbations appears to create a neurotoxic environment that ultimately leads to spiral ganglion cell death likely via the apoptotic mechanism. This review highlights some of the recent advances in the understanding of the pathophysiology of endolymphatic hydrops and progressive cochleovestibular deterioration, with emphasis placed on its potential therapeutic implications.

RECENT FINDINGS: Recent evidence supports that endolymphatic hydrops is possibly an epiphenomenon, and is preceded by perturbation of the normal ionic transport regulatory mechanisms. Furthermore, chronic cochleovestibular deterioration appears to be the result of an excitotoxic response to chronic hydrops. A recently described animal model, the Phex mouse, carrying a mutation in the Phex Hyp-Duk gene, provides a novel insight to genetically regulated postnatal endolymphatic hydrops and a useful tool to expand our understanding.

SUMMARY: Despite encouraging recent advances, there are considerable challenges that remain in the development of targeted therapeutic interventions that may offer new avenues of neuroprotection in known cases of Meniere’s disease. These advances will hopefully provide pharmacotherapeutic interventions aimed at preventing progressive cochleovestibular dysfunction.


Hong L, Kawaguchi Y.

*Dept of Orthopaedics, Peking University First Hospital, Beijing, China; Dept of Orthopaedic Surgery, Faculty of Medicine, University of Toyama, Toyama, Japan.

STUDY DESIGN: Retrospective study.

OBJECTIVE: To investigate the clinical effectiveness of polyetheretherketone (PEEK) cages-assisted anterior cervical discectomy and fusion (ACDF) to treat cervical spondylosis with sympathetic symptoms.

SUMMARY OF BACKGROUND DATA: The diagnosis and treatment of cervical spondylosis with sympathetic symptoms has remained controversial. To date, few reports have focused on the surgical efficacy of cervical spondylosis with sympathetic symptoms.

METHODS: Retrospective analysis was undertaken for 39 patients who were diagnosed as cervical spondylosis with sympathetic symptoms and underwent ACDF with PEEK cages. They were followed up for at least 1 year. The mean follow-up was 15.6 months. Radiographs obtained before surgery, after surgery, and at the final follow-up were assessed for quality of fusion. The sympathetic symptoms including vertigo, headache, tinnitus, nausea and vomiting, heart throb, hypomnesia, and gastroenterologic discomfort were scored by 20-point system preoperatively, 2 months postoperatively, and at the final follow-up. The recovery rate and clinical satisfaction rate were also evaluated. Surgical complications were also assessed.

RESULTS: Radiographs of the cervical spine at the last follow-up revealed a solid fusion with no signs of a pseudoarthrosis in 36 cases. In 2 patients delayed union and bony fusion were achieved at 9 and 11 months. Pseudoarthrosis was found in 1 case but the patient had no symptoms. The sympathetic symptoms improved in all patients and the score was significantly improved after surgery. There was one patient who had cerebral spinal fluid leakage but he recovered 1 week after surgery. Two patients felt a mild swallowing discomfort, but it disappeared within 1 month after surgery. Subcutaneous hematoma occurred in one patient due to obstructed drainage. It was cleared 2 days after surgery.

CONCLUSIONS: Cervical spondylosis patients with sympathetic symptoms may be managed successfully with ACDF using PEEK cages. Successful clinical results regarding symptom improvement and general satisfaction with the surgical procedure depend on obtaining successful decompression and radiographic fusion.
**Comparison of an Internet-based Guided Self-help and a Group Therapy for Chronic Tinnitus (MINT)**

<table>
<thead>
<tr>
<th>Current status</th>
<th>currently recruiting participants</th>
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<tr>
<td>Sponsors and collaborators</td>
<td>Johannes Gutenberg University Mainz; Linköping University</td>
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<tr>
<td>Information provided by</td>
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<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT01205906</td>
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<tr>
<td>Purpose</td>
<td>The aim of this study is to compare the efficacy of an internet-based guided self-help training for chronic tinnitus with a well-established outpatient group therapy and a discussion forum group.</td>
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<tr>
<td>Condition(s)</td>
<td>Tinnitus</td>
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</tbody>
</table>
| Interventions        | Behavioral: Internet-based guided self-help for tinnitus  
Behavioral: Cognitive-behavior group therapy for tinnitus  
Other: Internet discussion forum |
| Study type and design | Interventional;  
Allocation: Randomized  
Endpoint Classification: Efficacy Study  
Intervention Model: Crossover Assignment  
Masking: Open Label  
Primary Purpose: Treatment |
| Official title       | Comparison of the Efficacy of an Internet-based Self-help Training and a Well-established Outpatient Group Therapy for the Treatment of Chronic Tinnitus: A Randomized Controlled Trial |
| Arms                 | Internet-based guided self-help: Experimental  
This self-help training is exclusively provided via Internet over a period of 10 weeks. The treatment is based on the cognitive-behavioral approach and consists of 18 modules with helpful strategies to cope with tinnitus (e.g., applied relaxation, positive imagery, attention shift exercises, cognitive restructuring, sleep management, concentration management.). All modules include an information text, detailed practice instructions, worksheets and homework assignments. At the end of each treatment week, there is an e-mail contact between the participants and their therapist. The participants report on their work with the modules and if they had encountered any problems. The therapist provides feedback, support and recommendations on how to proceed.  
Cognitive-behavior group therapy: Experimental  
This well-established, cognitive-behavior group therapy was developed by Hiller and Haerkötter (2005) and consists of 10 weekly group sessions of 90 minutes. The strictly manualized program includes the following components focusing on the special needs of chronic tinnitus patients: Education, relaxation techniques, cognitive restructuring, the role of attentional processes for tinnitus perception, analysis of avoidance behaviors, tinnitus and the health care system as well as relapse prevention. For each session participants receive |
written materials, exercises and homework assignments to enhance understanding and to transfer the new information into the daily routine.

Discussion forum group: Active Comparator
To the participants of the control group the group therapy or the internet-based self-help after waiting time of 10 weeks is offered. During the waiting period participants receive access to a tinnitus online discussion forum.

Assigned Interventions:
Behavioral: Internet-based guided self-help for tinnitus
  Internet-based self-help for tinnitus: provided via Internet, duration of 10 weeks

Behavioral: Cognitive-behavior group therapy for tinnitus
  Cognitive-behavior group therapy for tinnitus: weekly group sessions of 90 minutes, duration of 10 weeks

Other: Internet discussion forum
  Tinnitus-specific internet discussion forum over 10 weeks (no therapeutic intervention)

Detailed Description
Chronic tinnitus can result in significant psychological suffering and reduce quality of life. Cognitive behavioral therapy (CBT) has been shown to be effective in decreasing the impairment caused by tinnitus. One recent way delivering CBT is an internet-based self-help intervention. Internet interventions for patients with chronic tinnitus, developed by Swedish scientists, showed promising results (Andersson et al., 2002; Kaldo et al., 2007; Kaldo et al., 2008). The main purpose of this study is to compare the efficacy of this internet-based self-help training for chronic tinnitus with a traditional well-established CBT group treatment and with a discussion forum group in a randomized controlled trial. Secondary goals are a process evaluation of both treatments, the identification of predictors of treatment success, an estimation of the cost-effectiveness of each treatment and the validation of the Tinnitus Cognitions Questionnaire (T-Cog; Hiller & Haerkötter, 2005).

Primary Outcomes
- Tinnitus Handicap Inventory (THI; Newman, Jacobson, & Spitzer, 1996; German version: Kleinjung et al., 2007) [ Time Frame: 18 months ] [ Designated as safety issue: No ]
  - The measure assesses tinnitus-related disability and handicap.
- MINI-Tinnitus Questionnaire (Mini-TQ; Hiller & Goebel, 2004) [ Time Frame: 18 months ] [ Designated as safety issue: No ]
  - The measure is a short version of the Tinnitus Questionnaire (TQ, Goebel & Hiller, 1998), to assess tinnitus-related psychological distress

Secondary Outcomes
- Hospital Anxiety and Depression Scale (HADS-D; Zigmond & Snith, 1983; German version: Herrmann-Lingen, Buss, & Snith, 2005) [ Time Frame: 18 months ] [ Designated as safety issue: No ]
  - The measure assesses depression and anxiety.
- Insomnia Severity Index (ISI; Bastien, Vallière, & Morin, 2001; German version: Pillmann, 2004) [ Time Frame: 18 months ] [ Designated as safety issue: No ]
  - The measure assesses the quality of sleep (sleep duration, sleep quality and negative impact on daily functioning).
Tinnitus Cognitions Questionnaire (T-Cog; Hiller & Haerkötter, 2005) [Time Frame: 18 months] [Designated as safety issue: No]
- The measure assesses dysfunctional beliefs and cognitions regarding the tinnitus.

Tinnitus Acceptance Questionnaire (TAQ; Westin, Hayes, & Andersson, 2008; self-translated) [Time Frame: 18 months] [Designated as safety issue: No]
- The measure assesses psychological acceptance of the tinnitus.

Anxiety Sensitivity Index - 3 (ASI-3; Taylor et al., 2007; German version: Kemper, Ziegler, & Taylor, 2007) [Time Frame: 18 months] [Designated as safety issue: No]
- The measure assesses the fear of anxiety-related sensations.

Fear Avoidance Questionnaire (FAQ; self-developed measure) [Time Frame: 18 months] [Designated as safety issue: No]
- The measure assesses fear-avoidance beliefs and behavior.

Working Alliance Inventory - Short Revised (WAI-SR; Horvath & Greenberg, 1986, 1989; German version: Wilmers et al., 2008) [Time Frame: 2 months] [Designated as safety issue: No]
- The measure assesses three aspects of the therapeutic alliance (development of an affective bond, agreement on the tasks of therapy and agreement on the goals of therapy).

Credibility Scale (Devilly & Borkovec, 2000; self-translated and adapted to an intervention for tinnitus) [Time Frame: 6 months] [Designated as safety issue: No]
- The scale assesses treatment credibility.

Therapy Expectancy Scale (self-developed) [Time Frame: baseline] [Designated as safety issue: No]
- The scale assesses therapy expectancy.

Therapy Satisfaction Scale (self-developed) [Time Frame: week 10] [Designated as safety issue: No]
- The scale assesses treatment satisfaction.

Web Screening Questionnaire for Common Mental Disorders (WSQ; Donker, van Straten, Marks, & Cuijpers, 2009; self-translated German version) [Time Frame: 3 months] [Designated as safety issue: No]
- The questionnaire screens for depressive disorder, alcohol abuse/dependence, GAD, PTSD, social phobia, panic disorder, agoraphobia, specific phobia, and OCD.

Big Five Inventory (BFI-10; Rammstedt & John, 2007; German version: Rammstedt & John, 2007) [Time Frame: baseline] [Designated as safety issue: No]
- The measure is the short version of the Big Five Inventory (BFI; John, Donahue, & Kentle, 1991) and assesses the five personality traits extraversion, agreeableness, conscientiousness, neuroticism, and openness.
### Process evaluation items (self-developed) [ Time Frame: 18 months ]
- 10 items assessing tinnitus loudness, tinnitus annoyance, perceived control, general mood, tinnitus acceptance, social functioning, behavioral avoidance and fear of sounds as well as the use of learned methods during the last week.

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<td>Eligibility Inclusion Criteria</td>
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  - Age of at least 18 years
  - Chronic tinnitus for at least 6 months
  - Medical examination of tinnitus by an ear, nose and throat physician (ENT)
  - Scoring 18 or above on the Tinnitus Handicap Inventory (THI) or scoring 12 or above in the Mini-Tinnitus Questionnaire (Mini-TQ)
  - Not currently receiving psychological treatment for tinnitus
  - Being able to access the Internet and print instructions
  - Sufficient knowledge of the German language to read and follow the internet-based self-help training
  - Being able to attend weekly group sessions in the Outpatient Department of the Psychological Institute of the University of Mainz, Germany
  - Sufficient time and motivation to work on the treatment programs

| Eligibility Exclusion Criteria |
  - Tinnitus caused by any other general medical condition or otologic disease (e.g., active Meniere’s Disease)
  - Clinical diagnosis of any severe mental disorder (especially a severe depressive disorder, suicidality, acute psychosis)
  - Clinical diagnosis of Dementia or another severe organic cerebral disorder
  - Clinical diagnosis of substance-related addiction/abuse

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<th>Contact</th>
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<tr>
<td>Maria Kleinstäuber, Ph.D.; phone +49-6131-3939201; <a href="mailto:kleinsta@uni-mainz.de">kleinsta@uni-mainz.de</a></td>
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<tr>
<td>Cornelia Weise, Ph.D.; <a href="mailto:cornelia.weise@liu.se">cornelia.weise@liu.se</a></td>
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<td>Department of Clinical Psychology and Psychotherapy, Johannes Gutenberg University Mainz, Rheinland-Pfalz, Germany, D-55122</td>
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<td>Wolfgang Hiller, Ph.D.</td>
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<td>Maria Kleinstäuber PhD</td>
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<td>Johannes Gutenberg University Mainz, Department of Clinical Psychology &amp; Psychotherapy ( Maria Kleinstäuber, PhD )</td>
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### Internet-based Guided Self-help for Chronic Tinnitus (TITUS)

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<th>Study ID Numbers</th>
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<td>Last Updated</td>
<td>September 20, 2010</td>
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<td>ClinicalTrials.gov Identifier</td>
<td>NCT01205906</td>
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<td>Health Authority</td>
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**Current status**
- currently recruiting participants

**Sponsors and collaborators**
- Johannes Gutenberg University Mainz; Linköping University

**Information provided by**
- Johannes Gutenberg University Mainz

**ClinicalTrials.gov Identifier**
- NCT01205919

**Purpose**
The purpose of this study is to determine the efficacy of a cognitive behavioral guided self-help training provided via the internet on tinnitus distress in a German sample.

**Condition(s)**
- Tinnitus

**Interventions**
- Behavioral: Internet-based guided self-help for tinnitus
- Other: Internet discussion forum

**Study type and design**
- Interventional;
  - Allocation: Randomized
  - Control: Active Control
  - Endpoint Classification: Efficacy Study
  - Intervention Model: Crossover Assignment
  - Masking: Open Label
  - Primary Purpose: Treatment

**Official title**
- Efficacy of an Internet-based Guided Self-help Training for Chronic Tinnitus: A Randomized Controlled Trial

**Arms**
- Internet-based self-help: Experimental
  - This self-help training is exclusively provided via Internet over a period of 10 weeks. The treatment is based on the cognitive-behavioral approach and consists of 18 modules with helpful strategies to cope with tinnitus (e.g., applied relaxation, positive imagery, attention shift exercises, cognitive restructuring, sleep management, concentration management). All modules include an information text, detailed practice instructions, worksheets and homework assignments. At the end of each treatment week, there is an e-mail contact between the participants and their therapist. The participants report on their work with the modules and if they had encountered any problems. The therapist provides feedback, support and recommendations on how to proceed.
Discussion forum group: Active Comparator
To the participants of the control group the internet-based self-help after waiting time of 10 weeks is offered. During the waiting period participants receive access to a tinnitus online discussion forum.

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<th>Detailed Description</th>
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<tr>
<td>Long waiting periods and the deficiency of outpatient therapies stimulated the development of internet-based interventions for a variety of mental disorders during the last years. A Swedish research group developed an internet-based self-help training for patients with chronic tinnitus showing promising results (Andersson et al., 2002; Kaldo et al., 2007; Kaldo et al., 2008). This self-help training was now adapted for German-speaking patients. The present study evaluates the efficacy of this treatment in a randomized controlled trial conducted in Germany. Further aims are a process evaluation of the treatment and the identification of predictors of efficacy.</td>
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<tbody>
<tr>
<td>Tinnitus Handicap Inventory (THI; Newman, Jacobson, &amp; Spitzer, 1996; German version: Kleinjung et al., 2007) [ Time Frame: 18 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>- The measure assesses tinnitus-related disability and handicap.</td>
</tr>
<tr>
<td>MINI-Tinnitus Questionnaire (Mini-TQ; Hiller &amp; Goebel, 2004) [ Time Frame: 18 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>- The measure is a short version of the Tinnitus Questionnaire (TQ, Goebel &amp; Hiller, 1998), to assess tinnitus-related psychological distress.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Anxiety and Depression Scale (HADS-D; Zigmond &amp; Snaith, 1983; German version: Herrmann-Lingen, Buss, &amp; Snaith, 2005) [ Time Frame: 18 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>- The measure assesses depression and anxiety.</td>
</tr>
<tr>
<td>Insomnia Severity Index (ISI; Bastien, Vallière, &amp; Morin, 2001; German version: Pillmann, 2004) [ Time Frame: 18 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>- The measure assesses the quality of sleep (sleep duration, sleep quality and negative impact on daily functioning).</td>
</tr>
<tr>
<td>Tinnitus Cognitions Questionnaire (T-Cog; Hiller &amp; Haerkötter, 2005) [ Time Frame: 18 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>- The measure assesses dysfunctional beliefs and cognitions regarding the tinnitus.</td>
</tr>
<tr>
<td>Anxiety Sensitivity Index - 3 (ASI-3; Taylor et al., 2007; German version: Kemper, Ziegler, &amp; Taylor, 2007) [ Time Frame: 18 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>- The measure assesses the fear of anxiety-related sensations.</td>
</tr>
<tr>
<td>Fear Avoidance Questionnaire (FAQ; self-developed) [ Time Frame: 18 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>- The measure assesses fear-avoidance beliefs and behavior.</td>
</tr>
</tbody>
</table>
Working Alliance Inventory - Short Revised (WAI-SR; Horvath & Greenberg, 1986, 1989; German version: Wilmers et al., 2008) [Time Frame: 2 months] [Designated as safety issue: No]
- The measure assesses three aspects of the therapeutic alliance (development of an affective bond, agreement on the tasks of therapy and agreement on the goals of therapy).

Credibility Scale (Devilly & Borkovec, 2000; self-translated and adapted to an intervention for tinnitus) [Time Frame: 6 months] [Designated as safety issue: No]
- The scale assesses treatment credibility.

Therapy Expectancy Scale (self-developed) [Time Frame: baseline] [Designated as safety issue: No]
- The scale assesses treatment expectancy.

Therapy Satisfaction Scale (self-developed) [Time Frame: week 10] [Designated as safety issue: No]
- The scale assesses treatment satisfaction.

Web Screening Questionnaire for Common Mental Disorders (WSQ; Donker, van Straten, Marks, & Cuijpers, 2009; self-translated German version) [Time Frame: 3 months] [Designated as safety issue: No]
- The questionnaire screens for depressive disorder, alcohol abuse/dependence, GAD, PTSD, social phobia, panic disorder, agoraphobia, specific phobia, and OCD.

Big Five Inventory (BFI-10; Rammstedt & John, 2007; German version: Rammstedt & John, 2007) [Time Frame: baseline] [Designated as safety issue: No]
- The measure is the short version of the Big Five Inventory (BFI; John, Donahue, & Kentle, 1991) and assesses the five personality traits extraversion, agreeableness, conscientiousness, neuroticism, and openness.

Process evaluation items (self-developed) [Time Frame: 18 months] [Designated as safety issue: No]
- 10 items assess tinnitus loudness, tinnitus annoyance, perceived control, general mood, tinnitus acceptance, social functioning, behavioral avoidance and fear of sounds as well as the use of learned methods during the last week.

Tinnitus Acceptance Questionnaire (TAQ; Westin, Hayes, & Andersson, 2008; self-translated) [Time Frame: 18 months] [Designated as safety issue: No]
- The measure assesses psychological acceptance of the tinnitus.

<table>
<thead>
<tr>
<th>Estimated Enrollment</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study start date</td>
<td>May 2010</td>
</tr>
<tr>
<td>Estimated Study Completion Date:</td>
<td>October 2011</td>
</tr>
<tr>
<td>Estimated Primary Completion Date:</td>
<td>October 2010 (Final data collection date for primary outcome measure)</td>
</tr>
<tr>
<td>Participants (age)</td>
<td>18 years and older</td>
</tr>
<tr>
<td>Gender</td>
<td>both</td>
</tr>
</tbody>
</table>
## Eligibility Inclusion Criteria
- Age of at least 18 years
- Chronic tinnitus for at least 6 months
- Medical examination of tinnitus by an ear, nose and throat physician (ENT)
- Scoring 38 or above on the Tinnitus Handicap Inventory (THI) or scoring 13 or above on the Mini-Tinnitus Questionnaire (Mini-TQ)
- Not currently receiving psychological treatment for tinnitus
- Being able to access the Internet and print instructions
- Sufficient knowledge of the German language to read and follow the Internet-based self-help program

## Eligibility Exclusion Criteria
- Tinnitus caused by any other general medical condition or otologic disease (e.g., active Meniere’s Disease)
- Clinical diagnosis of any severe mental disorder (especially a severe depressive disorder, suicidality, acute psychosis)
- Clinical diagnosis of Dementia or another severe organic cerebral disorder
- Clinical diagnosis of substance-related addiction/abuse

## Contact
- Cornelia Weise, PhD; phone: +46-13-282188; cornelia.weise@liu.se
- Maria Kleinstäuber PhD; kleinsta@uni-mainz.de

## Locations
- Department of Behavioural Sciences and Learning, Linköping University, Linköping, Sweden, SE-58183

## Study chair
- Gerhard Andersson, PhD, Lonkoeping University

## Principal Investigator
- Cornelia Weise, PhD, Lonkoeping University

## Responsible Party
- Linkoeping University, Department of Behavioural Sciences and Learning (Cornelia Weise, Ph.D.)

## Study ID Numbers
- TITUS-110510

## Record first received
- September 17, 2010

## Last Updated
- September 20, 2010

## ClinicalTrials.gov Identifier
- NCT01205919

## Health Authority
- Germany: Deutsche Gesellschaft für Psychologie (DGPs)
### Task-Based Functional MRI (fMRI) in Patients With Severely Bothersome Tinnitus

<table>
<thead>
<tr>
<th>Current status</th>
<th>not yet recruiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>Washington University School of Medicine</td>
</tr>
<tr>
<td>Information provided by</td>
<td>Washington University School of Medicine</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT01172262</td>
</tr>
</tbody>
</table>

#### Purpose
Tinnitus is a poorly understood symptom that is often described either as ringing, clicking, ocean sounds, or nature sounds. There is no cure for tinnitus. Approximately 50 million Americans are affected with a small minority being severely affected. This study targets patients with tinnitus who are severely bothered. Through MRI the investigators plan to evaluate the cortical networks of the brain in hopes to better understand this complex process.

#### Condition(s)
Tinnitus

#### Interventions
Procedure: MRI

#### Study type and design
Observational; Observational Model: Cohort; Time Perspective: Prospective

#### Official title
Task-Based Functional MRI (fMRI) Exploration of the Cortical Attention Network in Patients With Severely Bothersome Tinnitus

#### Groups/Cohorts
Bothered Tinnitus
Either responds with a Global Tinnitus Scale of Moderately or Severely Bothered. Score >30 on the Tinnitus Handicap Index (THI).

#### Assigned Intervention(s)
Procedure: MRI
This is an observational study, no intervention will occur.
Other Name: This is an observational study, no intervention will occur.

#### Detailed Description
Tinnitus is the perceived sensation of sound without actual acoustic stimulation that affects 50 million Americans, with 15 million being significantly bothered. Using functional connectivity MRI (fcMRI), the investigators have found distinct differences in the cortical attention networks between patients with bothersome tinnitus and age-matched controls. These novel findings suggest that some of the classic and most disturbing characteristics of tinnitus result from derangements in cortical pathways. Using a validated task-based functional MRI (fMRI) paradigm developed at Washington University, the investigators will explore the ventral and dorsal frontoparietal cortical attention networks in patients with bothersome tinnitus and non-tinnitus controls. This will be an experimental task-based fMRI pilot study involving the neurocognitive and neuroimaging assessment of patients with severely bothersome tinnitus.

The investigators plan to perform a pilot study and enroll a total of 10 subjects to undergo task-based imaging. These results will be compared to a control (no tinnitus) cohort (n=35) that has already undergone task-based fMRI. This task-based paradigm will allow us to advance knowledge about the role of the attention, control, and other...
cortical networks in the development and maintenance of bothersome tinnitus. The investigators anticipate it will take one year to successfully enroll and test a total of 10 patients. All scans will be performed on the Washington University grounds.

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>Perform task based functional imaging on severely bothered tinnitus patients [Time Frame: Analysis will begin after a participant is finished with the study, we anticipate two weeks per patient for complete analysis. Multiple patients can be analyzed at concurrently.] [Designated as safety issue: No] - By undergoing a task based function MRI, we are able to delineate the various attention networks involved with tinnitus. By isolating these networks, insight will be gained on why bothered tinnitus patients have such difficulty.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Outcomes</td>
<td>Perform neurocognitive testing on severely bother tinnitus patients [Time Frame: Analysis will begin after a participant is finished with the study, we anticipate two weeks per patient for complete analysis. Multiple patients can be analyzed at concurrently.] [Designated as safety issue: No] - Through our previously experiences, we have found that those patients with severely bothersome tinnitus have difficulty with neurocognitive testing involving memory and attention.</td>
</tr>
</tbody>
</table>

<p>| Estimated Enrollment | 10 |
| Study start date | February 2011 |
| Estimated Study Completion Date | February 2012 |
| Estimated Primary Completion Date | February 2012 (Final data collection date for primary outcome measure) |
| Participants (age) | 18 to 60 years |
| Gender | both |
| Accepts Healthy Volunteers | no |
| Sampling Methods | Non-Probability Sample |
| Eligibility Inclusion Criteria | • Men and women between the ages of 18 to 60 years • Subjective, unilateral or bilateral, non-pulsatile tinnitus of 6 month’s duration or greater • Either “moderately bothered” or “severely bothered” on the Global Bothersome scale • Able to give informed consent • Able to read, write, speak and understand English fluently • If applicable, a negative urine pregnancy test • An audiogram within the past 12 months • THI score &gt;38 |</p>
<table>
<thead>
<tr>
<th>Eligibility Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients experiencing tinnitus related to cochlear implantation, retrocochlear lesion, Ménière’s Disease, or other known anatomic lesions of the ear and temporal bone</td>
</tr>
<tr>
<td>• Patients with hyperacusis or misophonia (hyper-sensitivity to noises)</td>
</tr>
<tr>
<td>• Patients with cardiac pacemakers, intracardiac lines, implanted medication pumps, implanted electrodes in the brain, or any other contraindication for MRI scan</td>
</tr>
<tr>
<td>• Patients with an acute or chronic unstable medical condition which, in the opinion of the investigator, would require stabilization prior to initiation of magnetic stimulation</td>
</tr>
<tr>
<td>• Patients with any active ear disease that, in the opinion of the PI, needs to be further evaluated</td>
</tr>
<tr>
<td>• Patients with symptoms of depression as evidenced by a score of 14 or greater on the Beck Depression Inventory</td>
</tr>
<tr>
<td>• Any psychiatric co-morbidity that may complicate the interpretation of study results</td>
</tr>
<tr>
<td>• Any tinnitus related to a Workman’s Compensation claim or litigation-related event</td>
</tr>
<tr>
<td>• Weight over 300 pounds</td>
</tr>
<tr>
<td>• A Mini-Mental Status Exam score less than 27</td>
</tr>
<tr>
<td>• Patients with a history of claustrophobia</td>
</tr>
<tr>
<td>• Inability to lay flat for 2 hour</td>
</tr>
<tr>
<td>• Active alcohol and/or drug dependence or history of alcohol and/or drug dependence within the last year</td>
</tr>
<tr>
<td>• Any medical condition that, in the opinion of the investigators, confounds study results or places the subject at greater risk</td>
</tr>
<tr>
<td>• Unable to provide informed consent</td>
</tr>
<tr>
<td>• Currently pregnant</td>
</tr>
</tbody>
</table>

**Contact**

Andre M Wineland, MD; phone: 001 3143625296; winelanda@ent.wustl.edu

Joyce Nicklaus, RN; phone: 0013143627508; NicklausJ@ent.wustl.edu

**Locations**

Washington University, St. Louis, Missouri, United States, 63110

**Principal Investigator**

Andre M Wineland, MD, Washington University School of Medicine

**Responsible Party**

Washington University (Andre M. Wineland, PI)

**Study ID Numbers**

AMW04292010, Bothersome Tinnitus

**Record first received**

July 23, 2010

**Last Updated**

July 28, 2010

**ClinicalTrials.gov Identifier**

NCT01172262

**Health Authority**

United States: Institutional Review Board
**Tinnitus Retraining Therapy Trial (TRTT)**

<table>
<thead>
<tr>
<th>Current status</th>
<th>not yet open for patient recruitment</th>
</tr>
</thead>
</table>
| Sponsors and collaborators | Johns Hopkins Bloomberg School of Public Health; National Institute on Deafness and other Communication Disorders (NIDCD)  
University of Alabama, Tuscaloosa  
David Grant U.S. Air Force Medical Center  
Wilford Hall Medical Center  
United States Naval Medical Center, San Diego  
United States Naval Medical Center, Portsmouth  
National Naval Medical Center  
Naval Hospital Camp Pendleton |
| Information provided by | Johns Hopkins Bloomberg School of Public Health |
| ClinicalTrials.gov Identifier | NCT01177137 |

**Purpose**
The primary purpose of the Tinnitus Retraining Therapy Trial (TRTT) is to assess the efficacy of tinnitus retraining therapy (TRT) as a treatment for severe debilitating tinnitus. TRT is a non-medical intervention that uses directive counseling (DC) and sound therapy (ST) to habituate the patient's associated negative emotional reactions to tinnitus, its perception, and ultimately, its impact on the patient's life.

**Condition(s)** Subjective Tinnitus

**Interventions**
- Device: Conventional sound generator (SG)
- Device: Placebo sound generator (placebo SG)
- Behavioral: Standard of Care (SC)
- Behavioral: Directive Counseling (DC)

**Phase** III

**Study type and design**
- Interventional;  
  Allocation: Randomized  
  Control: Dose Comparison  
  Endpoint Classification: Efficacy Study  
  Intervention Model: Parallel Assignment  
  Masking: Double Blind (Subject, Outcomes Assessor)  
  Primary Purpose: Treatment

**Official title** Tinnitus Retraining Therapy Trial

**Arms**
TRT: Experimental  
TRT includes treatment with a conventional sound generator (SG) and directive counseling (DC)  
Interventions:  
- Device: Conventional sound generator (SG)  
- Behavioral: Directive Counseling (DC)
Partial TRT
Partial TRT includes treatment with a placebo sound generator (placebo SG) and directive counseling (DC).

Interventions:
• Device: Placebo sound generator (placebo SG)
• Behavioral: Directive Counseling (DC)

Standard of Care (SC)
The standard of care arm includes care as typically delivered in US military medical centers
Intervention: Behavioral: Standard of Care (SC)

Assigned Intervention(s)
- Device: Conventional sound generator (SG)
  Conventional SGs: Tranquil model sound generators (General Hearing Instruments, Inc.) are outside-the-ear devices that generate low-level noise, which is set at or just below the patient’s mixing point (i.e., the noise level that just blends with the study participant’s tinnitus)
- Behavioral: Directive Counseling (DC)
  Directive Counseling (DC): two-hour educational session during which the patient is given information regarding the nature of the tinnitus problem and related problems such as hearing loss and sound intolerance; visual aids to review the audiological/tinnitus/ hyperacusis evaluation, provide instruction on anatomy and physiology of hearing and tinnitus, introduce the Jastreboff neurophysiological model of tinnitus and related concepts of habituation, and describe and recommend the use of ST and environmental sound in the habituation process.
- Device: Placebo sound generator (placebo SG)
  Tranquil model placebo sound generators (General Hearing Instruments, Inc.) are outside-the-ear devices that generate a sound different from the active devices.
- Behavioral: Directive Counseling (DC)
  Directive Counseling (DC): two-hour educational session during which the patient is given information regarding the nature of the tinnitus problem and related problems such as hearing loss and sound intolerance; visual aids to review the audiological/tinnitus/ hyperacusis evaluation, provide instruction on anatomy and physiology of hearing and tinnitus, introduce the Jastreboff neurophysiological model of tinnitus and related concepts of habituation, and describe and recommend the use of ST and environmental sound in the habituation process.

Behavioral: Standard of Care (SC)
The standard of care treatment will be similar to that typically provided to patients with severe tinnitus at participating military medical centers and as described in the American Speech-Language-Hearing Association (ASHA) Preferred Practice Patterns in Audiology (ASHA, 2006). Tinnitus management will be based on the patient’s complaints, history, audiologic evaluation, and self-assessment. The goal of the tinnitus management is to reduce negative cognitive, affective, physical, and behavioral reactions to tinnitus and to improve the patient’s well-being and quality of life. Specific treatment recommendations will be individualized to reflect the participant’s concerns and abilities, as well as his or her engagement in the decision-making process regarding treatment options.
### Detailed Description

The Tinnitus Retraining Therapy Trial (TRTT), funded by the National Institute of Deafness and Other Communication Disorders, is a multi-center randomized clinical trial testing the efficacy of tinnitus retraining therapy (TRT) versus standard-of-care (SC) treatment in individuals who have self-perceived intolerable tinnitus. TRT is a non-medical intervention that uses directive counseling (DC) and low-level sound therapy (ST) achieved through sound generators (SGs) to habituate the patient’s associated negative emotional reactions (annoyance) to tinnitus, its perception (awareness) and, ultimately, its impact on the participant’s life. Study participants will include active and retired military personnel of the U. S. Armed Forces and their dependents who suffer from severe tinnitus. The study will be conducted at flagship Air Force, and Navy Medical Centers.

This trial will evaluate the efficacy of TRT and its components (DC and ST) versus the standard of care (SC) as administered in the military by comparing the efficacy of:

1. TRT (DC and ST achieved using conventional sound generators) versus SC;
2. TRT versus partial TRT (DC and placebo sound generators) to evaluate the separate effect of sound therapy, under the assumption that placebo noise generator will not provide any meaningful sound therapy beyond that found in SC;
3. Partial TRT versus SC to evaluate the separate effect of DC.

Eligibility will be determined at the Baseline Eligibility Visit, which will consist of a medical and tinnitus history, physical examination, and baseline audiological/tinnitus/hyperacusis evaluation. Study participants will also complete a series of quality of life and psychological profile tests. Study Audiologists will administer the randomly assigned treatment. Follow-up visits at Clinical Centers will take place at 3, 6, 12, and 18 months and include completion of tinnitus outcome questionnaires at all visits. Psychometric testing and audiological/tinnitus/hyperacusis evaluation will take place at the 6, 12, and 18 month visits.

The primary outcome to be measured in the TRTT will be change in scores on the Tinnitus Questionnaire (TQ) longitudinally assessed between baseline and follow-up (i.e., at 3, 6, 12 and 18 months following treatment). Secondary outcomes include changes in the sub-scales of the TQ, change in scores from the Tinnitus Handicap Inventory (THI), Tinnitus Reaction Questionnaire (TRQ), and TRT visual analogue scales, and change in the Digit Symbol Substitution Test (DSST). Psychometric secondary outcomes also include change in psychoacoustic variables related to the tinnitus sensation, including tinnitus pitch and loudness match, and loudness discomfort level.

The TRTT is designed to have sufficient power to detect a minimal clinically important difference in the Tinnitus Questionnaire (TQ) i.e., a 10 point difference between TRT and SC groups on change in TQ global scores longitudinally assessed over the course of follow-up and a 7-point difference on TQ score by TRT components, DC and ST.

### Primary Outcomes

- **Change in score on the Tinnitus Questionnaire (TQ) [ Time Frame: Baseline to 3, 6, 12, and 18 months follow-up ] [ Designated as safety issue: No ]**

Initial TQ administration will determine eligibility (score greater than or equal to 40) for the TRTT. The primary outcome is a repeated measures analysis of change in TQ score from baseline to follow-up.
<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Change in TQ sub-scale scores [Time Frame: Baseline to 3, 6, 12, and 18 months follow-up] [Designated as safety issue: No]</td>
<td>Repeated measures analysis of change in sub-scale scores from baseline to follow-up. Sub-scales include the following: psychological distress, intrusiveness, hearing difficulties, sleep disturbances, and somatic complaints.</td>
</tr>
<tr>
<td>• Change in Tinnitus Handicap Inventory (THI) score [Time Frame: Baseline to 3, 6, 12, and 18 months follow-up] [Designated as safety issue: No]</td>
<td>Repeated measures analysis of change in overall and sub-scale scores from baseline to follow-up. Subscales include the following: functional, emotional; and catastrophic.</td>
</tr>
<tr>
<td>• Change in Tinnitus Reaction Questionnaire (TRQ) score [Time Frame: Baseline to 3, 6, 12, and 18 months follow-up] [Designated as safety issue: No]</td>
<td>Repeated measures analysis of change in overall and sub-scale scores from baseline to follow-up. Subscales include the following: general distress, interference with work and leisure activities, severe signs of distress, and avoidance of activities subscales.</td>
</tr>
<tr>
<td>• Change in TRT Interview Visual Analogue scales [Time Frame: Baseline to 3, 6, 12, and 18 months follow-up] [Designated as safety issue: No]</td>
<td>Repeated measures analysis of change in score from baseline to follow-up.</td>
</tr>
<tr>
<td>• Change in Digit Symbol Substitution Test (DSST) [Time Frame: Baseline to 6 and 18 months follow-up] [Designated as safety issue: No]</td>
<td>Repeated measures analysis of change in score from baseline to follow-up. This test assesses cognitive function related to ability to focus attention to a task and recall and is an indirect measure of ability to ignore the tinnitus signal.</td>
</tr>
<tr>
<td>• Change in psychoacoustic variables [Time Frame: Baseline to 6 and 18 months follow-up] [Designated as safety issue: No]</td>
<td>Repeated measures analysis of change from baseline to follow-up in tinnitus pitch and loudness match and loudness discomfort level.</td>
</tr>
</tbody>
</table>

### Estimated Enrollment
228

### Study start date
November 2010

### Estimated Study Completion Date:
July 2015

### Estimated Primary Completion Date:
July 2015 (Final data collection date for primary outcome measure)

### Participants (age)
18 years and older

### Gender
both

### Accepts Healthy Volunteers
no
| Eligibility Inclusion Criteria | • Age 18 years or above  
• Subjective severe tinnitus, defined as a score on the Tinnitus Questionnaire (TQ) greater than or equal to 40  
• Eligible for care at a Department of Defense Clinical Center  
• Speaks English well enough to complete a series of questionnaires and benefit from counseling |
| Eligibility Exclusion Criteria | • Involvement in pending tinnitus-related financial claims or litigation  
• Tinnitus of less than 12 months duration  
• Treatment for tinnitus within previous 12 months  
• Routine unavoidable exposure to hazardous noise  
• Use of a cancer chemotherapeutic drug within previous 12 months  
• Treatment for head or neck injury within previous 24 months  
• Treatment for an emotional, psychological, or psychiatric condition within previous 12 months  
• Requirement for use of an ototoxic drug  
• Hearing impairment, defined by audiometric thresholds > 30 dB HL at and below 2,000 Hz and > 40 dB HL at 4,000 and 8,000 Hz  
• Required use of hearing aids  
• Fluctuating hearing loss at a level that would interfere with the reliability of study results  
• One or more prominent spontaneous otoacoustic emissions, defined as the presence of a spontaneous otoacoustic emission spike that is 3 or more times larger than the measured variation in amplitude across the remaining frequency range and/or if the emission corresponds in pitch to the tinnitus pitch  
• Pulsatile somatosounds suggesting presence of abnormal vasculature or high blood pressure contributing to the tinnitus  
• Feigning tinnitus or hearing loss  
• Evidence by audiological testing of a treatable etiology of the tinnitus, such as conductive hearing impairment as shown by pure-tone thresholds, abnormal acoustic immittance, abnormal stapedial reflex test, or abnormal auditory brainstem response  
• Predisposing disease with tinnitus symptoms amenable to medical or surgical intervention, including but not limited to; chronic otitis media, otosclerosis, vestibular disorder or dizziness, Eustachian tube, middle ear, or inner ear disease, Lyme disease or ear autoimmune disease, malocclusion or temporomandibular joint disease, uncontrolled allergies, aberrant ear, head, or neck blood vasculature or glomus tumor, neurological condition such as multiple sclerosis or ear-related demyelinating disease, perilymphatic fistula, or facial weakness or paralysis  
• Meniere’s disease  
• Uncontrolled diabetes, defined as blood glucose consistently ≥ 200 mg/dl or an HBA1c above 8%  
• Evidence from any laboratory study that suggests an etiology for the tinnitus that is treatable, including, but not limited to, abnormal thyroid stimulating hormone (TSH) or thyroid hormone (T3 or T4) levels, positive fluorescent treponemal antibody (FTA) test, or positive Lyme titer  
• Evidence of a tumor contributing to the tinnitus, including an acoustic neuroma (or vestibular schwannoma), cerebellopontive angle tumor, skull base tumor, or any other type of tumor that the examining physician believes is responsible for the tinnitus  
• Diagnosis of traumatic head or brain injury requiring treatment |
<table>
<thead>
<tr>
<th>Diagnosis of an emotional, psychological, or psychiatric condition requiring treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability or unwillingness of patient to comply with study requirements</td>
</tr>
<tr>
<td>Unwillingness of Clinical Center Director to randomize the patient to treatment due to the presence of any condition, physical, mental or social, which is likely to affect the patient returning for follow-up visits on schedule or which is likely to impair his or her performance on the functional tests</td>
</tr>
<tr>
<td>Inability or unwillingness of patient to provide informed consent</td>
</tr>
</tbody>
</table>

**Contact**

Roberta W. Scherer, PhD; phone: 001 (410) 502-4636; rscherer@jhsph.edu

**Locations**

United States California:
- Naval Hospital Camp Pendleton, Camp Pendleton, California, United States, 92055-5191
- Naval Medical Center, San Diego, California, United States, 92134
- David Grant Medical Center, Travis AFB, California, United States, 94535

United States, Maryland
- National Naval Medical Hospital, Bethesda, Maryland, United States, 20889-5600

United States, Texas
- Wilford Hall Medical Center, Lackland AFB, Texas, United States, 78236-5300

United States, Virginia
- Portsmouth Naval Medical Center, Portsmouth, Virginia, United States, 23705-2103

**Study chair**

C. Craig Formby, PhD, The University of Alabama, Tuscaloosa

**Study director**

Roberta W Scherer, PhD, Johns Hopkins School of Public Health

**Responsible Party**

Johns Hopkins School of Public Health (JHSPH) (Roberta Scherer, PhD, Director, Tinnitus Retraining Therapy Trial (TRTT) Coordinating Center)

**Study ID Numbers**

U01DC007422, U01DC007422

**Record first received**

August 5, 2010

**Last Updated**

August 31, 2010

**ClinicalTrials.gov Identifier**

NCT01177137

**Health Authority**

United States: Institutional Review Board
## Tinnitus Measured by MEG and Synchronous Neural Interaction™ Test: Template Development

<table>
<thead>
<tr>
<th>Current status</th>
<th>currently recruiting participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>Orasi Medical, Inc.; Novartis</td>
</tr>
<tr>
<td>Information provided by</td>
<td>Orasi Medical, Inc.</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT01185990</td>
</tr>
</tbody>
</table>

### Purpose

The study is designed to identify specific patterns of brain functional activity associated with chronic, moderate to severe tinnitus through the use of resting-state MEG scans. Robust patterns identified in this study will be used as a biomarker for subsequent clinical evaluation of experimental drug treatments for tinnitus. This study will conduct MEG scans on approximately 30 to 75 subjects with tinnitus and approximately 15 healthy control subjects. MEG scans will be obtained for each subject following screening, clinical and tinnitus evaluations. A subset of 6 subjects from the tinnitus cohort will be invited to undergo evoked auditory assessment during an extended MEG scan session to identify cortical regions that respond to the auditory stimulus. These six subjects also will be evaluated with a single structural MRI scan to support high-resolution mapping of the localized cortical regions. MEG data will be analyzed to identify patterns of brain activity that are specifically associated with the presence of tinnitus using both standard approaches and the Orasi Synchronous Neural Interaction™ (SNI) test. MEG scan results also will be evaluated to identify specific patterns of functional activity that correlate with other measures of tinnitus severity such as the Iowa Tinnitus Handicap Scale. This study will test the hypothesis that moderate to severe tinnitus is associated with altered patterns of brain functional activity measured by a brief, resting-state MEG scan. This hypothesis will be tested by comparing resting-state MEG scans of tinnitus patients with those of healthy control subjects collected during this study and available in Orasi’s existing MEG scan database.

<table>
<thead>
<tr>
<th>Condition(s)</th>
<th>Tinnitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study type and design</td>
<td>Observational; Observational Model: Case Control</td>
</tr>
<tr>
<td>Time Perspective:</td>
<td>Cross-Sectional</td>
</tr>
<tr>
<td>Official title</td>
<td>Moderate to Severe Tinnitus as Measured by MEG and the Synchronous Neural Interaction™ Test: Template Development Study</td>
</tr>
<tr>
<td>Groups/Cohorts</td>
<td>Tinnitus subjects: Subjects with chronic, moderate to severe unilateral tinnitus.</td>
</tr>
<tr>
<td></td>
<td>Healthy control subjects</td>
</tr>
</tbody>
</table>
### Primary Outcomes
Correlated brain activity [Time Frame: 1 day] [Designated as safety issue: No]
- MEG scan data will be analyzed using standard frequency domain approaches and the Orasi SNI test for correlated, synchronous activity.

### Secondary Outcomes
Tinnitus Severity Ratings [Time Frame: Up to 14 days] [Designated as safety issue: No]
- The degree of tinnitus severity also will be evaluated using the Iowa Tinnitus Handicap Questionnaire (THQ), Tinnitus Handicap Inventory (THI) and a Visual Analog Scale (VAS) of Tinnitus Severity.

### Estimated Enrollment
45

### Study start date
August 2010

### Estimated Study Completion Date:
February 2011

### Estimated Primary Completion Date:
February 2011 (Final data collection date for primary outcome measure)

### Participants (age)
18 Years to 75 Years

### Gender
both

### Accepts Healthy Volunteers
yes

### Sampling Method
Probability Sample

### Study population
Subjects with chronic, moderate to severe unilateral tinnitus

### Eligibility Inclusion Criteria
- Subject is between 18 and 75 years of age at the time of screening.
- Subject understands the study procedures and agrees to participate in the study by giving written informed consent.
- Subject is a non-smoker.
- Subject is judged to be in good health based on medical history and brief physical examination.
- Subject has a diagnosis of chronic, moderate to severe (Tinnitus Handicap Inventory score range of 38 - 76, inclusive), unilateral tinnitus of unknown etiology, or is participating in the study as a healthy control subject.

### Eligibility Exclusion Criteria
- Subject has severe hearing impairment, external or middle ear diseases or temporomandibular joint disorders.
- Subject has a diagnosis of a significant neurological condition including Alzheimer's disease, Parkinson's disease, vascular dementia, Lewy body dementia or frontal temporal dementia, human immunodeficiency virus, multiple sclerosis, or severe traumatic brain injury.
• Subject has a history of primary psychotic disorder (e.g. schizophrenia, schizoaffective disorder, delusional disorder) or bipolar disorder.

• Subject has a history of seizures, epilepsy, stroke, peripheral neuropathy, head trauma with persistent post-concussive symptoms, ADHD, dyslexia or other clinically significant neurological disease or cognitive impairment.

• Subject has a current episode of major depressive disorder.

• Subject has used antidepressants, anxiolytics, antipsychotics or antiepileptic medications in the past 6 months.

• Subject has a recent (within 2 years) history of alcohol or substance abuse/dependence.

• Subject has completed an MRI within 2 weeks prior to the MEG scan.

• Subject has metal braces or pacemaker that may interfere with the MEG scan.

• The investigator has any concern regarding the safe participation of a subject in the study, or if for any other reason the investigator considers the subject inappropriate for study participation

| contact       | Ann Rechtzigel, BSN, MN; phone: 001612-708-5357; rex5@frontiernet.net
                | Anne-Marie Tschida (radiant research); phone 001 952-922-7000 ext 4640; anne-marietschida@radiantresearch.com |
| Locations     | United States, Minnesota; Noran Neurological Clinic; Minneapolis, Minnesota, United States, 55407
                | Radiant Research: Minneapolis, Minnesota, United States, 55435 |
| Principal Investigator | Richard E Golden, MD; Noran Neurological Clinic
                        | Tami Helmer, MD; Radiant REsearch |
| Responsible Party | Orasi Medical, Inc. (Todd Verdoorn, PhD, Chief Scientific Officer) |
| Study ID Numbers | TTD 10 - 01 |
| Record first received | August 17, 2010 |
| Last Updated | August 19, 2010 |
| ClinicalTrials.gov Identifier | NCT01185990 |
| Health Authority | United States: Institutional Review Board |
### Caroverin and Inner Ear Diseases

<table>
<thead>
<tr>
<th>Current status</th>
<th>not yet open for participant recruitment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>Phafag AG</td>
</tr>
<tr>
<td>Information provided by</td>
<td>Phafag AG</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT01174979</td>
</tr>
<tr>
<td>Purpose</td>
<td>This trial is a randomized, double blind, placebo controlled study on patients suffering from inner ear diseases with tinnitus as a principal symptom. The study will investigate the transtympanic treatment with a 1,5 % caroverine solution. Each patient will undergo treatment for 2 cycles of 48 hours each.</td>
</tr>
<tr>
<td>Condition(s)</td>
<td>Tinnitus</td>
</tr>
<tr>
<td>Intervention(s)</td>
<td>Caroverin</td>
</tr>
<tr>
<td>Phase</td>
<td>III</td>
</tr>
<tr>
<td>Study type and design</td>
<td>Interventional; Allocation: Randomized Control: Placebo Control Endpoint Classification: Safety/Efficacy Study Intervention Model: Parallel Assignment Masking: Double Blind (Subject, Investigator) Primary Purpose: Treatment</td>
</tr>
<tr>
<td>Official title</td>
<td>Double Blind, Placebo-controlled, Randomized Clinical Trial to Evaluate the Efficacy and Safety of a Transtympanic Treatment of Tinnitus With Caroverine</td>
</tr>
<tr>
<td>Arms</td>
<td>Caroverin: Experimental - Intervention: Drug: Caroverin Placebo: Placebo Comparator - Intervention: Drug: Caroverin</td>
</tr>
<tr>
<td>Assigned Interventions</td>
<td>Drug: Caroverin - treatment with eardrops 2 times for 48 hours Drug: Caroverin - treatment with eardrops 2 times for 48 hours</td>
</tr>
<tr>
<td>Participants (age)</td>
<td>18 Years and older</td>
</tr>
<tr>
<td>Gender</td>
<td>both</td>
</tr>
<tr>
<td>Accepts Healthy Volunteers</td>
<td>no</td>
</tr>
<tr>
<td>Eligibility Inclusion Criteria</td>
<td>Men or women aged at least eighteen Written consent to take part in the study after receiving information from the trial physician</td>
</tr>
<tr>
<td>Eligibility Exclusion Criteria</td>
<td></td>
</tr>
<tr>
<td>-------------------------------</td>
<td></td>
</tr>
<tr>
<td>One of the following illnesses:</td>
<td></td>
</tr>
<tr>
<td>Decompensated tinnitus</td>
<td></td>
</tr>
<tr>
<td>Sudden hearing loss</td>
<td></td>
</tr>
<tr>
<td>Morbus Menière</td>
<td></td>
</tr>
<tr>
<td>Blast injury</td>
<td></td>
</tr>
<tr>
<td>Presbyacusis with Tinnitus</td>
<td></td>
</tr>
<tr>
<td>Chron. Otitis media</td>
<td></td>
</tr>
<tr>
<td>Patients who are not able to give their consent (e.g. dementia, coma, mental disability,…)</td>
<td></td>
</tr>
<tr>
<td>Women of childbearing age who are not using adequate contraception or who are (or plan to become) pregnant (a pregnancy test must be carried out by a doctor once a month in Austria) or are lactating</td>
<td></td>
</tr>
<tr>
<td>If there are solid reasons to doubt that the patient would be willing and able to cooperate</td>
<td></td>
</tr>
<tr>
<td>Known intolerance of/hypersensitivity to caroverine</td>
<td></td>
</tr>
<tr>
<td>Subjects who have taken part in another clinical trial within the 30 days preceding the start of this study or during this study</td>
<td></td>
</tr>
<tr>
<td>Pulse-synchronous tinnitus</td>
<td></td>
</tr>
<tr>
<td>Tinnitus caused by malposition of the jaw bone (bruxism)</td>
<td></td>
</tr>
<tr>
<td>Eardrum perforation</td>
<td></td>
</tr>
<tr>
<td>Subjects who have previously had a barotraumas, diving accidents or decompression sickness</td>
<td></td>
</tr>
<tr>
<td>Retrocochlear hearing disorder</td>
<td></td>
</tr>
<tr>
<td>Patients who have previously had a fracture of the petrous bone</td>
<td></td>
</tr>
<tr>
<td>Subjects suffering from acute or chronic accompanying conditions which severely impede their general health (NYHA stage IV, cancer, HIV etc.)</td>
<td></td>
</tr>
<tr>
<td>Accompanying conditions that according to the current state of scientific knowledge could affect the parameters used in this study to such an extent as to make it impossible to perform an objective assessment of those parameters, particularly ear conditions, including any conditions affecting the other ear or conditions like HI NYHA stage IV, cancer, HIV, Wallenberg Syndrome, massive Hypotension, Glaucoma.)</td>
<td></td>
</tr>
<tr>
<td>Accompanying medication that according to the current state of scientific knowledge are likely to affect the measurement techniques used in this study or the results obtained (cytostatics, aminoglycoside antibiotics, loop diuretics (furosemide, etacrynic acid), psycho pharmaceuticals, muscle relaxants, benzodiazepines, salicylates, quinine, cortisone and/or caroverine within the three days preceding the start of the study)</td>
<td></td>
</tr>
<tr>
<td>Drug treatment for tinnitus or sudden hearing loss (i.v. and oral) within seven days preceding the start of the study where the total duration of the course is less than four weeks</td>
<td></td>
</tr>
<tr>
<td>Diseases or conditions that may be associated with an altered perception or processing of stimuli, e.g. mental illness</td>
<td></td>
</tr>
</tbody>
</table>
Hearing Impairment, Cognitive Therapy and Coping

Current status not yet open for participant recruitment

Sponsors and collaborators Oslo University Hospital; South-Eastern Norway Regional Health Authority

Information provided by Oslo University Hospital

ClinicalTrials.gov Identifier NCT01206829

Purpose A randomized controlled study with hearing impaired workers, who have voluntarily signed up for an 8 session cognitive therapy (CBT) course. The CBT intervention will be compared to a waiting list control group. Participants who are allocated to the intervention group will be offered to start on the CBT-course immediately, while the control group that will be offered the same course 12 months later. Main outcome measures are assessments of mental distress and vocational coping. We will also assess the distress associated with tinnitus, which is a potential moderator variable.

Condition(s) Hearing Loss; Tinnitus; Stress; Psychological; Mental Fatigue

Intervention(s) Behavioral: 8-session CBT course
Hearing impaired workers voluntarily sign up for an 8 session cognitive therapy course. The study has a waiting list control group design. Participants will be randomized assigned to either an experiment group that will be offered to start on an immediate course, or a control group that will be offered the same course 12 months later.
### Phase I

**Study type and design**
- Interventional; Allocation: Randomized
- Endpoint Classification: Efficacy Study
- Intervention Model: Parallel Assignment
- Masking: Open Label
- Primary Purpose: Treatment

**Official title**
Hearing Impairment, Tinnitus, Mental Health and Vocational Coping. A Randomized, Controlled Study of a Cognitive Therapy Program to Reduce Social Safety Seeking.

**Detailed Description**
Although the relationship between hearing loss and mental distress is not linear, it is known that hearing impaired individuals have increased vulnerability for development of symptoms of distress and fatigue. It is assumed that distressed hearing impaired individuals will have a tendency to use maladaptive and passive coping strategies, such as social withdrawal or reluctance to make use of hearing aid devices. On the other side, it is well documented that hearing impaired employers who are open about their handicap and make others aware of their situation, i.e. take an active coping approach, have fewer symptoms of distress and have better vocational functioning. The level of knowledge is limited and mainly based on crosssectional studies, and the way people cope with hearing impairment has been measured indirectly by questionnaires focusing on communication problems. We plan to conduct a randomized controlled study with hearing impaired workers, who have voluntarily signed up for an 8 session cognitive therapy (CBT) course. The CBT intervention will be compared to a waiting list control group. Participants who are allocated to the intervention group will be offered to start on the CBT-course immediately, while the control group that will be offered the same course 12 months later. Main outcome measures are assessments of mental distress and vocational coping. We will also assess the distress associated with tinnitus, which is a potential moderator variable.

**Primary Outcomes**
- **Work Ability Index** [Time Frame: At recruitment, at time of course completement and at 6 months post-treatment] [Designated as safety issue: No]
  - Work Ability Index is a self report instrument that measures changes and variations in level of vocational functioning.
- **Current employment status** [Time Frame: At recruitment, at time of course completement and at 6 months post-treatment] [Designated as safety issue: No]
  - Participants are asked to describe their current vocational situation in some more detail. In addition, one item from the General Health Questionnaire, GQH-20 (World Health Organization, 2007) is included here: “To what degree is your ability to perform your ordinary work reduced today?”
- **Hospital Anxiety and Depression Scale; HADS** [Time Frame: At recruitment, at time of course completement and at 6 months post-treatment] [Designated as safety issue: No]
  - HADS consists of 14 items covering symptoms of anxiety and depression. HADS is a standarized and validated self report measure of general, mental health.
- **Fear of Negative Evaluation (FNE)** [Time Frame: At recruitment, at time of course completement and at 6 months post-treatment] [Designated as safety issue: No]
<table>
<thead>
<tr>
<th><strong>Estimated Enrollment</strong></th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study start date</strong></td>
<td>October 2010</td>
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<tr>
<td><strong>Estimated Study Completion Date:</strong></td>
<td>December 2013</td>
</tr>
<tr>
<td><strong>Estimated Primary Completion Date:</strong></td>
<td>December 2012 (Final data collection date for primary outcome measure)</td>
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<tr>
<td><strong>Participants (age)</strong></td>
<td>18 Years to 70 Years</td>
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<tr>
<td><strong>Gender</strong></td>
<td>both</td>
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<tr>
<td><strong>Accepts Healthy Volunteers</strong></td>
<td>yes</td>
</tr>
<tr>
<td><strong>Eligibility Inclusion Criteria</strong></td>
<td>Eligible participants need to be within the age range of 18-70 years, contain some formal employment and be able to document a mean, bilateral hearing loss of at least 40 dB.</td>
</tr>
<tr>
<td><strong>Eligibility Exclusion Criteria</strong></td>
<td>Individuals without a clear vocational status (for instance on permanent/temporarily sick leave) and a mean bilateral hearing loss beneath 40 dB.</td>
</tr>
<tr>
<td><strong>Contact</strong></td>
<td>Katharine C. Peterson, cand. psychol.; phone: +47 93482003 <a href="mailto:post@katherinepeterson.no">post@katherinepeterson.no</a></td>
</tr>
<tr>
<td><strong>Locations</strong></td>
<td>The Norwegian Centre for Hearing Impairment and Mental Health Oslo University Hospital, Oslo, Norway, 0424</td>
</tr>
<tr>
<td><strong>Study chair</strong></td>
<td>Egil W Martinsen, Prof. Dr.med., Oslo University Hospital</td>
</tr>
<tr>
<td><strong>Principal Investigator</strong></td>
<td>Katharine C Peterson, cand. psychol., The Norwegian Centre for Hearing Impairment and Mental Health</td>
</tr>
<tr>
<td><strong>Responsible Party</strong></td>
<td>The Norwegian Centre for Hearing Impairment and Mental Health (Egil W. Martinsen professor dr. med., Head of the Department for Research and Development)</td>
</tr>
<tr>
<td><strong>Study ID Numbers</strong></td>
<td>2009/2156 (REK), 52-2009 AUS</td>
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<tr>
<td><strong>Record first received</strong></td>
<td>September 21, 2010</td>
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<tr>
<td><strong>Last Updated</strong></td>
<td>September 21, 2010</td>
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<tr>
<td><strong>ClinicalTrials.gov Identifier</strong></td>
<td>NCT01206829</td>
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<tr>
<td><strong>Health Authority</strong></td>
<td>Norway: The National Committees for Research Ethics in Norway; Norway: Norwegian Social Science Data Services; Norway: Directorate for Health and Social Affairs</td>
</tr>
</tbody>
</table>
The Treatment of Tinnitus With Transcutaneous Non-invasive Vagus Nerve Stimulation

<table>
<thead>
<tr>
<th>Current status</th>
<th>recruiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>cerbomed GmbH</td>
</tr>
<tr>
<td>Information provided by</td>
<td>cerbomed GmbH</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT01176734</td>
</tr>
<tr>
<td>Purpose</td>
<td>The t-VNS CM02 device is a non-invasive, transcutaneous neurostimulator for influencing the afferent branches of the nervus vagus around the human ear. The clinical trial is designed as a pilot study addressing the treatment of tinnitus with transcutaneous vagus nerve stimulation</td>
</tr>
<tr>
<td>Condition(s)</td>
<td>Tinnitus</td>
</tr>
</tbody>
</table>
| Intervention(s)         | Device: Placebo  
Device: t-VNS® verum |
| Study type and design   | Interventional; Allocation: Randomized  
Endpoint Classification: Safety/Efficacy Study  
Intervention Model: Parallel Assignment  
Masking: Double Blind (Subject, Investigator)  
Primary Purpose: Treatment |
| Official title          | The Treatment of Tinnitus With Transcutaneous Non-invasive Vagus Nerve stimulation-a Controlled Randomized Pilot Study Assessing Safety, Compatibility and Clinical Performance |
| Primary Outcomes        | Effectiveness of t-VNS® stimulation [ Time Frame: 24 weeks ] [Designated as safety issue: No]  
- Determination of the effectiveness of the t-VNS stimulation vs. placebo, measured by the difference in the tinnitus score according to Goebel and Hiller between baseline vs. week 24 |
| Arms                    | Placebo: Placebo Comparator  
- Sham stimulation with the t-VNS device.  
Intervention: Device: Placebo  
Treatment with t-VNS: Active Comparator  
- Active treatment with t-VNS  
Intervention: Device: t-VNS® verum |
| Assigned Intervention(s) | Device: Placebo  
- Sham stimulation with the t-VNS device.  
Device: t-VNS® verum  
- Active stimulation with the t-VNS® device. |
<p>| Estimated Enrollment    | 30                                             |
| Study start date        | January 2010                                   |</p>
<table>
<thead>
<tr>
<th>Estimated Study Completion Date:</th>
<th>March 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated Primary Completion Date:</td>
<td>January 2011 (Final data collection date for primary outcome measure)</td>
</tr>
<tr>
<td>Participants (age)</td>
<td>18 Years to 75 Years</td>
</tr>
<tr>
<td>Gender</td>
<td>both</td>
</tr>
<tr>
<td>Accepts Healthy Volunteers</td>
<td>no</td>
</tr>
</tbody>
</table>
| **Eligibility Inclusion Criteria** | • Chronic tinnitus defined as a tinnitus over more than six months  
• ≥31 points in the tinnitus questionnaire according to Goebel and Hiller  
• Written informed consent  
• Both gender, aged from 18 -75 years  
• If the subject takes psychoactive medication (e.g antidepressants, anticonvulsives) therapy must be stable for at least 10 days. If a treatment with neuroleptics is necessary, only olanzapine and quetiapine should be used. The therapy should be constantly though a necessary change in medication is no reason for exclusion of the subject. |
| **Eligibility Exclusion Criteria** | • Objective tinnitus  
• Participating in other tinnitus treatments within 3 months before study start  
• Missing informed consent  
• Pregnancy  
• Bronchial asthma in medical history  
• Clinically relevant internistic, neurological or psychiatric diseases  
• Abuse of drugs or alcohol until 12 weeks before enrollment in the study  
• Indications of structural impairment of the basal ganglia or the brain stem  
• Active implants (e.g. cochlea implants, VNS, pacemaker)  
• Constant all-day use of hearing instruments or noisers on the left the part-time use in special situations (e.g. watching TV is no exclusion criteria  
• All dermatologic and infectious diseases which affect the area around the pinna and the ear canal  
• Severe malformation of the pinna  
• Other circumstances that in the opinion of the investigator might be an obstacle for enrolling the subject |
| **Contact** | Berthold Langguth MD, +49 941 941 ext 2099; berthold.langguth@medbo.de  
Michael Landgrebe MD, +49 941 941 ext 1226; michael.landgrebe@medbo.de  
Fax +49 941 941 2025 |
| **Locations** | Klinik für Psychiatrie und Psychotherapie Bezirksklinikum Regensburg  
Universitätsstr. 84 93053 Regensburg |
<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Goeran Hajak MD; Berthold Langguth MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Investigators</td>
<td>Michael Landgrebe MD</td>
</tr>
<tr>
<td>Responsible Party</td>
<td>cerbomed GmbH (Chief Medical Officer)</td>
</tr>
<tr>
<td>Study ID Numbers</td>
<td>cMPsTIN01</td>
</tr>
<tr>
<td>Record first received</td>
<td>August 5, 2010</td>
</tr>
<tr>
<td>Last Updated</td>
<td>August 17, 2010</td>
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<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT01176734</td>
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<tr>
<td>Health Authority</td>
<td>Germany: Federal Institute for Drugs and Medical Devices</td>
</tr>
</tbody>
</table>