10TH INTERNATIONAL TINNITUS RESEARCH INITIATIVE CONFERENCE AND 1ST EU COST ACTION (TINNET) CONFERENCE

Tinnitus: subtypes, mechanisms and interventions | 16-18 March 2016 Nottingham UK

MRC Institute of Hearing Research

NHS National Institute for Health Research

10th International Tinnitus Research Initiative Conference and 1st EU Cost Action (TINNET) Conference

16th – 18th March 2016

East Midlands Conference Centre, University of Nottingham, Nottingham, UK

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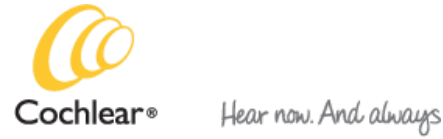

Wednesday 16th March			
08:00	**Registration opens. Closes at 15:30. Exhibitors open**		
09:00-9:05	**Welcome**		
09:05-10:00	**Keynote: Winny Schlee (TINNET)** **"Towards a better understanding of tinnitus heterogeneity"** **Chair: Deb Hall**		
10:00-10:30	**Keynote: Michael Landgrebe** **"The TRI database: Big data as a chance to improve clinical characterisation and development of new treatments for tinnitus"** **Chair: Deb Hall**		
10:30-11:00	**Coffee**		
Parallel 1 – location: Lecture Theatre **TINNET WG1 & WG5** **Clinical & Outcomes** **Chairs: Winfried Schlee & Kate Greenwell**		**Parallel 2 – location: Conference Suite 2** **TINNET WG3 & WG4** **Neuroimaging & Genetics** **Chairs: Jonas Dyhrfjeld-Johnsen & Katrin Krumbholz**	
11:00-11:40 **O1**	**TINNET COST Action BM1306 - Clinical WG1: Establishment of a standard for Tinnitus; patient assessment, characterization, and treatment options.** Cima R.F., Haider H., Mazurek B., Cederroth C.R., Lapira A., Kikidis D., Norena A.	11:00-11:40 **O2**	**TINNET COST Action BM1306 – Subtyping WG3.** Subtyping tinnitus and neuroimaging Pim van D., Norena, A., Langers D., Adjamian P
11:45-12:30 **O3**	**TINNET COST Action BM1306 - Outcome WG5: Systematic review of outcomes in tinnitus trials.** Presentation on behalf of Core Outcome Measures in Tinnitus (COMiT) Initiative.	11:45-12:30 **O4**	**TINNET COST Action BM1306 - Genetics WG4. Improving diagnosis and drug development through the understanding of tinnitus subtypes.** Lopez-Escamez J.A., Cima R.F., Mazurek B., Szczepek A., Knipper M., Bibas T., Van de Heyning P., Cederroth C.R., **Genetic susceptibility to tinnitus in a Swedish Twin cohort.** Requena Navarro M.T., Maas I.L., Brüggemann P., Edvall N., Szczepek A., Canlon B., Mazurek B., Lopez-Escamez J.A., Cederroth C.R.

12:30-13:30	**Lunch**		
Parallel 3 – location: Lecture Theatre Assessment Chairs: Rilana Cima & Kathryn Fackrell		**Parallel 4 – location: Conference Suite 2 Neural correlates (animal) Chairs: Pim van Dijk & Martin Holding**	
13:30-13:45 **O5**	**The Replicated Single Case Experimental Design as an innovative method for assessing effectiveness of treatment.** Fuller T.E., Cima R.F., Vlaeyen J.W.S.	13:30-13:45 **O6**	**Salicylate-induced changes in brain activity in awake guinea pigs.** Berger J.I., Coomber B., Hockley A., Wallace MN.., Palmer A.R.
13:45-14:00 **O7**	**Using Monte Carlo Markov Chain Methods to Assess Tinnitus Characteristics.** Lentz J.J., Silbert N.H.	13:45-14:00 **O8**	**Tinnitus-related neuroplasticity within the auditory system of Mongolian gerbils.** Schulze H., Tziridis K., Krauss P., Schilling A.
14:00-14:15 **O9**	**Patterns across outcome domains: a systematic review of tinnitus trials.** Haider H.F., Hall D.A.	14:00-14:15 **O10**	**Paired Auditory-Somatosensory Stimulation Therapy Reverses Tinnitus in Guinea Pigs.** Martel D.T., Wu C., Shore S.E.
14:15-14:30 **O11**	**Tinnitus is associated with reduced sound level tolerance in adolescents with normal audiograms and otoacoustic emissions.** Sanchez T.G., Roberts L.E.	14:15-14:30 **O12**	**Long-Lasting Sound-Evoked Afterdischarge in the Auditory Midbrain.** Oliver D., Ono M.
14:30-14:45 **O13**	**Tinnitus Concern Questioner.** Bauman N.	14:30-14:45 **O14**	**Effect of sound exposure on neuronal firing in the inferior colliculus of awake mice.** Longenecker R.J., Galazyuk A.V.
14:45-15:00 **O15**	**Pathognomonic tinnitus percepts, even when intermittent or intermixed with non-specific tinnitus, (i) identify tinnitus subtypes, (ii) suggest the tinnitus mechanism, and (iii) can lead to successful intervention.** Levine R.A.	14:45-15:00 **O16**	**Long-lasting suppression of spontaneous firing in auditory neurons: implication to the phenomenon of residual inhibition.** Galazyuk A.V., Voytenko S.V., Grimsley C.A., Longenecker R.J.
15:00-15:30	**Coffee**		

15:30-16:30	**Keynote: Karl Friston** **"Dynamic causal modelling of the auditory system"** **Chair: Adam McNamara**
16:30-17:30	**Posters & Drinks – P1-P57 (odd numbers)**
17:30-18:30	**Posters & Drinks – P1-P57 (even numbers)**
18:30	**Student event – meet in conference venue bar**

Thursday 17th March			
08:00	**Registration opens. Closes at 15:30**		
08:00-08:45	**Rüdiger Pryss** **Live Presentation of the new Tinnitus Database – Conference Suite 2**		
09:00-10:00	**Keynote: David Baguley** **"The association between tinnitus and hyperacusis: causal, indirect, or coincidence?"** **Chair: Mark Wallace**		
10:00-10:30	**Keynote: Veronica Kennedy** **"Management of Tinnitus in Children – the UK approach"** **Chair: Mark Wallace**		
10:30-11:00	**Coffee**		
Parallel 5 – location: Lecture Theatre **Co-morbidities** **Chairs: Haula Haider & Magdalena Sereda**		**Parallel 6 – location: Conference Suite 2** **Network connectivity** **Chairs: Agnieszka Szczepek & Joel Berger**	
11:00-11:15 **O17**	**CI in patients with single sided deafness influences the quality of life, tinnitus percept and psychological comorbidity.** Olze, H., Förster-Ruhrmann U., Szczepek A., Mazurek B.	11:00-11:15 **O18**	**Emerging network connectomics in phantom sound perception.** Mohan A.M., De Ridder D.D.R., Vanneste S.V.
11:15-11:30 **O19**	**Tinnitus after cochlear implantation.** Pierzycki R.H., Edmondson-Jones M., Dawes P., Munro K.J., Moore D.R., Kitterick P.T.	11:15-11:30 **O20**	**The resting state functional connectivity patterns in chronic subjective tinnitus.** Lewandowska M., Wolak T., Milner R., Ganc M., Niedzialek I., Skarzynski H.
11:30-11:45 **O21**	**Epidemiology of Tinnitus Incidence in Older Adults, 70+ Years: the Age, Gene/Environment Susceptibility–Reykjavik (AGES–R) Iceland**	11:30-11:45 **O22**	**Neural Correlates of White Matter Integrity in Tinnitus: Tract-Based Spatial Statistics.** Alhazmi F., Mackenzie I., Kay T., Kemp G.J., Sluming V.

	Longitudinal Cohort Study. Hoffman H.J., Dobie R.A., Li C.M., Losonczy K.G., Themann C.L., Cotch M.F, Launer L.J., Eiriksdottir G., Gudnason V., Petersen H.		
11:45-12:00 **O23**	**Hyperacusis: prevalence and risk factors in the US adult population.** Dobie R.A., Hoffman H.J., Losonczy K.G.	11:45-12:00 **O24**	**Abnormal Resting-state Functional Connectivity Study in Unilateral Pulsatile Tinnitus Patients: What is the Role of Posterior Cingulate Cortex?** Lv H ., Wang Z., Gong S., Zhao P., Liu Z., Yan F., Wang P., Zhang L., Li R
12:00-12:15 **O25**	**Impact of multiple factors on the degree of tinnitus distress.** Brueggemann, P., Szczepek A.J, Rose M., McKenna L., Olze H., Mazurek B.	12:00-12:15 **O26**	**Investigating tinnitus subgroups varying in severity using Diffusion Tensor Imaging.** Schmidt S., Romero, A., Husain, F.T.
12:15-12:30 **O27**	**Audiological and Psychosocial Predictors of Tinnitus Severity.** Wallhäusser-Franke E., Repik I., Delb W., Glauner A., Hörmann K.	12:15-12:30 **O28**	**Hearing tinnitus and reacting to tinnitus: two processes involving different networks.** Maudoux A., Gomez F., De Ridder D., Vanhecke W., Van de Heyning P., Cabay J.-E., Laureys S., Soddu A., Lefebvre P.H., Vanneste S.
12:30-13:30	**Lunch**		
Parallel 7 – location: Lecture Theatre Available interventions (neural) Chairs: Veronica Kennedy & Dean Thompson		**Parallel 8 – location: Conference Suite 2 Neural correlates (human) Chairs: Audrey Maudoux & Peyman Adjamian**	
13:30-13:45 **O29**	**---------Oral Presentation Withdrawn---------**	13:30-13:45 **O30**	**Tinnitus- and Task-Related Differences in Resting-State Networks.** Lanting C.P., Woźniak A., van Dijk P., Langers D.R.M.
13:45-14:00 **O31**	**Evaluation of tomographic vs. standard neurofeedback protocols for treatment of subjective tinnitus.** Meyer M., Güntensperger D., Neff P., Weidt S., Kleinjung T.	13:45-14:00 **O32**	**Decreased default mode network connectivity to the precuneus is common across tinnitus subgroups.** Schmidt, S., Carpenter-Thompson J.R., Husain F.T.
14:00-14:15	**Effectiveness, prognostic factors and safety of**	14:00-14:15	**Neural substrates predicting short-term**

O33	**microvascular decompression surgery of the eighth cranial nerve for the treatment of tinnitus and vertigo: a systematic review and meta-analysis of individual patient data.** van den Berge M.J.C., Posthumus I.A., Smidt N., Free R.H., van Dijk J.M.C., van Dijk P.	**O34**	**improvement of tinnitus loudness and distress after modified tinnitus retraining treatment.** Song, J.J., Vanneste S., De Ridder D., Jang J.H.
14:15-14:30 **O35**	**Prognostic Models for Tinnitus Change after Cochlear Implantation.** Kloostra, F., Arnold R., Hofman R., Van Dijk P.	14:15-14:30 **O36**	**The correspondence between audiometric profile and tonotopic organization of the primary auditory cortex in tinnitus.** Wolak T., Lewandowska M., Niedziałek I., Ciesla K., Pluta A., Rusiniak M., Skarzynski H.
14:30-14:45 **O37**	**Tinnitus suppression with electrical stimulation: broadening inclusion criteria for cochlear implantation.** George E.L.J., Arts R.A.G.J., Maes I.H.L., Van Tongeren J., Stokroos R.J.	14:30-14:45 **O38**	**The relation of cochlear synaptopathy to obscure auditory dysfunction and tinnitus with normal hearing thresholds.** Guest H.H., Munro K.J., Prendergast G., Plack C.J.,
14:45-15:00 **O39**	**Cochlear Implantation as a Long-Term Treatment for Ipsilateral Incapacitating Tinnitus in Subjects with Unilateral Hearing Loss up to 10 years.** Mertens G., Van de Heyning P.	14:45-15:00 **O40**	**Evidence for Hidden Hearing Loss in Tinnitus Subjects without Threshold Shifts.** Paul B.T., Bruce I.C., Roberts L.E.
15:00-15:30	**Coffee**		
15:30-16:30	**Posters – P58-P111 (odd numbers)**		
16:30-17:30	**Posters – P58-P111 (even numbers). Please remove all posters at the end of the session. Exhibitors close**		
17:30-18:30	**Keynote: Gerhard Andersson** **"Using the internet to develop and evaluate tinnitus treatments"** **Chair: Alan Palmer**		
19:30-23:00	**Conference Dinner**		

Friday 18th March			
08:00	**Registration opens. Closes at 13:30**		
08:00-08:45	**Desyncra Workshop - Conference Suite 2**		
09:00-10:00	**Keynote: Josef Rauschecker "Frontostriatal Dysfunction in Chronic Tinnitus" Chair: Berthold Langguth**		
10:00-10:30	**Keynote: Susan Shore "Mechanisms of tinnitus initiation in the cochlear nucleus" Chair: Berthold Langguth**		
10:30-11:00	**Coffee**		
Parallel 9 – location: Lecture Theatre Epidemiology & modelling Chairs: Martin Meyer & Derek Hoare		**Parallel 10 – location: Conference Suite 2 Preclinical interventions Chairs: Birgit Mazurek & Roland Schaette**	
11:00-11:15 **O41**	**The healthcare cost of tinnitus management in the UK.** Stockdale D., Brazier P., Kay T., Dowrick C., Hoare D.J., McFerran D.J.	11:00-11:15 **O42**	**High Definition Transcranial Direct Current Stimulation (HD-tDCS) for Tinnitus Relief: A New Kid in Town.** Shekhawat G.S., Mowbray R., Cooke C., Searchfield G.D.
11:15-11:30 **O43**	**Identifying a Minimal Important Change score for the Tinnitus Functional Index (TFI) questionnaire for different populations.** Fackrell K., Hall D.A., Barry J.G., Hoare D.J.	11:15-11:30 **O44**	**The effect of Transcranial Direct Current Stimulation in addition to tinnitus Retraining Therapy for treatment of chronic tinnitus patients.** Rabau S., Van Rompaey V., Van de Heyning P.
11:30-11:45 **O45**	**Reporting of sample size justifications: a systematic review of clinical trials in tinnitus.** Mehta R,L., Hall D.	11:30-11:45 **O46**	**Results from a patient-administered at-home tDCS treatment study for tinnitus: MEG markers for treatment response.** Hyvärinen P., Mäkelä J.P., Mäkitie A., Aarnisalo A.A.
11:45-12:00 **O47**	**Using regression modeling of survey data to better understand expectations of tinnitus treatment by audiologists and patients.** Jansen J.N., Gander P., Husain F.T.	11:45-12:00 **O48**	**Profiles of NMDA-R antagonists in clinical development for the treatment of tinnitus.** Piu F., Tsivkovskaia N., Wang X., Fernandez R., LeBel, C.

12:00-12:15 **O49**	**A cognitive model of tinnitus distress: results of path analysis.** Handscomb L., Hall D., Hoare D., Shorter G.	12:00-12:15 **O50**	**Immediate effects of nasal oxytocin in tinnitus patients.** Azevedo, A., Figueiredo R.R., Schlee W.
12:15-12:30 **O51**	**Tinnitus: Heterogeneous patterns of burden and complex types of causal pathways - a latent class mixture modelling approach.** Frick U., Langguth B., Frick H., Schlee W., Landgrebe M.	12:15-12:30 **O52**	**Individualizing the spectrum of tinnitus maskers can make them more efficient than white noise.** Brimijoin W.O., Porr B.
12:30-13:30	**Lunch**		
Parallel 11 – location: Lecture Theatre **Available interventions (psychological & auditory)** **Chairs: Alain Londero & Lucy Handscomb**		**Parallel 12 – location: Conference Suite 2** **Genetics** **Chairs: Jose Antonio Lopez-Escamez & Caroline Wilson**	
13:30-13:45 **O53**	**Mindfulness-Based Cognitive Therapy for Tinnitus: A Randomised Controlled Trial.** Marks E.M., McKenna L., Schaette R.	13:30-13:45 **O54**	**Neuregulin-1 Signaling in the Hippocampus Contributes to Tinnitus.** Bao, J., Nakamoto K., Zuo H., Nelson C.
13:45-14:00 **O55**	**The Development of Acceptance of Chronic Tinnitus in the Course of a Cognitive-behavioural Group Therapy.** Moschen R., Riedl D., Zorowka P.G., Rumpold G.	13:45-14:00 **O56**	**Characterization of tinnitus sub-types in a large Swedish family with multiple tinnitus cases for Whole Exome Sequencing.** Edvall N., Bibas T., Cima R.F., Canlon B., Knipper M., Lopez-Escamez J.A, Mazurek B., Szczepek A., Cederroth C.R.
14:00-14:15 **O57**	**Developing an audiologist-delivered psychological intervention for people with tinnitus.** Thompson D.M., Hall D.A., Walker D.M., Hoare D.J.	14:00-14:15 **O58**	**Genome-Wide Association Study on Tinnitus Heritability.** Gilles A., Fransen E., Van Camp G., Van de Heyning P.
14:15-14:30 **O59**	**Hearing training with fitted hearing aids to improve speech in noise perception in patients suffering from chronic tinnitus.** Ivansic-Blau D., Müller B., Reinhardt D., Guntinas-Lichius O.	14:15-14:30 **O60**	**ARHL and Tinnitus in Portuguese Population: what we can hear from a sample of elderly individuals.** FlooK M., Lopes S., Aparicio M., Santos R., Andrade C., Andrade S., Martins J.H., O'Neill A., Escada P., Arguello P., Alcântara, P., O'Neill J., Vilaverde Cabral M., Antunes

			M., Matos T.D., Fialho G., Caria H.
14:30-14:45 **O61**	**Neuro-Music Therapy: Impact of hearing aids on therapy outcome.** Argstatter, H., Grapp M.	14:30-14:45 **O62**	**Extreme Tinnitus Phenotype in Meniere's Disease.** Espinosa-Sanchez J.M., Frejo L., Batuecas-Caletrio A., Sanchez-Gomez H., Lopez-Escamez J.A.
14:45-15:00 **O63**	**Tinnitus Network and the results of the TMNM trial against tonal tinnitus.** Pantev, C.	14:45-15:00 **O64**	**Factors predicting hearing loss and associating with the compensation status in a cohort of 701 tinnitus patients.** Szczepek A.J., Mazurek B.
15:00-15:30	**Coffee**		
15:30-16:30	**Keynote: Charles Liberman** **"Cochlear synaptopathy - a possible role in the generation of tinnitus"** **Chair: Alan Palmer**		
	Close		

Keynote and invited speakers

Brief Biographies

Gerhard Andersson

"Using the internet to develop and evaluate tinnitus treatments"

Gerhard Andersson, Ph.D. is a professor of Clinical Psychology in the Department of Behavioural Sciences and Learning at Linköping University. He has also been a guest professor at Karolinska Institutet, Stockholm (2007-2012) in the Department of Clinical Neuroscience, Psychiatry (section for Internet Psychiatry), and now continues as an affiliated professor. His clinical work is mainly devoted to audiology, and he has a part-time position as a Clinical Psychologist in the Tinnitus team at the Department of Audiology, Linköping University Hospital. Professor Andersson received his M.Sc. in Clinical Psychology from Uppsala University in 1991. His first Ph.D. was in Clinical Psychology (1995), and his second Ph.D. was in Medicine (2000). He has also completed a B.A. in Theology (2010). Professor Andersson has published over 420 research papers and 15 books, and his research interests include: 1) Cognitive behavioural treatment and psychotherapy, 2) the biological mechanisms, epidemiology and psychological aspects of tinnitus and hearing loss, and 3) using the internet to provide guided psychological treatment.

David Baguley

"The association between tinnitus and hyperacusis: causal, indirect, or coincidence?"

David Baguley is Head of Service: Audiology/Hearing Implants at Cambridge University Hospitals, UK. His initial studies were at the University of Manchester in Psychology (BSc 1980-1983) and then Clinical Audiology (MSc 1984). David has worked in Audiology at Addenbrooke's Hospital since 1985, becoming the Consultant Clinical Scientist in 1989. He has over 140 peer-review publications, and a PhD on the subject of tinnitus from the University of Cambridge (2005). He is a co-author on the books: 'Tinnitus: a multidisciplinary approach' (second edition, Wiley, 2013) and 'Hyperacusis' (Plural, 2007) and co-edited the latest edition of Ballantyne's Deafness (2009) with John Graham. In 2006 David received an International Award in Hearing from the American Academy of Audiology, and has twice been awarded the Shapiro Prize from the British Tinnitus Association for tinnitus research (2005, 2008). He is a Visiting Professor at Anglia Ruskin University. David's clinical and research interests focus upon tinnitus and hyperacusis, with the aim of understanding these symptoms and designing and evaluating novel and innovative interventions.

Karl Friston

"Dynamic causal modelling of the auditory system"

Professor Karl Friston is a theoretical neuroscientist and authority on brain imaging. He is the Scien tific Director of the Wellcome Trust Centre for Neuroimaging at University College London. He invented statistical parametric mapping (SPM), voxel-based morphometry (VBM) and dynamic causal modelling (DCM). These contributions were motivated by schizophrenia research and theoretical studies of value-learning – formulated as the dysconnection hypothesis of schizophrenia. Mathematical contributions include variational Laplacian procedures and generalized filtering for hierarchical Bayesian model inversion. Professor Friston currently works on models of functional integration in the human brain and the

principles that underlie neuronal interactions. His main contribution to theoretical neurobiology is a free-energy principle for action and perception (active inference). He received the first Young Investigators Award in Human Brain Mapping (1996) and was elected a Fellow of the Academy of Medical Sciences (1999). In 2000 he was President of the international Organization of Human Brain Mapping. In 2003 he was awarded the Minerva Golden Brain Award and was elected a Fellow of the Royal Society in 2006. In 2008 he received a Medal, Collège de France and an Honorary Doctorate from the University of York in 2011. He became of Fellow of the Society of Biology in 2012, received the Weldon Memorial prize and Medal in 2013 for contributions to mathematical biology and was elected as a member of EMBO (excellence in the life sciences) in 2014.

Charles Liberman

"Cochlear synaptopathy - a possible role in the generation of tinnitus"

M. Charles Liberman, Ph.D. is the Schuknecht Professor of Otology and Laryngology at the Harvard Medical School and the Director of the Eaton-Peabody Laboratories at the Massachusetts Eye and Ear Infirmary, one of the largest and best-known research groups devoted to the study of hearing and deafness. The laboratory comprises 27 investigators, with research foci spanning all aspects of the auditory system from sound transmission in the middle ear, through signal transduction in the inner ear and neural processing in the central nervous system. Dr Liberman received his B.A. in Biology from Harvard College in 1972 and his Ph.D. in Physiology from Harvard Medical School in 1976. He has been on the faculty at Harvard since 1979, has published over 150 papers on a variety of topics in auditory neuroscience and is the recipient of the Award of Merit from the Association for Research in Otolaryngology, the Carhart Award from the American Auditory Society and Bekesy Silver Medal from the Acoustical Society of America. His research interests include 1) coding of acoustic stimuli as neural responses, 2) efferent feedback control of the auditory periphery, 3) mechanisms underlying noise-induced hearing loss, 4) the signaling pathways mediating nerve survival in the inner ear and 5) application of cell- and drug-based therapies to the repair of a damaged inner ear.

Josef Rauschecker

"Frontostriatal Dysfunction in Chronic Tinnitus"

Josef P. Rauschecker studied at TUM and LMU Munich (Electrical Engineering and Medicine) and at the Universities of Sussex and Cambridge, England (Artificial Intelligence and Physiology). He received his Ph.D. from TUM in 1980 for work performed at the Max Planck Institute (MPI) for Psychiatry in Munich and his habilitation (D.Sc.) for Neurophysiology in 1985 at Eberhard Karls University Tübingen. After working as Staff Scientist at the MPI for Biological Cybernetics from 1981-1989, he joined the National Institute of Mental Health (USA) as Senior Investigator in the Laboratories of Neuropsychology and Neurophysiology in 1989. Since 1995, he has been a Professor of Physiology and Biophysics, Neurology, and Neuroscience at Georgetown University, where he is also Director of the Laboratory of Integrative Neuroscience and Cognition (LINC) and has served on the university's Executive Council and on its Steering Committee.

Josef Rauschecker has 35 years of experience in systems and cognitive neuroscience, >25 years of experience in animal electrophysiology, and >15 years of experience with functional magnetic resonance imaging (fMRI). At Georgetown University Medical Center, he helped create the first human fMRI research facility and participated in the implementation of the first 7-Tesla small-animal MRI. He has numerous pertinent publications in peer-reviewed journals and has been the mentor of >30 graduate students and postdoctoral fellows. Josef P. Rauschecker's research is funded by the National Institutes of Health (USA) and the National Science Foundation (USA). He has also held visiting appointments at several institutions, including Harvard Medical School,

Rockefeller University, The Salk Institute, and Aalto University. He has been the recipient of a Humboldt Award and a Finland Distinguished Professorship and is currently Hans-Fischer Senior Fellow at the Institute for Advanced Study at TU Munich.

Winfried Schlee

"Towards a better understanding of tinnitus heterogeneity"

Winfried Schlee (born in 1978) is a German neuropsychologist at the University of Regensburg. He studied psychology, statistics and philosophy at the University of Konstanz and the University of Alabama at Birmingham. In 2009 he obtained his PhD in clinical neuropsychology at Konstanz where he introduced the concept of the Global Model of Tinnitus Perception to explain the neuronal mechanisms underlying the conscious perception of the tinnitus percept. Since then, Dr Schlee has studied various factors influencing the conscious perception of tinnitus, among them the influence of age, stress and emotional arousal, the interference with auditory, electric and magnetic stimulations, as well as intrinsic neuronal moment-to-moment fluctuations of the resting alpha activity in temporal brain regions. In 2013, he joined the Tinnitus Research Initiative (TRI) where his current work focuses on discovering new methods for the treatment and measurement of chronic tinnitus. He is also chair of the European COST project "TINNET - Better understanding the tinnitus heterogeneity to improve and develop new treatments", which started in April 2014.

Veronica Kennedy

"Management of Tinnitus in Children – the UK approach"

Dr Veronica Kennedy is an Audiovestibular Physician, based in Bolton, UK, specialising in hearing and balance disorders in children. She has had a long standing interest in tinnitus both in adults and children. She is a member of the TINNET Clinical Outcomes Working Group. As part of the British Society of Audiology multidisciplinary working group, she co-authored national Good Practice Guidance on the assessment and management of tinnitus in children. She is actively involved with the British Tinnitus Association who has developed leaflets and school resources for children with tinnitus.

Michael Landrebe

"**The TRI database: Big data as a chance to improve clinical characterisation and development of new treatments for tinnitus"**

Michael Landgrebe is a senior physician and specialist in psychiatry and psychotherapy at the University of Regensburg, Germany. He received his PhD and doctorate in medicine from the University of Göttingen in 1999 and moved to the University of Regensburg in 2004. He is the co-chair of the TINNET Working Group 2, focusing on standards for data management and analyses.

Susan Shore

"Harnessing multisensory metaplasticity to treat tinnitus"

Professor Shore received her B.A. in Speech Pathology and Audiology and her M.A. in Hearing Science (Cum Laude) in the Department of Speech Pathology and Audiology, University of Witwatersrand, Johannesburg, South Africa. She received her Ph.D. in Physiology at the Kresge Hearing Research Laboratory of the South in New Orleans, Louisiana. Postdoctoral studies were conducted at the University of Pittsburgh and Kresge Hearing Research Institute, University of Michigan Medical School. Currently, Dr Shore is a Professor of Otolaryngology, Molecular and Integrative Physiology and Biomedical Engineering at the University of Michigan in Ann Arbor, Michigan. She also holds the Joseph Hawkins Collegiate Research Professorship at the University of Michigan.

Professor Shore's laboratory studies the contributions of multisensory systems to auditory processing and discovered that 'touch-sensitive' neurons in the brain, that receive input from the face and head, send neural projections to the auditory brainstem. Most remarkably, after unilateral deafness, there is a strong enhancement in somatosensory influences on the cochlear nucleus, as if in compensation for the loss of input from the cochlea. Furthermore, in animals with tinnitus, there is increased excitation from the somatosensory system (http://www.uofmhealth.org/news/tinnitus-kresge-0201). Work extending these findings is now focused on stimulus-timing dependent synaptic plasticity as an underlying mechanism to explain the long-term nature of these changes (http://www.uofmhealth.org/news/archive/201312/u-m-tinnitus-discovery-opens-door-possible-new-treatment). Ongoing work is laying the groundwork for treatments that include specific, patterned stimulation that may 'reverse' the increased excitation that contributes to tinnitus.

Abstracts

Oral Presentations

Keynote: Winny Schlee (TINNET)

"Towards a better understanding of tinnitus heterogeneity"

The TINNET COST Action was established in 2014 to create a pan-European network of tinnitus researchers with the ultimate goal to reach a better scientific understanding of the heterogeneity of tinnitus. In order to effectively address the heterogeneity of tinnitus, a coordinated effort of all relevant disciplines is required to enable a European standard for the assessment of tinnitus characteristics and the joint analysis of a large database of tinnitus cases. Consequently, five workgroups were formed which concentrate on different aspects: 1) Clinical Workgroup, 2) Database Workgroup, 3) Neuroimaging Workgroup, 4) Genetics Workgroup and 5) Outcome Measures Workgroup. The TINNET Action is funded by the European COST framework, which specifically funds European networking activities in science and technology.
In this talk, I will first describe the organizational structure of the TINNET Action and how we can use this network together in order to advance the scientific effort towards a better understanding of tinnitus heterogeneity.
Second, I will outline the theoretical framework underlying the concept of tinnitus heterogeneity. The framework will be critically discussed and evaluated in light of the most recent scientific findings in the field.

Keynote: Michael Landgrebe

"The TRI database: Big data as a chance to improve clinical characterisation and development of new treatments for tinnitus"

Michael Landgrebe, Winfried Schlee, Susanne Staudinger, Berthold Langguth

Tinnitus represents a heterogeneous condition, which causes significant morbidity in many patients. Up to now, there are different treatment options available from which some patients benefit while they fail in others suggesting that there are different forms of tinnitus, which differ in their pathophysiology and their response to specific treatments. A challenge for tinnitus treatment is therefore the identification of the most promising therapy for the individual patient based on clinical criteria as well as the development of new, promising treatment approaches. However most available clinical treatment studies have only enrolled relative small patient samples, making it difficult to identify predictors of treatment response for specific approaches. Furthermore, inter-study comparability is limited due to the use of varying methods of tinnitus measures and different outcome parameters. Systematic data collection according to predefined methodological standards is one way to overcome these limitations. The TRI database is an international research initiative aiming at collecting data from clinical studies in tinnitus patients in a standardized manner based on an international consensus. Due to its multicentre approach ensuring compatibility of the data from different centers, clinical data from tinnitus patients can be collected in a reasonable time. With growing size, this database will provide the opportunity to test research hypothesis on big data samples and derive new treatment approaches or definition on predictor values for treatment outcome in an un-biased, data-driven way. In general, this

research project is open to every clinical researcher under the precondition that the defined standards of patient assessment and outcome measurement are followed.

O1: TINNET COST Action BM1306 - Clinical WG1: Establishment of a standard for Tinnitus; patient assessment, characterization, and treatment options.

Cima R.F[1, 2, 3]., Haider H[4]., Mazurek B[5]., Cederroth C.R[6]., Lapira A[7]., Kikidis D[8]., Norena A[9]. ([1]Department of Clinical Psychological Science, Maastricht University, The Netherlands, [2]Adelante, Centre for Expertise in Rehabilitation & Audiology, The Netherlands, [3]Behavioural Medicine, University of Leuven, Belgium, [4]ENT Department of Hospital Cuf Infante Santo - Nova Medical School, Travessa do Castro, Lisbon, Portugal,[5] Tinnitus Center, Charité, Germany, [6]Karolinska Institutet, Sweden, [7]Nova Southeastern University, Florida, USA, [8]National and Kapodistrian University of Athens, Athens, Greece,[91]University Aix-Marseille, Laboratory of Integrative and Adaptive Neuroscience, Marseille, France)

Tinnitus, the perception of a phantom sound, is a widespread auditory symptom [1]. Over 70 million people in Europe experience tinnitus, for 7 million it creates a debilitating condition. Tinnitus is a highly complex condition with a multifactorial origin, and therefore heterogeneous patient-profiles, standard treatment, assessment, and referral-trajectories are rare, inflexible and often insufficient. There is increasing need for European harmonized guidelines for demographic and clinical assessment of tinnitus sufferers, since lack of standard guidelines, leads to untreated, under-, as well as over-treated patients. This leads to increasing complaints, prolonged suffering, and loss of societal participation, health care overuse, endless referral trajectories and resulting in enormous psychological, societal and economic burden in Europe [2]. Through development and implementation of a European guideline we anticipate that management; assessment and treatment of tinnitus will be significantly more effective, leading to reduced suffering and frustration for patients, their families and clinicians alike.

Aim

The main goal of this working group is to establish consensus-based uniformity with regards to management, assessment and treatment of patients with different tinnitus profiles. In addition, we aim to establish consistency in policy regarding referral trajectories, thereby decreasing the need for multiple second opinions, and over- and under-diagnostics and treatment. Guidelines for detailed clinical definition and characterisation of cases will also be developed. Experts from different disciplines across Europe joined forces to further develop standardization procedures for easy, practicable and meaningful patient-profiling.

Method

The first step towards the development of meaningful and actionable guidelines for the assessment and treatment of tinnitus patients will involve a pan European survey amongst experts, clinicians and policy makers to investigate current standards in tinnitus care. This will lead to an updated description of the state of the art on standard care in Europe [3]. The second step is to review existing guidelines internationally, including but not limited to Europe alone. Third, the state of the art on clinical assessment of tinnitus (meaningful patient characterisation) and treatment options will be described. Results from the survey as well as the review of existing guidelines, and reviews on state of the art in assessment and treatment, will be used to develop an initial draft description of a European guideline. Finally, using Delphi consensus methodology, we aim to achieve harmonized and adaptive clinical European guidelines for the management, assessment and treatment for tinnitus patients

Results

Working group 1 'Clinical Guidelines', within the scope and duration of the TINNET project, aims to: Description of current European standard in tinnitus healthcare

Review existing guidelines
Describe the state of the art of clinical assessments and existing treatment options for tinnitus offer consensus-based European guidelines for assessment, treatment and clinical definition/characterization of tinnitus

References
1. Martinez et al. Ear Hear-2015
2. Maes et al. Ear Hear-2013
3. Langguth et al. ProgBrainRes-2007

O2: TINNET COST Action BM1306 – Subtyping WG3. Subtyping tinnitus and neuroimaging.
van Dijk P[1]., Norena A[2]., Langers D[1]., Adjamian P[3]. ([1]*University of Groningen, University Medical Center Groningen, Department of Otorhinolaryngology, The Netherlands, [2]Aix Marseille Université, Marseille, France [2]MRC Institute of Hearing Research, Nottingham, United Kingdom)*

Although tinnitus appears to be associated with some form of peripheral damage in nearly all cases, the function of the brain is believed to be essential in (1) the generation of tinnitus, (2) the transition from acute to chronic tinnitus and (3) the burden of tinnitus. Neuroimaging offers the possibility to investigate neurophysiological brain mechanisms that are involved in tinnitus. Most neuroimaging tinnitus studies have compared a specific groups of tinnitus subjects to e.g. subjects without tinnitus. In this approach a limited number of subjects are included, having putatively the same tinnitus sub-type (i.e. acute tinnitus caused by noise trauma). However, the ambition of TINNET is the definition of multiple tinnitus subtypes. Hence, another approach is to investigate a large group of tinnitus subjects and compare them against each other. The large scale of such an approach requires a multi-center collaboration. An inherent step in setting up multi-center neuroimaging tinnitus studies is standardization of the study procedures. TINNET Workgroup 3 has decided to focus on EEG and fMRI, and to focus on standardization of application of these techniques for tinnitus research. During the presentation, we will present the current status of this standardization process. Also, it will be important to connect human and animal research, such that human neuroimaging findings can be translated to animal experiments and animal findings can be validated in human subjects. Our presentation will also outline some thoughts on this translational aspects of tinnitus imaging.

O3: TINNET COST Action BM1306 - Outcome WG5: Systematic review of outcomes in tinnitus trials.

Presentation on behalf of Core Outcome Measures in Tinnitus (COMiT) Initiative.

Awaiting abstract.

O4: TINNET COST Action BM1306 - Genetics WG4. Improving diagnosis and drug development through the understanding of tinnitus subtypes.

Lopez-Escamez J.A., Cima R.F.F., Mazurek B., Szczepek A., Knipper M., Bibas T., Van de Heyning P., Cederroth C.R.

Awaiting abstract.

O4: Genetic susceptibility to tinnitus in a Swedish Twin cohort.

Requena Navarro M.T[1]., Maas I.L[2]., Brüggemann P[2]., Edvall N[3]., Szczepek A[4]., Canlon B[3]., Mazurek B[2]., Lopez-Escamez J.A[1]., Cederroth C.R[3]. ([1]University of Granada, GENYO, Spain, [2]Tinnitus Center, Charité, Germany, [3]Karolinska Institutet, Sweden, [4]Charité-Universitätsmedizin Berlin, Germany)

Tinnitus, the phantom perception of sounds in their physical absence, is a prevalent condition that affects near 15% of the population. Whereas it is thought that tinnitus has a major environmental component, potential genetic contributions have been overlooked. Here, the TINNET Genetics Working Group IV evaluated the relative importance of genetic influences on self-reported tinnitus in a sample of monozygotic (MZ) and dizygotic (DZ) Swedish twins. The study sample consisted of 48,676 twin pairs who participated to two large studies, namely STAGE and SALT, and that answered to the question "Do you have buzzing in your ears?". Probandwise concordance rates (the risk for one twin to be affected given that his/her twin partner has tinnitus) were evaluated for MZ and DZ twin pairs of either same or opposite sex. Heritability coefficients (the proportion of the total variance attributable to genetic factors) were calculated using standard biometrical model fitting procedures. The results showed near twice-higher concordance of tinnitus in MZ than in DZ twins, which is indicative of genetic influences on tinnitus development. Genetic factors explained 27.8% of the individual differences in bilateral tinnitus. We attribute this low genetic contribution to the imprecise nature of self-reporting cases. Subtyping strategies in twin cohorts might help defining the true contribution of genetic factors to tinnitus vulnerability.

O5: The Replicated Single Case Experimental Design as an innovative method for assessing effectiveness of treatment.

Fuller T.E[1, 2]., Cima R.F[1, 2, 3]., Vlaeyen J.W.S[1, 3]. ([1]Department of Clinical Psychological Science, Maastricht University, The Netherlands, [2]Adelante, Centre for expertise in Rehabilitation & Audiology, The Netherlands, [3]Behavioural Medicine, University of Leuven, Belgium)

Background

Randomised controlled trials based on group designs are typically considered the gold standard of experimental design in establishing the effectiveness of an intervention as through randomisation and blinding they are designed to minimise threats to internal validity. However, while they can tell us if an intervention was effective, RCTs provide information about mean differences between groups rather than differences at an individual level. Additionally, the self-report data upon which they often rely is limited by inherent problems associated with retrospective data collection. A method to study which part of an intervention was particularly effective at an individual level is the experimental single case series design. This method features frequent, repeated data collection and can yield information that leads to increases in efficiency and/or effect sizes of treatments as ineffective components can be removed, and effective ones introduced earlier, increased or intensified.

In this replicated single-case series we aim to examine the effects of two components (hearing and tinnitus education; and exposure) from a stepped care, cognitive behavioural therapy based intervention for tinnitus distress that was recently found in a RCT to be highly effective in reducing tinnitus related distress (Cima et al, 2012). Both education and exposure are hypothesised to reduce levels of catastrophic misinterpretations and tinnitus related fear.

Method
We propose to examine the effects of no-treatment (component "A"), education (component "B") and exposure (component "C") within multiple-baseline, ABC and ACB study designs respectively in a single case series of N=16. This study design allows for participants to act as their own control and while also making it possible to exclude external factors as an explanation for any observed changes in the dependent variables. Importantly for strengthening the internal validity of the study, start dates and duration of the intervention components will be randomly determined. Frequent, repeated observations of the tinnitus related variables (e.g., fear, distress), will be collected applying ecological momentary assessment methods, with a purpose built smartphone application. Data will be analysed using randomisation tests, visual analytical methods and effect sizes will be calculated.

Results and discussion
The "in the moment" assessment of tinnitus catastrophizing and related fears, will provide ecologically valid data less affected by recall bias that will reveal the timing and extent of any intervention effects that occur. The results of this study will begin to shed light into the black box of CBT treatment for tinnitus fear and distress that in turn should lead to improvements in intervention efficiency and effect sizes.

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O6: Salicylate-induced changes in brain activity in awake guinea pigs.
Berger J.I., Coomber B., Hockley A., Wallace MN., Palmer A.R. (MRC Institute of Hearing Research, University Park, Nottingham, UK)

Studies conducted in human subjects with tinnitus have shown altered patterns of resting-state oscillatory brain activity. However, to date this has not been extensively explored using animal models, which allow more invasive examination of changes in neural activity and their correlation with objective behavioural measures of tinnitus.

Here, we describe the development of an awake preparation for examining tinnitus-related changes in resting-state and auditory-evoked brain activity. Guinea pigs were implanted with electrocorticography (ECoG) electrode arrays, with electrodes positioned on the surface of the dura over left and right auditory cortex and over the cerebellum, to monitor auditory brainstem responses (ABRs). ECoG responses were subsequently compared before and two hours after tinnitus induction with sodium salicylate (350 mg kg-1; i.p.), a drug which reliably induces tinnitus in both humans and animals.

Subtle salicylate-induced changes in oscillatory activity were observed in all animals recorded from electrodes over auditory cortex. Click-evoked cortical field potentials were dramatically enhanced (~100% increase) following salicylate treatment, potentially indicating increased sensitivity to sound (hyperacusis). This was despite the presence of reduced sensitivity at high frequencies in the periphery, as measured by ABRs. These salicylate-induced changes in spontaneous and auditory-evoked cortical potentials may be due to direct effects on neuronal excitability. Furthermore, in a separate group of animals, significant gap detection deficits in both behavioural and neural responses were observed following salicylate administration. Tinnitus induction with salicylate is widely used as an acute tinnitus model. The next stage will involve a chronic tinnitus model (induced by acoustic over-exposure), that will allow us to track neural changes throughout tinnitus development in an awake-behaving model.

O7: Using Monte Carlo Markov Chain Methods to Assess Tinnitus Characteristics.
Lentz J.J[1]., Silbert N.H[2]. ([1]Indiana University, Bloomington, Indiana, USA [2]University of Cincinnatti, Cincinnatti, USA)

A common tinnitus evaluation begins at the level of the case history, in which patients describe their tinnitus using descriptive terminology (e.g., "noisy, tonal"). Follow up testing relies on using pure tones or bands of noise to estimate the pitch of tinnitus. Together, these procedures provide an estimate of what tinnitus may sound like for a patient, but only yield a general estimation and cannot provide the details of that tinnitus perception to the audiologist. As many studies have demonstrated that the tinnitus percept can be more complex than is easily characterized using these tests, better methods of assessing the characteristics of the tinnitus percept are needed. The work presented here proposes a new method that, once fully developed, can provide a more sophisticated descriptor of the tinnitus percept without requiring an intractable amount of time for data collection. Here, we describe our initial data on the application of Markov Chain Monte Carlo methods to assess tinnitus characteristics. As this work is in the early stages, we present data on the ability of this method to characterize tinnitus pitch and degree of "noisiness," as quantified via bandwidth. Data from both normally hearing subjects and tinnitus subjects will be presented. The data from normally hearing subjects are used to validate this method and illustrate how well this method is able to converge on the perception of known acoustic tokens. Data from tinnitus patients will be compared to those from other methods of tinnitus assessment, such as audiometric pitch matching, rating methods, and categorization methods. Results will be discussed in terms of the reliability of this new method and its ability to yield similar results to other assessment methods.

O8: Tinnitus-related neuroplasticity within the auditory system of Mongolian gerbils.
Schulze H., Tziridis K., Krauss P., Schilling A. (Experimental Otolaryngology, University of Erlangen-Nürnberg, Germany)

Current models of tinnitus development postulate a damage of the receptor epithelium of the cochlea being etiologic for neuroplastic changes within the central auditory system up to the auditory cortex (AC) that finally lead to the perception of subjective tinnitus. Recently we have demonstrated that there seems to be a predisposition for the development of tinnitus after noise trauma (Ahlf et al., 2012; Tziridis et al., 2015): In our animal model, the Mongolian gerbil, noise trauma (2 kHz, 115 dB SPL, 75 min) led to behavioral signs of tinnitus in about 75% of subjects (group T), while the remaining animals (group NT) did not develop the condition. Neuronal activity in AC of both groups did differ already before noise trauma: In contrast to T animals, NT animals showed significantly higher overall evoked activity in AC, especially to frequencies up to 4 kHz. Post trauma, these animals reduced this AC activity to levels seen in group T before trauma. In contrast, T animals did not show such reduction of AC activity, but rather an increase in AC response strength to high tone frequencies which possibly corresponds to the tinnitus percept.

Based on these data we here postulate a model for tinnitus development, where a bottom-up mechanism initially increases neuronal gain within damages frequency channels by means of stochastic resonance (SR) to compensate for noise induced hearing loss caused by the noise trauma. There, the optimal level of neuronal noise for SR at the receptor output is adjusted via an autocorrelation based mechanism (Krauss et al., 2015). In addition, a global top-down inhibitory mechanism secondarily counteracts an activity increase in more central parts of the auditory pathway to prevent the development of tinnitus as an epiphenomenon of hearing threshold restoration by gain increase. This top-down mechanism requires high activity levels in AC to be effective which are only available in group NT. T animals on the other hand show low AC activity already before noise trauma that cannot be reduced further, so that they cannot counteract the compensatory gain increase from the periphery and in the consequence develop central tinnitus.

This model therefore not only explains how central tinnitus develops but also why some subjects develop tinnitus while others with the same hearing loss do not.

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O9: Patterns across outcome domains: a systematic review of tinnitus trials.

Haider H.F[1]., Hall D.A[2]. ([1]ENT Department of Hospital Cuf Infante Santo - Nova Medical School, Travessa do Castro, Lisbon, Portugal, [2]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK)

Rationale
Tinnitus is a hearing disorder which consists in the perception of a sound in the absence of a corresponding auditory stimulus. Tinnitus is experienced by 10-20% of the population and no cure has been found yet. However the suffering and que quality of life from these patients can be improved with the establishment of consensual general guidelines, a core set of outcome domains, patient outcome measures and assessment tools. Being such a subjective condition, as a first step, it is crucial to determine the primary outcome aspects (domains) underlying Tinnitus, in order to contribute to the progress in the development of successful treatments.

Objective
The goal of this presentation is to analyze the patterns across primary outcome domains included in Tinnitus research. Through systematic review of recent literature (from July 2006) we examined the main aspects which have previously been used in clinical trials of interventions for patients with tinnitus. Therefore, the current study will contribute to the development of a core domain set for future controlled trials on tinnitus treatment effectiveness.

Methods
Records were identified by searching electronic databases of research literature, such as PubMed, Embase and CINAHL, and electronic trial registers of ongoing clinical trials. Some additional records were identified by hand-searching methods, performing a total of 3029 records in total. After a rigorous selection by two independent raters, this number was reduced to a final set of 228 records. Studies were eligible for inclusion if they were related to tinnitus as primary outcome, even when it was not specified. All the participants were adults and the sample size of each study considered should be equal or greater than 20 participants. Also these studies had to be written in English and published in print on or after July 2006. Data collection was then conducted by a pool of 20 project team members of COMiT in which two independent raters collected the data according to detailed guidance for notes.

Results

The 228 records included 505 primary domains outcomes, describing 35 different types of primary domain. The most popular primary outcome domain directly relating to tinnitus was "tinnitus loudness" (70, 14%), followed by "tinnitus distress" (33, 7%) and "tinnitus annoyance" (21, 4%). Over half (279, 55%) of the data entries did not clearly describe the complaint of interest. Authors did not specified what domain their trial intended to assess on 128 occasions (25%), not possible to code (58, 12%).

Discussion. This review is a first step to better understand domains patterns through Tinnitus research. The fact that a significant amount of these studies did not clearly describe the primary outcome domain reinforces the need for standardization of this aspect. Our findings highlight the urgency in standardize outcomes domains as well as outcomes measurements in order to become more reliable the comparison among different Tinnitus trials and to increase tinnitus treatment effectiveness in a near future.

O10: Paired Auditory-Somatosensory Stimulation Therapy Reverses Tinnitus in Guinea Pigs.

Martel D.T., Wu C., Shore S.E. (University of Michigan, Ann Arbor, Michigan, USA)

Introduction

Tinnitus, the phantom perception of sound, has been linked to increased spontaneous activity in the dorsal cochlear nucleus (DCN). The principal output neurons of the DCN, fusiform cells, integrate auditory nerve and somatosensory inputs through the process of stimulus-timing dependent plasticity (STDP)(Koehler and Shore, 2013a). In animals that develop tinnitus after noise exposure, STDP timing rules are broader in the excitatory phase. Further, spontaneous activity is increased compared to sham exposed or animals that did not develop tinnitus (Koehler and Shore, 2013b), suggesting that tinnitus arises from heightened excitability in the somatosensory-fusiform cell circuit. The suppressive phase of STDP timing rules predict that properly applied transdermal stimulation could reduce DCN circuit excitability (Wu et al., 2015). In this study, by combining auditory and somatosensory stimulation at a specific bimodal interval, we induced long-term suppression in noise-damaged guinea pigs with tinnitus as a non-invasive tinnitus therapy.

Methods

Guinea pigs were noise-exposed with a 7 kHz-centered, half-octave band at 97 dB SPL for 2 hours to induce a temporary threshold shift, measured with auditory brainstem responses (ABRs). Gap-Prepulse Inhibition of Acoustic Startle (GPIAS) was used to assess tinnitus. Somatosensory stimulation was provided via transdermal stimulating electrodes placed near the C2 cervical vertebrae. Electrical stimuli were presented within 20 ms of 40 dB SL sounds matching the tinnitus spectra. Tinnitus animals were treated for four weeks concurrently with biweekly tinnitus assessments. A control group of tinnitus animals received a sham-treatment. Following treatment cessation, single unit recordings from fusiform cells were performed with multichannel recording electrodes placed stereotaxically into the DCN after ketamine/xylazine anesthesia.

Results

Noise-exposed animals exhibited 20-40 dB ABR threshold shifts, which recovered within two weeks. Animals with tinnitus showed inverted STDP rules and elevated spontaneous activity at the confirmed tinnitus frequencies. In contrast, exposed animals without tinnitus showed decreased spontaneous activity compared to the tinnitus animals and unexposed controls. Animals receiving STDP therapy showed frequency-specific decreases in spontaneous activity, which correlated with a reduction in behavioral evidence of tinnitus.

Conclusions

These results demonstrate that non-invasive, long-term alterations of fusiform cell activity through STDP can be used to alleviate behavioral and neural correlates of tinnitus. This treatment strategy has the potential to provide relief to a large number of human tinnitus sufferers.

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O11: Tinnitus is associated with reduced sound level tolerance in adolescents with normal audiograms and otoacoustic emissions.

Sanchez T.G[1, 2]., Roberts L.E[3]. ([1]Instituto Ganz Sanchez, São Paulo, Brazil, [2]University of São Paulo Medical School, São Paulo, Brazil, [3]McMaster University, Hamilton, Canada)

Introduction

Recent research in animals and humans suggests that tinnitus can reflect synaptic loss in the cochlea that does not express in the audiogram but leads to neural changes in auditory pathways that reduce sound level tolerance (SLT). Such findings lead one to ask whether persistent tinnitus experienced by adolescents is associated with changes in SLT that could be indicative of hidden hearing loss not detected by clinical audiometry. Moreover the prevalence of tinnitus among adolescents is also of interest, since its experience could have relevance for later hearing.

Objective

We sought (1) to estimate the prevalence of tinnitus among teenagers both by questionnaire and by psychoacoustic measurements; (2) contrast psychoacoustic measurements of tinnitus in adolescents with those established for adult chronic tinnitus sufferers; (3) assess loudness discomfort levels (LDL, a measure of SLT) in adolescents; (4) compare LDL, audiometry, and otoacoustic emissions at several frequencies between individuals reporting and not reporting tinnitus; and (5) assess the prevalence of potentially risky leisure listening habits in adolescents and their relation to their reports of tinnitus and loudness perception.

Methods: 170 adolescents completed a detailed questionnaire addressing their present or prior experience with tinnitus, potentially risky listening habits, and annoyance with ordinary sounds. All adolescents then underwent psychoacoustic measurements in a sound booth, comprising pure tone audiometry (0.25 to 16 kHz), LDLs, transient and distortion product otoacoustic emissions, and, for the adolescents with tinnitus, their pitch and loudness matching.

Results

By questionnaire, 54.7% of the adolescents reported that they had previously experienced tinnitus within the last 12 months. In the sound booth, 28.8% of the adolescents heard tinnitus; their pitch and loudness matches corresponded with those reported by chronic adult tinnitus sufferers. Neither hearing thresholds (≤15 dBHL to 16 kHz) nor otoacoustic emissions discriminated between adolescents reporting or not reporting tinnitus in the sound booth. However, LDL did so significantly, being 11.3 dB lower in adolescents experiencing tinnitus in the acoustic chamber ($p<0.00001$).

Risky listening habits were near universal among the adolescents. Interestingly, reports of these habits by teenagers experiencing tinnitus and reduced SLT in the sound booth indicated, not that they were exposed to higher levels of sounds, but that they tended to protect their hearing.

Conclusions
Tinnitus and reduced SLT could be interpreted as early prevalent indications of a vulnerability to develop hidden synaptic injury in adolescents exposed to high level environmental and recreational sounds. Moreover, this hidden damage is not perceived as hearing complaint nor expressed in the pure tone audiometry or otoacoustic emissions. If the findings of animal research – showing that such injury is followed by a gradual loss of spiral ganglion cells in the cochlea that progresses over a human time scale of decades – would happen in adolescents, our findings suggest that they could become a generation with persistent tinnitus and hearing difficulties later in life, but earlier than previous generations.

O12: Long-Lasting Sound-Evoked Afterdischarge in the Auditory Midbrain.
Oliver D[1]., Ono M[1,2]. ([1]University of Connecticut - UConn Health, Connecticut, USA, [2]Kanazawa Medical University, Japan)

Different forms of plasticity are known to play a critical role in the processing of information about sound. Here, we report a novel neural plastic response in the inferior colliculus, an auditory center in the midbrain of the auditory pathway. A vigorous, long-lasting sound-evoked afterdischarge (LSA) is seen in a subpopulation of both glutamatergic and GABAergic neurons in the central nucleus of the inferior colliculus of normal hearing mice. These neurons were identified with single unit recordings and optogenetics in vivo. The LSA can continue for up to several minutes after the offset of the sound. LSA is induced by long-lasting, or repetitive short-duration, innocuous sounds. Neurons with LSA showed less adaptation than the neurons without LSA. The mechanisms that cause this neural behavior are unknown but may be a function of intrinsic mechanisms or the microcircuitry of the inferior colliculus. Since LSA produces long-lasting firing in the absence of sound, it may be relevant to temporary or chronic tinnitus or to some other aftereffect of long-duration sound.

O13: Tinnitus Concern Questioner.
Bauman N. (Tinnitus Practitioners Association, Hamden, Connecticut, USA)

As early as in 1988 Hallam et al and later Wilson et al in 1991 considered various factors which may affect person's reactivity to tinnitus. Reaction or over-reaction can create in some a catastrophic response to tinnitus.

Each tinnitus patient may have a very specific reason for their reaction to tinnitus which may explain why tinnitus becomes a debilitating problem to some and a benign event to others.

Many tinnitus inventories have been developed in order to help to assess the tinnitus handicap. Such questioners also serve as a validation tool of the tinnitus treatment program. However, there is a need to be able to identify the specific factors which are than responsible for different degrees obtained by the handicap tests.

The Tinnitus Concern Questioner (TCQ) was developed to help to identify the main concern/s tinnitus patient identifies as the primary reason for over-reacting to this perceived "evil" sound event.

Clinical observations over several years of treating tinnitus patients helped to identify what are some of the main concerns responsible for how strong the dislike and aversion to tinnitus becomes. In other words, we tried to recognize what are the factors which categorize the tinnitus patient on the spectrum from acceptable tinnitus to perceiving tinnitus as a catastrophic event.
The results of this clinical study will be presented. Preliminary data will be shown as to the application of such focused tinnitus treatment based on the results of the TCQ.

O14: Effect of sound exposure on neuronal firing in the inferior colliculus of awake mice.
Longenecker R.J., Galazyuk A.V. (Northeast Ohio Medical University, Ohio, USA)

Aims and Objectives
It is well established that acoustic over exposure can increase the risk of suffering from hearing loss and/or tinnitus. Sound trauma often leads to reduced input to the central auditory system. Compensatory plastic changes often result in pathologic hyperactivity developed in auditory neurons, which may underpin tinnitus. Recordings from anesthetized animals have shown coincidence of hyperactivity and burst firing in the cochlear nucleus, inferior colliculus, medial geniculate body, and auditory cortex after sound exposure. However, it is not well understood which of these abnormal activities are linked to tinnitus.

Methods
A possible relationship between abnormal brain activity, tinnitus, and hearing loss was tested in individual CBA/CaJ mice following sound exposure. An improved method utilizing gap-prepulse inhibition of the acoustic startle reflex was used to detect tinnitus whereas PPI audiometry was used to assess for possible hearing loss following sound exposure. Extracellular single unit recordings were conducted to assess firing activity in inferior colliculus neurons. Both spontaneous and bursting activity in IC neurons were measured and compared in sound exposed tinnitus positive and tinnitus negative animals as well as in control unexposed mice. Recordings were conducted in awake animals to exclude a possible effect of anesthesia on the test results

Results
We found that hyperactivity is a typical phenomenon following sound exposure and it is largely independent whether animal exhibits tinnitus. In contrast to previous findings, we found an increase in bursting activity of IC neurons is likely to be linked to severe hearing loss rather than to tinnitus.

Conclusions
Hyperactivity seems to be a ubiquitous feature of sound-induced damage to the auditory system rather than a specific hallmark of tinnitus. Bursting activity might be a feature of highly damaged auditory systems. Future research is necessary to determine what features of these maladaptive changes are specifically linked to tinnitus.

This research was supported by grant R01 DC011330 and 1F31DC013498-01A1 from the National Institute on Deafness and Other Communication Disorders of the U.S. Public Health Service.

O15: Pathognomonic tinnitus percepts, even when intermittent or intermixed with non-specific tinnitus, (i) identify tinnitus subtypes, (ii) suggest the tinnitus mechanism, and (iii) can lead to successful intervention.
Levine R.A. (Tel Aviv Medical Center, Israel)

The tinnitus percept can vary in multiple dimensions including: loudness, quality (including pitch), location, temporal pattern, and how it interacts with activation of both the auditory and non-auditory neural systems (e.g. acoustic masking and somatic testing). From this matrix of possibilities has emerged two pathognomonic tinnitus percepts that have specific (1) etiologies, (2) generating mechanisms, and (3) treatments. The two pathognomonic tinnitus percepts are as follows:
[A] Clicking ("Typewriter") Tinnitus: its percept is pathognomonic (monaural, staccato, irregular, and intermittent); it is caused by auditory nerve distortion usually from vascular compression, that results in ephaptic cross-talk between individual auditory nerve fibers. It can be suppressed by (a) carbamazepine or (b) auditory nerve decompression.

[B] Somatosensory Pulsatile Tinnitus Syndrome: its percept is pathognomonic (cardiac synchronous pulsations that can be abolished by intense head or neck muscle contractions). It is caused by a somatic myofascial dysfunction that leads to abnormal CNS interactions between the somatosensory and auditory systems. In some cases it can be abolished by (a) dry needling of head and neck trigger points or (b) auricular electrical stimulation.

A case series will be presented, supporting the notion that when a constant non-specific tinnitus percept is intermixed even intermittently with a forme fruste of one of these two types of pathognomonic tinnitus, detection of the pathognomonic component will point to the underlying cause of the constant non-specific percept, which in turn will lead to treatment that can abolish both percepts.
We conclude that in the case of monaural non-specific tinnitus, it is incumbent upon the physician to inquire whether there is ever the presence of typewriter-like clicking, even if very minor (infrequent and very soft). If such clicking is sometimes present, then the etiology is auditory nerve distortion, which will then lead to specific treatment options.

Similarly with any kind of non-specific tinnitus whether lateralized or not, the patient must be questioned whether it is sometimes pulsatile, even if very occasional and of low intensity. If it is sometimes pulsatile and the pulsations can be suppressed somatically, then the etiology is head or neck somatic myofascial dysfunction, which will then lead to a different set of specific treatment options.

O16: Long-lasting suppression of spontaneous firing in auditory neurons: implication to the phenomenon of residual inhibition.
Galazyuk A.V., Voytenko S.V., Grimsley C.A., Longenecker R.J. (Northeast Ohio Medical University, Ohio, USA)

Aims and Objectives
Tinnitus can be briefly eliminated/reduced after a masking stimulus has been terminated, the phenomenon known as "residual inhibition" (RI). About 80% of patients with tinnitus indicate some degree of RI (Vernon and Meikle, 2003; Roberts et al, 2006). Although RI was first described more than 100 years ago (Spaulding, 1903) the underlying mechanisms remains unknown. Recently we have demonstrated that sounds can trigger a long lasting suppression of spontaneous firing in auditory neurons after sound cessation (Voytenko and Galazyuk 2010; 2011). It is well known that hyperactivity or elevated spontaneous firing in the auditory system has been linked to tinnitus. If so, suppression of this activity by a sound should lead to tinnitus

suppression. Therefore this suppression might be an underlying mechanism of RI. The goal of this research was to test this hypothesis by determining whether major characteristics of this sound-triggered suppression resemble psychoacoustic properties of the RI.

Methods
Experiments were conducted on both the unexposed CBA/CaJ mice and mice with behavioral evidence of tinnitus. For tinnitus induction animals were exposed to a narrow-band noise centered at 12.5 kHz presented at 116 dB SPL unilaterally for 1 hour under Ketamine/Xylazine anesthesia. Tinnitus was assessed by using gap-induced prepulse inhibition of the acoustic startle reflex. Extracellular recordings were performed in the inferior colliculus (IC) and auditory cortex (AC) in awake restrained animals. Pure tones at neurons' characteristic frequency and/or wideband noise stimuli which lasted 5 or 30 seconds were used for sound stimulation.

Results
We found that about 50% of IC and AC neurons showed long-lasting suppression of their spontaneous firing following a long sound stimulus that typically induces RI in humans. Interestingly, both normal (unexposed) and tinnitus positive animals exhibited this suppression. There are several striking similarities between this suppression and RI observed in tinnitus patients. First of all, the duration of suppression in response to a typical sound used for RI induction correlates with the duration of RI. Second, increasing the sound duration makes both the suppression and RI last longer. Third, pure tones are more effectively induce both robust suppression and RI compared to wideband noises. Fourth, multiple attempts to induce suppression or RI with relatively short time intervals make both much weaker.

Conclusions
Striking similarities between RI and sound-induced suppression of spontaneous firing strongly suggests that this suppression is the underlying mechanism of RI.

Since both the normal animals and animals with behavioral signs of tinnitus exhibited similar suppression, we conclude that this suppression is a normal phenomenon of sound processing.People with tinnitus perceive sound-induced suppression of their tinnitus only because they perceive hyperactivity in their auditory system as tinnitus. Spontaneous firing in tinnitus free people remains below their level of sensation. Therefore they cannot perceive suppression of this firing.

Supported by grants R01 DC011330 and 1F31DC013498-01A1 from the National Institute on Deafness and Other Communication Disorders.

Keynote: Karl Friston
"Dynamic causal modelling of the auditory system"

The past decade has seen tremendous advances in characterising functional integration in the brain. Much of this progress is set against the backdrop of a key dialectic between functional and effective connectivity. My talk will focus on the application of dynamic causal modelling to induced brain responses and endogenous neuronal activity as measured with neuroimaging. A special focus will be on advances in network discovery and Bayesian model reduction. I will survey recent (and rapid) developments in modelling distributed neuronal fluctuations (e.g., stochastic, spectral and symmetric DCM for fMRI) – and how this modelling rests upon functional connectivity. I hope to highlight the intimate relationship between functional and effective connectivity and the implications for studies of auditory perception and predictive coding.

Live Presentation of the new Tinnitus Database
Pryss, R. (University of Ulm)

The Tinnitus Database is one of the major developments of the TINNET Action. The database is specifically designed for a standardized assessment of tinnitus characteristics, both in the clinical and scientific context. The new Tinnitus Database was implemented to allow an intuitive data entry at all platforms: standard computers, tablets and smartphones. The clinical data are fully anonymized and data security is ensured using the most current standards in data protection. The data export functions will provide all major data types to allow further statistical analysis with all statistical software tools. Dr. Pryss is a software engineer specialized for databases in the clinical context. He will present the current stage of the Tinnitus Database development in a live presentation to the audience.

Keynote: David Baguley
"The association between tinnitus and hyperacusis: causal, indirect, or coincidence?"

Epidemiological studies indicate that tinnitus and hyperacusis often co-occur in both adults and children with such symptoms. For some clinicians and researchers this may potentially lead to an assumption that there may be common causes or mechanisms, or that one symptom is somehow causal of the the other. In this lecture I will consider the various potential relationships between the symptoms and examine what evidence we have, and what evidence we need, to be able to understand the relationships between tinnitus and hyperacusis. As a clinician I will conclude with reflections on the clinical implications of what has been described.

Keynote: Veronica Kennedy
"Management of Tinnitus in Children – the UK approach"

Surveys of paediatric audiology departments in the UK had shown that only a few included services for children with tinnitus. In the surveys, some respondants didn't think that children experienced tinnitus. There was also an expressed reluctance to ask children about tinnitus because of the lack of local facilities or in case questioning prompted a worsening of the tinnitus. There was also a reported lack of guidelines in this area. In 2012, a Priority Setting Partnership of patients, researchers and clinicians, the James Lind Alliance, collated proposed research priorites and uncertainties in the treatment of tinnitus. One of the top 10 priority areas identified to address was 'what is the optimal set of guidelines for assessing children with tinnitus?'

While the underlying principles of managing tinnitus in adults can be applied to the management of tinnitus in children and young people, there are important differences. The cognitive and linguistic development of a child plays a significant role in the presentation, assessment and management of tinnitus in a child. A multidisciplinary working group, consisting of clinicians experienced in managing tinnitus in children, was set up to develop good practice guidance for the British Society of Audiology. As there are currently no evidence based guidelines for managing tinnitus in children, this guidance was based on the experiences of the working group as well as on the evidence base underlying adult tinnitus practice principles and general paediatric practice principles. After national and international consultation, the practice guidance was published in 2015. Complementing this document,

leaflets for children with tinnitus were developed by the British Tinnitus Association which were aimed at different age groups. Workshops were held at all national audiology conferences on managing children with tinnitus. The British Tinnitus Association has also held 2 day courses on a practical approach to managing children with tinnitus. A recent survey shows that more departments are now offering tinitus services for children and that there has been an increase in the confidence and knowledge of those offering the service.

The presentation looks at the process behind the development of the good practice guidance and other resources in the UK, and, in keeping with the EU COST Action principles, how the bottom up approach of a network of clinicans and the national patient group has led to a co-ordinated national approach for the management of children with tinnitus.

O17: CI in patients with single sided deafness influences the quality of life, tinnitus percept and psychological comorbidity.

Olze, H[1]., Förster-Ruhrmann U[1]., Szczepek A[1]., Mazurek B[2]. ([1]Charité-Universitätsmedizin Berlin, ENT-Department, Berlin, Germany [2]Charité-Universitätsmedizin Berlin, Tinnitus Center, Berlin, Germany)

Introduction

The indication criteria for cochlear implantation (CI) have expanded greatly in the recent time. Not only bilaterally but also unilaterally deafened patients are meeting the CI criteria. The main goal of our study was to assess additional benefit of cochlear implantation in this group of patients regarding the tinnitus distress, quality of life and psychological comorbidities.

Methods

Twenty adult patients, who were unilaterally implanted with a CI for at least 6 months prior to this study, were included. We have evaluated the HRQoL, tinnitus impairment, perceived stress and depressive and anxiety symptoms using 5 validated questionnaires: the Nijmegen Cochlear Implant Questionnaire (NCIQ), the Tinnitus Questionnaire by Göbel and Hiller, the Perceived Stress Questionnaire and finally the General Depressions Scale and the General Anxiety Disorder- 7 questionnaire. In addition, speech perception for the implanted ear and in the binaural condition in quiet and noise was tested using the Freiburg monosyllable test and OLSA-test. The Oldenburg Inventory (OI) was used to quantitatively evaluate the subjective hearing after CI.

Results

CI in SSD patients resulted in a statistically significant improvement of HRQoL, as measured by the NCIQ and its 6 subscales. The subjective assessment of auditory abilities measured by the OI also revealed significant improvements for hearing in noise and localization. Seventeen of 20 patients (85%) reported tinnitus before implantation. Tinnitus had decreased in 12 patients, 3 patients reported total disappearance of tinnitus, and 1 patient has not reported changes. In the three patients who were tinnitus- free before surgery, implantation has not induced tinnitus. The mean total score of the TQ in patients with tinnitus before CI was decreasing significantly following CI. Of the six TQ subscales, the three scales Em, InTi, and Aku were found to be significantly reduced following CI. In addition, psychometric tests revealed a significant reduction of anxiety and decrease in the number of patients with depressive symptoms.

Conclusion

The present study provides evidence that cochlear implantation constitutes a very successful procedure of auditory rehabilitation for SSD patients. In addition, an additional advantage of implantation in SSD patients was manifested by increased quality of life and reduced tinnitus and psychological comorbidities.

O18: Emerging network connectomics in phantom sound perception.

Mohan A.M[1]., De Ridder D.D.R[2]., Vanneste S.V[1]. ([1]The University of Texas at Dallas, Texas, USA, [2]University of Otago, North Dunedin, New Zealand)

Tinnitus, the perception of a phantom sound, is a multi-symptom, clinically debilitating condition which affects about 30 million Americans. Although the etiology of tinnitus occurrence encompasses a variety of peripheral inconsistencies there are several studies that now show a central trait to tinnitus. The brain is proposed to be a complex adaptive system that is constantly changing in order to update itself with the dynamic environment. With this in mind, tinnitus is hypothesized to be a neuromodulatory coping mechanism of the brain to conflicting bottom-up and top-down information. As an evidence, tinnitus has been identified to be the outcome of different auditory and non-auditory brain areas working in tandem within a functional network. Further, the different symptoms of tinnitus has been proposed to be the consequence of multiple, separable but overlapping subnetworks encoding its each behavioral correlate such as pitch, loudness, distress, laterality and type.

The current study aims to provide empirical evidence for network reorganization in tinnitus using graph theory. Graph theory is the science of computing a pairwise relationship between objects, in this case brain regions, in order to model the network they make up as a whole. These graphs were calculated using source-localized EEG data collected from 311 tinnitus patients and 256 healthy adults in eight frequency bands (delta, theta, alpha1, alpha2, beta1, beta2, beta3 and gamma). The network topology of the two groups in the various frequency bands were contrasted using different network connectivity measures, by examining the network hubs or regions of concentrated information flow and inducing a virtual focal lesion to these and other brain regions.

The results of the current study reveal the adaptive nature of the brain in the advent of a disorder in a frequency specific manner. We observe that the brain is indeed orchestrated as multiple, separable but overlapping subnetworks in the different frequency bands with a resilient core and a manipulatable periphery that is organized in communities and is detachable from the core. Although this basic organization is retained in the presence of a disorder, the change in the network connectivity with tinnitus manifests either as a modification in the hubs, or modification in the connectivity among similar hubs or a combination of the two. The hubs of the various tinnitus subnetworks also reflect the areas that have been shown to encode its different behavioral correlates confirming the theoretical model of the tinnitus network. Although, these changes accompany an increase in efficiency in the higher frequencies that seemingly compensate the decrease in efficiency in the lower frequencies, the networks correspondingly shift to a more random network and a more lattice network. This would mean that the networks in general become less efficiently wired in the presence of a disorder.

In conclusion, the presence of a neuropathology drives the brain to exploit its complex adaptive nature to rewire itself to try to compensate for the changes thus brought about in its environment, in a frequency specific way.

O19: Tinnitus after cochlear implantation.

Pierzycki R.H[1, 2]., Edmondson-Jones M[1, 2]., Dawes P[3]., Munro K.J[3, 4]., Moore D.R[1, 2, 5]., Kitterick P.T[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, [3]School of Psychological Sciences, Ellen Wilkinson Building, University of Manchester, Manchester, UK, [4]Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, [5]Cincinnati Children's Hospital Medical Center and Department of Otolaryngology, University of Cincinnati College of Medicine, Cincinnati, USA)

Background and objectives

The management of tinnitus in those with profound hearing loss and of tinnitus-related insomnia are among top priorities identified by patients and clinicians [1]. Cochlear implants (CIs) are an established intervention to restore useful aspects of hearing in the profoundly deaf. CIs have also a suppressive effect on tinnitus and have been recommended as an intervention for tinnitus in these patients [2]. As suppression occurs mostly when the CI is switched on [3], tinnitus can still lead to sleep difficulties in CI users when CIs are switched off at night time. Compatibly, an observational study has shown that sleep difficulties are not reduced in all patients using CIs [4]. Therefore, to infer the effects of implantation on tinnitus and sleep difficulties the present study estimated and compared the prevalence of tinnitus and sleep difficulties in a sample of UK adult CI users and potential candidates for implantation.

Methods

Self-report data on hearing, tinnitus, sleep difficulties and demographic variables were collected from CI users (n = 194) and individuals identified as potential 'candidates' for cochlear implantation (n = 211) participating in the UK Biobank study. The potential candidates were selected based on impaired hearing sensitivity, inferred from self-reported hearing aid use, and impaired hearing function. Function was measured as the ability to report words accurately at negative signal-to-noise ratios on an unaided, closed-set speech discrimination test. Data on the presence and persistence of tinnitus, related emotional distress, and on sleep difficulties were analysed using logistic regression models controlling for gender, age, deprivation and neuroticism.

Results

The prevalence of tinnitus was similar amongst CI users (50%) and candidates (52%). However, CI users were less likely to report that their tinnitus caused distress at its worst (41%) compared to candidates (63%). The regression model suggested that the lower tinnitus distress in CI users was due to their tinnitus being less persistent (46%) than in candidates (72%). The prevalence of self-reported sleep difficulties was similar among CI users (75%) and candidates (82%), and not related to tinnitus persistence or the extent of distress from tinnitus.

Conclusions

CI users showed reduced tinnitus persistence and tinnitus distress compared to potential candidates for implantation. The lack of any association between tinnitus persistence and sleep difficulties is in line with the observation that tinnitus is suppressed primarily during active electrical stimulation, and possibly returns when the implant is switched off at night time. The data suggest that cochlear implantation may not be an appropriate intervention if the primary aim is to improve tinnitus-related sleep difficulties.

Acknowledgments

This research has been conducted using the UK Biobank resource.

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O20: The resting state functional connectivity patterns in chronic subjective tinnitus.

Lewandowska M., Wolak T., Milner R[1]., Ganc M., Niedzialek I., Skarzynski H. ([1]Department of Experimental Audiology, World Hearing Center, Institute of Physiology and Pathology of Hearing, Nadarzyn, Poland)

Previous studies have shown alternations in resting-state functional connectivity (rs-fc) of the auditory, attentional, emotional and default mode networks in people with tinnitus [1 for a review]. However, there is a high variability in rs-fc outcomes in this group which may, in part, result from the heterogeneity of the tinnitus population. The aim of the present study was to determine rs-fc patterns corresponding to tinnitus subgroups, identified based on various tinnitus characteristics and comorbid symptoms. Forty eight patients of the Institute of Physiology and Pathology of Hearing in Warsaw/Poland (28 M, mean age=42.8±14.1years) who suffered from subjective tinnitus from at least 6 months, and 22 healthy controls with no tinnitus (22 M, mean age=42.1±12.6years) participated in a medical interview and an otolaryngological and pure-tone audiometry (125 Hz-16 kHz) examinations. The Polish versions of depression and anxiety questionnaires were administered to all subjects (patients also completed the THI and a tinnitus characteristics questionnaire). The resting-state fMRI protocol was performed in a 3T MR scanner using a 12-channel head coil. The parameters of rs imaging session were: TR=2000ms, TE=25ms, flip angle=90°, FOV=192mm, matrix size: 64×64, 41 axial slices of 3mm thickness (no gap), 150 volumes. Subjects were presented with a black screen and asked to lie still and relax with their eyes open. The data were pre-processed using SPM12 software and rs-fc was analyzed in CONN toolbox.

Cluster analysis revealed 3 tinnitus subgroups. Subgroup 1 (n=23) was characterized by normal hearing, increased depression and anxiety and described their tinnitus as severe, loud, mainly tonal sound. Subgroup 2 (n=19) showed no depressive and anxiety symptoms and did not much suffer from tinnitus. Instead, they had mild to moderate high-frequency hearing loss (3-16 kHz). Subgroup 3 (n=6) experienced bothersome tinnitus accompanied by depression, anxiety and the most profound hearing loss (this group was excluded from rs-fc analysis due to insufficient number of participants to perform any statistics). Subgroup 1, compared to controls, showed increased rs-fc of the seeds in the default mode network (with the right occipital cortex), the visual network (with the right fusiform gyrus), the left amygdala (with the precuneus/posterior cingulate and subcallosal area), the left and right parahippocampal gyrus (with the precuneus and medial frontal cortex, respectively) and the right hippocampus (with the left supramarginal gyrus). Subgroup 2 demonstrated increased connectivity of the attentional networks with the right paracingulate cortex, right frontal and left occipital poles and decreased rs-fc with the precuneus. Furthermore, there was increased rs-fc in the visual and sensorimotor networks and decreased rs-fc of the seed in the right nucleus accumbens with the right occipital cortex and of the right amygdala with the posterior cingulate gyrus and bilateral occipital area. Grouping the patients into subtypes reduced the high variability of tinnitus rs-fc outcomes. Normalization of abnormal functional connectivity patterns could help to alleviate tinnitus sensation

O21: Epidemiology of Tinnitus Incidence in Older Adults, 70+ Years: the Age, Gene/Environment Susceptibility–Reykjavik (AGES–R) Iceland Longitudinal Cohort Study.

Hoffman H.J[1]., Dobie R.A[2]., Li C.M[1]., Losonczy K.G[1]., Themann C.L[3]., Cotch M.F[4]., Launer L.J[5]., Eiriksdottir G[6]., Gudnason V[6, 7]., Petersen H[7, 8]. ([1]Epidemiology and Statistics Program, Division of Scientific Programs, National Institute on Deafness and Other Communication Disorders (NIDCD),

National Institutes of Health (NIH), [2]Department of Otolaryngology-Head and Neck Surgery, The University of Texas Health Science Center at San Antonio, [3]National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), [4]Division of Epidemiology and Clinical Applications, National Eye Institute (NEI), National Institutes of Health (NIH), [5]Laboratory of Epidemiology and Population Science, National Institute on Aging (NIA), National Institutes of Health (NIH), [6]Icelandic Heart Association (Hjartavernd), Kopavogur, Iceland, [7]Faculty of Medicine, University of Iceland, Reykjavik, Iceland, [8]Department of Otolaryngology-Head and Neck Surgery, Landspitali University Hospital)

Background
AGES-R was designed to assess risk factors and detailed phenotypes in an older population in Iceland. Prior studies in Australia, Europe and the United States have shown that tinnitus prevalence increases until about age 70, plateaus, then declines slowly with advancing age. Risk factors from prior studies include noise exposure, hearing acuity, chronic health conditions, and behavioral or lifestyle characteristics. Few studies have investigated risk factors for tinnitus incidence (TI) among older adults.

Objective
To examine associations between new onset of tinnitus (TI) and risk factors based on a longitudinal cohort study of older adults.

Methods
AGES-R was established using a population cohort followed since 1967 by the Icelandic Heart Association; it began in 2002 (AGES_1, 2002-2006, ages 66-96; n=5,764) and the surviving cohort was followed-up five years later (AGES_2, 2007-2011, ages 71-98; n=3,411). TI (AGES_2) was defined as being bothered for a duration less than five years by ringing, roaring, or buzzing in the ears or head that lasted five minutes or longer during the past 12 months. Information was also obtained on migraine headaches, sleep problems, arthritis, diabetes, cardiovascular disease, depression, vision loss, otitis media, other ear diseases, work or leisure noise exposure, and self-reported hearing difficulties. Hearing impairment (HI) was defined for better ear (BE) and worse ear (WE) using the 2010 Global Burden of Disease classification of air-conduction, pure-tone average (PTA) thresholds for 0.5, 1, 2, and 4 kHz: mild HI (BE, 20 to 34 dB HL [hearing level]) and disabling HI (BE, 35 dB HL or worse). Multivariable logistic models were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) in SAS and SUDAAN.

Results
Tinnitus prevalence in AGES_1 was 20.3% and in AGES_2 was 16.1%; 8.6% had new onset tinnitus (TI) between AGES_1 and AGES_2. Factors associated with increased TI were: other ear diseases, OR=3.08 (CI: 1.66-5.72), temporary loss of eyesight for less than 24 hours (past five years), OR=2.92 (CI: 1.43-5.95), patient in hospital one or more nights (past five years), OR=1.42 (CI: 1.001-2.01). Protective factor was: walking for exercise each week in winter months, OR=0.55 (CI: 0.38-0.82). Borderline associations ($p<0.10$) were: work/occupational noise exposure, disabling WE HI, depression, and chronic lung disease. In AGES_1, tinnitus prevalence was associated with many factors, including younger age, male sex, cigarette smoking, cardiovascular disease, migraine headaches, sleep problems, frequent childhood otitis media, work noise exposure, BE mild and disabling HI, and self-reported hearing difficulties.

Conclusion
Many associations with tinnitus prevalence were found in AGES_1, reflecting similar findings in the literature; however, fewer associations were discovered for new onset of tinnitus among older adults. The two most significant factors for TI were other (non-otitis) ear diseases (e.g., cholesteatoma, otosclerosis, Meniere's disease) and temporary vision loss. Clinicians who see older patients presenting with tinnitus of recent-onset may need to screen for ear diseases and other co-morbidities.

O22: Neural Correlates of White Matter Integrity in Tinnitus: Tract-Based Spatial Statistics.

Alhazmi F[1, 2]., Mackenzie I[3]., Kay T[4]., Kemp G.J[2, 5]., Sluming V[1, 2]. ([1]Department of Molecular and Cellular Physiology, Institute of Translational Medicine, University of Liverpool, UK, [2]Magnetic Resonance and Image Analysis Research Centre, University of Liverpool, UK, [3]Liverpool School of Tropical Medicine, Liverpool, UK, [4]Aintree University Hospital NHS Foundation Trust, Liverpool, UK, [5]Institute of Ageing and Chronic Diseases, University of Liverpool, UK)

Background

Tinnitus and hearing loss are usually considered as a related phenomenon [1], which was estimated that approximately 85-96% subjects with tinnitus often associated with some forms of hearing loss [2]. Recently, the thought of the origin of tinnitus generation has been shifted to the central nervous system as research studies have demonstrated that the maladaptive plasticity could be caused by tinnitus perception in the brain.

Purpose

The aim of this study is to investigate the effect of tinnitus perception on white matter integrity.

Material and methods: 46 participants were recruited in this study: 20 mild to moderate hearing loss subjects without tinnitus (MH) and 26 tinnitus subjects with hearing loss (TI) (13 tinnitus bothersomes and 13 tinnitus non-bothersomes, and 16 bilateral and 10 unilateral tinnitus participants). For tinnitus group, two different tinnitus questionnaires (Tinnitus Handicap Inventory (THI) and Tinnitus Functional Index (TFI)) were used to investigate the influence of tinnitus perception on the quality of life. Routine clinical audiometry was performed at different frequencies (0.5- 8 kHz). Diffusion-weighted images (DWI) were acquired using MRI scanner with 8-chennels head coil. Tract-based spatial statistics (TBSS) [3] was applied to investigate white matter integrity differences between normal controls and tinnitus patients, and explore the influence of tinnitus severity, lateralization and duration on white matter integrity.

Results

The mean of FA values was found significantly lower in tinnitus patients comparing to MH group. A significant reduction of white matter integrity (fractional anisotropy) was found in tinnitus group at corpus callosum (body and splenium), bilateral inferior longitudinal fasciculus (Auditory cortex) and corticospinal tract, inferior-occipital fasciculus (Prefrontal cortex), left anterior thalamic radiation (Thalamus), and superior longitudinal fasciculus (middle temporal gyrus) comparing with mild to moderate hearing loss group. No significant difference of white matter integrity was found between tinnitus bothersome and non-bothersome groups. Bilateral tinnitus subgroup showed a significant reduction of white matter integrity comparing to unilateral tinnitus participants at left inferior frontal occipital fasciculus. Correlation analysis found that no significant correlation between the changes of FA values and tinnitus severity (THI and TFI scores), onset and hearing loss thresholds.

Conclusion

Abnormality of white matter integrity was found in tinnitus group, which may suggest that tinnitus perception could cause brain plasticity on different brain regions including auditory, limbic and attention networks.

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O23: Hyperacusis: prevalence and risk factors in the US adult population.

Dobie R.A[1]., Hoffman H.J[2]., Losonczy K.G[2]. ([1]University of Texas Health Science Center at San Antonio, San Antonio, USA [2]National Institute on Deafness and other Communication Disorders, Bethesda, MD USA)

For the first time in 2014, the US National Health Interview Survey asked respondents about hyperacusis: "Some people are bothered by everyday sounds or noises that don't bother most people. Do everyday sounds, such as from a hair dryer, vacuum cleaner, lawnmower, or siren, seem too loud or annoying to you?" Responses were weighted to ensure nationally representative estimates of prevalence and risk factors: 14.1 million civilian, non-institutionalized US adults (5.9% of adults) have "hyperacusis" by this definition. While most consider this to be no problem or a small problem, about 4.3 million US adults (1.8% of adults) consider it a moderate problem or worse. Univariate predictors of "hyperacusis" included self-reported hearing impairment (especially difficulties communicating in noise), female sex, older age, higher education level, tinnitus (especially tinnitus severity), current hearing aid use, occupational noise exposure, severe emotional problems, and severe headaches or migraine. In multivariate models, all of these except for hearing aid use were significant risk factors for "hyperacusis" and/or "moderate or worse problem." However, the age effect was reversed: after accounting for hearing impairment and other variables, adults aged 40 or more were less likely to have a moderate or worse problem than younger adults.

Other variables significantly associated with "hyperacusis" or "moderate or worse problem," in analyses accounting only for age and sex, included current unemployment, poor sleep, prior medical diagnoses (coronary heart disease, stroke, diabetes, asthma, sinusitis, and arthritis), joint pain, and difficulty walking or climbing steps. The association of hyperacusis with self-reported poor health and disability is reminiscent of findings in previous population-based surveys of tinnitus.

O24: Abnormal Resting-state Functional Connectivity Study in Unilateral Pulsatile Tinnitus Patients: What is the Role of Posterior Cingulate Cortex?

Lv H [1]., Wang Z[1]., Gong S[1]., Zhao P[1]., Liu Z[1]., Yan F[2]., Wang P[1]., Zhang L[1]., Li R[1]. ([1]Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]Beijing Tongren Hospital, Capital Medical University, Beijing, China)

Objects

Functional magnetic resonance imaging (fMRI) has been widely used to characterize the abnormal neural activities in tinnitus patients. Various studies have demonstrated altered activations in the PCC (posterior cingulate cortex) in patients with tinnitus. However, few studies have investigated the relationship between the resting-state brain functional connectivity and the perception of PT (pulsatile tinnitus).

Methods

In this study, we recruited 38 unilateral PT patients and 38 healthy controls to identify the functional connectivity pattern between the PCC and the whole brain. Correlation analyses with clinical variables were also performed.

Results
Compared with healthy controls, PT patients showed significant decreased functional connectivity to the right MTG (middle temporal gyrus), bilateral insula and right thalamus. By contrast, PCC demonstrated increased functional connectivity between the PCC and precuneus, bilateral fusiform gyrus/parahippocampa gyrus, bilateral MOG (middle occipital gyrus) and SFG (superior frontal gyrus). Positive correlations were also found between PT duration and FC of PCC-right MTG, and between THI score and FC of PCC-precuneus.

Conclusions
Our results indicated the key role of MTG in the brain of PT patients. The connectivity between bilateral MOG and PCC might be a modulation pathway to habituate the pulsatile tinnitus. The connectivity pattern in unilateral PT patients could also be bilaterally altered. This study may yield a more comprehensive functional connectivity framework for PT patients.

O25: Impact of multiple factors on the degree of tinnitus distress.
Brueggemann, P., Szczepek A.J, Rose M., McKenna L., Olze H., Mazurek B. (Tinnitus Center Charité University Medicine, Berlin, Germany)

Objective
The primary cause of subjective tinnitus is an auditory system dysfunction; however, the distress caused by tinnitus depends largely on the psychological status of a patient. Our goal was to simultaneously analyze the association between the grade of tinnitus-related distress and the psychological distress, physical or psychological discomfort, hearing and social parameters.

Methods
We determined the level of tinnitus-related distress in 531 tinnitus patients using the German version of tinnitus questionnaire (TQ). In addition, we used Perceived Stress Questionnaire (PSQ); General Depression Scale (ADS), Berlin Mood Questionnaire (BSF); somatic symptoms inventory (BI) and SF-8 health survey as well as auditory parameters and general informations collected in medical history.

Results
TQ score significantly correlated with the score obtained by using PSQ, ADS, BSF, BI, SF-8 and with other psychosocial factors, such as age, gender or marital status. The level of hearing loss, auditory properties of tinnitus together with perceived stress and the degree of depressive mood and somatic discomfort were identified as medium-strong predictors of chronic tinnitus. Social factors such as gender, age or marital status also had impact on the degree of tinnitus distress. Obtained results were implemented in a specific cortical distress network model.

Conclusions
Using the large representative sample of patients with chronic tinnitus has permitted the simultaneous statistical measurement of psychometric and audiological parameters influencing tinnitus distress. We have demonstrated that single factors influencing tinnitus-related distress can be tell apart, explaining their causative association during the induction of tinnitus-related distress

O26: Investigating tinnitus subgroups varying in severity using Diffusion Tensor Imaging.
Schmidt S., Romero, A., Husain, F.T. (University of Illinois at Urbana-Champaign, Illinois, USA)

Diffusion Tensor Imaging (DTI) is a tool used to examine the orientation of white matter tracts in the brain. A few studies have examined the microstructural integrity of white matter tracts in tinnitus patients using fractional anisotropy (FA), but they have produced conflicting results. In our previous study (Husain et al., 2011), we found that the presence of mild tinnitus did not have an effect on FA values. Instead, the degree of hearing loss of the participants accounted for the most significant changes in the orientation of the tracts.

The present study has two components. First, we attempted to replicate our previous results in new populations of patients with mild tinnitus (average Tinnitus Handicap Inventory (THI) score 10.6 ± 11.5) and both normal hearing and hearing loss controls. The mild tinnitus and hearing loss groups had matched, sloping sensorineural hearing loss. Second, we speculated that variable results seen across DTI studies could be because they examined different subgroups of tinnitus patients. To investigate this further, we examined two subgroups of tinnitus participants that differed in their tinnitus severity: a low severity group (average THI score 9.44 ± 5.17) and a high severity group (average THI score 30.22 ± 10.95). Hearing thresholds for each group ranged from normal to moderate hearing loss, but the two groups did not significantly differ in hearing profile. Note that there was no overlap between these additional groups and the tinnitus group in the first portion of the study.

In our first analysis comparing a mild group to the two controls, we found similar results as in the Husain et al. (2011) paper. The only significant differences at a $p<0.1$ FWE corrected threshold were decreases in FA values in the hearing loss group compared the mild tinnitus patients. This difference was located in the right corticospinal tract, anterior thalamic radiation, inferior fronto-occipital fasciculus, and superior longitudinal fasciculus. In the second analysis contrasting the additional tinnitus groups, no significant differences were found between the high and low severity groups at $p<0.1$ FWE corrected. There was, however, a trend for decreased FA values in the high severity group compared to low in right anterior thalamic radiation and cingulum.

These results support our previous finding that hearing loss and not mild tinnitus causes alterations in white matter tract organization. Further, the lack of significant differences between the high and low severity tinnitus groups suggests that white matter tracts may not be affected by moderate severity but the trend leaves open the possibility for an effect of more profound severity. None of the groups differed in their scores on the Beck Depression Inventory, which has recently been shown to be associated with white matter alterations in tinnitus patients (Ryu et al., 2015). For a more complete examination of tinnitus subgroups related to white matter tracts, differences related to depressive symptoms should be examined.

O27: Audiological and Psychosocial Predictors of Tinnitus Severity.

Wallhäusser-Franke E[1]., Repik I[2]., Delb W[3]., Glauner A[1]., Hörmann K[1, 2]. ([1]Heidelberg University, Medical Faculty Mannheim, Department of Otorhinolaryngology and Audiology, Germany, [2]University Hospital Mannheim, Department of Otorhinolaryngology, Germany, [3]HNO-Kooperation Südwestpfalz, Germany)

To date most studies on the relation between chronic tinnitus and predisposing factors are based on retrospective data and may not sufficiently distinguish between tinnitus-promoting factors and consequences of tinnitus. Aim of the study is to investigate relations of hearing threshold, mental health, and personality at tinnitus onset with tinnitus severity after six months to identify early predictors of chronic severity. Short self-report questionnaires were used to allow future routine use in ENT-practices.

Data were gathered at the Ear, Nose and Throat Clinic of University Hospital Mannheim and at four ENT practices in the area. Inclusion criteria were acute tinnitus of no longer than four weeks, no prior history of tinnitus, sufficient knowledge of German, and an age of at least 18 years. Patients fulfilling the inclusion criteria were asked to participate in a study on tinnitus development. An audiogram was recorded at T1. Participants filled out paper and pencil questionnaires at inclusion (T1), and three (T3) and six months (T4) after tinnitus onset. Six weeks after tinnitus onset they were interviewed on the phone. Tinnitus loudness and sound sensitivity were assessed by numeric rating scales, tinnitus-related distress was recorded with the short form of the tinnitus questionnaire (Hiller and Goebel, 2006). Mental health and personality factors were measured by the depression, anxiety and somatic severity scales of the Patient Health Questionnaire (Löwe et al., 2010), and the resilience scale (Wagnild 2009).

Remission rate was low, tinnitus loudness and distress were stable throughout the investigation period whereas sound sensitivity decreased. Resilience did not represent a predictor for chronic tinnitus severity in this sample. Analyses revealed an effect of the amount of hearing loss and of the amount of depression at T1 on tinnitus loudness at T4, while amount of depression and age at T1 showed an effect on sound sensitivity and tinnitus-related distress at T4.

Stability of subjective tinnitus-loudness and tinnitus-related distress during the six months after tinnitus onset supports the hypothesis of tinnitus manifestation within a few days after onset. Moreover, results of this study support the hypothesis that later tinnitus severity is related to hearing impairment and psychosocial distress at tinnitus onset. Therefore the use of hearing aids should be considered whenever justified by audiometry and by absence of sound hypersensitivity. Furthermore, tools for the identification of psychosocial problems in particular depression need to be employed at an early stage of tinnitus progression to identify patients that might benefit from psychotherapeutic interventions.

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O28: Hearing tinnitus and reacting to tinnitus: two processes involving different networks.

Maudoux A[1, 2]., Gomez F[2]., De Ridder D[3]., Vanhecke W[4]., Van de Heyning P[5]., Cabay J.-E[6]., Laureys S[2, 7]., Soddu A[2]., Lefebvre P.H[1]., Vanneste S[8]. ([1]OtoRhinoLaryngology Head and Neck Surgery Department, CHU Sart Tilman Hospital, University of Liège, Belgium, [2]Coma Science Group, Cyclotron Research Centre, University of Liège, Belgium, [3]Surgical Sciences, Surgery, Neurosurgery, Dunedin School of Medicine, New Zealand, [4]Brain, TRI & Department of Neurosurgery, Antwerp University Hospital, Antwerp, Belgium, [5]OtoRhinoLaryngology Head and Neck Surgery Department, Antwerp University Hospital, Antwerp, Belgium, [6]Radiology Department, CHU Sart Tilman Hospital, University of Liège, Belgium, [7]Neurology Department, CHU Sart Tilman Hospital, University of Liège, Belgium, [8]Lab of Auditory & Integrative neuroscience. School of Behavioral and Brain Science. University of Texas at Dallas. Dallas, USA)

Background

It is known that peripheral lesions in the cochlea or the auditory nerve produce dysfunctional input to central auditory structures and induce changes in the auditory system. Associated to plastic changes in central auditory structures, extra-auditory regions have been implicated in the tinnitus pathophysiology.

The role of these extra-auditory regions is still debated. Some proposed that the tinnitus percept is a combination of multiple overlapping dynamic brain networks, each encoding a specific tinnitus characteristic (De Ridder et al., PNAS 2011). Other suggested that these regions are part of noise cancellation system (Rauschecker et al., TICS 2015). If regions are indeed part of a noise canceling system then activity in those regions should be related to the perceived tinnitus loudness. If regions are implicated in the reaction to the sound then activity in those regions might be more related to the distress associated with tinnitus.

The aim of our study is to investigate the neuronal activation patterns associated with tinnitus characteristics related to perception/reaction to the sound. By correlating these tinnitus clinical characteristics with resting-state fMRI connectivity patterns we hope to retrieve the networks that are associated with each clinical features.

Methods
We prospectively assessed 133 tinnitus patients (40 women; mean age 50 years). In all patients resting-state fMRI time series were acquired on a 3T scanner. Preprocessing steps were performed using SPM12 following the preprocessing pipeline provided in the CONN functional connectivity toolbox. The hearing level, the age, the tinnitus duration, the tinnitus distress as measured by the tinnitus questionnaire (TQ) score, the subjective tinnitus intensity as measured by a visual analog scale (VAS) and the objective tinnitus loudness measured during the audiological assessment were entered as second level covariates.

The connectivity analysis was performed using the CONN toolbox. We looked at correlation between clinical characteristics and functional connectivity between 38 ROIs selected based on the literature. We included the rostral ACC, pregenual ACC, subgenual ACC, dorsal ACC, parahippocampus, ventromedial PFC, medial geniculate body, habenulla, PCC, nucleus accumbens, primary and secondary auditory cortices, amygdala, hypothalamus and ventral tegmental area.

Results
We focused on three tinnitus characteristics: the objective tinnitus loudness, the subjective tinnitus intensity and the tinnitus related distress.

The objective tinnitus loudness seems to be associated with a modification of the interaction between the NAc and the VTA. The subjective tinnitus intensity correlates with increased connectivity among limbic regions (vmPFC, pgACC and amygdala). Tinnitus distress seems to be associated to a modification of interaction between regions of the negative reward system linked to dysregulation of the autonomic nervous system (ANS) (habenulla, hypothalamus, NAc and amygdala).

In conclusion, it seems that modification of connectivity pattern across regions that are part of the hypothesized gating system influence to what extend the tinnitus signal is perceived. The reaction to the tinnitus sound seems associated to a dysfunction of the reward system leading to modification of the ANS.

O29: Transcranial magnetic stimulation-induced neuroplasticity underlying therapeutic response in chronic tinnitus.
Poeppl T.B., Langguth B., Lehner A., Rupprecht R., Kreuzer P.M., Landgrebe M., Schecklmann M. (University of Regensburg, Germany)

Tinnitus, the perception of sound in the absence of a corresponding external acoustic stimulus, is an excellent paradigm to gain insight into the neural basis of phantom sensations. Non-invasive brain stimulation can modify phantom sounds for longer periods by modulating neural activity and putatively inducing regional neuroplastic changes. Using voxel-based morphometry, we show that transcranial magnetic stimulation-induced neuroplasticity determines therapeutic outcome. More specifically, we found macroscopic gray matter changes of the left ventrolateral prefrontal cortex in responders (but not non-responders) that were strongly correlated with a reduction of tinnitus distress. Our results support the implication of non-auditory brain regions in phantom sounds and the dependence of therapeutic response on their neuroplastic capabilities.

O30: Tinnitus- and Task-Related Differences in Resting-State Networks.
Lanting C.P[1, 2]., Woźniak A[1, 2]., van Dijk P[1, 2]., Langers D.R.M[1, 2]. ([1]University of Groningen, University Medical Center Groningen, Department of Otorhinolaryngology/Head and Neck Surgery, The Netherlands, [2]Graduate School of Medical Sciences Research School of Behavioural and Cognitive Neurosciences, University of Groningen, The Netherlands)

We investigated tinnitus-related differences in functional networks in adults with tinnitus by means of a functional connectivity study. Previously it was found that various networks show differences in connectivity in patients with tinnitus compared to controls. How this relates to patients' ongoing tinnitus and whether the ecological sensory environment modulates connectivity remains unknown.

Twenty healthy controls and twenty patients suffering from chronic tinnitus were enrolled in this study. Except for the presence of tinnitus in the patient group, all subjects were selected to have normal or near-normal hearing. fMRI data were obtained in two different functional states. In one set of runs, subjects freely viewed emotionally salient movie fragments ("fixed-state") while in the other they were not performing any task ("resting-state"). After data pre-processing, Principal Component Analysis was performed to obtain 25 components for all datasets. These were fed into an Independent Component Analysis (ICA), concatenating the data across both groups and both datasets, to obtain group-level networks of neural origin, each consisting of spatial maps with their respective time-courses. Subject-specific maps and their time-course were obtained by back-projection (Dual Regression). For each of the components a mixed-effects linear model was composed with factors group (tinnitus vs. controls), task (fixed-state vs. resting state) and their interaction.

The neural components comprised the visual, sensorimotor, auditory, and limbic systems, the default mode, dorsal attention, executive-control, and frontoparietal networks, and the cerebellum. Most notably, the default mode network (DMN) was less extensive and shows significantly less connectivity in tinnitus patients than in controls. This group difference existed in both paradigms. At the same time, the DMN was stronger during resting-state than during fixed-state in the controls but not the patients. We attribute this pattern to the unremitting engaging effect of the tinnitus percept.

O31: Evaluation of tomographic vs. standard neurofeedback protocols for treatment of subjective tinnitus.
Meyer M[1]., Güntensperger D[1]., Neff P[1]., Weidt S[2]., Kleinjung T[2]. ([1]University of Zurich, Zurich, Switzerland [2]University Hospital of Zurich, Zurich, Switzerland)

We introduce a study that evaluates sLORETA-based vs. standard neurofeedback (NFB) for treatment of subjective tinnitus.

The study includes 52 individuals who suffer from chronic subjective tinnitus.While half of the participants undergoes tomographic NFB (n of electrodes = 31) the remaining half takes part in conventional NFB protocols (n of electrodes = 4).

Irrespective of group participants use neurofeedback over the course of 15 weeks. They train an increase of resting-state alpha activity and a down-regulation of delta power, While the group partaking in the conventional protocol does not modulate brain activity in a particular region, the tomographical training is focused on auditory cortex regions. To achieve the latter we combined the tomographical sLORETA-based approach with the Cygnet software (EEGinfo).

Furthermore, we collect pre and post resting-state EEG recordings (immediately before and after each training session and 3 months after completion of trainings). We always combine EEG recording with a numerous psychometric, health-related questionnaires and audiometric testing. The compilation of behavioral and neurophysiological data and thorough analysis devoid of any a priori assumptions will enable the evaluation of treatment success at both a group-related and individual level. Long-term we aim at classifying subtypes of groups and individuals who are supposed to mainly benefit from different tomographic protocols that will be developed based on comprehensive analysis of psychmetrical and psychopathological data.

The talk is meant to introduce first results and to discuss pros and cons of tomographic NFB in the treatment of chronic subjective tinnitus.

O32: Decreased default mode network connectivity to the precuneus is common across tinnitus subgroups.
Schmidt, S., Carpenter-Thompson J.R., Husain F.T. (University of Illinois at Urbana-Champaign, Illinois, USA)

Recently, we have published functional MRI studies on differences between subgroups of tinnitus patients that vary in severity. Tinnitus severity appears to have a strong impact on emotional processing; patients with mild tinnitus utilize frontal regions to mediate emotional responses to sounds, while patients with severe tinnitus use the amygdala and parahippocampus to a greater extent compared to the mild tinnitus group (Husain, 2015, Hear Res; Carpenter-Thompson et al., 2015, PLoS One). To enhance our understanding of the neural correlates of tinnitus and how they vary based on tinnitus subgroups, we conducted a resting state functional connectivity study.

We examined four groups of tinnitus patients in this study. These include two groups of mild tinnitus patients (LTIN and LOW; average Tinnitus Handicap Inventory (THI) scores of 10.6 ± 11.5 and 9.44 ± 5.17 respectively), a group of patients with mild tinnitus who had had their percept for under one year (RTIN; average THI score of 15.7 ± 10.2), and a group of patients with higher tinnitus severity (HIGH; average THI score of 30.22 ± 10.95). Two age-matched normal hearing and hearing loss groups served as controls. The LTIN and LOW groups were not combined because they were collected on separate MRI scanners; the LTIN, RTIN, and control data were collected on a Siemens Allegra scanner, while the LOW and HIGH groups' data were collected on a Siemens Trio scanner. All tinnitus patients had hearing loss that was not significantly different across groups; the hearing loss control group was matched to the LTIN group. A seed-to-voxel approach using the Conn toolbox was performed to examine the connectivity of the default mode network. Seeds were located in the posterior cingulate cortex and medial prefrontal cortex.

A main effect of group showed decreased connectivity between seed regions and the precuneus. Post-hoc t-tests revealed this decrease in the HIGH group compared to both normal hearing and hearing loss controls and the LTIN, LOW and HIGH groups compared to the RTIN group. Trends for this decrease where also found in the LTIN group compared to both control groups, and the LOW group compared to the hearing loss group. This suggests that decreased correlations between the default mode network and the precuneus may indicate the presence of tinnitus. Further, the severity of tinnitus may mediate the strength of the decrease. No differences in connectivity were noted in the RTIN group compared to either control group, suggesting that longer durations of the disorder are required to cause alterations in resting state functional connectivity. Additionally, correlations between seeds and the cerebellum were also altered across tinnitus subgroups. Weakened correlations between the cerebellum and seeds were noted in the LOW group compared to normal hearing controls and the HIGH group compared to both normal hearing and hearing loss controls. Despite the confounding use of two scanners, our results shed light on the possible commonalities across different tinnitus subgroups.

O33: Effectiveness, prognostic factors and safety of microvascular decompression surgery of the eighth cranial nerve for the treatment of tinnitus and vertigo: a systematic review and meta-analysis of individual patient data.

van den Berge M.J.C [1]., Posthumus I.A [1]., Smidt N[2]., Free R.H [1]., van Dijk J.M.C[3]., van Dijk P [1].([1]University Medical Center Groningen, Department of Ear, Nose and Throat surgery, Netherlands, [2]University of Groningen, department of Epidemiology, The Netherlands, [3]University Medical Center Groningen, Department of Neurosurgery, The Netherlands)

Background

Microvascular decompression (MVD) surgery is a well accepted treatment for trigeminal neuralgia, hemifacial spasms and glossopharyngeal neuralgia. MVD of the cochleovestibular nerve for the treatment of tinnitus and vertigo is still controversial. The objective of this systematic review was firstly to assess the effectiveness and safety of MVD surgery of the cochleovestibular nerve in patients with tinnitus and/or vertigo and secondly to investigate the prognostic factors of complete relief.

Methods

A systematic review was conducted, including an individual patient data meta-analysis, using the methods of the Cochrane Collaboration and using the PRISMA-IPD guidelines. A comprehensive search (February 2015) in MEDLINE, EMBASE and Google Scholar was done to identify eligible studies, consisting of studies that investigated the effectiveness of MVD surgery of the cochleovestibular nerve in patients who were referred to the hospital for tinnitus and/or vertigo. The collected outcome was a global measurement of improvement, indicating the success of the treatment. The study selection, data extraction and quality assessment of the included studies was performed by two reviewers independently. If needed, authors of the included studies were contacted to provide the individual patient data. The protocol for this review was published in PROSPERO database (CRD42015017437).

Results

Thirty-five studies (527 patients) consisting of 13 case reports and 22 case series were included in this systematic review. Overall, 34% of the tinnitus patients and 32% of vertigo patients reported complete relief after MVD surgery. When patients had with both tinnitus and vertigo, complete relief was found in 62%. In 10.8% of the patients, one or more complications following MVD surgery were reported, of which permanent hearing deterioration was the most frequent (4.9%). The individual patient data meta-analysis included 165 patients from 26 studies. No prognostic factors for success were identified.

Discussion
This systematic review demonstrated a low success rate for MVD surgery for tinnitus and vertigo, especially when compared to success rates of MVD surgery for other cranial nerves. Moreover, the complication rate of surgery is considerably high. We could not demonstrate any prognostic factors for success of MVD surgery, mainly due to missing individual patient data. Considering the low success rate and high complication rate, it is concluded that MVD surgery for tinnitus and vertigo should not be considered as standard treatment method. Future research is needed to gain more insight in adequate selection criteria for MVD surgery for tinnitus and/or vertigo and the use of a standardized outcome tool is needed.

O34: Neural substrates predicting short-term improvement of tinnitus loudness and distress after modified tinnitus retraining treatment.

Song, J.J[1]., Vanneste S[2]., De Ridder D[3]., Jang J.H[4]. ([1]Department of Otorhinolaryngology, Seoul National University Bundang Hospital, South Korea, [2]School of Behavioral and Brain Sciences, The University of Texas at Dallas, USA, [3]Unit of Neurosurgery, Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand, [4]Department of Otorhinolaryngology, Ajou University School of Medicine, South Korea)

Background
Although the majority of previous studies indicated that tinnitus retraining therapy (TRT) is effective in most patients with tinnitus, neither the exact mechanism of tinnitus improvement nor the predictors of the degree of improvement in tinnitus after TRT are fully understood yet. In this regard, by correlating the degree of tinnitus improvement with pre-TRT resting-state source-localized quantitative electroencephalography (qEEG) findings, we attempted to find the pretreatment neural substrates of tinnitus improvement.

Methods
Thirty-one patients complaining of subjective tinnitus were prospectively enrolled for the TRT program, and their resting-state EEGs were recorded before the initial TRT session. At 3 months after the initial TRT session, source-localized cortical activities were correlated with percent improvement in numeric rating scale (NRS) tinnitus loudness, tinnitus distress, and tinnitus perception.

Results
The enrolled patients showed statistically significant improvements with regard to NRS loudness, distress, and perception 3 months after the initial TRT session. By a median-split approach, we have confirmed that the improvements in NRS loudness, distress, and perception were not affected by the level of hearing loss. Percent improvement of NRS tinnitus loudness was negatively correlated with the activity of the parahippocampus (PHC). Meanwhile, the activity of the insula showed significantly positive correlation with percent improvement of NRS tinnitus distress. Also, the activity of the rostral anterior cingulate cortex (rACC) was positively correlated with percent improvement of NRS tinnitus perception.

Conclusion
The current study may underpin roles of decontexturizing ability of PHC with regard to the improvement of tinnitus loudness, parasympathetic activity control by the insula for tinnitus distress improvement, and noise canceling system for tinnitus perception improvement. The current study has partly replicated classical Jastreboff's neurophysiologic model of tinnitus, and these results may role as a milestone toward patient-tailored application of TRT.

O35: Prognostic Models for Tinnitus Change after Cochlear Implantation.
Kloostra F., Arnold R., Hofman R., Van Dijk P. (University Medical Center Groningen, Department of Otorhinolaryngology, Head & Neck surgery, The Netherlands)

Background
Cochlear implantation is the standard treatment to restore hearing in functionally deaf patients. Recently, some medical centers have started implanting cochlear implants as a treatment for tinnitus in patient with single sided deafness. Since cochlear implantation not always reduces tinnitus and may even deteriorate tinnitus, it is important to know which factors influence the outcome of cochlear implantation on tinnitus. From the studies done so far no clear conclusions can be drawn concerning these influencing factors. In this study we created prognostic models predicting positive or negative changes in tinnitus after cochlear implantation.

Material and Methods
We created these models by means of two retrospectively send questionnaire booklets; one assessed the situation before implantation and one assessed the situation after cochlear implantation. In our analyses we used a question about the presence of tinnitus pre- and post-surgery as dependent outcome factor. Based on previous studies and our own expectations we included the following continuous pre-operative predictors: tinnitus handicap (THI/THQ), hearing handicap (APHAB), personality characteristics (DS14, LOT), anxiety and depression (HADS), pre-operative phoneme scores, mean pre-operative hearing loss in decibels, years of tinnitus before implantation, age at time of inclusion. By means of t-tests and Mann Whitney U-tests we tested which of these variables were relevant to include in further binary logistic regression analyses.

Results
In the binary logistic regression analyses to predict a positive of cochlear implantation on tinnitus we included THI and DS14-negative affectivity. However with these two variables we could not create a significant model. In the binary logistic regression analysed to predict a negative effect of cochlear implantation on tinnitus we initially included THI, APHAB, DS14-negative affectivity, DS14-social inhibition, HADS-anxiety and HADS-depression. With all these variables included we created a significant model ($p<0.001$, Nagelkerke $R2 = 0.559$). However, not all separate variables in this model were significant predictors of a negative effect. Therefore, we performed an additional analysis in which we only include a selection of the initial variables based on the most significant variables in the first model. In this model we included the APHAB, THQ and DS14-social inhibition. With these variables we created a significant model in which also the separate variables were significant or nearly significant ($p<0.001$, Nagelkerke $R2 = 0.584$). This model indicates that the lower the preoperative tinnitus handicap, the lower the preoperative hearing handicap and the less social inhibition, the higher the chance a patient has on a negative effect of cochlear implantation on tinnitus.

Conclusion
Based on binary logistic regression analyses we could not create a good predictive model for a positive effect of cochlear implantation on tinnitus. Concerning a negative effect of cochlear implantation on tinnitus we created a model with good reliability in which patients with low preoperative tinnitus and hearing handicap scores and little social inhibition have more chance of a negative effect on tinnitus.

O36: The correspondence between audiometric profile and tonotopic organization of the primary auditory cortex in tinnitus.
Wolak T., Lewandowska M., Niedziałek I., Ciesla K., Pluta A., Rusiniak M., Skarzynski H. (World Hearing Center, Institute of Physiology and Pathology of Hearing, Kajetany, Warsaw, Poland)

Animal models have shown tonotopic maps reorganization in tinnitus but only when hearing loss is>25dB. In humans, a MEG study has shown differences in tonotopic maps between tinnitus patients and controls [1] whereas fMRI data [2] have suggested no macroscopic changes in tonotopic map in tinnitus patients. These inconsistent outcomes motivated the authors to explore the relationship between audiometric profile and tonotopy of the primary auditory cortex (PAC) in tinnitus.

Thirty two patients with bilateral tinnitus and 27 controls participated in pure-tone audiometry (125Hz-16kHz) examination. Based on 3 different functions that were fit to the individual hearing levels [3], tinnitus patients were assigned to a group with normal hearing up to 8kHz (T, n=15) or a group with high-frequency hearing loss (T+HL, n=17). Analogically, controls were subdivided into those with normal audiograms (C, n=13) or with high-frequency hearing loss (C+HL, n=14).
fMRI data were acquired in a 3T scanner Three 9min20s EPI runs (56 brain volumes per one run in a sparse sequence: TR=10s, TA=2s, TE=30ms, FA=90, matrix 96x96x37, resolution 2x2x2mm) were applied. Stimulation involved 8-s FM tone bursts with central frequencies: 0.4, 0.8, 1.6, 3.2, 6.4kHz, presented binaurally at 80dB(A).

After pre-processing steps in SPM12, fMRI data were analyzed using GLM, by implementing time courses of all presented sounds compared to silence. One-sample t-test maps were produced for each tone burst (0.4, 0.8, 1.6, 3.2, 6.4kHz). In each group the specific area in the PAC was determined, in which there was significant activation for a given T-stat threshold for at least 1 of 5 frequencies. The area was determined individually for the left and right PAC as a function of the T-stat threshold (in the range from 2 to 12). Then, the part of the area that was activated by particular frequencies and a common region representing all 5 frequencies were determined.

There were no significant differences between T+HL and C+HL groups, which means that representations of each frequency in the PAC were very similar in tinnitus and hearing loss-matched control groups. Interestingly, T group showed an overrepresentation of 1.6-3.2kHz frequencies compared to C group (25% larger activation area for 3.2kHz). Audiogram profile analysis revealed that the averaged hearing thresholds for T and C groups were comparable for all frequencies, however, in T group the outcome variance was twice higher than in C for 3-4kHz (there were similar variances for other frequencies in both these groups). Thus, a correspondence between the audiometric profile and tonotopic organization of PAC in tinnitus was observed but only in normal hearing (up to 8kHz) patients.

O37: Tinnitus suppression with electrical stimulation: broadening inclusion criteria for cochlear implantation.
George E.L.J., Arts R.A.G.J., Maes I.H.L., Van Tongeren J., Stokroos R.J. (Maastricht UMC+, Maastricht, The Netherlands)

Tinnitus is an unsolved neurotological problems, with a large impact on the quality of life of millions. Our university medical center focuses on translational tinnitus research, combining clinical knowledge with basic animal model interventions, advanced fMR imaging and reimbursed care model development. A main theme of this research program is tinnitus suppression by electrical stimulation with cochlear implants. This presentation gives an overview of the current results, and provides directions for future research trials.

Tinnitus has yet remained refractory to medical treatment, although it is widely accepted that tinnitus may be suppressed by restoring peripheral auditory neural activity. Applying a cochlear implant (CI) to stimulate the auditory pathway enables a customised, patient specific treatment. In

clinically implanted CI-recipients who suffer from pre-implant tinnitus and who are profoundly deaf, a suppressive effect on tinnitus is reported in 65% to 93% of cases.

Based on these effects, a prospective clinical trial was performed in which ten patients with Single Sided Deafness and unilateral tinnitus were fitted with a CI. The primary goal was to compare the effect on tinnitus complaints of individually optimized looped stimulation with the effect achieved by standard clinical fitting of the CI, both in short and long term.

Results show that tinnitus can be suppressed by clinically obtained CI-fittings (with environmental sounds being perceived), but also by looped intracochlear electrical stimulation (without environmental sounds). Tinnitus suppression was observed both short-term and long-term. This indicates that tinnitus is connected to unwanted neuroplasticity as a consequence of hearing loss. Optimal stimulus parameters for suppression were highly subject-specific, making customization necessary for each individual user. In some cases, even inaudible stimulation appeared to be able to significantly suppress tinnitus.

These results open up further possibilities for developing a novel hearing implant for tinnitus, and contribute to the viability of cochlear implantation based on tinnitus complaints.

O38: The relation of cochlear synaptopathy to obscure auditory dysfunction and tinnitus with normal hearing thresholds.
Guest H.H., Munro K.J., Prendergast G., Plack C.J. (School of Psychological Sciences, University of Manchester, Manchester, UK)

Some individuals with audiometrically normal hearing experience hearing deficits, including difficulty hearing speech in noise ("obscure auditory function", OAD) and tinnitus. It has been suggested that these disorders may be consequences of cochlear synaptopathy (or "hidden hearing loss"), although central factors may also be involved. In an ongoing study we are investigating the neural basis of these disorders, and determining the relation to noise exposure history.

Audiometrically normal individuals with tinnitus, OAD, or both are paired with non-symptomatic controls matched in age, sex, years of education, and pure tone thresholds. Auditory nerve and brainstem function are evaluated using transient-evoked auditory brainstem responses and envelope following responses, while high frequency audiometry and otoacoustic emissions provide measures of cochlear mechanical function. Speech perception abilities are assessed via self-report and psychoacoustic methods, along with self-reported noise exposure history.

In this talk we will present our latest findings, including the relation of OAD and tinnitus to cochlear synaptopathy.

O39: Cochlear Implantation as a Long-Term Treatment for Ipsilateral Incapacitating Tinnitus in Subjects with Unilateral Hearing Loss up to 10 years.
Mertens G[1, 2]., Van de Heyning P[1, 2].([1]Antwerp University Hospital, Belgium, [2]University of Antwerp, Belgium)

Introduction:

The authors previously demonstrated that tinnitus resulting from unilateral hearing loss (UHL) can be treated with electrical stimulation via a Cochlear Implant (CI).

Aim of the study
The study aimed to do a long-term (LT) evaluation of CI in subjects suffering from UHL and accompanied incapacitating tinnitus up to 10 years. The primary focus of the study is on LT tinnitus reduction.

Methods
LT evaluation was derived from 23 subjects suffering from UHL and accompanied incapacitating tinnitus (Pre-operative Tinnitus Loudness Visual Analogue Scale (VAS) score >6/10). They were cochlear implanted at a median age of 55 years (22 - 71 yr) and had 8 years (3 - 10 yr) experience with their CI at the LT testing. The subjects were categorized into two groups: a Single-Sided Deaf Group (SSD) and an Asymmetric Hearing Loss Group (AHL). In order to obtain a LT structural overview of the CI use in UHL subjects, a structured interview was conducted including questions about daily amount of CI use, residual inhibition of the tinnitus after switch off, tinnitus type, etc. The VAStinnitus loudness and the Tinnitus Questionnaire were obtained pre-operatively, one, three, six, 12, and 36-months post-operatively and at the long-term test interval (8 (3-10 years) post-operative). The Hyperacusis Questionnaire was administered in the CION and the CIOFF condition.

Results
The structural interview revealed that all patients (23/23) still wear their CI seven days a week, eight (3-10) years after cochlear implantation. In the SSD group, tinnitus suppression is still the primary benefit reported (83%), whereas in the AHL the majority of the subjects (55%) report that the primary benefit shifted to improved hearing. In the majority of the subjects the tinnitus reduction starts within one minute (in 70% of the cases) and the residual inhibition after CI switch-off is less than a minute (in 65% of the cases). The VAS and TQ scores significantly improved up to three months after the first-fitting and remain stable up to the LT test interval. The median score on the Hyperacusis Questionnaire was 17 (7-36) in the CIOFF condition and improved to 23,5 (12-39) in the CION condition in the SSD group.

Conclusion
Structured interviews shows that 100% of the subjects wears their CI seven days a week. The tinnitus reduces significantly up to three months after the first-fitting and the tinnitus reduction remain stable up to the LT test interval. The SSD group report tinnitus reduction as the primary benefit, whereas the majority of the AHL group report improved hearing as the primary benefit, eight (3-10) years after implantation. In addition to the tinnitus reduction, the CI provides also a benefit regarding reported.

O40: Evidence for Hidden Hearing Loss in Tinnitus Subjects without Threshold Shifts.
Paul B.T., Bruce I.C., Roberts L.E. (McMaster University, Hamilton, Canada)

Background
Evidence from human and animal studies suggests that chronic subjective tinnitus occurs after central auditory structures are deafferented by cochlear damage caused by noise exposure or the aging process [1]. However, not all cases of tinnitus are associated with audiometric hearing loss. One explanation is that tinnitus may be associated with cochlear damage not expressed in the audiogram [2]. High spontaneous rate (HS) auditory nerve fibers (ANFs) with low firing thresholds may have been comparatively well preserved for these tinnitus subjects, resulting in a normal

audiogram. However, low spontaneous rate (LS) ANFs with high thresholds may have been damaged in the tinnitus subjects, which could be expected to affect the processing of suprathreshold sounds but would not be expected to affect threshold measures.

Methods
We tested this hypothesis in tinnitus (N=12) and control (N=25) subjects with clinically-normal thresholds. In a behavioural task subjects were required to detect the presence of 19 Hz amplitude modulation (AM) in a suprathreshold 5 kHz tone (75 dB SPL), which lies in the frequency region where tinnitus is typically experienced and where hidden hearing loss was expected to be present in the tinnitus subjects. All tones were presented against narrowband noise (40 dB spectrum level centered at 5 kHz) intended to saturate HS ANFs such that their ability to contribute to encoding of AM was greatly reduced [3]. In a second test we measured by 32-channel EEG the "envelope following response" (EFR) which originates from the auditory midbrain and is sensitive to AM coding by ANFs [4]. The EFR was evoked by an 85 Hz AM, 5 kHz tone (75 dB SPL) at modulation depths of 100%, 75%, and 50%, against narrowband background noise. A no-noise control condition was also included.

Results and Conclusions
Tinnitus subjects had worse AM detection thresholds in noise compared to controls ($p = 0.03$). Tinnitus subjects also had reduced EFRs in all conditions compared to controls, including the no-noise condition in which HS-ANFs were not saturated by noise ($p = 0.004$). In control subjects, the slope of EFR decline as AM depth decreased correlated with AM detection thresholds ($p = 0.02$), but neither correlated with the audiogram. Simulations of ANF responses based on the auditory periphery model of Zilany, Bruce and Carney [5] found that, in addition to ~100% loss of LS ANFs, an additional ~30% loss of HS fibers was needed to account for the reduced EFRs observed in the tinnitus subjects, and for the differing effects of the background noise in tinnitus and non-tinnitus subjects. A loss of ~30% of HS ANFs would not have been expected to affect hearing thresholds.

Supported by NSERC of Canada

Keynote: Gerhard Andersson
"Using the internet to develop and evaluate tinnitus treatments"

Awaiting abstract.

Keynote: Josef Rauschecker
"Frontostriatal Dysfunction in Chronic Tinnitus"

Awaiting abstract.

Keynote: Susan Shore
"Mechanisms of tinnitus initiation in the cochlear nucleus"

The cerebellar-like circuitry of the dorsal cochlear nucleus (DCN) is unique in its role as the entry point of the central auditory nervous system for integration of sensory and motor information. Fusiform cells, the principal DCN output neurons and gateway to the inferior colliculus and thalamus,

integrate multimodal information for adaptive localization and suppression of internally generated sounds. Fusiform cells are also second-order neurons that display physiological correlates of tinnitus, which are transmitted to higher centers for interpretation and salience.
Multimodal signals, including those from the somatosensory, vestibular and even motor systems are transmitted to cochlear nucleus granule cells, whose axons relay the information to fusiform cells via their apical dendrites. This information is integrated with input from the auditory nerve, which synapses on fusiform cell basal dendrites. Whether combined auditory-multimodal information produces long term depression or long term potentiation depends on whether activation of the parallel fibers precedes or follows activation of the fusiform cell by auditory nerve inputs. This process is termed stimulus-timing dependent plasticity (StDP), the macroscopic equivalent of spike-timing-dependent plasticity.

Following tinnitus-inducing noise-exposure, StDP timing rules are inverted so that stimuli that previously weakened the circuit (anti-Hebbian plasticity) now strengthen the circuit (Hebbian plasticity) and move the fusiform cell to a more excitable state in which spontaneous activity, burst firing and cross-unit synchrony are increased. These physiological markers correlate with behavioral measures of tinnitus. Factors contributing to heightened excitation in the circuit include an upregulation of excitatory inputs from somatosensory structures. These non-auditory projections require a threshold-level of cochlear damage for their upregulation, beyond which they no longer increase. The threshold-limiting cross-modal compensation suggests that while tinnitus-related circuit changes are triggered by cochlear damage, they are not dependent on the amount of hearing loss. The development of tinnitus after "hidden" hearing loss supports this hypothesis.

This talk will elucidate how knowledge of the underlying circuitry is essential for developing effective treatments for tinnitus.

O41: The healthcare cost of tinnitus management in the UK.

Stockdale D[2]., Brazier P[3]., Kay T[4]., Dowrick C[5]., Hoare D.J[6]., McFerran D.J[1]. ([1]Colchester Hospital University NHS Foundation Trust, Colchester, UK [2]British Tinnitus Association, Sheffield, UK, [3]Optimity Matrix, London, UK, [4]Aintree University Hospital NHS Foundation Trust, Liverpool, UK, [5]University of Liverpool, Liverpool, UK, [6]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK)

Background

There is no standard treatment pathway for tinnitus patients in the UK. Possible therapies include education and reassurance, cognitive behavioural therapies, modified tinnitus retraining therapy, or therapies combined with the treatment of hearing loss. However, the effectiveness of most therapies is somewhat controversial. As health services come under economic pressures to deploy resources more effectively there is an increasing need to both demonstrate the value of tinnitus therapies and to substantiate how that value may be continuously enhanced. The objective of this project was to quantify the economic value of tinnitus therapies provided by the NHS from the patient's perspective, differentiating between the common tinnitus therapies currently available.

Methods

Current treatment pathways, costs and health outcomes were determined from the tinnitus literature, national statistics, a patient survey and expert opinion. This information was used to create an Excel-based economic model for the therapy options for tinnitus patients. The probabilities associated with the likelihood of an individual patient receiving a particular combination of therapies was used to calculate average cost of treatment per patient, average health outcome per patient, measured in QALYs gained and cost-effectiveness, measured by the average cost per QALY gained.

Findings

The average cost of treatment per patient per year is GB£717, equating to an NHS healthcare bill of GB£750 million per year. Societal costs are estimated at GB£2.7billion per year. Across all pathways, tinnitus therapy costs GB£10,600 per QALY gained. Sensitivity analyses to test the effect of limited access to cognitive behaviour therapy, and a subsequent reliance on other therapies, had little effect on the estimate.

Interpretation
NHS provisions for tinnitus are cost-effective against the National Institute for Health and Clinical Excellence cost-effective threshold and spending on other comparable conditions. Most interventions help, but education alone offers very small QALY gains. The most effective therapies in the model were delivered within audiology.

O42: High Definition Transcranial Direct Current Stimulation (HD-tDCS) for Tinnitus Relief: A New Kid in Town.
Shekhawat G.S., Mowbray R., Cooke C., Searchfield G.D. (University of Auckland, Auckland, New Zealand)

Tinnitus processing and perception is the by-product of altered neuronal activity in the central nervous system. Modification of this pathological neuronal activity for tinnitus management is referred as neuromodulation for tinnitus relief. Neuromodulation techniques are hypothesised to work based on modulating neuronal excitability and/or synaptic strength and disturbing the pathological neural networks responsible for tinnitus. One such non-invasive neuromodulation technique is Transcranial Direct Current Stimulation (tDCS), depending on the polarity of the stimulation; tDCS can increase or decrease the cortical excitability in the brain region to which it is applied. TDCS has been used for tinnitus research since 2006 and results in transient suppression of tinnitus loudness and annoyance; however, it does not lead to long-term impact on tinnitus-related emotion and yet to be a standalone clinical treatment [1].

Recently a modification of tDCS: High Definition tDCS (HD-tDCS) has been used for tinnitus research [2]. HD-tDCS is more focal and has longer lasting impact on neural plasticity compared to the tDCS [3]. In HD-tDCS the conventional large sponges electrodes of tDCS are replaced with smaller gel electrodes. TDCS uses 2 electrodes placed across the head this is believed to produce deep brain current flow, since current is not lost as it crosses gray matter. tDCS stimulates large tracts of white matter, deep and mid-brain structures. In contrast, 4 × 1 HD-tDCS produces current flow that is restricted to areas below the 4 electrodes and with limited depth of penetration. A further advantage of the 4 × 1 HD-tDCS montage is that the diffusion of return current along the 4 electrode forming the ring results in a more unidirectional modulation such that the polarity of the center electrode (anode or cathode) determines the primary change in excitation; this is compared with conventional tDCS where both anodal and cathodal effects must always be considered.

A series of studies aimed at optimizing HD-tDCS for tinnitus relief and understanding the neurophysiological basis of this technique for tinnitus management were carried out. The result of these trials will be presented to discuss the scope of HD-tDCS for tinnitus relief.

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O43: Identifying a Minimal Important Change score for the Tinnitus Functional Index (TFI) questionnaire for different populations.

Fackrell K[1, 2]., Hall D.A[1, 2]., Barry J.G[3, 4]., Hoare D.J[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and hearing group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, [3]MRC Institute of Hearing Research, University Park, Nottingham, UK, [4]Nottingham University Hospitals NHS Trust, Nottingham, UK)

Background
Sensitively measuring changes in questionnaire scores is essential to identifying whether outcomes are valid and clinically meaningful in a given population. Minimal Important Change (MIC) scores facilitate this interpretation. For people with tinnitus, who often present with a number of co-morbid complaints, recommended methods of evaluating the effectiveness of treatments is to use self-report questionnaires. The Tinnitus Functional Index (TFI) questionnaire is reported to specifically provide a responsive measure of change in tinnitus severity. However, no valid MIC score exists. The present study aimed to identify MIC scores relevant to clinical or research populations, using a combination of distribution-based and anchor-based methods.

Methods
TFI questionnaire data was collected from 255 tinnitus patients recruited from 12 NHS audiology clinics around the UK on four occasions over a nine month period. TFI scores were categorised based on participants ratings of perceived change in severity over the 3, 6 and 9 months (Much-to-moderately improved/worsened, Slight improved/worsened and unchanged). Forty four volunteers who previously participated in a multi-site randomised controlled trial provided TFI questionnaire data at baseline and second visit (within 7-21 days) before receiving any intervention

Analysis involved calculating and integrating Standard Error of Measurement (SEM), Smallest Detectable Change (SDC) (Distribution-based), Receiver Operating Characteristic curve optimal value (ROC) and the global ratings of improvement scores (clinical population).

Results
In the research population, an SDC score of 22.4 was identified based on the variance in the TFI scores between the two time points and the SEM of 8.1. In the clinical population, an SDC score of 22.2 and SEM of 7.4 were identified using the data from 50 participants who rated their tinnitus as unchanged at 3 and 6 months. ROC analysis identified a score of -7.6 as an optimal value for identifying improvement. Difference in the mean TFI change scores between unchanged and slight improved groups indicated a change of -8.7 as important, whilst the difference between unchanged and much-to moderately groups indicated a change of -18 as an important improvement. The scores were integrated using a visual anchor-based MIC distribution plots and an MIC score of a decrease in TFI score of -18 was identified.

Conclusion
This is the first report to integrate approaches using both anchor-based and distribution-based methods to identify a minimal important change score that accounts for both patient perceived benefit and measurement error for the TFI. The findings indicate a minimal important change score of -18 points in TFI global score was associated with higher measurement precision and less variability in scores and measurement error. The similarity in

SDC scores between the populations indicates that researchers, in particular, need to be aware of the natural history of tinnitus (variability) when making judgements on the significance of treatment effects and when claiming that a scale is responsive to change.

O44: The effect of Transcranial Direct Current Stimulation in addition to tinnitus Retraining Therapy for treatment of chronic tinnitus patients.

Rabau S[1, 2]., Van Rompaey V[1, 2]., Van de Heyning P[1, 2].([1]Faculty of Medicine, Campus Drie Eiken, University of Antwerp, Antwerp, Belgium, [2]University Department of Otorhinolaryngology and Head & Neck Surgery, Antwerp University Hospital, Edegem, Belgium)

Background

Currently, there still is no treatment that eliminates tinnitus in all patients. Recent studies have shown that Tinnitus Retraining Therapy (TRT) significantly improves quality of life for tinnitus patients. Also, several studies have reported that transcranial Direct Current Stimulation (tDCS) has a positive effect on attention, working memory, long-term memory and other cognitive processes. The aim of this randomised placebo-controlled double-blind study is to evaluate the added effect of tDCS to TRT in chronic tinnitus patients. To our knowledge, this is the first study to combine both methods.

Methods

Patients with chronic, non-pulsatile tinnitus were randomised in two treatment groups: TRT and real tDCS versus TRT and sham tDCS. Evaluations took place at baseline before therapy started, at the end of the TRT and three months after therapy started. The Tinnitus Functional Index was used as the primary outcome measurement. Secondary outcome measurements were the Visual Analogue Scale of Loudness, Hospital Anxiety and Depression Scale (HADS), hyperacusis questionnaire, psychoacoustic measurements and Late Evoked Potential (P300). The objective was to evaluate whether tDCS can provide faster and/or more relief from the annoyance experienced in patients' daily lives.

Results

Study is still on-going at the moment. Final results will be presented at the conference.

O45: Reporting of sample size justifications: a systematic review of clinical trials in tinnitus.

Mehta R.L., Hall D. (NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK)

Rational

A sample size calculation has become a mandatory entity for transparent reporting of trials. The primary objective of sample size calculations is to determine the number of subjects needed in each treatment arm to detect a clinically relevant treatment effect for a pre-specified primary outcome. Conventionally, the prerequisite to perform a formal sample size calculation involves four parameters: (i) expected treatment effect, (ii) uncertainly measured with a standard deviation (SD), (iii) power, and (iv) significance level (one or two-sided)(www.consort-statement.org). Significance level is normally fixed at 5% (two-sided) and power at 80% or 90%.

Methods

We searched PubMed, EMBASE, Cumulative Index to Nursing and Allied Health Literature, and trials registers: ClinicalTrials.gov, the International Standard Randomised Controlled Trials Number registry, International Clinical Trials Registry Platform and the Cochrane Database of Systematic Reviews. We also searched the Cochrane Central Register of Controlled Trials. Two review eligibility characteristics were specified: first, English language articles only and second, articles to be published on or after July 2006. The justification for this date was to follow from the first international consensus meeting for patients with tinnitus assessment and treatment outcome measurements. The quality assessment considered seven criteria recommended by the CONSORT statement as the minimum set of recommendations for reporting formal power calculations. These criteria were: 1. Identification of the primary outcome variable on which the calculation is based, 2. Clear definition of the hypothesis (the minimal clinically important difference), 3. Power, 4. One or two sided hypothesis testing, 5. Statistical significance level, 6. Derived Sample size per group, and 7. Whether the sample size calculation is based on a prior summary statistics that are sufficiently reported in the text. An independent statistician conducted a blinded review of the formal sample size/power calculations based on the text that had been extracted from the article. Each article was then assessed according to the seven criteria, scoring each item with 1 (present) or 0 (absent) with a total score of seven depicting completeness.

Results
Of the 228 identified articles, 91 (39.9%) were trial registrations where there was no field in the template to include sample size. The remaining 137 (60.1%) were publications of a study protocol or study findings where opportunities did exist to report sample size. Among them, 37 (27%) did report a sample size calculation, but 100 (73%) did not. Of the 37 studies, 29 (78.4%) were RCTs, 5 (13.5%) were cross-over designs, 2 (5.4%) were non-randomised controlled trials or case control studies and 1 (2.7%) was a before and after study. The calculated mean (SD) quality score for the 37 articles that reported sample size calculation was 3.76 (1.71). Note that this represents insufficient information to replicate the calculation since four prerequisites are required.

Conclusion
From what we have observed, sample size calculations are poorly reported in tinnitus studies and do not permit replication.

O46: Results from a patient-administered at-home tDCS treatment study for tinnitus: MEG markers for treatment response.
Hyvärinen P[1, 2]., Mäkelä J.P[3]., Mäkitie A [1]., Aarnisalo A.A [1].([1]Department of Otorhinolaryngology — Head and Neck Surgery, Helsinki University Hospital and University of Helsinki, Finland, [2]Department of Neuroscience and Biomedical Engineering, Aalto University School of Science, Findland, [3]BioMag Laboratory of HUS Medical Imaging Center, Helsinki University Hospital and University of Helsinki, Finland)

Transcranial direct current stimulation (tDCS) has been suggested as a possible treatment for tinnitus after showing promising short-term results in early pilot and open-label studies. However, these findings have not translated into long-term improvements in tinnitus, as shown by recent double-blind sham-controlled tDCS trials. A possible explanation for this discrepancy could be that the long-term treatment trials have included far less patients, leading to less statistical power. One major difficulty in transitioning from one-session experiments to multi-session treatment studies is in the increased labor in running many in-hospital treatment sessions per participant. Also, if numerous visits to the clinic are required, it may also hinder the recruitment of participants —this is especially true for patient groups who have challenging schedules due to e.g. work or family. Thus, approaches that reduce the number of visits to the clinic in long-term tDCS trials are needed.

We studied the safety and feasibility of patient-administered at-home tDCS treatment with either LTA or bifrontal montage in a double-blind sham-controlled setting. 43 patients with chronic tinnitus received 20 minutes of either active 2 mA tDCS or sham tDCS treatment on 10 consecutive days.

The tDCS devices were designed for patient use and included custom-made EEG-caps with electrode positioning guides to assist treatment preparation. We collected pre- and post-treatment (4 weeks after first session) questionnaire data (THI, mTQ, BDI, BAI, loudness and annoyance VASs) and additionally performed 5-minute resting-state MEG measurements on 15 patients. MEG measurements were recorded before and after the first treatment session as well as on the 4-week post-treatment visit. The aim of the MEG measurements was to identify objective measures for treatment response and to relate immediate first-session changes to long-term treatment outcomes.

The treatment was completed by 40 patients and five more patients had to be excluded from final analysis. Additionally, five patients had THI scores under 18 points and were assigned to a control group. For the non-control groups (LTA: 10 patients, bifrontal: 9 patients, sham: 11 patients), we found an overall decrease in THI scores across all treatment groups (average THI change -5.0, $t(29) = -2.41$, $p < 0.05$), but there was no difference between active and sham groups. TDCS treatment was well tolerated and was found to be easy to administer by patients. We also found evidence for thalamocortical dysrhythmia in the resting-state MEG recordings. Gamma, alpha and theta power was modulated by tDCS in some treatment responders with changes in MEG activity linked to VAS changes. Positive MEG markers could be seen in some cases already after the first treatment session and lasted to the 4-week post-treatment measurement session.

Self-administered tDCS is a feasible and safe method for conducting tDCS treatment studies. Our results are in line with recent findings from double-blind controlled in-hospital trials in that there was no advantage of active tDCS over sham treatment in tinnitus. However, we found an overall

O47: Using regression modeling of survey data to better understand expectations of tinnitus treatment by audiologists and patients.
Jansen J.N[1]., Gander P[2]., Husain F.T[1].([1]University of Illinois at Urbana-Champaign, Illinois, USA, [2]University of Iowa, Medical School, Iowa, USA)

Our study compared audiologists' and patients' responses to similar survey questions about their expectations regarding tinnitus treatment. Two surveys were created, one for patients with tinnitus, and one for practicing audiologists who may treat such patients, and included many similar questions, such that comparison of the two could reveal where patients' and audiologists' expectations for tinnitus care were in agreement and areas in which they differed. We also wanted to explain the variance in each of these expectations based on other demographic factors, such as severity of tinnitus (patients) or years practicing (audiologists).

The survey for audiologists and patients was a 31 and 38-item questionnaire respectively. Both surveys were comprised of demographic questions followed by several tinnitus-related questions in multiple choice or Likert scale format. All survey recruitment was completed online. Responses were collected via the Survey Monkey (http://www.surveymonkey.com/) webtool. We received 230 completed patient and 68 completed audiologist surveys. Responses were analyzed within and between surveys and grouped into topical categories (assessment, counseling, current available tinnitus information, satisfaction and expectations, improving tinnitus management). For data within surveys, descriptive statistics and correlation analyses were used. All correlations were generated with SPSS software. The primary means for analyzing data across surveys was by comparison of frequency counts and descriptive statistics from the individual surveys. In some cases independent t-tests were also used to compare data generated from both participant groups. We followed this with linear regression modeling to better understand the sources of variance in the expectations for definition and expectation of treatment outcomes in the two groups.

An important difference was found between the two groups' responses to the question on the definition of treatment success; audiologists reported decreased awareness (77%), stress/anxiety relief (63%) and increased knowledge of tinnitus (63%) most commonly, while patients reported reduction of tinnitus loudness (63%) and complete elimination of tinnitus (57%) most often. The topic of greatest agreement was the desire for more information on tinnitus; 62% of patients felt more information from their healthcare provider would be the most important for improved tinnitus management, and 67% of audiologists reported 'some access' or less to appropriate resources for tinnitus treatment.

For models of patient ratings of treatment outcomes, the most explanation is provided by the answers to the questions "your treatment outcome has been…", followed by "how pleased do you think your care provider…" . For the models of audiologist ratings of treatment outcomes, caseload and experience explain very little of the variance and the biggest contributor is "how satisfied would you say your patients are…", with a little added by "access to resources". In both groups, most of the variance could be explained by each individual imagining how happy the other person would be with the treatment. Further, providing credible tinnitus information resources to audiologists, and focusing resources on training a small number of tinnitus specialist audiologists could greatly improve patient satisfaction with the current state of tinnitus palliative care.

O48: Profiles of NMDA-R antagonists in clinical development for the treatment of tinnitus.

Piu F., Tsivkovskaia N., Wang X., Fernandez R., LeBel, C. (Otonomy Inc., San Diego, California, USA)

The contribution of cochlear N-Methyl-D-Aspartate receptors (NMDA-R) to the pathology of tinnitus has been extensively described in a number of preclinical models. In particular, pharmacological modulation of NMDA-R function using antagonists has been pursued as an approach to mitigate symptoms of tinnitus1. More recently, several NMDA antagonists have been advanced into clinical development for the treatment of tinnitus, including S-ketamine (AM-101)2 and gacyclidine (OTO-311)3.

A comparison of the binding profiles of the non-competitive NMDA receptor antagonists S-ketamine and gacyclidine (racemate and enantiomeric forms) was performed by an independent contract research laboratory. A total of 87 primary molecular targets were assessed, including ion channel receptors, G-protein coupled receptors (GPCRs), transporters, nuclear receptors, tyrosine kinase receptors and enzymes. Gacyclidine racemate and enantiomers exhibited an affinity for NMDA-R in the low nM range, compared to the affinity of S-ketamine which was observed in the high nM range. Off target activity of gacyclidine was limited, indicating a 600-fold selectivity over a variety of molecular targets. S-ketamine demonstrated a 40-fold selectivity over non-NMDA receptor targets. Binding dissociation studies showed more rapid on-rate binding for gacyclidine compared to S-ketamine, and a slower off-rate dissociation for gacyclidine compared to S-ketamine.

Data from these investigations suggest that gacyclidine offers a number of attractive features over S-ketamine as an NMDA-R antagonist, including significantly greater affinity, greater selectivity, and longer binding kinetics. Results from ongoing clinical trials will provide important insight into the correlation between NMDA-R antagonism and tinnitus symptomology.

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O49: A cognitive model of tinnitus distress: results of path analysis.

Handscomb L[1,2]., Hall D[1]., *Hoare D[1]*., *Shorter G[3]*. *([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]UCL Ear Institute, London, UK, [3]Trinity College, University of Dublin, Ireland)*

Tinnitus is known to be a much more distressing experience for some individuals than for others (Davis and El Refaie, 2000), but the reasons for these individual differences are not fully understood (Andersson et al., 1999). A cognitive model of tinnitus distress has been proposed by McKenna et al. (2014). This suggests that tinnitus becomes and is maintained as a distressing problem through a process of interaction between thoughts, emotional distress, attention, perceived loudness, beliefs and behaviour.

In order to investigate the predictions made by this model, a survey was compiled which consisted of nine published questionnaires (or parts of questionnaires) which measure tinnitus-related distress, thoughts, beliefs, attention and avoidance behaviour, perceived tinnitus magnitude and general emotional distress. The survey was completed (mostly online) by 342 members of the public with tinnitus.

Respondents were divided into five categories depending on whether they rated their tinnitus as not a problem or a small, moderate, big or very big problem. Comparison of mean questionnaire scores between categories showed a clear tendency for questionnaire scores to be higher amongst those who rated their tinnitus as a greater problem, except on one questionnaire measuring control beliefs. This suggests that all the components of the model do contribute to people's perception of how problematic their tinnitus is, although there is some ambiguity over the role of beliefs.

Factor analysis was carried out on all the questionnaires used and a satisfactory factor structure was identified for all of them. Path analysis was then carried out using the factor scores derived from all the factors identified. Several adapted versions of the cognitive model of tinnitus distress (testable using structural equation modelling techniques) were found to be an acceptable fit to the data, with certain elements of the model being shown to mediate or partially mediate the relationships between other variables.

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O50: Immediate effects of nasal oxytocin in tinnitus patients.

Azevedo, A[2]., Figueiredo R.R[1]., 1 Schlee W[3]. ([1]TRI Pharmagroup, Porto Alegre, Brazil, [2]Federal University of São Paulo, Brazil, [3]Tinnitus Research Initiative, Germany)

Introduction

Chronic tinnitus is a phantom auditory sensation affecting around 20 % of the general population. To date, there is no FDA approved pharmacological treatment to cure tinnitus. Oxytocin is an endogenous hormone with neurotransmitter and neuromodulator properties.

Aim
To evaluate the immediate effects of nasal oxytocin on tinnitus intensity and distress.

Method
Randomized double-blind placebo-controlled, cross-over study. The clinical global impression scale (CGI) was used to measure the treatment-related improvement at two time points after the intervention (30 min and 24 hours). A visual analog scale (VAS) was used to measure the tinnitus-related distress before and after (30 min and 24 hours) the intervention. For treatment, the patients received 2 puffs of Oxytocin per nostril. In the placebo condition, patients received 2 puffs of distilled water.

Results
17 patients (6 female, average age 63.5 years) with chronic tinnitus were enrolled in the study with average tinnitus duration of 78.8 months. The mean tinnitus distress as measured by Tinnitus Handicap Inventory (THI) was 50.7 ± 30.7 points. An analysis of variance with the CGI scores as dependent variable revealed a strong effect ($p = 0.005$) for the treatment condition. The mean CGI rating after the oxytocin condition was 2.97 compared to 3.68 after the placebo condition.

Discussion
Oxytocin shares neural pathways with dopamine and serotonin and its activity in the temporal cortex has been related to maternal affective bonding in rats. This study data suggest that there may be an immediate effect of oxytocin in tinnitus.

Conclusion
Oxytocin has an immediate positive effect on tinnitus sensation when compared to placebo. Further studies are needed to evaluate its' potential therapeutic role.

O51: Tinnitus: Heterogeneous patterns of burden and complex types of causal pathways - a latent class mixture modelling approach.
Frick U[1]., Langguth B[2]., Frick H[3]., Schlee W[2]., Landgrebe M[4]. ([1]HSD University of Applied Sciences, Cologne, Germany, [2]Psychiatric University Hospital, Regensburg, [3]University College London, Department of Statistical Science, London, UK, [4]kbo-Lech-Mangfall-Hospital, Agatharied, Germany)

Tinnitus sometimes is thought of as a syndrome embedded in different patterns of disease burden that might be caused by partly differing and partly overlapping risk factors. Thus, a latent class approach to separate more or less distinct „types" of tinnitus seems promising. In order to adjust for concomitant variables and to explore potential causal relationships, statistical analysis should be performed simultaneously regressing the latent classes to be identified by a list of potential confounding and/or causal variables. Thus, latent class mixture modelling (B. Muthén) was chosen as statistical approach using MPLUS for computations.

Syndromatic patterns were established from a list of 17 anamnestic variables (like age at onset, prior trauma, psychiatric comorbidity, sex, headache, vertigo, pattern of hearing loss, etc.). Because continuous variables (age at onset, age at help seeking) and an ordinal variable (anxiety) were part of

this list, a latent profile approach was chosen for the classificatory part of the model. The statistical impact of a list of 27 variables were evaluated within a framework of multinomial logistic regressions on the emerging latent classes of tinnitus. Among these concomittant variables were characteristics of the course of illness, measures of burden of disease caused by tinnitus, quality and quantity of symptoms, and subscales of validated psychometric assessments for tinnitus patients like THI or TQ.

N = 2567 patients from the Regensburg Tinnitus Database were included for analysis. Ten latent classes comprising 4.9% to 14.9% of the total sample could be distinguished with only very low risk for missclassification error. Examples for these subtypes were "patients with psychiatric comorbidity" (12.7%) or "young patients with normal hearing" (8.1%) or "females with somatic comorbidities" (11.6%). Our presentation will discuss these subtypes in detail and give the results of the statistical impact of 7 psychometric scales on each of these latent classes. The modelling approach reached its limits when adding nominal or ordinal regressor variables to the model. Substantial and methodological consequences from this innovative modelling approach will be discussed as outlook for future research.

O52: Individualizing the spectrum of tinnitus maskers can make them more efficient than white noise.

Brimijoin W.O[1]., Porr B[2]. ([1]MRC/CSO Institute of Hearing Research, Glasgow, Scotland, [2]School of Engineering, University of Glasgow, Scotland)

Aim

Tinnitus can severely affect quality of life. A tinnitus masker is a sound that is played to lessen the apparent loudness or annoyance of a person's tinnitus, and achieves varying degrees of success. There exist devices that play masking sounds, most often consisting of a pre-set library of sounds that the tinnitus sufferer can select from. The method we propose could allow a listener to train a piece of software (or device) to deliver a customized, highly efficient masker or set of maskers for different situations.

Methods

The algorithm is based on that found in Brimijoin et al. (2013) where we demonstrated that it is possible to use random noise stimuli to estimate the internal representation of vowel sounds like [a] or [:i]. Analysis of the relationship between listeners' responses and the noise stimuli yielded average signal spectra that closely matched those of actual [a] and [:i] vowels. In our method to estimate efficient (or "ideal") tinnitus maskers, the listener is presented with a noise constructed so as to have a particular identifiable spectral structure at any given moment. This structure changed over time and listeners were asked to listen over headphones and press and hold a button whenever their tinnitus became harder to hear. The time and duration of each press was recorded and response-triggered averaging was used to determine the signal spectrum that most frequently occurred with or preceded a response. A signal with this spectrum is the presumptive ideal masker.

Outcomes

The masking strength of these ideal maskers was then evaluated as a function of presentation level. This function was contrasted with that measured for signals with inverted spectra ("worst" maskers) and white noise of the same sound pressure level. Our preliminary pilot data suggests that for some listeners our technique did not result in maskers that were more efficient (effective at lower SPLs) than either worst maskers or white noise, but in others the individualized ideal maskers were at least 12 dB more efficient than white noise.

Conclusions

This method shows promise for some patients and could be readily incorporated into current hearing aids, combi devices, apps, and/or standalone tinnitus noise generators.

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O53: Mindfulness-Based Cognitive Therapy for Tinnitus: A Randomised Controlled Trial.

Marks E.M[1,2]., McKenna L[2]., Schaette R[3]. ([1]University of Bath, Bath, UK, [2]Royal National Throat Nose & Ear Hospital, London, [3]Ear Institute, UCL, London, UK)

Introduction

Recent developments in treatments for chronic tinnitus have demonstrated potential benefits of including 'acceptance based' approaches within more standard psychological treatments. This is a radically different approach to mainstream audiology practice. Mindfulness-Based Cognitive Therapy (MBCT) is a group-based intervention that draws together aspects of Cognitive Behavioural Therapy (CBT) and Mindfulness meditation. Recent studies of mindfulness-based approaches have reported beneficial effects, however these have been from uncontrolled or small clinical trials. We describe results of a larger randomized-controlled trial of MBCT, based on the standard UK approach and adapted to be specific to tinnitus, compared to an active control group (Relaxation Therapy) and a waiting period

Method

Patients reporting chronic and distressing tinnitus were assessed. Those meeting eligibility criteria were randomized to receive either Mindfulness Based Cognitive Therapy (MBCT) or Relaxation Training (RT). Both were group treatments, delivered in groups over eight weekly, 2-hour sessions, by two clinical psychologists. Primary outcome measures included questionnaires assessing tinnitus-related distress (Tinnitus Questionnaire – TQ) and psychological distress (Clinical-Outcomes on Routine Evaluation - CORE-OM). Secondary outcomes included measures of anxiety, depression, tinnitus loudness, tinnitus catastrophizing, tinnitus acceptance and mindfulness. Participants completed measures at 5 time-points (8-weeks pre-therapy, week 1 and week 8 of therapy and at 1 and 6-month follow-up).

Results

70 patients completed the study. Initial results of pre-post differences demonstrated significant improvements in both groups on primary and secondary outcomes. Between-group analyses showed that a significantly greater proportion of patients in the MBCT group (50%) reported clinically significant reduction in psychological distress compared to the RT group (21%) (X2= 0.02). There was a trend effect of the MBCT to be associated with greater improvement in tinnitus distress (TQ) compared to RT ($p = 0.088$). Compared to the RT group the MBCT group showed significantly greater reductions in tinnitus-catastrophizing and greater improvements in tinnitus acceptance. Further analyses are due to be conducted to measure outcomes at 1 and 6 months, and explore potential mediators and moderators of change, and these results will be presented.

Discussion

MBCT and RT both led to significant clinical improvements in tinnitus-related distress and psychological well-being. Patients in the MBCT group showed some significantly greater changes than those in the RT group in a number of domains. This included changes in tinnitus acceptance and

catastrophizing, cognitive and behavioural correlates of tinnitus which have previously been associated with long-term outcomes. We discuss the implications for these findings in future developments of treatments for chronic and distressing tinnitus.

O54: Neuregulin-1 Signaling in the Hippocampus Contributes to Tinnitus.
Bao J., Nakamoto K., Zuo H., Nelson C. (Northeast Ohio Medical University, Ohio, USA)

Tinnitus is a major health problem and is often associated with noise induced or age-related hearing loss. There are no drug treatments for the prevention or alleviation of this disabling condition due to the lack of knowledge about the underlying cellular and molecular mechanisms. Recent studies suggest that the central auditory system and the limbic systems such as hippocampus may be involved. This study demonstrates a significant suppression of noise-induced tinnitus in a transgenic animal model with a conditional over-expression of neuregulin-1 (NRG1) gene in the hippocampus.

NRG1 was the first gene implicated in the pathophysiology of schizophrenia, and is highly expressed in certain neurons, such as adult neurons in the hippocampus. In our previous work, we discovered a novel NRG1 signaling pathway involved in synaptic plasticity in the cochlea and established conditional tissue-specific transgenic mouse lines with different NRG1 over-expression patterns. The major advantage of these transgenic lines is that NRG1 over-expression occurs in specific tissues, such as the hippocampus, can be easily turned on or off during aging with an antibiotic drug. Using an improved tinnitus detection method, which is based on operant conditioning, we have discovered that NRG1 over-expression in the hippocampus can suppress tinnitus genesis in a noise induced tinnitus model. Furthermore, this suppression can be reversed by pharmacological modulation of gamma-aminobutyric acid (GABA) receptors, consistent with previously identified NRG1 signaling cascades for regulating GABA receptors. Therefore, our studies revealed a novel functional role of the NRG1 signaling pathway in the hippocampus. Our future studies will focus on the mechanisms underlying NRG1 suppression of tinnitus in order to developing drug therapies against tinnitus.

O55: The Development of Acceptance of Chronic Tinnitus in the Course of a Cognitive-behavioural Group Therapy.
Moschen R[1]., Riedl D[1]., Zorowka P.G[2]., Rumpold G[1]. ([1] Department of Medical Psychology, Medical University of Innsbruck, Austria, [2]Department for Hearing, Speech and Voice Disorders, Medical University of Innsbruck, Austria)

Objective
Recent findings show the importance of acceptance in the treatment of chronic tinnitus. Cognitive-behavioral treatment (CBT) is considered an effective treatment for tinnitus distress. Recently, acceptance-based approaches have received growing attention within the treatment of chronic tinnitus. Recent studies show that acceptance plays an important role in the reduction of tinnitus distress, but also that the process of acceptance is influential in therapeutic treatments which do not include specific acceptance oriented methods. This study investigates the efficacy of a CBT group therapy and the corresponding change in tinnitus acceptance.

Methods
68 outpatients took part in a CBT group therapy over a 3-month period. Effect sizes and paired t-tests were used to evaluate the effectiveness of the CBT treatment and to investigate the development of acceptance.

Results

Results showed a significant decrease in tinnitus distress and an increase in tinnitus acceptance. Improvements were maintained over a 6-month follow-up period in which large effect sizes were observed.

Conclusions
CBT is an effective treatment for tinnitus distress in patients with chronic tinnitus. Acceptance of chronic tinnitus clearly improved within a CBT group therapy.

O56: Characterization of tinnitus sub-types in a large Swedish family with multiple tinnitus cases for Whole Exome Sequencing.
Edvall N[1]., Bibas T[2, 3]., Cima R.F.F[4]., Canlon B[1]., Knipper M[7]., Lopez-Escamez J.A[8,], Mazurek B[5]., Szczepek A[6]., Cederroth C.R[1]. ([1]Karolinska Institutet, Sweden, [2]National & Kapodistrian University of Athens, Greece, [3]UCL Ear Institute, London, UK, [4]Maastricht University, The Netherlands, [5]Tinnitus Center, Charité, Germany, [6]Charité-Universitätsmedizin Berlin, Germany, [7]Hearing Research Centre Tübingen, Germany, [8]University of Granada, GENYO, Spain)

Tinnitus is a prevalent condition that is experienced by near 15% of the population. While a molecular basis of tinnitus is emerging from animal studies, the translation of this knowledge to therapeutic tools is lagging. The multiple forms of tinnitus, and the numerous aetiologies, make it a challenging task and new approaches are needed to identify new targets. In a recent twin study, we found that tinnitus has a genetic component, which prompted us to investigate the potential genetic factors underlying the vulnerability to tinnitus development. The TINNET Genetics Working Group IV identified a large Swedish family with multiple cases of tinnitus (mainly due to noise overexposure) of potential value for Whole Exome Sequencing. Since many of the genetic studies have failed to identify variants associated with tinnitus, we sought to develop an approach for the in-depth characterization of tinnitus profiles in this family using questionnaire, psychoacoustic and audiological instruments. Our selection of instruments differed slightly from that suggested by the Tinnitus Research Initiative in 2008. Tinnitus and emotional questionnaire instruments included the TSCHQ, THI, TFI, FTQ, TCS, HADS, PSQ-30 and WHOQoL, of which the THI, the FTQ, the TCS and the HADS have been successful in measuring positive outcomes in a recent large clinical trial on cognitive behavioral therapy. Psychoacoustic measures included tinnitus pitch and loudness matching, MML, Residual Inhibition. Finally, audiometric assessments included tympanometry, pure-tone audiometry (up to 16 kHz), DPOAEs (up to f2 = 8 kHz) and LDLs. Inspired from a current effort from our companion Working Group V to identify core outcomes measures in tinnitus trials (COMiT), we represented the overall burden of each individual using a flower plot, whereby each petal represented a domain (tinnitus severity, hearing loss, emotional burden, and affects in quality of life), with greater size of the petals corresponding to greater burden according to the scores obtained from a selection of the above instruments. Using a combination of regression and t-tests, we were able to identify cases and matching controls for their selection, which genetic analysis is ongoing. We believe this type of approach could prove relevant for the identification of tinnitus endophenotypes facilitate the identification of genuine allele variants for tinnitus.

O57: Developing an audiologist-delivered psychological intervention for people with tinnitus.

Thompson D.M[1, 2]., Hall D.A[1, 2]., Walker D.M[3].,Hoare D.J[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and Hearing group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, UK, [3]Health Sciences, University of Southampton, UK)

Rationale

Tinnitus is associated with depression and anxiety disorders, severely and adversely affecting the quality of life and functional health status for some patients. Cognitive Behavioural Therapy (CBT) and other psychological therapies that challenge negative thinking and maladaptive behaviours have been tested with this population, resulting in a convincing level of evidence, enough to warrant its recommendation for use in practice in the UK and the US. However this evidence is limited to psychologist-delivered therapy.

Objective
The overarching aim of this work is to develop an evidence-base for audiologist-delivered psychological therapies designed for people with tinnitus-related distress. The present work approaches the field by way of three consecutive stages. Here we begin with the question of 'what is known from the existing literature about the identity of components of psychological therapies designed to affect causal processes that regulate cognition and behaviour for people with tinnitus?'

Methods
A scoping review of the literature was conducted as part of the development and testing of a manual for audiologist-delivered psychological intervention for people with tinnitus. Searches were performed of medical databases and the grey literature for articles written in the English language and published from 1980. Records returned by these searches were eligible for inclusion if they reported an intervention or guidance of a psychological talking therapy or part of one; while excluding reviews or treatments that included biofeedback, hypnosis or sound therapy. No records were excluded on the basis of their research design. Extracted data included author, year of publication, components of psychological therapy, outcome measures, participants (including sample size, type/severity of tinnitus and comorbid mental health problem), delivering clinician, research methods and results concerning the primary hypothesis. The components of psychological therapies were collated and summarised using inductive thematic analysis.

Results
A total of 5043 record were retrieved of which 64 were retained. Twenty-five themes of components of psychological therapy were identified, derived from 1085 individual components of treatment extracted from the literature of Cognitive Behavioural Therapy; Acceptance and Commitment Therapy; Mindfulness; Existential Patient Centred Therapy; Gestalt Therapy; Eclectic Therapy; Tinnitus Activities Treatment and Directive Counselling.

Discussion
This scoping review did not seek to synthesise the quality of the evidence from which data were extracted. As a result it is difficult to assess the relative importance of the components of psychological therapy extracted here. Moreover, the potential for taking therapy techniques named in the literature and employing them in a novel package of psychological therapy is stymied by a lack of replicability of psychological therapies in the literature. Further research will take this opportunity to involve patients and clinicians using the Delphi methodology to survey how as well as what should be included in a novel psychological intervention package of treatment before testing it.

O58: Genome-Wide Association Study on Tinnitus Heritability.
Gilles A[1, 2, 3]., Fransen E[4, 5]., Van Camp G[5]., Van de Heyning P[1, 2]. ([1]University Department of otorhinolaryngology and Head & Neck surgery, Antwerp University Hospital, Edegem, Belgium, [2]Faculty of Medicine, Campus Drie Eiken, Antwerp University, Wilrijk, Belgium, [3]Department of Human and Social Welfare, University College Ghent, Ghent, Belgium, [4]Center for Medical Genetics, Antwerp University, Belgium, [5]StatUa center for Statistics, Antwerp University, Belgium)

Introduction
Tinnitus, the perception of an auditory phantom sound in the form of ringing, buzzing, roaring or hissing in the absence of an external sound source, is perceived by approximately 15% of the population of which 2.5% experiences a severely bothersome tinnitus. The contribution of genes on the development of tinnitus is still under the debate but based on epidemiological studies the heritability is estimated around 40-50%.

Methods
We performed a genome-wide association study (GWAS) on 916 independent individuals, of whom 18% reported episodes of tinnitus lasting for longer than 5 minutes. After imputation and quality checking, we tested the association between the tinnitus phenotype and 4 000 000 SNPs using PLINK (v1.07) assuming an additive model.

Results
None of the SNPs reached the threshold for genome-wide significance ($p<5E-8$). The most significant SNPs, which are situated outside coding genes, reach a p-value of 3.4E-7. Using the Genetic Analysis of Complex Traits (GACT) software, we estimated the percentage of the variance explained by all SNPs in the GWAS. This analysis showed a very low heritability of tinnitus (3.2%).

Conclusions
To our knowledge, this is the first GWAS study on tinnitus. The present study suggests that tinnitus has very low heritability and is merely due to environmental influences.

O59: Hearing training with fitted hearing aids to improve speech in noise perception in patients suffering from chronic tinnitus.
Ivansic-Blau D., Müller B., Reinhardt D., Guntinas-Lichius O. (Tinnitus-Center at the Department of Otorhinolaryngology, Jena University Hospital, Germany)

Objective
Tinnitus patients, although to some extent having a normal pure tone audiogram, complain often difficulties in speech perception in background noise. This is why our multidisciplinary day-care tinnitus-therapy also contains a hearing training, where speech perception in background noise is trained.

Methods
We investigated 308 consecutive patients with chronic decompensated tinnitus treated in Tinnitus-Center at the Jena University Hospital. The interdisciplinary day-care treatment goaled habitation to tinnitus, consisted of counseling, cognitive-behavioral therapy and physiotherapy and lasted for 5 days. The hearing training combined wearing fitted hearing aids for 3.5 weeks with hearing training which took an hour a day. During hearing training tinnitus patients heard different voices in 65dB background noise, and had a task e.g. to listen only to one female voice and to repeat what it said. After every task, to give a feedback, the correct answer was presented in written form. We measured the speech-in-noise-perception with Freiburger monosyllable speech test in quiet, 55 dB and 65 dB noise before (T1), after 3.5 weeks hearing training (T2) and 6 months later (T3).

Results
Grades of hearing impairment were calculated as 4 frequency-pure-tone hearing average (4f-PTA) on better ear: 89.9% of this population had normal hearing (WHO-grade 0=64.7%, grade 1=25.2%) and only 10.1 % had a disabling hearing impairment (grade 2=8.5% and grade 3=1.6%). In all

background noise settings speech perception was better with fitted hearing aids than without. In overall, speech-perception improved significantly in all background noises after hearing-training at T2 and remained stable over 6 months at T3. The post-hoc analysis showed that only tinnitus patients with no disabling hearing impairment (WHO-grade 0 and 1) improved their speech-in-noise-perception significantly and stable. Nevertheless, almost 90% of our patients with chronic decompensated tinnitus have no disabling hearing impairment according to WHO.

Conclusion
Speech perception difficulties are frequent complaints among tinnitus patients and can be improved by specialised hearing training, but only in tinnitus-patients without disabling hearing impairment seem to profit.

O60: ARHL and Tinnitus in Portuguese Population: what we can hear from a sample of elderly individuals.
FlooK M[2, 3].,Lopes S[2]., Aparicio M[4]., Santos R[5]., Andrade C[6]., Andrade S[7]., Martins J.H[8]., O'Neill A[7, 9, 10]., Escada P[15, 10]., Arguello P[11]., Alcântara, P[6]., O'Neill J[9, 10]., Vilaverde Cabral M[6]., Antunes M[12]., Matos T.D[2]., Fialho G[2]., Caria H[2, 11]. ([2]Deafness Research group, BTR Unit, BioISI- Biosystems & Integrative Sciences Institute, Faculty of Sciences, University of Lisbon (FCUL), Portugal, [3]ESTSP- School of Health Tecnologies, Polytechnic Institute of Porto, Porto, Portugal, [4]FCUL-Faculty of Sciences, University of Lisbon, Portugal, [5]ENT Service CHLO, HEM-Centro Hospitalar de Lisboa Ocidental EPE, Hospital Egas Moniz, Portugal, [6]ICS, IE-Social Sciences Institute, Ageein Institute, University of Lisbon, Portugal, [7]ENT Service, Hospital José Luciano de Castro, União das Misericórdias, Anadia, Leiria, Portugal, [8]ENT Service – CHUC, Centro Hospitalar e Universitário de Coimbra, EPE, Coimbra, Portugal, [9]FCM/UNL-Department of Anatomy, Faculty of Medical Sciences, New University of Lisbon, Portugal, [10]CEFITEC/FCT/UNL-Faculty of Sciences and Technology, New University of Lisbon, Portugal, [11]ESS/IPS-School of Health, Polytechnic Institute of Setubal, Portugal. [12]CEAUL, Faculty of Sciences, University of Lisbon, Portugal)

Currently it is known that 1/3 of individuals with more than 65 years old can have presbyacusis or age-related hearing loss (ARHL). The WHO estimates that in 2025, there will be 1.2 billion people over 60 years of age worldwide, with more than 500 million individuals who will suffer from significant presbycusis. Many individuals will wait several years before seeking help for the hearing loss (HL), due to the insidious onset of the disorder as well as the negative stigma associated with hearing aid. Generally, even in developed societies, individuals accept some degree of HL as inevitable and do not consider it a treatable disorder. ARHL can lead to progressive social withdrawal, depression, isolation and significant familial stress. The impact of HL can be further compounded by the higher incidence of HL in individuals with other coexisting functional limitations. It is reported that about 30% of the individuals with ARHL also have tinnitus, this leading to the increase of elderly frailty. Several studies referred the possibility of common metabolic pathways between ARHL and tinnitus, all damaging the cochlea at the level of the organ of Corti, by affecting hair cells and the stria vascularis cells.

Considering the pathophysiological mechanisms of ARHL, it is assumed that with aging occurs a progressive hypoperfusion within the cochlea leading to ischemia and an increase of free radicals, highly toxic and harmful to the auditory neuroepithelium. These free radicals contribute for genome mutations and mtDNA alterations, thus leading to the reduction of mitochondrial membrane potential, contributing for the formation of bioenergetically inefficient mitochondria.

The genetic susceptibility associated with ARHL has been described through the association between presbycusis and different genes involved in hereditary deafness or oxidative metabolism as well as with specific mitochondrial haplogroups.

In the present study, epidemiological and psychological data are presented for about 450 elderly individuals (over 65 years old) from the Portuguese population. The results of the study of genetic variants concerning NAT2 and GRM7 genes are presented. We also report a wide range of mtDNA haplogroups identified in the subjects, which was expected in the Portuguese population. Gender comparisons are discussed considering hearing loss and audiological patterns. Elderly individuals aged 70-80 or >80 years have significantly more probability of having ARHL, as already described. As regard emotional and social difficulties, the worst listeners present more difficulties and more depressive symptoms, being this more common in women. Of the total of the individuals from our sample, about 39% reported tinnitus, being observed several differences in the age of onset, severity or even laterality. We discuss the differences and similarities at the genetic and epidemiological levels for this subgroup with tinnitus as compared with the other individuals as an attempt of contribution for the association between ARHL and tinnitus.

O61: Neuro-Music Therapy: Impact of hearing aids on therapy outcome.

Argstatter, H., Grapp M. (Deutsches Zentrum für Musiktherapieforschung/German Center for Music Therapy Research, DZM e.V. Heidelberg, Germany)

Background

Many patients suffering from tinnitus also present some degree of hearing loss. Consequently, auditory stimulation procedures are promoted as important therapy option. One music-based intervention is the Neuro-Music Therapy according to the Heidelberg Model. This therapy consists of different modules comprising an auditory discrimination training and a tinnitus reconditioning grounded on the individual tinnitus pitch. Main parts of the intervention depend on the patients' ability to segregate auditory stimuli. Hearing aids might have considerable impact on therapy effectivity.

Objectives

The main question of the current trial was to find out if and to what extent hearing aids influence therapy outcome. We expected that patients presenting hearing loss would benefit from the use of hearing aids and achieve better therapy results than patients not provided with suitable hearing aids.

Methods

A retrospective analysis of adult patients suffering from chronic tonal tinnitus attending a neuro-music therapy was conducted considering three subgroups of patients. Patients in Groups A and B groups presented hearing loss (i.e. WHO grades I-III); patients in Group C presented normal hearing thresholds hearing level better than 25 dB, WHO grade 0). Patients fitted with sufficient hearing devices (ensuring at most moderate hearing loss in the tinnitus frequency region) were allocated in Group A. An audiologist rechecked appropriate hearing thresholds prior to the treatment. Patients diagnosed with hearing loss not compensated for were allocated in Group B. Data from samples of n = 40 patients in each group were analyzed.

All patients attended a Neuro-Music Therapy. This is a manualized short term music therapeutic intervention comprising nine 50-minutes sessions of individualized therapy over a period of five consecutive days.
Primary outcome measure was the change in Tinnitus Questionnaire Total Scores (TQ) from baseline (admission) to end of treatment. Apart from statistical significance (ANOVA), individual changes were assessed according to the concept of clinical significance.

Results

Mean overall reduction in TQ-scores was estimated to about 10.1 ± 9.7 points. About two thirds of all patients in our sample were positive responders in the sense of clinical significance. These numbers are in line with results from previous trials. However, the groups performed unequally: Patients in Group A (hearing loss with hearing aid) and Group C (normal hearing) achieved a nearly equal reduction in TQ-scores and similar proportions of responders (about 8 out of 10) while patients in Group B (hearing loss without hearing aid) were significantly worse off with 3 out of 10 responders. An ODD's ratio calculation revealed an about three times higher chance for positive therapy outcome for patients from Groups A (2.6) and C (3.3) contrasted with patients from Group B.

Conclusions
Based on these results, we conclude that a hearing aid can compensate for a hearing loss and improve the chance for positive therapy outcome while if a hearing loss is not compensated for, success rate declines considerably.

O62: Extreme Tinnitus Phenotype in Meniere's Disease.
Espinosa-Sanchez J.M[1, 2]., Frejo L[1]., Batuecas-Caletrio A[3]., Sanchez-Gomez H[3]., Lopez-Escamez J.A[1, 4]. ([1]Otology and Neurotology Group CTS495, Department of Genomic Medicine, Centre for Genomics and Oncology Research, Pfizer/Universidad de Granada/Junta de Andalucía (GENyO), Granada, Spain, [2]Department of Otolaryngology, Hospital San Agustin, Linares, Jaen, Spain, [3]Department of Otolaryngology, Hospital Universitario, Salamanca, Spain, [4]Department of Otolaryngology, Complejo Hospitalario Universitario de Granada (CHUGRA), Granada, Spain)

Introduction
Tinnitus is a symptom that can appear in many different etiological conditions and that varies widely in its perceptual characteristics. This clinical heterogeneity makes difficult not only to assess different treatment approaches, but also to investigate the underlying causes. So, the delineation of tinnitus subtypes has been proposed as an imperative need in tinnitus research. Persistent tinnitus clearly possesses a dual mechanism that emerges from peripheral dysfunctions leading to changes in central activity likely influenced by an emotional counterpart that feeds tinnitus-related distress. In this sense, Meniere´s disease (MD) is a well-defined cochlear disorder that can be used as a disease model to investigate tinnitus. One step further in this strategy is to select individuals with a strong disabling tinnitus to define a homogeneous endophenotype for genetic studies.

Aims
To analyse the clinical characteristics of extreme tinnitus phenotype (ETP) in MD patients.

Patients and Methods
Patients with definite MD according to 1995 criteria of the AAO-HNS were prospectively recruited at three hospitals between December 2014 and December 2015. Pure-tone hearing thresholds from 250 to 8000 Hz were obtained and patients filled out the Tinnitus Handicap Inventory (THI). We defined ETP as those patients with a THI score greater than 90th percentile. Acufenometry was not performed as psychoacoustic measures do not related with tinnitus distress. Clinical features were compared between patients with and without ETP. Statistical analysis was performed using SPSS and regression analysis.

Results
A total of 160 MD patients were included (61 males, 99 females; mean age 57 ± 13 years). Mean age of onset of MD was 47±14 years and mean duration of disease was 10 ± 9 years. Medium THI score was 38.66 ± 26.59 and THI 90th percentile was 80, thus 15 patients were classified as ETP.

We compared current age, sex, age of onset, uni/bilateral involvement, hearing stage, antecedent of headache, type of headache, existence of hypertension or history of autoimmunity between patients with and without ETP, but no differences were found. ETP was most commonly found in familial MD 6/47 (13%) vs sporadic cases 9/113 (8%), although with a marginal statistical significance [OR=1,691 (0.566-5,052), p= 0.0495].

THI score was related with hearing thresholds at all frequencies, with strong correlation at 250 Hz (r=0.218, p=0.007) and 4000 Hz (r=0.219, p=0.007) in the whole cohort. This effect was increased in patients without ETP at 4000 Hz (r=0.241, p=0.004). Nevertheless, patients with MD and ETP did not show correlation with hearing threshold at any frequency in the audiogram (p>0.5).

Conclusions
1. THI score in ETP is not related with hearing thresholds in MD patients.
2. Extreme tinnitus phenotype seems to be more common in familial MD.

O63: Tinnitus Network and the results of the TMNM trial against tonal tinnitus.
Pantev C. (Institut für Biomagnetismus und Biosignalanalyse, Wilhelms-Universität Münster, Germany)

Abstract
Tinnitus is a result of hyper-activity/hyper-synchrony of auditory neurons coding the tinnitus frequency, which has developed due to synchronous mass activity owing to the lack of inhibition. We assume that removal of exactly these frequencies from a complex auditory stimulus will cause the brain to reorganize around tonotopic regions coding the tinnitus frequency through inhibition-induced plasticity. Based on this assumption, we introduced a novel treatment for tonal tinnitus – "tailor-made notched music" (TMNM).

The prevailing research regarding the neural underpinnings of tinnitus focuses on the role that the auditory cortex has in the generation of this phantom percept. Nevertheless, recent evidences suggest that the cortical reorganization underlying tinnitus involves a widespread network of cortical sources, which operate in a dynamical state. Our own event related studies have demonstrated tinnitus related activity in the cortical tinnitus network comprising temporal, parietal and frontal brain regions.

Further I will report the results of the first study on TMNM that was planned and conducted following the CONSORT statement standards. Our primary outcome measures were the Tinnitus Handicap Questionnaire and Visual Analog Scales. Participants rated their tinnitus before and after the training as well as one month after cessation of the training. While no effect was found for the primary outcome measures, at the follow-up, tinnitus loudness in the treatment group was significantly reduced as compared to the control group. Post hoc analysis, accounting for low reliability scores in the Visual Analog Scales, showed a significant reduction of the overall Visual Analog Scale mean score in the treatment group even at the post measurement.

O64: Factors predicting hearing loss and associating with the compensation status in a cohort of 701 tinnitus patients.
Szczepek A.J[1]., Mazurek B[2]. ([1]ORL Department, Charité University Hospital, Berlin, Germany, [2]Tinnitus Center, Charité University Hospital, Berlin, Germany)

We have conducted progressive, non-interventional study in a sample of 701 patients with chronic tinnitus, who were admitted to Tinnitus Center Charité over a period of one year. The local ethics committee has granted the permit and all patients included have signed a written consent. There were 361 men and 340 women included; the mean age was 55 (range from 19 to 85). Of 701 included subjects, 616 fully answered the German version of Tinnitus Questionnaire (TQ). Based on the TQ score, we found that 442 individuals had compensated (non-severe) and 174 – compensated (severe) form of tinnitus. We have determined that in our sample, the significant predictive factors for hearing loss included age and the severity of TQ grade (decompensation). Interestingly, diabetes was significantly predictive factor for hearing loss (OR 2.23) whereas bruxism associated negatively with hearing loss (OR 0.38). The risk factor for decompensated tinnitus as compared to compensated tinnitus included bilateral (but not unilateral) hearing loss (OR 4.1), depression (OR 2.61) and insomnia (OR 1.97). Our results suggest existence of subcategories of tinnitus that may be helpful for categorizing and further studies of tinnitus

Keynote: Charles Liberman
"Cochlear synaptopathy - a possible role in the generation of tinnitus"

Hidden Hearing Loss: Synaptopathy in noise-induced and age-related cochlear damage

The classic view of sensorineural hearing loss (SNHL) is that the "primary" targets are hair cells, and that cochlear-nerve loss is "secondary" to hair cell degeneration. Our recent work in mouse and guinea pig has challenged that view. In noise-induced hearing loss, exposures causing only reversible threshold shifts (and no hair cell loss) nevertheless cause permanent loss of >50% of cochlear-nerve / hair-cell synapses. Similarly, in age-related hearing loss, degeneration of cochlear synapses precedes both hair cell loss and threshold elevation. This primary neural degeneration has remained hidden for two reasons: 1) the spiral ganglion cells, the cochlear neural elements commonly assessed in studies of SNHL, survive for years despite loss of synaptic connection with hair cells, and 2) the degeneration is selective for cochlear-nerve fibers with high thresholds. Although not required for threshold detection in quiet (e.g. threshold audiometry or auditory brainstem response threshold), these high-threshold fibers are critical for hearing in noisy environments. Our research suggests that 1) primary neural degeneration is an important contributor to the perceptual handicap in SNHL, 2) it may be key to the generation of tinnitus and hyperacusis, and 3) in cases where the hair cells survive, neurotrophin therapies can elicit neurite outgrowth from spiral ganglion neurons and re-establishment of their peripheral synapses.

Abstracts
Poster presentations

Assessment

P1: Measuring fear as an emotional marker of tinnitus distress: psychometric properties of the Fear of Tinnitus Questionnaire.

Fuller T.E[1, 2]., Cima R.F[1, 2, 3]., Vlaeyen J.W.S[1, 3]. ([1]Department of Clinical Psychological Science, Maastricht University, The Netherlands, [2]Adelante, Centre for expertise in Rehabilitation & Audiology, The Netherlands, [3]Behavioural Medicine, University of Leuven, Belgium)

Background

Fear is strong emotional response to a perceived threat that has inherent survival value; it sets in motion the fight or flight response and alerts people to employ safety behaviours to mitigate the threat. However when a fear is triggered by a persistent, internal signal such as subjective tinnitus there is little survival benefit to be gained from these behaviours. It has been postulated (Kleinstäuber et al, 2013) that in people with bothersome tinnitus, fear of tinnitus is a product of catastrophic interpretations of the tinnitus sound that subsequently leads to safety behaviours that are not functional in the long term, but contribute to impairment and additional emotional distress. Tinnitus-related fear has been previously implicated to play a key role in the chronic nature of tinnitus distress and serves as a predictor of overall tinnitus related distress levels. This study aimed to assess the psychometric properties of the Fear of Tinnitus Questionnaire (FTQ) and examine the association between of fear of tinnitus with tinnitus-related distress. The FTQ is a 17 item self-report measure assessing fear of tinnitus, using a binary scale with use of a series of statements (e.g. I am afraid that tinnitus will become worse) applies to them or not. Items for the FTQ were derived from the Tampa Scale for Kinesiophobia (Miller, Kori & Todd, 1991) and Pain Anxiety Symptom Scale (McCracken, Zayfert & Gross, 1992) that are two commonly used measures of fear but applied in the context of experiencing pain.

Methods

An open invitation to participate in study about tinnitus was posted on the Dutch Tinnitus Platform and Dutch Association for Hearing Disorders websites respectively. Participants (N=594) completed a battery of questionnaires that included the FTQ and measures of relevant tinnitus domains such as distress, catastrophising, attention and quality of life. Two weeks after first completing the questionnaires a subset of participants (n=146) completed them a second time to enable test-retest reliability to be calculated.

We used the statistical program R to conduct exploratory factor analysis for binary measures to examine the factor structure of the FTQ, calculated internal consistency, assessed test-retest reliability after a two-week period, and construct validity by examining the relationship between the FTQ and other tinnitus related measures.

Results and Discussion

Results relating to scale and test-retest reliability, convergent and construct validity as well as the factor structure will be presented. Recommendations will also be made regarding the suitability of the FTQ for research and clinical purposes and using fear as a marker of tinnitus distress.

Reference

Kleinstäuber, M., Jasper, K., Schweda, I., Hiller, W., Andersson, G. & Weise C. (2013) The Role of Fear-Avoidance Cognitions and Behaviors in Patients with Chronic Tinnitus, CognitiveBehaviour Therapy, 42:2, 84-99, doi:10.1080/16506073.2012.717301

P2: Clinical patterns for the tinnitus management.

Lai, J.T (Taiwan Tinnitus Association, Taichung City, Taiwan)

A simplified clinical patterns is very useful for the management of chronic tinnitus patients. Since 1995 we have set up tinntus special clinic for severe chronic patients. From the expierence of 3500 subjects in 20yrs we have developed a new clinical patterns for the tinnitus management. The clinical patterns as follow: 1. Disturbances of tinnitus modulating systems

Many patients c severe chronic tinnitus are not really related to the hearing loss revealed by audiogram but related to "tinnitus control system."The most important two systems that regulating the tinnitus to be perceived by patients are eustian tube systems t and sleep systems connected in the central cortex. Mild to moderate E tube dysfunction was often neglected by the otologist. The sleep disturbance related to menopsuse in the female subjects and obstructive sleep apnea (OSA) in the male suffers are common major causes of provocating thechronic tinnitus. After treating these underlying trigger factors we usually could manage the chronic tinnitus with very good result. Others causes often missed by clinician including silent chronic rhinosinusitis, laryngopharyngeal reflux and stress.

2. Disturbance of hearing systems

Tinnitus are presented with directed to the ear diseases just in processing. Sudden deafness & Meniere disease, Significant hearing loss are three diseases that often encountered in the tinnitus clinic. This pattern should treat with good counselling about the natural courses of diseases. Deceasing the fear and emphasizing the protecting effect offered by tinntus.Also hearing rehabilitation with hearing aids is important for facilliating habituation of tinnitus.

3. Potential dangerous tinnitus

Some chnonic tinnitus patients with underlying risky disease in proceeding. The most important one is psychiatric disesase. Most ofen are major depression and panic disorder. Bil tinnitus due to ototoxicity and drug abuse of sedatives are another condition we often noticed in Taiwan.

4. Idiopathic subjective tinnitus

After detailed evaluations of realated systems nasal, throat, LPR, sleep, menopause syndrome,OSA and etc…The real idiopathic is about 10 % only. Of these idiopathic group some are "physiologic tinnitus "but reaction presentrd as very nervous (may be termed "tinnitus hypersensitivity"). Some might have minor defect we did not detected.

P3: Clinically significant tinnitus in 12 years old children.

Raj-Koziak D[1]., 1 Skarzynski P.H[1, 2, 3]., Skarzynski H[1]. ([1]World Hearing Center, Institute of Physiology and Pathology of Hearing, Kajetany/ Warsaw, Poland, [2]Heart Failure and Cardiac Rehabilitation Department of the Medical University of Warsaw, Poland, [3]Institute of Sensory Organs, Kajetany, Poland)

Applied diagnostic criteria to assess the prevalence of tinnitus in children are included in a questionnaire that is filled in by children during hearing screening examination in schools in Poland. The criteria are broad and include questions concerning clinically relevant and irrelevant tinnitus.
Our aim was to evaluate the prevalence of tinnitus heard for at least 5 minutes per day and its characteristics in a group of 12-year old children attending randomly selected secondary schools in Warsaw.

During realization of the hearing screening program in schools children were asked to answer a few basic questions. One of the questions concerned perception and occurrence of tinnitus. The children who indicated one of the following answers: "rarely", "often", "very often", have been asked to complete additional questionnaire consisting of seven questions assessing the prevalence of clinically significant tinnitus and its characteristics.

Clinically significant tinnitus (lasting more than 5 minutes) was found in 18.6%. 5.2% of the children reported permanent tinnitus. The most commonly described sound heard by the children was a squeal. The most of the surveyed children were unable to indicate the source of their tinnitus.

There is a need to introduce a time criterion to the basic questionnaire to evaluate the prevalence of tinnitus in the continued hearing screening program in polish schools. The time criterion will allow us to collect the real data on the existing clinically significant tinnitus among children in Poland.

P4: Assessing catastrophising as a cognitive marker for tinnitus distress: psychometric properties of the Tinnitus Catastrophising Scale.
Fuller T.E[1]., Cima R.F[1, 2, 3]., Vlaeyen J.W.S[1, 2]. ([1]Maastricht University, Maastricht, The Netherlands, [2]Adelante, Centre for expertise in Rehabilitation & Audiology, The Netherlands, [3]Behavioural Medicine, University of Leuven, Belgium)

Background
Catastrophising, defined as an overly negative interpretation of a stimulus, is a process, implicated in the cause of distress associated with many physical and mental health conditions. Within the context of chronic subjective tinnitus, the fear avoidance model predicts that catastrophising triggers a cycle that leads to elevated levels of fear, distress and interference in daily life activities. The Tinnitus Catastrophising Scale (TCS) was recently developed to assess the level of catastrophic misinterpretation of the tinnitus. The TCS, which is based on the Pain Catastrophising Scale (Sullivan, Bishop, & Privik, 1995), is a 13-item self-report measure that asks people to indicate, using a 5-point Likert-type scale the extent to which a series of statements applies to them. We assessed the psychometric properties of the TCS and tested the prediction that catastrophic interpretations of subjective tinnitus would be associated with greater levels of tinnitus-related fear, distress and interference in daily life.

Methods
An open invitation to participate in a study to assess processes associated with tinnitus was posted on the Dutch Tinnitus Platform and Dutch Association for Hearing Disorders websites respectively. Participants (N=591) completed a battery of questionnaires that included the TCS and measures of relevant tinnitus domains such as distress, fear, attention and quality of life. Two weeks after first completing the questionnaires a subset of participants (n=146) completed them a second time to enable test-retest reliability to be calculated.

We conducted exploratory and confirmatory factor analysis to examine the factor structure of the TCS, calculated internal consistency, assessed test-retest reliability after a two-week period, and assed construct validity by examining the relationship between the TCS and other tinnitus related measures.

Results and Discussion
Exploratory and confirmatory factor analysis indicated that a three-factor model of the 13-item TCS was the best-fitting model. Internal consistency of the TCS subscales was very good (Cronbach's alpha between .78 and .86) and that the TCS was strongly correlated with measures of tinnitus related fear (r = .72), disability (r = .50) and distress (r = .77) respectively. The analysis indicates that the TCS is a reliable measure with which to assess the extent to which people catastrophically misinterpret tinnitus-perceptions. Evidence indicates that catastrophizing about tinnitus is a strong predictor of levels of tinnitus related distress.

Reference
Sullivan, M.J.L., Bishop, S.R., & Pivik, J. (1995) The Pain Catastrophizing Scale: Development and validation. Psychological Assessment, 7(4), 524-532. doi:http://dx.doi.org/10.1037/1040-3590.7.4.52

P5: Correlates of optimism and Spirituality in individuals with complaints of tinnitus.
Oliveira A.V[1, 2, 3]., Meneses R.F[3]., Trigueiros-Cunha N[4]. ([1]ENT Department - Hospital das Forças Armadas, Porto, Portugal, [2]Audiology Department - School of Alied Health Sciences/Polytechnic Institute of Porto, Portugal, [3]Human and Social Sciences Faculty - University Fernando Pessoa, Porto, Portugal, [4]ENT Department - Hospital de Pedro Hispano, Matosinhos, Portugal)

The optimism and spirituality are related to a positive and dynamic perspective, either of life as of the relationship to health, which could lead the person to face his/her problem, particularly if it is a chronic problem, in a more constructive way. For example, using coping strategies to address this problem more effectively, by better managing stress and negative life events associated with it.

It appears that the most optimistic individuals deal better with tinnitus and that optimism is a predictor of QOL in patients with tinnitus. Spirituality is an important dimension in QOL in its relationship to health and disease, particularly in situations of chronic problems, however, there are no studies concerning their presence in tinnitus problems.

The objectives of the study undergo are characterize optimism and spirituality of individuals with tinnitus complaints and explore its relationship with socio-demographic and clinical variables.

From the results, it is emphasized that 12.3% of individuals in the sample (N = 57) showed average values below the midpoint (assumed to be cut) for the optimism scale (LOT-R), not finding statistical relations significant with regard to the variables. For spirituality, 27.6% of subjects (N = 58) are below the midpoint (cutoff) to the spirituality of scale. Relations were found between spirituality and age, verifying that older individuals have higher values in the spirituality scale. It was also found correlations between spirituality and education, verifying that individuals with higher levels of spirituality have lower levels of education.

These indicators reinforce the perception that spirituality is an important aspect to explore in a therapeutic intervention with these individuals, which is reinforced by the fact that there is a considerable percentage of individuals who perceive their spirituality as low. Optimism, which does not replicate the values found in the literature, should also be considered in a therapeutic intervention for this type of individuals.

Keywords: Tinnitus, Spirituality, Lot-r, Optimism

P6: The Evaluation of a New Tinnitus Pitch Matching Method.

Williams, M., Hauptmann C. (*Institute of Neuroscience and Medicine - Neuromodulation (INM-7), Jülich Research Center, Jülich, Germany and DESYNCRA Technologies Ltd., London, UK)*

Purpose

A number of modern sound based therapies for primary tinnitus are designed to target specific regions of the auditory cortex by utilising the tonotopic organisation of the system with the user's perceived tinnitus pitch acting as a guide (Pantev et al, 2012, Tass et al 2012, Wan Suhailah et al 2015). It is, therefore, reasonable to assume that the efficacy of such targeted sound therapies is dependant upon acquiring an accurate pitch match of a patient's tinnitus percept. Authors have proposed a variety of tinnitus pitch matching protocols; however, reliability has not yet been either demonstrated or reported. The present study proposes a new mixed methods approach to pitch matching that combines the utilisation of bracketing, similarity grading, two-alternative forced-choice (2AFC) paradigm and individual fine tuning.

Methods

50 pitch match recordings (left and right ear) were carried out with 25 normal hearing subjects with simulated tonal tinnitus, of a known frequency. Their simulated tinnitus was matched using a modified pre-existing protocol, by Vernon et al, which has been well documented for clinical tinnitus evaluation. This was subsequently compared to the mixed method approach to enable comparison and validation. Repeatability was also investigated by carrying out successive pitch match measurements with 10 subjects who presented with primary tonal subjective tinnitus. For subjects attempting to pitch match a simulated tinnitus frequency a range of ±5% was chosen to represent a threshold of accuracy.

Results

The mixed methods protocol provided a significantly more accurate pitch match value for all subjects. 76% of subjects matched the artificial tinnitus tone within the required accuracy range for the mixed methods protocol with only 32% of subjects achieving this level of accuracy with the Vernon method. The mean deviation from the known artificial tinnitus frequency was recorded as being 10.4% (SD:4.4) for the Vernon et al method and 3.8% (SD: 6.1) for the mixed methods protocol. Repeatability testing, in subjects with primary tinnitus, revealed that 75.5% of recorded pitch matching values to be within the ±5% threshold around the mean tinnitus pitch.

Conclusion

In this study the proposed new tinnitus pitch matching method appears to be a promising option for obtaining an accurate tinnitus frequency value.

P7: Validation of the Chinese Tinnitus Functional Index.

Kam A.C.S[1]., Leung E.K.S[2]., Chan P.Y.B[3]., Cheung A.P.P[4]., Tong M.C.F[5]. ([1]Department of Special Education & Counselling, The Hong Kong Institute of Education, Hong Kong, [2]ENT Department, Prince of Wales Hospital, Hong Kong, [3]ENT Department, Youde Nethersole Eastern Hospital, Hong Kong, [4]ENT Department, Yan Chai Hospital, Hong Kong, [5]Department of Otorhinolaryngology, Head & Neck Surgery, The Chinese University of Hong Kong)

Purpose of study

The objective of this study was to translate the Tinnitus Functional Index (TFI) into Chinese and then validate its use in Chinese Hong Kong patients who are suffering from chronic tinnitus.

Methods
The subjects were 83 adults who attended audiology clinics with a primary or secondary complaint of tinnitus. They completed the Chinese versions of the Tinnitus Questionnaire and the Short-Form 36 Health Survey (SF-36). The subjective severity of tinnitus and tinnitus-related problems were scored using rating scales. Statistical analysis was performed to determine the psychometric properties of the questionnaire.

Results
The TFI-CH had good internal consistency reliability estimate (α = 0.86), which was comparable to that of the original version of TFI. Significant correlations were observed between the TFI-CH and psychological distress, tinnitus-related problem ratings, and severity ratings.

Conclusion
The results suggest that the TFI-CH is a reliable and valid measure of tinnitus severity and it can be used in measuring treatment outcomes.

P8: Validation of a Dutch version of the Tinnitus Functional Index in a tertiary referral tinnitus clinic.
Arnold R[1]., Tuinstra J[2]., Van Dijk P[1]. ([1]University of Groningen, University Medical Center Groningen, Department of Otorhinolaryngology/Head and Neck surgery, The Netherlands, [2]University of Groningen, University Medical Center Groningen, Dept. of Health Sciences, The Netherlands)

Background
In recent years, the Tinnitus Functional Index has received increasing interest and has shown good qualities, both for clinical and research purposes. Furthermore, research has shown the TFI to be responsive to treatment-related changes, which was one of the main purposes of the instrument. Our study presents the results of the validation of a Dutch version of the TFI in a population of tinnitus patients seen in a specialised multidisciplinary outpatient clinic in the North of the Netherlands.

Materials and methods
The original TFI was translated by means of a translation-back translation procedure. The Dutch version of the TFI was administered to a group of consecutive tinnitus patients, who visited a tertiary referral tinnitus clinic. The self-report questionnaire consisted of the TFI, THI, HADS, and Rand-36. In total, 79 patients (aged 53 ± 12; 61% male) were included.

Results
The internal consistency of most of the subscales as well as the total TFI was quite good (Cronbach's alpha .81-.97). Only subscale "sense of control" showed a lower, though acceptable, internal consistency (Cronbach's alpha .67).
With respect to convergent validity, the results show significant correlations (r = .26-.66) between the subscales of the TFI and related subscales of the THI. Subscales "sense of control", "concentration" and "auditory" show low correlations with anxiety and depression (HADS; r = .04-.19), which is indicative of a good divergent validity. However, subscales "intrusive" and "sleep" were significantly related to anxiety and depression scores, whereas subscale "relaxation" was significantly related to depression scores. These last results show a modest divergent validity.

Conclusions

Overall, the Dutch version of the TFI has shown to be a reliable and valid instrument. However, significant correlations of a few TFI subscales with anxiety and depression scores show a modest divergent validity.

P9: Which tinnitus-related characteristics affect current health-related quality of life and depression? A cross-sectional cohort study.
Peter N[1]., Kleinjung T[1]., Delsignore A[2]., Meyer M[3]., Rufer M[2]., 2 Weidt S[2]. ([1]Department of Otorhinolaryngology, University Hospital Zurich, Zurich, Switzerland, [2]Department of Psychiatry and Psychotherapy, University Hospital Zurich, Zurich, Switzerland, [3]Neuroplasticity and Learning in the Healthy Brain, University of Zurich, Switzerland)

Tinnitus is sometimes associated with lower health-related quality of life (HRQoL) and depressive symptoms. However, only limited evidence exists identifying which tinnitus characteristics are responsible for these associations. The aim of this cross-sectional study was to assess associations between tinnitus, HRQoL, depressive symptoms, subjective tinnitus loudness and audiometrically assessed tinnitus characteristics (e.g., hearing threshold).

Two hundred and eight outpatients reporting tinnitus completed questionnaires on tinnitus (Tinnitus Handicap Inventory, THI), HRQoL (World-Health-Organisation Quality of Life Short Form Survey, WHOQOL-BREF), and depressive symptoms (Beck Depression Inventory, BDI), and underwent audiometry.
Patients with higher THI scores exhibited significantly lower HRQoL, and higher depression scores. THI total-score, THI subscales, and subjective tinnitus loudness explained significant variance of WHOQOL-BREF and BDI. Audiometrically measured features were not associated with WHOQOL-BREF or BDI.
Overall, we confirmed findings that different features of tinnitus are associated with HRQoL and depressive symptoms but not with audiometrically assessed tinnitus characteristics. Consequently, physicians should evaluate THI total score, its sub-scores, and subjective tinnitus loudness to reliably and quickly identify patients who potentially suffer from depressive symptoms or significantly lower HRQoL. Supporting these patients early might help to prevent the development of reactive depressive symptoms and impairment of HRQoL.

P10: A systematic review of the global reporting of tinnitus prevalence and severity.
McCormack A[1]., Edmondson-Jones M[1, 2]., Somerset S[1, 2]., Hall D.A[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, [3]MRC Institute of Hearing Research, University Park, Nottingham, UK)

Objectives
Tinnitus prevalence figures vary widely depending on the populations studied, and the definition and methodologies used. There is no standard diagnostic test for tinnitus. Within epidemiological studies presence of tinnitus is usually by self-report, typically in response to a single question. However the precise wording of that question varies. It is likely that the definition of tinnitus, characterisation of tinnitus, and other factors, have a significant effect on the figures for tinnitus prevalence and severity. Given the variety of international studies we proposed to assess and collate published tinnitus prevalence and severity estimates, creating a narrative synthesis of the data, and examining variability.

Methods

A systematic review included all adult population studies reporting the prevalence of tinnitus post 1980. We searched five databases (Embase, Medline, PsychInfo, CINAHL and Web Of Science), using a combination of medical subject headings (MeSH) and relevant text words.

Results
The databases identified 875 papers and 16 were identified through manual searching. After duplicates were removed, 515 remained. At title, abstract and full text screening, 400, 48 and 28 papers respectively were removed, leaving 39 papers for data extraction. Sixteen countries were represented, with the majority of studies from the European region (44%). Studies published since 2010 represented half of all studies (51%). There were 8 different types of definitions of tinnitus, the most common being "tinnitus lasting for more than five minutes at a time" (36%). Only 18% of studies gave justification for the question that was used, or acknowledged the lack of standard questions for tinnitus. Twenty-four studies (65%) reported tinnitus prevalence by age groups, and generally show an increase in prevalence as the age increases. Half (54%) of the studies reported tinnitus prevalence by gender. The pattern generally shows higher tinnitus prevalence among males than females for the majority of studies. Overall prevalence figures for each study ranged from 5.1% to 42.7%. Prevalence figures for studies that used the same definition of tinnitus ranged from 11.9% to 30.3%.

Conclusion
There is widespread inconsistency in defining and reporting tinnitus, leading to variability in prevalence estimates among studies. The risk of bias assessment results showed that more than half of the included studies had a high risk of bias and this limits the generalisability of prevalence estimates. In addition, the available prevalence data is heterogeneous thereby preventing the ability to pool the data and perform meta-analyses. Sources of heterogeneity include different diagnostic criteria, different age groups, a different study focus and therefore differences in reporting and analysis of the results, thus making comparison among studies impracticable. Deriving global estimates of the prevalence of tinnitus involves combining results from many surveys which are consistent in the definitions and measurement of tinnitus, the survey methodology and in the reporting and analysis of the results. Ultimately comparison among studies is unachievable without such consistency, however the strength of this review is in providing a record of all the available, recent epidemiological data in each global region.

P11: Why is tinnitus a problem? A qualitative analysis of problems reported by tinnitus patients.
Watts E[1]., Fackrell K[2]., Smith S[2]., Sheldrake J[3]., Hoare D[2]. ([1]School of Medicine, University of Nottingham, Nottingham, UK, [2]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [3]The Tinnitus and Hyperacusis Centre, London, UK)

Introduction
Tinnitus is a prevalent and currently incurable condition. Individuals often experience a wide range of associated problems. The negative consequences of tinnitus can be categorised into 'domains', i.e. distinct symptoms which are theoretically similar. There is however, no universal agreement on what these domains are, how many domains of tinnitus problem there are, or how these domains should be assessed. Using qualitative analysis, the primary aim of the study was to identify the domains of tinnitus problem, and secondly to examine the relevance of the Tinnitus Functional Index (TFI) questionnaire (Meikle et al., 2012) as a clinical measure against those domains.

Methods

We performed a retrospective analysis of a large anonymised clinical data set from 988 patients who attended a single tinnitus treatment centre in the UK, between 1989 and 2014. The Tinnitus and Hyperacusis Initial Interview Form (Jastreboff and Hazell, 2004) was completed in clinic during the first consultation. Free text responses to the interview question 'Why is tinnitus a problem?' were analysed using summative content analysis. Cluster analysis of the data was also conducted to determine whether any of the domains identified by patients were consistently linked with each other, e.g. whether patients with problem x also generally report problem y. This would indicate which tinnitus problems are likely to co-occur. The TFI questionnaire (introduced as part of the standard assessment in the clinic during 2011) items and subscales were compared to patient self-reported.

Results
Our analysis identified 21 distinct domains of tinnitus-associated problems. Tinnitus-related fear was notably a common problem. Other domains included constant awareness, loss of peace, annoyance, and inability to concentrate. All eight TFI subscales related to problem domains we identified from patient self-report and that the TFI includes items relevant to 14 of the 21 domains.

Discussion
Fear, the most common problem as identified during this study, is not represented in the TFI and so the use of a questionnaire measure of 'fear' is recommended. This work will inform a core outcome set for tinnitus research currently under development in Europe, and the development of any future tinnitus questionnaires.

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P12: A systematic review of domains relating to the everyday impact of hearing loss, as reported by patients or their communication partner(s).
Vas V[1]., Hall D.A[1]., Akeroyd M.A[2].
([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]MRC Institute for Hearing Research, University Park, Nottingham, UK)

Introduction
Hearing loss is a highly prevalent condition that affects approximately one in six people in the UK alone. The consequences of hearing loss are multifaceted, as it is a complex condition that can detrimentally affect various aspects of an individual's life, including communication and personal relationships. Currently the most common intervention for hearing loss is amplification with hearing aid(s) which serves to address the degradation of audibility due to hearing loss, but may not address all of its consequences. As such, there is a pressing need for appropriate outcome measures that capture the most significant effects that hearing loss has on an individual's life (Boothroyd 2007). However, it is unclear whether current outcome measures adequately match what patients report as the major consequences of hearing loss (Taylor 2007). This systematic review will collate independent evidence from studies that have reported what adults with hearing loss and their communication partners consider as the most important problems as a result of their hearing loss in their everyday lives. This includes reported problems with aided listening, but not with using listening devices themselves.

Methods
Methods are defined according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses for Protocols (PRISMA-P) 2015. Searches were conducted in Web of Science, PubMed, Embase, Cos Conference Papers, CINAHL and Google scholar (earliest to August 2015). Following a screen of the titles of each study, 559 potentially relevant studies were identified. Two researchers conducted parallel screens of the abstracts to exclude studies that did not fit into the scope of the review. To assess inclusion based on the abstracts of the articles, each researcher referred to the objectives of the systematic review, inclusion criteria and the language of the abstract.

Results
Data extraction for studies that have been taken forward to full-text review is currently on-going. Thus far, most of the included records have reported data that is qualitative. All relevant information extracted from the studies will be used in a narrative synthesis to form themes that represent the most commonly reported complaints of hearing loss.
Discussion: The dimensions of complaints could be used to inform diagnostic assessment, as well as to inform the choice of outcome measures to assess treatment benefit.

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Taylor, B. (2007). "Changes in hearing aid benefit over time: an evidence-based review." Audiology Online.

P13: Tinnitus Handicap Inventory as a disease-specific questionnaire assessing tinnitus distress in Polish patients - preliminary study.
Skarzynski P.H[1, 2, 3]., Raj-Koziak D[1]., Rajchel J[3]., Pilka A[1]., Skarzynski H[1]. ([1]World Hearing Center, Institute of Physiology and Pathology of Hearing, Kajetany/Warsaw, Poland, [2]Heart Failure and Cardiac Rehabilitation Department of the Medical University of Warsaw, Poland, [3]Institute of Sensory Organs, Kajetany, Poland)

Currently there are in the world a lot of questionnaires that asses the effect of tinnitus on the lives of the people affected by this condition. The aim of our study was to establish the degree of tinnitus distress among Polish patients using polish version of Tinnitus Handicap Inventory (THI-POL).

For this purpose we've chosen worldwide validated and reliable questionnaire Tinnitus Handicap Inventory (THI-E) developed by Newman et al. The interdisciplinary team of specialists translated and adopted English version of THI into Polish language (THI-POL). We examined 75 patients of the Institute of Physiology and Pathology of Hearing seeking help due to tinnitus as their primary complaint. After initial interview we obtained informed consent from every person. Patients were asked to fulfill THI- POL questionnaire at their first and last day of hospitalization (at two days interval) providing data for test-retest analysis.

Currently the research is in progress and the results will be collected by the end of January. We will present results and conclusions concerning psychometric evaluation.

P14: Interaction of autonomic nerve system function and sleep quality on the severity of chronic subjective tinnitus.
Lin C-Y., Wu J-L. (Department of Otolaryngology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan. Taiwan)

Sleep difficulties are among the frequent complaints associated with chronic tinnitus. Most studies reporting on this problem are questionnaire-based. The perceived distress in tinnitus patients seems to be sympathetically mediated was also proposed recently. We aimed to investigate the significant predictors of chronic subjective tinnitus, and to assess the interaction of autonomic nerve system (ANS) function and sleep quality on the tinnitus severity. Adult patients with subjective tinnitus were recruited. The duration of tinnitus complaint was required to be at least 6 months. According to previous medical records, subjects with the pure-tone averages for 500 Hz, 1000 Hz, and 2000 Hz frequencies above 25 dB HL were excluded. Objective assessments included pure-tone audiometry, over-night hospital polysomnography (PSG) and ANS function test. Subjective questionnaire assessment of tinnitus severity was Tinnitus Handicap Inventory (THI). Participants (with and without tinnitus) were matched for health and relevant socioeconomic factors. There were 40 tinnitus patients and 40 control subjects without tinnitus completed the whole protocol. Tinnitus patients were older than non-tinnitus subjects ($p<0.05$). Characteristics of hearing status among tinnitus patients included worse 4k-Hz hearing threshold and worse 4k-Hz uncomfortable loudness level. Longer sleep latency and lower sleep efficiency were found among tinnitus patients ($p<0.05$). 4k-Hz uncomfortable loudness level, sleep latency and ANS function hyperactivity were significant predictors of the tinnitus severity. Furthermore, combination with longer sleep latency and ANS function hyperactivity led to higher score level of THI. Our study showed that longer sleep latency and ANS function hyperactivity aggravated the tinnitus severity. Further clinical interventions to improve the ANS function hyperactivity and sleep difficulties among chronic subjective tinnitus patients should be considered.

P15: Alexithymia is associated with the impact of tinnitus on daily life.

Hemsley C[1]., Peter N[1]., Wielopolski J[2]., Kleinjung T[1]., Wichser M[1]., Meyer M[3]., Rufer M[2]., Weidt S[2]. ([1]Department of Otorhinolaryngology, University Hospital Zurich, Zurich, Switzerland, [2]Department of Psychiatry and Psychotherapy, University Hospital Zurich, Zurich, Switzerland, [3]Neuroplasticity and Learning in the Healthy Brain, University of Zurich, Switzerland)

Background

Alexithymia is a personality trait with a tendency to express psychological distress in somatic rather than emotional form and is considered a triggering factor for somatization. Although, such a tendency is often observed in patients with tinnitus, the association between alexithymia and tinnitus severity remains yet unclear.

Design

We assessed 207 patients with tinnitus from a tinnitus outpatient unit for tinnitus severity (Tinnitus Handicap Inventory, THI), depression (Beck Depression Inventory, BDI) and characteristics of alexithymia (Toronto Alexithymia Scale, TAS-20). Correlation analyses and multiple regression analyses were performed to evaluate the relationship between alexithymia, depression and tinnitus severity.

Results

Highly significant correlations were found between THI total score and BDI score as well as TAS-20 total score and two subscales (difficulty in identifying feelings and difficulty in describing feelings). Multiple regression analyses revealed that only BDI and the difficulty in identifying feelings-subscale significantly predicted tinnitus severity measured by THI.

Conclusions

An independent link exists between tinnitus severity and the difficulties identifying feelings dimension of alexithymia which is conducive to a better understanding of affect regulation and annoyance among patients with tinnitus.

P16: Clinical validation of a new tinnitus assessment technology.

Fournier, P[1, 3]., Hébert S. [1, 2, 3], ([1]International Laboratory for Brain, Music and Sound Research (BRAMS), [2]École d'orthophonie et d'audiologie, Faculty of Medicine, Université de Montréal, Canada, [3]Centre de Recherche, Institut Universitaire de Gériatrie de Montréal, Canada)

The clinical assessment of tinnitus mainly relies on patients' self-report. The psychoacoustic measurements of pitch and loudness are not widely used in clinical settings but when they are, the standard procedure is passive, with clinicians controlling the stimulus parameters presented to the patient. These techniques are usually performed by highly skilled clinicians and do not provide stable measurements of the tinnitus percept within a session or between sessions over time. Recently, an active method allowing the patient to control the parameters using a touchscreen has shown good test-retest reliability for pitch and loudness matching over several months. Moreover, psychoacoustic loudness matches were sensitive and specific to the presence of tinnitus, contrary to pitch matches. The purpose of the present study was to compare the performance of the touchscreen platform with a new stand-alone prototype, both using an active method for pitch and loudness matching. Fifteen tinnitus patients and fifteen tinnitus stimulators (i.e. individuals without tinnitus instructed to simulate this sound perception with the intention to convince an experimenter that they have tinnitus) were tested with both devices in a counterbalanced order. Prior to the tinnitus assessment, a standard audiology evaluation including otoscopy and hearing thresholds by conventionnal Hughson-Westlake from 0.25 to 16 kHz was performed. The tinnitus assessment for both devices consisted of three-seconds pure tones ranging from 0.25 to 16 kHz. Participants were first asked to rate the likeness of the tone to their tinnitus pitch on a Likert-type scale in which 0 = ''does not match my tinnitus at all'' and 10 = ''perfectly match my tinnitus.'' During the same trial, they matched the loudness of the tone -that is, the sound level at which that specific frequency contributed to their tinnitus- by moving a visual gauge (Touchscreen) or a potentiometer (Stand-alone prototype) that increased and decreased the sound level by 1 dB steps. Both the touchscreen platform and the new device showed very similar results in pitch and loudness matching. On pitch matches there were no main effect or interaction with type of device (Touchscreen or Stand-alone prototype). A Frequency by Group interaction was significant ($p=.048$), with simulators rating low frequencies more like their tinnitus than the tinnitus group. The correlation between the likeness ratings of all frequencies between the two devices was high ($r=.743$, range: .53 to .95, all ps < .003). On loudness matches there were no main effect or interactions with type of device. There was a significant Group effect ($p=.015$), with simulators rating loudness higher (Mean: 19 dB SL) compared to tinnitus patients (Mean: 8.6 dB SL). The correlation between the loudness ratings of all frequencies between the two devices was also high ($r=.673$; range: .32 to .85, all ps < 0.01, except at 750 Hz, $p=.08$). In conclusion, both devices show very similar results and replicate previous findings that have shown higher low frequency pitch matching and higher loudness mathcing for simulators compared to tinnitus participants.

P17: Music-induced hearing disorder - a clinical and psychophysical characterization.

Szibor A[2]., Ylikoski J[1]., Lehtimäki J[1]., Hyvärinen P[2]., Ylikoski M[1]., Aarnisalo A[2]., Mäkitie A[2]. ([1]Helsinki Ear Institute, Helsinki, Finland, [2]Department of Otolaryngology-Head and Neck Surgery, University of Helsinki, Finland)

Loud music and excessive noise levels are the two most prominent causes of acute noise trauma to which adolescents and young adults expose themselves voluntarily at music and social events. In some night clubs noise levels between 104-112 dB(A) are not unusual but relatively little is known about the clinical and audiological features of music-induced hearing disorders (MIHD). In this study the clinical and psychophysical data of

104 patients attending the Helsinki Tinnitus Clinic were examined retrospectively. In all cases the tinnitus was triggered by an exposure to loud music with the event being less than 3 months before the visit.
Tinnitus was experienced most often (83%) as a high frequency tone such as whining, ringing, beeping, whistling or TV tuning sound at 8.0 kHz or10.0 kHz (both 24%), 12.0 kHz (14%) and 6.0 kHz (10%). The level of tinnitus-matched tones was relatively low (n=98). In 68% of the cases, tinnitus was matched to a tone below 30 dB HL. The Tinnitus Handicap Inventory (THI) scores ranged from 0-94 with an average score of 43.1. According to the THI-based classification, most of the patients (60%) had either mild (THI 18-36, 27%) or moderate (THI 38-56, 33%) tinnitus. Others complained of slight (THI 0-16, 14%), severe (THI 58-76, 16%) or catastrophic tinnitus (THI >78, 10%). Tinnitus loudness as assessed by Visual Analogue Scales (VAS) ranged from 10-90 with an average value of 42.4. VAS values for tinnitus annoyance and awareness ranged from 10-100 with an average value of 54.2 for annoyance and 60.3 for awareness. Importantly, all VAS values correlated strongly with THI scores (loudness $r2=0.302$, $p<0.001$, $n=101$; annoyance $r2=0.474$, $p<0.001$, $n=101$; awareness $r2=0.273$, $p<0.001$, $n=93$ respectively).

A key finding of this study is that the hearing was normal in about two-thirds of the patients (64%, n=101), 26% had a (chronic) high frequency and 10% a mild low frequency hearing impairment. None of the patients had acute hearing impairment at the time of the examination but two of them reported a verified temporary thresholds shift immediately after the insult. Hyperacusis was present in 71% of the cases (n=96) of which 65% described the symptom as mild, 15% as moderate and 12% as severe with a LDL average ranging from74.3 to 82.2 dBHL. In addition, 79% of the patients reported sleeping disorders due to their tinnitus (n=94).

This study shows that, in music-induced acute acoustic trauma, there is typically no hearing impairment, as tested by conventional pure tone audiometry. In contrast, the main symptom is tinnitus in all cases, accompanied by intolerance to louder sounds (hyperacusis) in three quarters of cases. These results suggest that our patients represent individuals with "silent hearing loss". Thus, the pathophysiological basis for the entity of the patients might be the recently described afferent nerve terminal damage rather than hair cell loss.

P18: Central component of presbycusis identified by specific auditory tests.

Profant O[1]., Jilek M[1]., Bures Z[1, 3]., Lindovsky J[1]., Betka J[2]., 2 Syka J[1]. ([1]Department of Auditory Neuroscience, Institute of Experimental Medicine, Academy of Sciences of the Czech Republic, Prague, Czech Republic, [2]Department of Otorhinolaryngology and Head and Neck Surgery, 1st Faculty of Medicine, Charles University in Prague, University Hospital Motol, Prague, Czech Republic, [3]Department of Electrical Engineering and Computer Science, College of Polytechnics, Jihlava, Czech Republic)

Age related hearing loss (presbycusis) is one of the most prevalent sensory deficits that affect the elderly population. Disorders of the inner ear expressed by loss of functional hair cells, however people with presbycusis suffer also from deterioration in the processing of temporal sound detection, thus indicating a central component.

The aim of our project is to develop a battery of auditory tests that will provide us with detailed information about the central component of presbycusis with future goal to improve compensation of speech processing in presbycusis.

The following auditory tests were employed: laterogram (time-intensity interchangeable ratio), binaural speech chopper, gap detection threshold difference limen for frequency and amplitude modulation as a function of frequency, hearing threshold as a function of the tone-pip time duration,

threshold for masking of tone by white-noise and difference limen for intensity as a function of intensity, speech audiometry, speech audiometry in noise, high frequency pure tone audiometry, dichotic speech tests, otoacoustic emissions with and without contralateral suppression.

A clear difference between results of the young and old volunteers showed in all the tests. For further correlations the elderly subjects were divided in four subgroups: prevalence of the central impairment, prevalence of the peripheral impairment and two subgroups with a mixed impairments. Our preliminary data suggest different processing deficits at central levels in patients with presbycusis.

P19: Hyperacusis Questionnaire (HQ) as a tool for measuring hypersensitivity to sound in a tinnitus research population.

Fackrell K[1, 2]., Fearnley C[3].,Hoare D.J[1, 2]., Sereda M[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, [3]School of Medicine, University of Nottingham, Nottingham, UK, [4]Nottingham University Hospitals NHS Trust, Nottingham, UK)

Introduction

Hyperacusis can be extremely debilitating, impacting on daily life with emotional, cognitive and behavioural consequences. It is estimated to affect 2% of adults in the UK. Hyperacusis (hypersensitivity to external sounds) is often comorbid with tinnitus and may be significant for the acceptability and adherence to certain tinnitus management options such as sound therapy. It is important to accurately diagnose hyperacusis in a tinnitus population. The Hyperacusis Questionnaire (HQ) was developed by Khalfa and colleagues (2002) to specifically assess and quantify hyperacusis, with three subscales measuring attentional, social and emotional aspects. The aim of this study was to evaluate the psychometric properties of the HQ for use as a measurement tool in tinnitus research.

Methods

A retrospective analysis of data from 264 tinnitus volunteers who participated in research studies between 2008 and 2014. At the initial assessment, participants were tested for Uncomfortable Loudness Levels (ULLs) and completed questionnaires; the HQ; Tinnitus Handicap Inventory (THI); Tinnitus Handicap Questionnaire (THQ); Beck's Depression Inventory-II (BDI-II); Beck's Depression Inventory fast screen (BDI-fast); and the Beck's Anxiety Inventory (BAI). We evaluated the HQ factor structure (Confirmatory Factor Analysis (CFA) and Exploratory Factor Analysis (EFA)), reliability (internal consistency), validity (convergent and discriminant validity), and responsiveness (floor and ceiling effects).

Results

CFA revealed that the three factor structure to the HQ originally proposed was not a good fit of the data (N:264). The internal consistency for the 14-item HQ was high (0.877). However, the follow-up one-factor CFA using half the sample (N:132) showed similar misfit. Four problematic items (Items 1, 5, 6, and 11) were identified and removed. An EFA (N:132) identified a two-factor solution (10-items) with attentional and social components. Moderate correlations were observed between the HQ and the ULLs (r =0.55), the THI (r = 0.49), THQ (r = 0.40), BDI-II (r = 0.37), BDI-fast (r = 0.32) and BAI (r = 0.38). Floor and ceiling effects were present in four items in particular.

Conclusion

The original three-factor structure of the HQ was not confirmed. The evidence suggests that all 14-items do not accurately assess hypersensitivity to sound in a tinnitus population. We propose a 10-item (2 factor) version of the HQ, which may provide a more reliable indicator of hyperacusis in tinnitus population. Further evaluation is needed; the proposed structure will need to be confirmed.

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P20: Investigating the inter-subject variability of tinnitus characteristics in patients with tonal and noise tinnitus.
Wrzosek M[1]., Norena A[2]. ([1]Adam Mickiewicz University in Poznan, Poznan, Poland, [1]University Aix-Marseille, Laboratory of Integrative and Adaptive Neuroscience, Marseille, France)

In the present study we examined psychoacoustic properties of tinnitus: lateralization, audiogram, central frequency, width and level. We tested 63 patients (36 males, 27 females) from the IMERTA Clinic in Marseille. Patients with noise tinnitus (tinnitus different from pure tone) formed 40% of tested population. Significant differences were observed between groups of patients with tonal and noise tinnitus concerning central frequency of tinnitus ($F(1,61)=4.322$, $p<0.05$; tonal tinnitus: mean=6164.47Hz, SD=2956.98; noise tinnitus: mean=4538Hz, SD=2747.05). Audiograms between groups did not differ significantly. In a subgroup of patients we measured the tinnitus masking curve (the level required for masking tinnitus for several maskers with different masker frequencies). The psychophysical tuning curve was also assessed with a target tone chosen to correspond to the tinnitus center frequency presented at the tinnitus loudness (condition 1) or at 10-15dB above the hearing threshold (condition 2). Significant differences between patients with tonal and noise tinnitus were found for the PTCs (condition 2) – ($F(1,6)=6.124$, $p<0.05$), indicating that tonal tinnitus was easier to mask than a tone presented 10-15dB above the hearing threshold (and below tinnitus level). Moreover, we found that tinnitus is easier to mask in subjects with tonal tinnitus than in subjects with noise tinnitus.

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P21: Correlation of Minimal Masking Levels and the Tinnitus Functional Index as Tinnitus Outcome Measures.
Stecker N.A., Stocking C.T. (University at Buffalo, New York, USA)

Two frequently used outcome measures of tinnitus management effectiveness are the Tinnitus Functional Index (TFI) and minimal masking levels (MMLs). Two separate studies were recently carried out at the University at Buffalo; one investigating the effectiveness of the components of the Widex Zen Therapy program and the other evaluating the use of vagal nerve stimulation (VNS) as a treatment for tinnitus. In both studies, minimal masking levels (MMLs) and the Tinnitus Functional Index (TFI) were used as outcome measures... In the Widex Zen Therapy study, twenty participants with disturbing tinnitus were followed over twelve months. Each participant completed the Widex Zen counseling protocol, was fit with Mind 440 hearing aids when appropriate, and received Zen sound therapy. Outcome measures at 2-week intervals included the TFI. MMLs were obtained at the

beginning, six and twelve month visits. In the VNS study, six participants underwent surgery to implant an electrode on the left vagal nerve. One week post-surgery, the participants were stimulated and the tinnitus treatment of paired VNS along with tones presented via headphones was initiated. Participants were required to complete the treatment for a continuous two and a half hour session daily. On site visits were every two weeks for three months, quarterly and yearly. At each visit, audiometric data was collected along with MMLs and the TFI.

The Tinnitus Functional Index was developed by consortium of tinnitus experts, (Meikle, Henry et al.) and published in 2012. It is a 25-item self-assessment questionnaire specifically designed for responsiveness to treatment. It has eight subscales to measure various dimensions of the tinnitus problem: Intrusive, Sense of Control, Cognitive, Sleep, Auditory, Relaxation, Quality of Life, and Emotional. The score is expressed as a percentage with 100% being the most severe. MMLs were measured using broadband noise that was increased from threshold until it masked the subject's tinnitus for the right and left ears separately and for a binaural presentation. Measures are repeated several times and an average was recorded. A significant change was considered as a5 dB change in MML. TFI overall score and subtest scores were correlated with MMLs and analyzed from these two studies. This poster will report on these results and discuss the usefulness of the TFI and MMLs as outcome measures of the effectiveness of tinnitus management programs.

P22: Dimensions of tinnitus-related complaints reported by patients and their significant others: a systematic review.

Haider H[2]., Li A.B[1]., Thavayogan R[3]., Kennedy V[3]., Fackrell K[4]., Hall D.A[4]. ([1]School of Medicine, The University of Nottingham, Notttingham, UK, [2]ENT Department, Hospital Cuf Infante Santo - Nova Medical School, Lisbon, Portugal, [3]Department of Audiovestibular Medicine, Halliwell Health and Children, Bolton, UK, [4]NIHR Nottingham Hearing Biomedical Research Unit, Otology and hearing group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK)

Dimensions of tinnitus-related complaints reported by patients and their significant others: a systematic review

Background

Tinnitus is a multi-dimensional concept. Each patient complaint has the potential to be defined as a domain: a distinct element (or dimension) of tinnitus such as how loud or how emotionally distressing a patient may find his or her tinnitus. It is probably fair to say that none of the existing questionnaires covers all possible domains of tinnitus-related complaints, and questionnaire developers typically do not explain how they established that the included domains are important to patients, even though they may be informed by clinical experience. There is no current consensus. This systematic review therefore concerns the patient perspective and seeks to find what complaints are reported by people who experience tinnitus and by their significant others. The primary research question is about what dimensions of tinnitus-related complaints patients and their significant others report as being a problem. Secondary research questions include: (i) about whether patients and significant others have similar or different perspectives, (ii) whether tinnitus sub-types (acute/chronic, intermittent/constant, pulsatile/non-pulsatile, and severity grading) influence the nature of the tinnitus complaints that are reported, and (iii) whether a health-related comorbidity influences the nature of the tinnitus complaints that are reported. This work is presented on behalf of Core Outcome Measures in Tinnitus (COMiT) and is supported by EU COST Action BM1306.

Methods

For the systematic review, written documents will be included from grey literature searches (Open Grey, PsychEXTRA, DART, ProQuest, NDLTD, Web of Science) and electronic research databases such as PubMed, EMbase (OVID), and CINAHL. Those tinnitus-reported complaints reported in the final set of included documents will be collated in a narrative synthesis with information presented in a table to summarise and explain the characteristics

and findings. We will seek to preserve the original descriptive labels for domains wherever possible, then use this information to cluster together related concepts across studies. We also plan to conduct three assessments of study quality in terms of collecting, defining and reporting the domains of tinnitus-related complaints. The systematic review protocol is registered on PROSPERO (International Prospective Register of Systematic Reviews): CRD42015020629. We also report on progress to date.

Results
The literature search of academic research and grey literature has identified a total of 3561 documents so far. After the first stage of duplicate removal, this left 3509. The first selection step considered the title information to determine inclusion according to pre-defined eligibility criteria. Two team members performed each step independently for every record, with a third person resolving any discrepancies. This first selection step reduced the number of potentially eligible documents down to 391, with a further 30 duplicates being identified and removed. At the time of writing this abstract, we are in the middle of screening the remaining 361 abstracts for eligibility. Data extraction is ongoing.

P23: Influence of tinnitus on auditory spectral and temporal resolution and speech perception in tinnitus patients.
Shim H.J[1]., Won J.H[2]., Moon I.J[3]., Kang H.W[1]., Kim D.H[1]., 1 Ahn Y.H[1]. ([1]Department of Otorhinolaryngology-Head and Neck Surgery, Eulji University School of Medicine, Eulji Medical Center, Seoul, Korea, [2]Department of Audiology and Speech Pathology, University of Tennessee Health Science Center, Knoxville, Memphis, Tennessee, USA, [3]Department of Otorhinolaryngology-Head and Neck Surgery, Samsung Medical Center, Sungkyunkwan University, Seoul, Korea)

Objective
We can sometimes find unilateral tinnitus patients who have symmetric hearing thresholds. Our research question was what kind of difference would be responsible for the tinnitus in the tinnitus-affected ears (TEs) but not in the non-tinnitus ears (NTEs) of subjects with symmetric hearing thresholds. We evaluated the potential influence of tinnitus upon the subjects' auditory spectral and temporal resolution and speech perception in noise by comparing these psychoacoustic performances between TEs and NTEs in the same subjects.

Subjects and methods
Human subjects with tinnitus and symmetric hearing thresholds were divided into three groups: nine unilateral tinnitus subjects with normal and symmetric hearing thresholds up to 20 kHz (group 1), twelve unilateral tinnitus subjects with hearing loss and symmetric hearing thresholds up to 8 kHz (group 2), and nine bilateral tinnitus subjects with hearing loss and symmetric hearing thresholds up to 8 kHz (group 3). Fifteen normal-hearing subjects without tinnitus were also tested as a control group. Four different tests were administered: 1) spectral-ripple discrimination, 2) temporal modulation detection, 3) Schroeder-phase discrimination, and 4) speech recognition threshold (SRT) in noise.

Results
There were no significant differences in spectral-ripple discrimination, temporal modulation detection, and Schroeder-phase discrimination between the TEs and NTEs in subject groups 1 and 2 ($p > 0.05$). In contrast, the TEs showed higher SRTs (i.e. poorer performance) in noise than the NTEs in in subject groups 1 and 2 ($p = 0.022$ and 0.049). The multiple comparisons among the TEs, NTEs, and normal ears of the control group with the Bonferroni correction confirmed that TEs showed poorer speech perception in noise compared to the normal ears. The within-subject comparison between the right TEs and the left TEs showed that there was no difference in SRTs in noise between the right and left TEs.

Conclusion
Tinnitus can constrain patients' speech perception ability in noise regardless of their hearing sensitivity despite the fact that tinnitus had no influence upon spectral and temporal resolution of hearing. This finding suggests that tinnitus may affect central auditory system as 'a central masker' to interrupt speech perception and there may be no more outer hair cell (OHC) damage in tinnitus side, given that damaged OHCs are associated with broaden the auditory filters. On the other hand, the decoupling of the SRT results from the spectral/temporal resolution data could imply that the occurrence of tinnitus does not depend upon the degree of end-organ damage, but upon different plastic changes in central auditory system following cochlear damage.

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Neural correlates

P24: Inducing temporary tinnitus without auditory over-exposure or long-term auditory deprivation.
Gurer B[1, 2]., Besle J[1]., Krumbholz K[1]. ([1]MRC Institute for Hearing Research, University Park, Nottingham, UK, [1]School of Psychology, University of Nottingham, Nottingham, UK)

Tinnitus research is starting to illuminate the neural mechanisms that lead to phantom auditory perceptions. It has been suggested that deprivation to the central auditory system, as a result of hearing loss or auditory deafferentation, causes a reduction in inhibitory activity in the auditory pathway through homeostatic plasticity or tonotopic reorganisation. Reduction in inhibition, in turn, is thought to lead to increase in spontaneous activity and neural synchrony, and thus cause tinnitus.

Chronic tinnitus is a hard condition to study, partly due to the difficulty in finding appropriate controls with matched hearing loss. Temporary tinnitus, however, offers the exciting possibility to study phantom auditory perceptions in normal-hearing participants, which may help to elucidate the mechanisms underlying chronic tinnitus. However, current ethical methods of induction would benefit from further development. Schaette et al. (2012) found that simulation of high-frequency hearing loss through auditory deprivation with earplugs for a prolonged period of time (about seven days) induced temporary tinnitus in the majority of their normal-hearing subjects. The current study expands on the method reported by Schaette and shows that it is possible to induce temporary tinnitus in a much shorter time span and with better control of relevant parameters. For that, we used sustained presentation of filtered sound sources.

Here, we will present subjective measurements of the spectral characteristics of temporary tinnitus as a function of the spectral characteristics of the inducing stimulus as well as objective measurements of the associated neural activity. We will also present systematic measurements showing how the strength and stability of the percept depend on the level and spectral characteristics of, and time of exposure to, the inducing stimulus. The subjective tinnitus measurements use the 'tinnitus spectrum' approach proposed by Norena et al. (2002). The objective measurements will involve electroencephalography (EEG) recordings of spontaneous oscillatory activity.

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P25: Effects of a cannabinoid agonist in guinea pig models of tinnitus.

Coomber B[1]., Berger J.I[1]., Owen W[1]., Alexander S.P.H[2]., Palmer A.R[1]., Wallace M.N[1]. ([1]MRC Institute of Hearing Research, University Park, Nottingham, UK, [2]School of Life Sciences, University of Nottingham, Nottingham, UK)

Animal models of tinnitus have revealed long-term hyperexcitability and altered neural synchrony, thought to arise from a pathological imbalance between excitatory and inhibitory neurotransmitter systems. The release of all neurotransmitters is regulated by neuromodulators, such as endogenous cannabinoids (endocannabinoids). Endocannabinoids are produced on-demand in response to depolarisation and act to regulate presynaptic neurotransmitter release. Cannabinoid drugs are potent anti-nociceptive agents in models of chronic neuropathic pain, a condition that shares substantial parallels with tinnitus, i.e. phantom sensory percept in the absence of sensory input, initiated peripherally through deafferentation and subsequently involving central mechanisms.

In the present study, tinnitus was induced by either (1) subjecting guinea pigs (GPs) to unilateral acoustic over-exposure (AOE) or (2) administering sodium salicylate. Both models involve central changes, i.e. they are not reliant solely on altered peripheral input. In animals subjected to AOE, tinnitus was objectively identified with the gap prepulse inhibition of acoustic startle (GPIAS) behavioural test, eight weeks after AOE. Hearing status was assessed using auditory brainstem responses. Animals were then retested on five occasions after being administered either the cannabinoid CB1 receptor agonist arachidonyl-2'-chloroethylamide (ACEA; 1 mg kg-1, i.p.) or drug vehicle. In the second group of animals, GPs were first implanted with electrocorticography (ECoG) multi-electrode arrays, before being administered with sodium salicylate (350 mg kg-1; i.p.) to induce tinnitus, and either ACEA (1 mg kg-1, i.p.) or drug vehicle. Resting-state and auditory-evoked neural activity recorded in awake, freely-moving animals was compared between groups.

Treatment with ACEA induced variable effects in animals with AOE-induced tinnitus, but neither augmented nor attenuated tinnitus behaviour. In the second group of animals, sodium salicylate altered resting-state activity and enhanced auditory-evoked responses. In animals co-administered ACEA and salicylate the changes in resting-state oscillations were smaller than for salicylate alone.

These data indicate that manipulating endocannabinoid signalling can affect tinnitus-related neural activity, but these changes may be too subtle to detect using the GPIAS behavioural approach. The next step will be to implant animals before AOE and then study the electrophysiological changes produced by ACEA after tinnitus has developed.

P26: Involvement of parahippocampus in tinnitus percept.

Gander P.E[1]., Sedley W[2]., Kumar S[2, 3]., Kovach C.K[1]., Oya H[1]., Nourski K.V[1]., Kawasaki H[1]., Howard M.A[1]., Griffiths T.D[2, 3]. ([1]University of Iowa, Iowa, USA, [2]Newcastle University, Newcastle, UK, [3]University College London, London, UK)

Awaiting abstract.

P27: Noise Exposure Leads to Increased Synchrony Between Primary Auditory Cortex and Anterior Auditory Field Neurons.
Basura G., Takacs J., 1 Shore S. (Department of Otolaryngology, University of Michigan, USA)

Aims and Objectives
Noise-exposure leads to increased spontaneous firing rates (SFR) and enhanced neural synchrony in multiple central auditory brain stations including primary auditory cortex (A1). These putative neural correlates of tinnitus have yet to be investigated in associative auditory cortical areas, including the anterior auditory field (AAF); a know modulator of A1 function that also processes auditory information in a parallel manner. Here we investigated whether a temporary threshold shift (TTS) following noise over exposure leads to changes in SFR and neural synchrony in A1, AAF and between the two regions.

Methods
Three weeks following unilateral, left ear noise over exposure (exposed group) or anesthesia alone (sham), adult guinea pigs with auditory brainstem response-confirmed recovered TTS underwent concurrent extracellular neural recordings from A1 and AAF to measure SFR and neural synchrony.

Results
As compared to sham, A1 neurons in exposed animals showed significant increases in SFR and neural synchrony as previously published. Within AAF, noise exposure led to a modest increase in SFR when compared to sham, but no significant increases in neural synchrony. Interestingly, when the two regions were analyzed, noise exposure enhanced neural synchrony between A1 and AFF as compared to sham.

Conclusions
These findings confirm previously documented increases in SFR and neural synchrony, putative neural correlates of tinnitus, within A1 following noise exposure. Moreover, our data suggest that tinnitus neural correlates, in part, may also exist in AAF. Increases in synchrony between A1 and AAF neurons following noise, suggests that adjacent, non-A1, associative auditory cortices may be contributing to tinnitus generation and ultimately perception.

P28: Blocking potassium currents desynchronises the firing of dorsal cochlear nucleus principal cells.
Olsen T[1]., Capurro A[1]., Pilati N[2]., Large C[2]., Hamann M[1].([1]University of Leicester, Leicester, UK, [2]Autifony Therapeutics, Department of Cell Physiology & Pharmacology, University of Leicester, Leicester, UK)

Numerous studies postulate that tinnitus, the phantom perception of sound, originates as a hyperactivity in the cochlear nucleus in response to peripheral auditory nerve damage (reviewed in Wu et al., 2015). Our previous study has shown that exposure to loud sound leading to hearing loss triggers bursts in the dorsal cochlear nucleus principal (fusiform) cells, due to a down regulation of high voltage activated potassium currents (Pilati

et al., 2012). One theory behind the perception of tinnitus considers that it arises as an initial dys-synchrony within the auditory system (Schulman and Goldstein, 2006). Here we studied whether blocking K+ currents with tetra-ethylammonium (TEA) introduced changes in the firing pattern of dorsal cochlear nucleus fusiform cells, and in particular if it introduced dys-synchrony.

Fusiform cells were recorded in slices from P13-P18 CBA mice, using current clamp whole cell recordings. Synchronicity was measured using a variation of the shuffled autocorrelation method (Joris et al., 2006). High degree of synchronicity would translate into action potentials firing at the same time throughout repetitive 1 nA current injections. Conversely, lower degrees of synchronicity would result in action potentials firing at irregular times.

Fusiform cells were held at -80 mV and action potentials were elicited by applying step currents (from 50 pA to 1.5 nA). In control conditions, fusiform cells fired in a regular manner, up to ~150 Hz, as previously described (Zhang & Oertel 1994). TEA (0.5 mM) decreased the firing frequency, eliminated the action potential undershoot normally observed in the control condition, and caused action potentials to fire with varying peak amplitudes. TEA also decreased the regularity of the firing, as indicated by an increase in a coefficient of variation of the inter-spike interval. Finally, TEA disrupted the ability for action potentials to fire at the same point in space in response to a repetitive pulse, and therefore decreased the amount of synchronicity.

In conclusion, TEA disrupts the ability for fusiform cells to fire regular, synchronous action potentials. The changes here described could represent the initial network imbalance arising in the dorsal cochlear nucleus, and underlying the emergence of tinnitus.

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P29: Cortical magnification measurements in human auditory cortex using 7 Tesla fMRI and potential application to measuring cortical re-organization in hearing-impairment and tinnitus.

Besle J[1]., Gurer B[1]., Sanchez-Panchuelo R-M[2]., Francis S[2]., Krumbholz K[1]. ([1]MRC Institute of Hearing Research, University Park, Nottingham, UK, [2]Sir Peter Mansfield Imaging Centre, School of Physics and Astronomy, University of Nottingham, Nottingham, UK)

A general organisation principle of sensory cortices is that the cortical surface dedicated to a given part of sensory space is proportional to its behavioural relevance. In visual cortex for instance, proportionally more cortical area is devoted to the fovea than to the periphery. This visual cortical magnification function has been well characterized in human V1 using fMRI and is known to be closely linked to localization ability across the visual field. In primary auditory cortex (PAC), the cortical magnification function has not been measured, partly because it is still unclear which tonotopic gradients belong to primary auditory cortex.

Being able to measure cortical magnification in PAC is important for tinnitus research because animal models suggest that tinnitus generation could be linked to cortical tonotopic re-organization following peripheral deprivation of auditory input (e.g. high-frequency hearing loss). The re-organization could consist in an over-representation of frequencies at the edge of the hearing loss (i.e. a change in cortical magnification).

In this study, we used structural and functional MRI at 7T to identify tonotopic gradients in PAC in normal-hearing listeners and estimate the cortical magnification function along them. We estimated voxelwise preferred frequency and frequency selectivity using functional MRI (sparse 2D GRE EPI, 1.5 mm resolution, phase-corrected for B0-related distortions) and trains of narrowband noises at 7 centre frequencies spaced on a cochlear filter scale. For structural mapping of myelination, we estimated the R1 longitudinal relaxation rate (3D PSIR, 0.6 mm resolution). All structural and functional measures were projected onto a flattened model of the supra-temporal cortex, segmented from the high-resolution processed PSIR volume.

In all subjects/hemispheres, we identified core (primary) auditory cortex as an area of increased frequency selectivity and myelination aligned with Heschl's gyrus (HG). In all subjects/hemispheres, we also identified 2 mirror tonotopic gradients of preferred frequency centred on Heschl's gyrus (HG), each oriented at 70° relative to the long axis of HG (and 140° with each other). Although there was considerable inter-subject variability in the relative location of core auditory cortex and tonotopic gradients, these 2 gradients are the most likely to correspond to core auditory areas and we will estimate cortical magnification along them. We expect the cortical magnification function in primary auditory cortex to be proportional either to cochlear tuning width, or to frequency discrimination threshold, as a function of frequency.

However, because we spaced the frequencies of our tonotopic sampling stimuli on a cochlear tuning width scale (rather than a frequency discrimination threshold scale), we will also conduct simulations using a neuronal population model to investigate how a particular choice of stimulus frequency spacing and range influences the estimation of cortical magnification function (given different possible actual cortical magnifications).

We discuss how this type of cortical magnification measurements could be used to study tonotopic re-organization in hearing-impaired and tinnitus patients and how inter-subject variability in the measured functional organization of auditory cortex is likely to complicate the measurement and interpretation of this re-organization, if observed.

P30: DCN microglia in rat tinnitus models: density, activation and possible roles.

Perin P[1]., Venturino A[1]., Solinas S[2]., Bertone V[1]., Pizzala R[1]. ([1]University of Pavia, Corvino San Quirico PV, Italy, [2]University of Sassari, Sassari SS, Italy)

Although tinnitus has been associated to aberrant plasticity phenomena in the auditory system, it is still unclear whether different causes converge on common final processes and at what levels. In animal models, protocols for tinnitus induction exert different effects on several auditory centers. In particular, DCN output is increased after noise trauma and decreased after salicylate [1].

Fusiform cells are the target of multiple inputs, and several plastic phenomena are seen in the circuits regulating them [2].

Microglia has been found to regulate neural plasticity, especially in pathological conditions [3]. Therefore, we investigated changes in DCN microglia after inducing tinnitus with noise trauma, unilateral cochlear destruction, or salicylate, by observing Iba-1 immunofluorescence in DCN slices by

confocal microscopy. Although all treatments induced tinnitus (tested by GPIAS), salicylate significantly increased microglia density (from 117±47, n=15 to 215±55 cell/mm2, n=18), without inducing activation, whereas cochlear destruction also increased microglia density (466±186; n=14) but also induced activation. Noise trauma increased microglia density (242±49, n=7) especially in DCN regions corresponding to trauma frequencies.

Microglia activation was necessary for tinnitus onset after cochlear destruction: in animals treated with minocycline (a blocker of microglia activation) after surgery, neither microgliosis (after 5 days, ipsilateral DCN density was 144+33, n=5) nor behavioural signs of tinnitus were observed. Tinnitus induced by salicylate (n=3) and noise trauma (n=5) was less clearly dependent on microglia activation, since behavioural signs of tinnitus were still observed after treatment with minocycline.

On the other hand, DCN microglia activation was sufficient for tinnitus onset: a monolateral stereotaxic injection of LPS (a microglial activator) in the DCN was able to induce a very localized focus of strong microglial activation and behavioural signs of tinnitus (n=3). Our results suggest that DCN microglia follows different functional pathways upon different tinnitus-inducing treatment.

The observed microglial density increase would agree with the presence of chemoattractant mechanisms, such as local increases in ATP or glutamate release. Given that the small size of microglial cells would allow them to selectively regulate apical and basal dendrites of fusiform cell circuits, we built a computational model where "microglial domains" in a DCN circuit were able to locally modulate several synaptic parameters (ECl, spine density, basal Ca2+), trying to reproduce our morphological distribution and literature data for fusiform cell behaviour after tinnitus-inducing protocols

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P31: Exploring the amygdala response to emotionally evocative soundscapes in people with tinnitus: a sound-evoked fMRI study.

Davies J[3]., Gander P[2]., Hall D.A[1, 4]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Human Brain Research Laboratory, Department of Neurosurgery, The University of Iowa, Iowa City, USA, [3]Division of Audiology, Faculty of Health and Life Sciences, De Montfort University, Leicester, UK, [4]Otology and Hearing group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK.

Background

Tinnitus is often associated with strong negative feelings which can lead to the manifestation of a distressing and chronic experience. Key to this process is the amygdala, the "feeling and reacting" part of the brain. Although implicated in a number of well-known tinnitus models, the quantification of human amygdala activity has only been made possible in more recent years through neuroimaging methods such as functional magnetic resonance imaging (fMRI). Several fMRI studies have investigated the role of the amygdala in the processing of emotionally evocative sound, but only two have targeted a tinnitus population. Interestingly, neither study found heightened amygdala activation in individuals with tinnitus as originally hypothesised.

One possible reason for this is their choice of fMRI parameters, which were not optimally suited for amygdala detection; a brain region with exhibits a poor signal to noise ratio.

This study investigated how the presence of chronic tinnitus impacts upon emotional processing using a novel double-echo imaging sequence for optimal detectability of subcortical activity. Our hypotheses were: (1) sound clips rated with the highest and lowest levels of emotional valence elicit stronger amygdalar activity than neutral sound clips, (2) people with tinnitus have greater amygdalar activity in response to emotionally evocative sounds (relative to neutral sounds) compared to age and hearing-matched controls.

Methods
Twelve participants (seven male; mean age 66 years) all with chronic, (2 years minimum duration) constant tinnitus took part. We also recruited eleven age and hearing matched controls (eight male; mean age 68 years). Participants with a history of neurological disorder, hyperacusis or unilateral/asymmetrical hearing loss were excluded. Participants listened to a range of emotionally evocative sound clips which had previously been rated as very pleasant, very unpleasant or neutral. A region-of-interest (ROI) analysis was chosen to test our a priori hypotheses. Amygdala ROIs were functionally defined on an individual basis using voxel co-ordinates which corresponded to peak maxima amygdala activity in response to salient versus neutral sound conditions.

Results
Both groups displayed a robust and similar overall response to sounds versus silence in the following ascending auditory pathways; inferior colliculus, medial geniculate body and the primary auditory cortex. In support our first hypothesis the amygdala's response to very pleasant and very unpleasant sound clips was significantly greater than neutral sounds. Contrary to our second hypothesis, we found no significant main effect of group, indicating that the amygdala's overall response to emotionally evocative sounds was similar between groups. However, further examination revealed a consistent trend for lower activation in response to either very pleasant or very unpleasant sounds compared with neutral sounds was observed in the tinnitus group.

Conclusions
Based on these findings, the amygdala does appear to provide information which could be key in differentiating between the true presence or absence of tinnitus. Future studies targeting amygdala function should carefully consider fMRI parameters to ensure sufficient signal quality from the amygdala regions.

P32: The brain neural activity in patients with etiology confirmed unilateral vascular pulsatile tinnitus: why it is frequency-dependent?
Lv, H[1]., Zhao P[1]., Liu Z[2]., Yan F[2]., Li R[1]., Wang P[1]., Zhang L[1]., Gong S[1]., Wang Z[1]. ([1]Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]Beijing Tongren Hospital, Capital Medical University, Beijing, China)

Objects
Previous resting-state functional magnetic resonance imaging (RS-fMRI) studies have shown that neurological changes are important findings in vascular pulsatile tinnitus (PT) patients. Frequency-dependent phenomenon was also found in other patients with Alzheimer disease, schizophrenia etc. but not patients with PT.

Methods
Here we utilized RS-fMRI to measure the amplitude of low-frequency fluctuations (ALFF) in forty patients with unilateral PT and forty age-, gender-, education-matched normal control subjects. Two different frequency bands (slow-4, 0.027-0.073 Hz; slow-5, 0.010–0.027 Hz) were analyzed to examine the intrinsic brain activity in detail.

Results
Widespread ALFF differences between the two bands were observed, predominantly including the aMPFC (anterior medial prefrontal cortex)/ ACC (anterior cingulate cortex), PCu (precuneus) etc. Compared to controls, PT patients had increased ALFF values mainly in the PCu, bilateral IPL (inferior parietal lobule), left IFG (inferior frontal gyrus), right IFG/anterior insula, and decreased ALFF values in the multiple occipital areas including bilateral middle-inferior occipital lobe etc. The ALFF abnormalities in aMPFC/ACC, PCu, right IPL and some regions of occipital and parietal cortices were greater in the slow-5 band compared to the slow-4 band. Additionally, the THI score of PT patients was positively correlated with changes in slow-5 and slow-4 band in PCu.

Conclusions
The pathophysiological mechanism of these results should be carefully determined to be helpful in the neurological studies of PT patients. Studies are still needed to understand the underlying physiological mechanisms of changed ALFF in each frequency band.

P33: Abnormal Regional and Circuit Synchronization in Resting-state Brain Networks Associated with Pulsatile Tinnitus.
Lv, H[1]., Zhao P[1]., Liu Z[2]., Yan F[2]., Zhang L[1]., Li R[1]., Wang P[1]., Gong S[1]., Wang Z[1]. ([1]Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]Beijing Tongren Hospital, Capital Medical University, Beijing, China)

Objects
The abnormal neural activities revealed by the resting-state functional magnetic resonance image (rs-fMRI) are defined by the regional and circuit synchronization of the networks in the brain. This study was designed to demonstrate the network alternations in the patients with pulsatile tinnitus (PT).

Methods
In this study, we recruited 45 patients with unilateral PT and 45 normal controls. We used the ReHo and seed-based functional connectivity analysis method to reveal the resting-state brain activities associated with pulsatile tinnitus.

Results
Compared with healthy controls, PT patients showed regional abnormalities mainly in the left MOG, PCC, precuneus and right AI. When set as seeds, we demonstrated widespread plasticity between different brain networks, including the auditory network, visual network, default mode network (DMN), cognitive control network (CCN) etc. Positive correlations were found between the core structures within the DMN. However, the right anterior insula, a key node in CCN, showed negative relationship with the DMN due to the perception of PT.

Conclusions
The enhanced relationship between the auditory and visual network were considered due to an indirect mediation of self-protection mechanism reflected by the AOAs (auditory occipital activations). The plasticity in the higher order control networks were mainly focused on the DMN and CCN.This

study will yield a valid and comprehensive neurological framework to understand the regional and the circuit synchronization of the brain networks in PT patients.

P34: Measuring the effects of transcranial direct current stimulation on auditory cortical activity using magnetoencephalography.
Holding M[1]., Weisz N[2], Demarchi G[2]., Hall D.A[3]., Schurrman M[4]., Adjamian P[1]. ([1]MRC Institute of Hearing Research, University Park, Nottingham, UK, [2]Centre for Cognitive Neuroscience, University of Salzburg, Salzburg, Austria, [3]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [4] School of Psychology, University of Nottingham, Nottingham, UK)

It is widely believed that tinnitus is generated and maintained by abnormal neural activity in various areas of the brain including the auditory cortex. Numerous magneto- and electro- encephalography (MEG/ EEG) studies show that neural oscillations are altered in tinnitus. Transcranial direct current stimulation (tDCS) involves the passing of mild electrical currents through the scalp, and has been shown to modulate neural oscillations. If it can be shown that tDCS is capable of modulating the neural oscillations implicated in tinnitus, it could be used as a potential therapeutic option. Indeed, studies have found that the use of tDCS in combination with residual inhibition (the temporary suppression of tinnitus following application of a noise masker) could increase the length of time the tinnitus remains suppressed. Both noise maskers and tDCS devices are becoming more widely available to the public, and so it is vital that the effects of both masker noises and tDCS on cortical activity is properly explored. This study aimed to investigate the combined effect of tDCS and noise masking on brain oscillatory activity recorded with MEG. We took 13 non-tinnitus participants and exposed them to a paradigm known to induce residual inhibition in tinnitus patients, whilst also recording brain data in a MEG scanner. Participants were also exposed to sham (a weak positive current) and anodal (a strong positive current) tDCS on alternating trials. Increases in alpha band activity and modulations of delta were found across all subjects when they were undergoing anodal tDCS as opposed to the sham stimulation. These results indicate that tDCS does appear capable of modulating oscillatory frequency bands implicated in tinnitus generation. More work is needed to assess the precise effects of these modulations on tinnitus, but these initial results offer a promising avenue to explore.

P35: Frontiers Research Topic: Towards an Understanding of Tinnitus Heterogeneity.
Adjamian P., Cederroth C.R., Gallus S., Hall D.A., Langguth B., Kleinjung T., Lopez-Escamez J.A., Mazurek B., Meyer M., Moriotti A., Norena A., Probst T., Schlee W., Searchfield G., Shekhawat R., Van Dijk P., Vanneste S., Weisz N.

Within the dissemination aims of TINNET, we have launched a Research Topic with Frontiers, with the aim of gathering the latest research that will help the scientific community understanding better the heterogeneity of tinnitus with the aims of improving patient care and treatment outcomes. Here we announce the launch of this research topic, which is connected to a variety of Frontiers journals, to allow the multiple areas of tinnitus research to contribute to TINNET's endeavors. The Frontiers platform offers a unique opportunity for dissemination, debate and discussions around a specific research area, here tinnitus heterogeneity. This Research Topic is launched within a recent competition "The Spotlight Conference Award" in which the topic that shows the greatest dissemination, scientific interaction, and debate within 2016 will be awarded 100'000 US$ for the organization of a meeting at the SwissTech Convention Center in Lausanne. We want you to join this call for proposals, and involve as many of your team members in the debate to improve knowledge around the complexity of tinnitus heterogeneity, and ultimately lead TINNET to a final conference in Switzerland at the end of the COST funding scheme. Industry companies are welcome to sponsor publications in exchange of increased visibility in our Frontiers page.

http://journal.frontiersin.org/researchtopic/4725/towards-an-understanding-of-tinnitus-heterogeneity#overview

P36: The Plasticity of the Brain and Tinnitus.
Kemp H.

Accessing brain plasticity to address tinnitus in 12 weeks.
The aim of the study was to reduce tinnitus and increase the quality of life of the client. Various neurological, vascular and somatic disorders have been linked to the development of tinnitus, which is often seen as an auditory phantom sensation and the result of increased neural synchronicity (Eggermont, 2007). Tonotopic map reorganisation (Benson, 2009;2013; Rauschecker, Leaver and Muhlau, 2010; Manzoor, Gao, Licari & Kaltenbach, 2013), altered synchronised cortisol activity (Weisz, Moratti, Meinzer, Dohrman & Elbert, 2005; Weisz & Obleser, 2013) and enhanced spontaneous firing rates in various structures of the auditory pathway (Eggermont & Roberts, 2004) sets tinnitus as a phenomenon in the central nervous system.

Interventions for the management of Tinnitus
A multimodal approach was followed as Pantev et al., (2012) found that there is a greater response to a stimulus consisting of a combination of modalities compared to the sum of neural responses to each modality separately (Bourjaily & Miller, 2011; James & Stevenson, 2012).

By targeting different parallel loops in the interconnected hierarchial structure of the brain, the inherent balance between the inhibitory and excitatory neuron activity were addressed. The interventions were chosen to bring about change in the auditory, limbic and cortical systems.

The Auditory Network
Berard AIT (Auditory Integration Training) was used for activation of the auditory pathways through musical stimulation. The neuro-habilitative potential of music (Pantev & Herholz, 2011) leads to a decrease in tinnitus related hyper-synchronous cortical activity and activation of the lateral inhibition in the auditory cortex (Lanting, de Kleine & van Dijk, 2009; Pantev et al, 2012).

The Emotional Network
As the limbic system is actively involved in the generation as well as suppression of tinnitus, it was essential to make it a focus point in tinnitus treatment (Krauss & Canlojn, 2012). Several researchers have emphasized the strong link between the auditory cortex and the limbic system (Alpini & Cesarani, 2006; Pirodda, Brandolini, Raimondi, Ferri & Borghi, 2009).

Biofeedback, which has been used by several researchers and clinicians, was used as an intervention to calm the autonomic nervous system (Weise, Heinecke & Rief, 2008).

The Cortical Network
Neurofeedback was used to direct neural plasticity, restore dysfunctional neural networks (Engineer et al., 2013) and balance cortical and subcortical inhibition and excitation potentials (Egner, Zech & Gruzelier, 2004; Schenk, Lamm, Gundel & Ladwig, 2005; Dohrmann, Elbert, Schlee & Weisz, 2007; Dohrmann, Weisz, Schlee, Hartmann & Elbert, 2007; WEisz, Dohrmann, Schlee, Hartmann & Elbert, 2007; Kahlbrock & WEisz, 2008).

Conclusion

Stabilizing the maladaptive functioning of the brain, increasing flexibility in cortical control and increasing parasympathetic versus sympathetic dominance, led to increased inhibition, a calming of the ANS and an amelioration of tinnitus symptoms.

P37: Whole scalp resting state EEG of oscillatory brain activity shows no parametric relationship with psychoacoustic and psychosocial assessment of tinnitus: A repeated measures study.

McNamara J.A[1]., Pierzycki R.H[1, 2]., Hoare D.J[1, 2]., Hall D.A[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK)

Introduction

Tinnitus is a perception of sound that can occur in the absence of an external stimulus. A brief review of electroencephalography (EEG) and magnetoencephalography (MEG) literature demonstrates that there is no clear relationship between tinnitus presence and frequency band power in whole scalp or source oscillatory activity. Yet a preconception persists that such a relationship exists and that resting state EEG could be utilised as an outcome measure for clinical trials of tinnitus interventions, e.g. as a neurophysiological marker of therapeutic benefit.

Methods

Data was collected during an intervention study (intervention n = 20, placebo n = 22) examining the effects of the T30 Neurostimulator device. Inclusion criteria at screening were as follows: adults (≥18 years) experiencing chronic subjective tinnitus (i.e. constant and experienced for >3 months prior to the study); pure tone audiometric average < 60 dB (0.5, 1, 2, 4 kHz) in the ear where tinnitus is perceived and the ability to hear all stimulation tones presented by the sound therapy device; the dominant tinnitus frequency measured between 0.2 and 10 kHz; at least 'mild' tinnitus defined by a score of ≥18 on the Tinnitus Handicap Inventory (THI). Participants also had to be willing to wear the device 4–6 h daily during the trial.

Sixteen psychosocial variables collected were the subdomains of the "Tinnitus Functional Index", "World Health Organization Quality of Life and THI questionnaires. Three psychoacoustic variables were captured: 'duration' and 'loudness' of tinnitus and 'hearing ability'. We first examined the test-retest correlation of EEG band power measures in tinnitus patients. Second we examined the evidence for a parametric relationship between numerous commonly used tinnitus variables (psychoacoustic and psychosocial) and whole scalp EEG power spectra, directly and after applying factor reduction techniques.

The whole scalp power spectra were divided into normalized EEG frequency bands: delta (1–4 Hz), theta (4.2–7.8 Hz), alpha (8–12 Hz), beta (12.2–29.8 Hz), gamma low (30–48 Hz) and gamma high (52–90 Hz). Agreement of band power between sessions was determined using intraclass correlation coefficients (ICC) to avoid an effect of order. Band spectra were additionally analyzed for correlations with the 19 psychosocial/acoustic variables.

Results

Test-retest correlation for both EEG band power measures and tinnitus variables were high (ICC > 0.7), exceeding (ICC> 0.9) for delta, alpha and gamma bands. Yet we found no relationship between whole scalp EEG band powers and psychoacoustic or psychosocial variables in either group.
Conclusion: Test-retest measures for whole scalp EEG recordings are very reliable yet no correlation between these measures and psychosocial/acoustic variables were found. We conclude from these data that resting state whole scalp EEG should not be used as a biomarker for

tinnitus and that greater caution should be exercised in regard to reporting of findings to avoid confirmation bias. The data was collected during a randomised controlled trial registered at ClinicalTrials.gov (Identifier: NCT01541969).

P38: Oscillatory power change in tinnitus resolved in source space – the role of auditory and prefrontal cortices.

Adjamian P[1]., Zobay O[1]. Sereda M[2, 3]., Hall D.A[2, 3]., Palmer A.R[1]. ([1]MRC Institute of Hearing Research, Nottingham, UK, [2]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [3]Otology and Hearing group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, UK

A number of MEG and EEG studies indicate that tinnitus is associated with various changes in oscillatory brain activity, including delta (~3 Hz,) theta (~7 Hz), alpha (~10 Hz), and gamma (> 30 Hz). The majority of these studies have provided a coarse spatial estimate of the observed effects, roughly implicating the auditory cortex or the frontal regions. In a previous MEG study (Adjamian et al., 2012), we showed that delta and theta activity were enhanced in the region of auditory cortex in patients with tinnitus compared to controls with no tinnitus, regardless of the presence or degree of hearing loss. However, in a recent EEG study we failed to find any relationship between oscillatory responses and measures of tinnitus over the whole brain (Pierzycki et al 2016). In several studies, we have evaluated source-space inter-regional connectivity (Zobay et al., 2015) and auditory cortex amplitude-amplitude frequency coupling (Zobay and Adjamian, 2015) with mixed results. Overall we showed that there are specific differences between participants with tinnitus and non-tinnitus controls in the way that various parts of the brain communicate with each other. Importantly, our analysis was based on source-space and focused on specific brain regions that have been suggested to be involved in tinnitus generation and maintenance.

Here we present a follow up analysis of MEG data in source space using specific Brodmann areas to assess changes in localised oscillatory activity. Using the Global Brain model (Schlee et al., 2011) we evaluated functional and effective connectivity between Brodmann areas in specific frequency bands when tinnitus is present and when it is masked. When tinnitus was perceived, we found significant increase in power in the right insula, right temporal, and left frontal cortices in the delta band. Furthermore, increased alpha activity was observed in tinnitus participants compared to non-tinnitus controls. There was no clear relationship between oscillatory power and tinnitus laterality. Our results provide further indication that tinnitus involves non-auditory areas of the brain which require interaction with the auditory cortex for the tinnitus sensation to emerge.

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P39: Steady-State Auditory Evoked Fields in Normal Subjects and Tinnitus Patients.
Li L.P.H. (Department of Otolaryngology, Cheng-Hsin General Hospital, Taipei, Taiwan)

Steady-state auditory evoked fields (SSAEFs) are the net effect of entrained background activity and overlaid cortical evoked responses. SSAEF is a sinusoidal magnetic response in the brain induced by periodically presented auditory stimuli which has been regarded as a potential tool to provide information for assessment of hearing loss and evaluation of aural rehabilitation. The present study adopted empirical mode decomposition (EMD) to extract SSAEF. With EMD, one signal can be decomposed into a series of intrinsic mode functions (IMFs) by iteratively conducting the sifting process. Pertinent IMFs were selected to reconstruct noise-suppressed SSAEFs. We have studied twelve normal subjects and twelve patients with tinnitus. SSAEFs in both group showed activation dominance in their right auditory cortex, which echoed the right hemispheric laterality of SSAEFs proposed by Ross et al. (2005). Comparing the source strengths of SSAEFs in both groups, the source amplitudes in patients with tinnitus were significantly stronger than those in normal subjects ($p<0.01$) which might indicate decreased inhibition in central auditory structures. In addition, the EMD-based approach presented a better interpretation of SSAEFs signal than traditional average (goodness-of-fit: 89.2% v.s. 80.1%). The study results can demonstrate the feasibility of the proposed method in auditory studies.

P40: Using auditory brainstem responses (ABRs) to measure hearing loss-induced increases in neural gain and its implications with tinnitus.
Hardy A.J., de Boer J., Krumbholz K. (MRC Institute of Hearing Research, University Park, Nottingham, UK)

The homeostatic plasticity model posits that tinnitus is triggered by an increase in neural gain due to a reduced input from a damaged periphery. Evidence for this mechanism in humans has come from click-evoked auditory brainstem responses (ABR) (Schaette & McAlpine, 2011; Schaette & Kempter, 2006). It is thought that the wave I to V amplitude ratio reflects neural gain, with wave I reflecting activity at the auditory nerve and the wave V at the upper brainstem. Schaette (2011) found that tinnitus patients had a reduced wave I but their wave V was the same as normal hearing participants, indicating that there was an increase in neural gain. However, wave I is mainly dependent on high frequencies, whereas wave V integrates over low and high frequencies. This means that high frequency hearing loss commonly associated with tinnitus can affect the wave amplitudes differently, which could be a driving factor behind the increased wave I/V ratio. We aimed to address this confound by measuring frequency-specific ABRs, which are obtained by restricting the response from the cochlea using intense high pass masking noise with a variable cut off frequency. Responses recorded with different cut off frequencies are subtracted to produce a response which contains contributions only from a band-limited frequency region. However, we found that wave I was barely detectable using this approach, in particular low frequency responses. We also found that a very high stimuli sound level was required and therefore a very intense noise would be needed to effectively mask it. Therefore our aim is to develop a method of recording frequency specific ABRs with improved signal to noise ratios but without exposure to very high intensity sound that is used in traditional ABR recordings.

Our first step is to replace the eliciting click with a rising 'chirp' stimulus which starts at a low frequency and rises to a high frequency over a short period of time. The chirp causes the high and low frequency auditory nerves to fire simultaneously, by delaying the high frequencies relative to the low frequencies. This is done to counter the desynchronization caused by the travelling wave delay in the cochlea. This results in a larger response compared to the click (Wegner & Dau, 2002) . A second step is to use low-pass filtering of the stimulus, which will reduce the high pass noise level required to eliminate contributions outside the targeted frequency band. This method has been optimised it can be used to compare the wave I to

wave V ratio in normal hearing, tinnitus and matched hearing groups in both high and low frequency regions. If there is a neural gain increase we will expect to see an increase in wave I to V ratio at hearing loss regions in the tinnitus group compared to normal/hearing matched groups but not in regions where hearing is intact.

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P41: The effect of Transcranial Direct Current Stimulation in addition to tinnitus Retraining Therapy for treatment of chronic tinnitus patients.

Rabau S[1, 2]., Van Rompaey V[1, 2]., Van de Heyning P[1, 2]. ([1]Faculty of Medicine, Campus Drie Eiken, University of Antwerp, Antwerp, Belgium, [2] University Department of Otorhinolaryngology and Head & Neck Surgery, Antwerp University Hospital, Edegem, Belgium)

Background

Currently, there still is no treatment that eliminates tinnitus in all patients. Recent studies have shown that Tinnitus Retraining Therapy (TRT) significantly improves quality of life for tinnitus patients. Also, several studies have reported that transcranial Direct Current Stimulation (tDCS) has a positive effect on attention, working memory, long-term memory and other cognitive processes. The aim of this randomised placebo-controlled double-blind study is to evaluate the added effect of tDCS to TRT in chronic tinnitus patients. To our knowledge, this is the first study to combine both methods.

Methods

Patients with chronic, non-pulsatile tinnitus were randomised in two treatment groups: TRT and real tDCS versus TRT and sham tDCS. Evaluations took place at baseline before therapy started, at the end of the TRT and three months after therapy started. The Tinnitus Functional Index was used as the primary outcome measurement. Secondary outcome measurements were the Visual Analogue Scale of Loudness, Hospital Anxiety and Depression Scale (HADS), hyperacusis questionnaire, psychoacoustic measurements and Late Evoked Potential (P300). The objective was to evaluate whether tDCS can provide faster and/or more relief from the annoyance experienced in patients' daily lives.

Results

Study is still on-going at the moment. Final results will be presented at the conference.

P42: Parietal operculum OP3 and tonal phantom auditory perception in Human: Is there a link with middle ear kinesthesia?

Job A[1, 2]., Pons Y[3]., Raynal M[3].,Kossowski M[3]., Gauthier J[4]., Lombard B[4]., Schmerber S[5]., Delon-Martin C[6]. ([1]Institut de Recherche Biomédicale des Armées, France, [2]University of Grenoble Alpes, Grenoble Institut des Neurosciences, France. [3]Service ORL, HIA Percy, France, [4]Service ORL, HIA Desgenettes, France, [5]Service ORL, CHU-Grenoble, France, [6]INSERM, U836, Grenoble, France)

The phantom sound perception mechanism by which a sound perception occurs without any external sound source is still enigmatic. According to our previous fMRI study, a small region in the parietal operculum 3 was hyperactivated as a function of tinnitus periodicity in subjects with acoustic trauma tinnitus sequelae. This region was localized in the vicinity of neural correlates of middle-ear tympano-ossicular chain movements due to pressure variations. Disturbed proprioceptors are known to trigger illusory perceptions; therefore, we hypothesized that a disturbance of middle-ear proprioceptors may originate phantom sound perceptions. We designed an fMRI study that aimed to stimulate middle-ear proprioceptors by repetitive vibrations using various rates of click trains. In this study, we report that exposure to specific rates of stimuli for a few minutes at comfortable intensity level in healthy subjects distinctly triggered transient tinnitus-like aftereffects. The fMRI neural correlates of the aftereffects were unequivocally localized in the same parietal region as in acoustic trauma tinnitus sufferers. Our results strongly suggest that a middle-ear kinesthetic/proprioceptive illusion exists at the origin of acoustic trauma tinnitus via a somatosensory pathway encompassing the trigeminal system.

P43: Adaptive auditory gain in the brainstem.
de Kleine E., van Dijk P., Hoekman Turkesteen S. (University Medical Centre Groningen, Groningen, The Netherlands)

It has been suggested that abnormal loudness perception, as in hyperacusis, originates from pathological mechanisms in the brainstem. We investigated the relation between loudness perception and brainstem processing in humans by testing changes in brainstem responses due to temporary hearing loss.

In this study fifteen normal hearing test subjects were followed for four weeks. In each of them a temporary hearing loss was achieved by means of custom made earplugs in both ears. They wore the earplugs for two weeks. At the baseline (week 0) a categorical loudness scaling (CLS), acoustic reflex thresholds (ART) and click evoked auditory brainstem responses (ABR) were measured. Directly after these measurements the test subjects started wearing the earplugs. After two weeks (week 2) the measurements were repeated immediately after removal of the earplugs and finally two weeks later (week 4) again.

After wearing the earplugs in week 2 a stimulus was reported to be louder in the CLS. In week 4 a stimulus was reported to be softer, instead of returning to the baseline as in week 0. ARTs are obtained at lower thresholds in week 2 and at slightly higher thresholds in week 4 compared to week 0. From the ABR data the latencies and amplitudes of wave I, III and V were collected, analysis of ABR data is, however, ongoing.

Co-morbidities

P44: Association between tinnitus and arterial hypertension.
Figueiredo, R., Azevedo A.A., Penido N.O. (Federal University of São Paulo, Brazil)

Introduction
Tinnitus is the perception of noise in the absence of an external source and is considered by most authors as a multifactorial symptom. A systematic review concerning the association of tinnitus and systemic arterial hypertension (SAH) retrieved suggestions of a positive association, but the articles included failed to perform a detailed analysis on the theme.

Purpose
To analyze the presence and characteristics of tinnitus in hypertensive patients. To analyze differences between tinnitus impact and psychoacoustic measurements in hypertensive and normotensive patients and to evaluate the association between the presence of tinnitus and the diverse antihypertensive drugs employed.

Method
Cross-sectional transversal study, comparing two groups of subjects (144 in the study group with tinnitus and 140 in the control group, without tinnitus). Clinical, demographical, audiometrical and psychoacoustics characteristics of the subjects were compared.

Results
Hypertension prevalence in tinnitus subjects was 44.4% against 31.4% in subjects without tinnitus (p=0.024). Age was significantly higher for patients with tinnitus and hypertension (median of 66 for the group with tinnitus and hypertension against 52.5 for the group with hypertension only - p=0.0001). Positive associations with tinnitus were found with hypertension treatment with angiotensin-converting enzyme inhibitors (p=0.006), tiazidic diuretics (p<0,0001), potassium-sparing diuretics (p=0.016) and calcium channels blockers (p=0.004).

Conclusions
There is an association between systemic arterial hypertension and tinnitus. This association is potencialized by ageing. Hypertension treatment with diuretics, angiotensin-converting enzyme inhibitors and calcium channels blockers was more prevalent in tinnitus patients.

P45: Subtyping of tinnitus patients - implications for diagnosis and therapy.
Golenhofen M.P. (Tinnitus Center, Prien, Germany)

100 consecutive patients, investigated for their acute or chronic tinnitus percetion in a specialized center were categorized for their subtype, using a procedure of different clinical diagnostics (general medical, psychological, otological, orthopedic, orthodontic, immunological, dental). Further, tinnitus-specific features were: localization of tinnitus perception, tinnitus-pitch, presence of sensorineural hearing loss with/without acustic trauma, somatosensory modulation characteristics, onset description of the patient, vertigo symptoms, hyperacusis and perception pattern during daytime. Subtyping led to 5 clinically relevant clusters, mirroring known pathophysiological pathways of tinnitus perception in humans, described in the literature: From cochlea to cortex: deafferentiation of sensorineural (1) and endolymphatic (2) origin, dysfunctional integration process in cranial nerve nuclei of the brainstem (3), toxic influences on structures of the auditory pathway (4) and functional changes in the auditory cortex, following plasticity-driven pathologies (5).

As results, the five subtypes are described in their quantiative distribution, clinical features, interdependence to psychiatric comorbidity, pathophysiological markers and treatment implications.

As conclusion, relevance and form of a state-of-the-art medical differential diagnosis and the rationale behind a subtype-specific treatment is shown. Further subtype-specific treatment implications are outlined.

The value of tinnitus studies in humans, working without subtype-specification is discussed.

P46: Tinnitus and autoimmune ear disorder: A Case Report.

Fioretti A[1]., Di Rubbo V[2]., Peri G[3]., Eibenstein A[2]. ([1]Tinnitus Center - European Hospital, Rome. Italy, [2]L'Aquila University – DISCAB, Italy, [3]Audin Clinic, Rome, Italy)

Background

The incidence of autoimmune inner ear disease (AIED) is rare, accounting for < 1% of all cases of hearing impairment or dizziness. Nevertheless, the diagnosis of AIED might be overlooked for the lack of a specific diagnostic test.

Materials and Methods

A 50-year-old Caucasian woman came to our attention complaining severe disabling bilateral tinnitus, ear fullness and headache. The patient reported previous thyroidectomy for autoimmune thyroid disease (ATD) at 29 years and 3 breast surgeries for cancer and implant. The onset of tinnitus was associated to the last breast surgery (breast implant asportation after infection) and prolonged antibiotic therapy, which occurred about 1 month before. In spite of different medical therapies, there was no tinnitus improvement. Meanwhile the tinnitus worsened with a pitch of 8 kHz. Insomnia and concentration problems due to tinnitus lead to severe disability and a poor quality of life based on Tinnitus Handicap Inventory score (THI: 96). Pure tone audiometry testing revealed bilateral fluctuating mild hearing loss on high frequencies. Tympanogram was normal bilaterally. Auditory evoked potentials were normal. Computed tomography (CT) of temporal bone was normal. Magnetic resonance imaging (MRI) and angio-MRI resulted normal and negative for cerebral ischemia and acoustic neuroma. 2 transient unilateral facial paralysis were promptly treated with corticosteroids and completely resolved. The following serological markers of autoimmunity were positive: antinuclear antibodies (ANA), anti-extractable nuclear antibodies (ENA), anti-smooth muscle antibodies (ASMA) and Scl-70 antibodies. A diagnosis of mixed connective tissue disease with notes of fibromyalgia was made.

Results

The tinnitus was successfully treated with bilateral sound generators (listening 8-9 hours per day). Shortly after 1 month of a standard fitting procedure the patient reported a significant reduction of her tinnitus (THI: 36). The tinnitus worsened after 2 months in relation to a transient facial emiparesis and ear fullness (THI: 65). At 4 months follow up the tinnitus was stable (THI: 36).

Conclusion

the frequency of fibromyalgia is higher in women with breast implant rupture or extracapsular silicone. The literature doesn't account a clear evidence of an effective treatment for AIED from high-quality prospective trials. We can consider, in conclusion, ear fullness and tinnitus as aspects of a central sensitivity syndrome.

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P47: A possible role of inner ear melanocytes in tinnitus and audiovestibular disorders.

Barozzi S[1]., Del Bo L[2]. ([1]Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milano, Italia, [2]Fondazione Ascolta e Vivi. Milano, Italia)

Melanocytes are present in the skin and hair follicles, as well as in the eye, the leptomeninges, the anal canal and the inner ear. In the inner ear melanocytes are found both in the intermediate layer of the stria vascularis of the cochlea and in the dark cells of the vestibular organs. They are believed to play an important role in the production of endolymphatic potentials and in the maintenance of normal volumes of the inner ear fluids. Melanocytes disorders have been associated to some audiological abnormalities such as the Waardenburg syndrome and/or the Vogt-Kayanagi-Harada syndrome, characterized by both hearing impairment and pigmentation abnormalities. We propose that melanocytes could potentially be involved with inner ear fluid pressure dysfunction influencing conditions such as endolymphatic hydrops and Ménière's disease.

Recently, we reported the case of a patient in whom the appearance of a choroidal melanoma coincided with the exacerbation of tinnitus and vertigo spells in a unilateral Ménière's disease that had been clinically silent for more than ten years. The symptoms disappeared after the radiotherapy treatment and did not show up again during the following three years. We suggest that inner ear melanocytes could be a target of an autoimmune process in patients affected by melanoma as well retinal melanocytes in melanoma-associated retinopathy. The immune system could produce antibodies that cross-react with both the melanoma cells and the labyrinth melanocytes, causing an altered homeostasis of endolymphatic liquids. In this perspective, audiovestibular disorders could be interpreted as an attempt by the individual immune system to develop anti-tumoral response.

Autoimmune processes affecting inner ear melanocytes could be considered as a potential cause of tinnitus and audiovestibular disorders.

P48: Emotional stress influences ABR and mitochondria in the auditory cortex of experimental rats.

Mazurek B[1]., Szczepek A.J[2]. ([1] Tinnitus Center, Charité University Hospital, Berlin, Germany, [2]ORL Department, Charité University Hospital, Berlin, Germany)

Previously, we have reported that the emotional stress influences the auditory system of Wistar rats by inducing auditory hypersensitivity. In the present work, we have studied possible differences in the reaction to stress between the Wistar and Lewis strains of rats. Our work concentrated on the functional (auditory brainstem responses) and the protein expression levels in the auditory cortex. The animals were subjected to controlled stress. Various times after finishing stress, the rats were anesthetized and their auditory performance was measured with the evoked auditory brainstem response. Finally, the animals were sacrificed, their brains removed and processed immediately. Obtained proteins were separated on the SDS-PAGE, blotted onto PVC membranes and incubated with antibodies specific for Bax and Bcl-XL. We have confirmed our previous observations about stress-induced hypersensitivity in Wistar rats and found in addition, that Lewis rats react to stress in a different way, namely by developing auditory hyposensitivity. Consistent with this, we found strain-specific changes in the amounts of Bax and Bcl-XL, both of the proteins important for the preservation of mitochondrial structure and metabolic activity. We conclude that emotional stress may induce functional and molecular changes in the auditory cortex of experimental rats and that these changes are strain-specific.

P49: The Impact of Tinnitus on N-back Performance in Normal Hearing Individuals.
Waechter S., Brännström K.J., Hallendorf L., Malmstein E., Olsson A. (Lund University, Sweden)

Objective
The present study examines whether there are any differences between individuals with tinnitus and carefully matched controls in terms of response time and accuracy on a visual nback task, and whether hearing thresholds in the high-frequency range correlate with n-back task performance.

Design
All participants had their hearing thresholds measured (0.125 to 16 kHz) and performed a visual n-back test with and without presence of simultaneous speech. Thereafter all participants completed the Hospital Anxiety and Depression Scale (HADS), in addition tinnitus participants answered the Tinnitus Questionnaire (TQ).

Study sample
A total of 40 individuals were included, 20 had tinnitus (tinnitus group) and 20 had not (control group). Groups were age- and sex matched and all participants had hearing thresholds of 20 dB HL or better at 0.125 to 8 kHz.

Results
Results showed no significant differences between the groups regarding n-back task performances, however, high-frequency hearing thresholds of the right ear (10 to 16 kHz) correlated with response time for less demanding n-back conditions.

Conclusion
This suggests that the perceived decline in cognitive performance in tinnitus sufferers might be explained by deteriorated high-frequency hearing thresholds.

P50: Interaction of autonomic nerve system function and sleep quality on the severity of chronic subjective tinnitus.
Cheng-Yu L., Jiunn-Liang W. (Department of Otolaryngology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan. Taiwan)

Sleep difficulties are among the frequent complaints associated with chronic tinnitus. Most studies reporting on this problem are questionnaire-based. The perceived distress in tinnitus patients seems to be sympathetically mediated was also proposed recently. We aimed to investigate the significant predictors of chronic subjective tinnitus, and to assess the interaction of autonomic nerve system (ANS) function and sleep quality on the tinnitus severity. Adult patients with subjective tinnitus were recruited. The duration of tinnitus complaint was required to be at least 6 months. According to previous medical records, subjects with the pure-tone averages for 500 Hz, 1000 Hz, and 2000 Hz frequencies above 25 dB HL were excluded. Objective assessments included pure-tone audiometry, over-night hospital polysomnography (PSG) and ANS function test. Subjective questionnaire assessment of tinnitus severity was Tinnitus Handicap Inventory (THI). Participants (with and without tinnitus) were matched for health and relevant socioeconomic factors. There were 40 tinnitus patients and 40 control subjects without tinnitus completed the whole protocol. Tinnitus patients were older than non-tinnitus subjects ($p<0.05$). Characteristics of hearing status among tinnitus patients included worse 4k-Hz hearing threshold and worse 4k-Hz uncomfortable loudness level. Longer sleep latency and lower sleep efficiency were found among tinnitus patients ($p<0.05$). 4k-Hz uncomfortable

loudness level, sleep latency and ANS function hyperactivity were significant predictors of the tinnitus severity. Furthermore, combination with longer sleep latency and ANS function hyperactivity led to higher score level of THI. Our study showed that longer sleep latency and ANS function hyperactivity aggravated the tinnitus severity. Further clinical interventions to improve the ANS function hyperactivity and sleep difficulties among chronic subjective tinnitus patients should be considered.

P51: Relationship between co-morbid factors and psychological outcome in tinnitus patients.

Pajor A.M[1]., Ormezowska E.A[2]., Józefowicz-Korczyńska M[1]. ([1]Department of Otolaryngology,Medical University of Lodz, Poland, [2]Department of Neurosurgery, Medical University of Lodz, Poland)

Introduction

Tinnitus is frequently associated with sensorineural hearing loss and sometimes with dizziness or vertigo. These co-morbid symptoms, as well as some tinnitus parameters, may influence emotional state and cognitive functioning as it was demonstrated that psychological factors play an important role in the perception of other otological symptoms.

Material and methods

The study was carried out to determine the impact of some co-morbid otological symptoms and demographic factors on the emotional distress and cognitive functioning in patients with tinnitus. One hundred consecutive patients, complaining of constant idiopathic tinnitus (mean duration – 2.4 yrs), were enrolled into the study. Four tests were administered: Beck Depression Inventory (BDI), Hospital Anxiety Depression Scale (HADS, A - anxiety, D – depression), Mini-Mental State Examination (MMSE) and Trail Making Test (TMT). A multivariate stepwise linear regression analysis was performed to estimate the relationship between the results of each of the tests and following co-morbid factors: age, sex, tinnitus duration, tinnitus laterality, hearing status (normal hearing, unilateral hearing loss, bilateral hearing loss) and vertigo/dizziness.

Results

It was found that the scores of MMSE and TMT were negatively correlated with age and with hearing status and the scores of HADS-A were slightly correlated with sex. In regression analysis, the model reached statistical significance for HADS-A, MMSE and TMT, although the multivariate correlation for all variables was weak for HADS-A (multiple correlation coefficient $R=0.25$, $p<0.05$) and moderate for MMSE and TMT ($R=0.41$ and 0.56 respectively, $p<0.001$). In HADS-A, sex and to a lesser extent tinnitus duration, in MMSE and TMT, age and to a lesser extent tinnitus laterality were the variables that were comprised in the final model.

Conclusion

It was demonstrated that age had contributed to the results of cognitive tests while sex had affected the anxiety level in tinnitus patients. The other co-morbid factors, like hearing status, vertigo, tinnitus duration and laterality had very limited impact on psychological outcome in these patients.

P52: Tinnitus as a symptom of hidden lesions of the middle ear.

Djeric D[1]., Arsovic N[1]., Pavlovic S[2]. ([1]Clinic for Otorhinolaryngology and Maxillofacial Surgery, Clinical Centre of Serbia, Medical Faculty University of Belgrade, Serbia, [2]Institute of Molecular Genetics and Genetic Engineering University of Belgrade, Serbia)

Tinnitus does not represent a disease itself, but is a symptom of a variety of underlying diseases. Any pathologic lesion in the auditory pathway or any reduction in auditory nerve function has the potential to produce tinnitus. Otologic causes include numerous pathological conditions in the external, middle and inner ear. Most common causes are: cerumen, trauma, otitis, tymopanosclerosis, otosclerosis, cholesteatoma, Meniere's disease, tumors, and other causes. Neurologic causes include various diseases (multiple sclerosis, vestibular schwannoma and other cerebellopontine-angle tumors.). Infectious causes include various types of otitis media and otogenic complications and other infectious or inflammatory processes that affect hearing. Tinnitus is also caused by some oral medications or dysfunction of temporomandibular-joint and other dental disorders. It is known that about 40% of patients cannot identify any cause associated with tinnitus onset. In clinical practice, a presence of potential tumor (vestibular schwannoma, acoustic neuroma, meningioma) should be considered in cases with tinnitus and unilateral high-frequency hearing loss combined with poor speech discrimination. The purpose of this report is to present cases with tinnitus as an initial symptom of hidden lesionsin the middle ear. We present clinical, imaging and surgical findings in patients and point out the importance of early diagnosis for diseases, such as cholesteatoma, paraganglioma and other tumors of this region

P53: Spontaneous brief unilateral tapering tinnitus: Converging evidence supports the hypothesis that they arise ipsilaterally from the lateral pterygoid muscle.

Singh P.P. (University College of Medical Sciences & GTB Hospital, Delhi, India)

About 75% of people have experienced the sudden onset of a tone in one ear that fades away within seconds and has no definite precipitant. We have referred to this phenomenon as "sudden brief unilateral tapering tinnitus" (SBUTT's).

P54: Changes of co-morbid psychic symptoms in patients with chronic tinnitus: ICD-10-Symptom-Rating.

Seydel C.S., Brueggemann P.B., Mazurek B.M. (Tinnitus Center, Charité University Medicine Berlin, Berlin)

Introduction

Previous studies demonstrated the relationship between tinnitus and mental disorders. In spite of a great variety of psychometric instruments measuring psychic comorbidities of tinnitus there are rarely instruments that measure in a differentiated and comprehensive way. To analyze changes of co-morbid psychic symptoms after an outpatient multimodal 7-day tinnitus treatment, we used the ICD-10-Symptom-Rating (ISR) in our study. Furthermore we wanted to find out about the correlation between the ISR and tinnitus associated symptoms and if the ISR is determines symptoms in tinnitus patients that are not collected hitherto.

Method

313 patients were assessed using ICD-10-Symptom-Rating (ISR), Tinnitus Questionnaire (TQ), Perceived Stress Questionnaire (PSQ) und General Depressions Scale (ADS).

Results

Therapy resulted in significant reductions of ISR total score (especially on the subscales „additional scale", „depression", „anxiety" und „eating disorder"), TF total score (with the strongest effect on the subscales „emotional and cognitive distress", "intrusiveness", „hearing problems" und „sleep

disturbances") and PSQ total score (concerning all the four scales). The ADS scores also significantly improved after the outpatient multimodal 7-day therapy.

Conclusion
The ISR appears to be an effective instrument for measuring psychic symptoms in patients with tinnitus in a differentiated way. The instrument is appropriate in terms of tinnitus diagnostics and evaluating treatment

P55: A Physical Therapist's View on Somatic Tinnitus
Michiels S., De Hertogh W., Van de Heyning P. (University of Antwerp, Department of Rehabilitation Sciences and Physiotherapy, Antwerp, Belgium)

Background/Aims
Tinnitus can be related to many different aetiologies such as hearing loss or a noise trauma, but it can also be related to the somatosensory system of the cervical spine. It is however still unclear whether or not altered somatosensory information can actually cause tinnitus and very little information is available on the altered cervical somatosensory afference. As such, the need for thorough cervical spine assessment rises, as well as the need for prognostic indicators that can predict the effect of cervical physical therapy in patients with somatic tinnitus.

Methods
Cervical spine dysfunction was investigated in a group of patients with chronic subjective non-pulsatile tinnitus, using manual cervical spine investigation techniques.

Prognostic indicators, for the effect of cervical physical therapy in patients with somatic tinnitus, were investigated by exploring tinnitus and neck related baseline variables in patients with somatic tinnitus. After baseline measurements, all patients were treated using a multimodal cervical physical therapy treatment.

The effect of the treatment on the tinnitus complaints was measured using the Tinnitus Functional Index (TFI) and global perceived effect (GPE) after treatment and after 6 weeks follow-up.

Results
Cervical spine dysfunction is highly prevalent in a chronic subjective non-pulsatile tinnitus population. The somatic tinnitus group was mainly characterized by: a decreased mobility of the cervical spine, pain provocation during a combination of extension, rotation and lateral flexion of the neck and the presence of sensitive trigger points. No differences in ability to modulate the tinnitus were found between both groups.

Patients who experience co-variation of their tinnitus and neck complaints are significantly more likely to benefit from cervical physical therapy treatment. This co-variation of tinnitus and neck complaints was present in 49% of the study population. The co-varying group had significantly lower TFI-scores after treatment ($p=0.001$) and after 6 weeks follow-up ($p=0.03$).

Additionally, patients suffering from low-pitched tinnitus are more likely to benefit from the applied treatment than patients suffering from high-pitched tinnitus (87% versus 48%) ($p=0.04$). When combining the low-pitched tinnitus with the 'increase of tinnitus during inadequate postures during rest,

walking, working or sleeping', a group of patients could be identified that all experienced substantial improvement of their tinnitus immediately after treatment and after 6 weeks follow-up.

Conclusions
Although a higher prevalence of neck dysfunction was found in the somatic tinnitus group, neck dysfunction is also often present in non-somatic tinnitus patients. The group of patients that benefited most from cervical physical therapy were patients with low-pitched tinnitus, covarying with neck complaints and increasing during inadequate cervical spine postures.

P56: Experience with tinnitus, audiology services, the management options offered to them and effective interventions: views and experiences of (profoundly) deaf adults
Ng Z-Y., Archbold S., Sereda M., Harrigan S., Mulla I.

Introduction: Tinnitus is perceived in 75-80% of the hearing loss population (Shao et al. 2009), and the combination has been related to concentration and sleep problems (Axelsson & Sandh, 1985); however, there are mixed findings about the impact on quality of life (Zarenoe & Ledin, 2014; Joo et al. 2015). This poster will illustrate a study which explored the experiences of deaf adults with tinnitus on the impact of their tinnitus and their access to services and support.

Methods: Over 1,400 responses were collected through an online questionnaire and in-depth interviews, which were analysed using quantitative and qualitative methodologies. Comparisons were made between those with mild-moderate hearing losses versus those with severe-profound hearing losses.

Results: Preliminary results show that tinnitus has a great impact on the daily life of both groups, including difficulties in different areas between the groups. The respondents showed difficulties in
separating the impact of hearing loss and tinnitus, and a deep sense of desperation to stop or reduce the tinnitus. Both groups reported on mixed feelings regarding the help and support they received from professionals. Effective interventions included information education, hearing technology, leaflets/articles and internet resources.

Discussion: In comparison with previous literature, tinnitus deeply impacts the lives of those with various levels of hearing loss, including concentration and sleep problems, but also on (other) mental, physical and social aspects, and overall quality of life. Those with hearing loss and tinnitus could benefit from more tinnitus awareness, support groups, training of professionals and research on tinnitus.

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P57: Genetic study of familial cases of otosclerosis associated with tinnitus.

Pavlovic S[1]., Djeric D[2]., Stojiljkovic M[1]., Arsovic N[2]. ([1]Instiute of Molecular Genetics and Genetic Engineering University of Belgrade, Serbia, [2]Clinic for otorhinolaryngology and maxillofacial surgery, Clinical Centre of Serbia, Medical Faculty University of Belgrade, Serbia)

Tinnitus is commonly defined as the sensation of hearing a sound in the absence of external sounds and may be caused by the dysfunction of different parts of the hearing system. Causes of tinnitus, associated with the middle ear disorders/diseases, include various conditions, such as congenital malformations, inflammatory process, tympanosclerosis and uncommon ones, such as otosclerosis. Here we report the results of genetic study of familial cases of otosclerosis associated with tinnitus and hearing loss. We have investigated genetic profile of two affected family members from two generations. The otosclerosis was diagnosed during surgical intervention. Tinnitus and hearing loss affected both ears. Clinical and audiological findings confirmed otosclerosis. We have collected blood samples from two affected family members from different generations, and investigated their genetic profile using Illumina MiSeq and TruSightOne Sequencing Panel which targets 4 813 genes associated with known clinical phenotypes. Bioinformatics analysis has been conducted using VariantStudio software. In both affected relatives we have found the same rare genetic variants, not present in healthy individuals: BMP2: p.Arg190Ser, COL1A1: p.Thr1075Ala, ACE: c.1922-288C>T, c.2306-11A>C, c.3692-6G>A and RELN: c.8843+7G>C, 3:c.578-3T>C, p.Ser630Arg. It is worth noting that detected variants are located in genes coding the proteins involved in development of bone and cartilage (BMP2 gene), strengthening and supporting cartilage and bone tissues, collagen (COL1A1gene), development of vascular disease (ACE gene) and regulation of synaptic plasticity (RELN gene). The variations in the same genes have previously been associated with otosclerosis. Additional studies of familial cases of tinnitus and diseases associated with tinnitus as a symptom, would contribute to elucidating genetic basis of tinnitus.

Behavioural models

P58: Behavioural animal model for Tinnitus and Hyperacusis.

Rüttiger L., Möhrle D., Knipper M. (University of Tübingen, Tübingen, Germany)

In humans, loss of hearing function comprises increased thresholds, altered sound processing of temporally and spatially modulated auditory stimuli, but also through abnormal perception of above-threshold sounds or phantom perceptions, like hyperacusis and tinnitus (for review see Knipper et al., 2013). Previous studies on the rodent had already demonstrated the degeneration of auditory fibres following mild auditory trauma (Kujawa and Liberman 2009, Furman et al. 2013, Rüttiger et al., 2013, Singer et al., 2013) and over age (Sergeyenko et al. 2013). Here we demonstrate how a mild auditory trauma induces hyperacusis or tinnitus in a rat animal model. Hyperacusis and tinnitus sensation were tested using a behavioral approach

(Rüttiger et al. 2003), and hearing function was studied using auditory evoked brainstem responses (ABR) and otoacoustic emissions (DPOAE). To gain insight into the central brainstem function above-threshold responses to click and frequency specific stimuli were analysed in detail for fibre recruitment and latencies of ABR wave deflections (wave amplitudes and latencies). Results from behavior studies on differentially aged rats, before and after auditory overstimulation, are presented in correlation with individual hearing functions and morphological specifications of the hair cell molecular phenotype and hair cell ribbon loss.
Supported by Action on Hearing Loss, RNID G45 (Rü)

P59: Developing an objective test for tinnitus in humans using the post auricular muscle reflex.
Wilson C.A[1, 2]., Berger J[1]., Coomber B[1]., de Boer J[1]., Sereda M[2, 3]., Palmer A.R[1]., Hall D.A[2, 3]., Wallace M.N[1]. ([1]MRC Institute of Hearing Research, University Park, Nottingham, UK, [2]Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, [3]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK)

Gap-induced pre-pulse inhibition of the acoustic startle (GPIAS) (behavioural test for tinnitus in animals) relies on a short gap in continuous background noise providing a cue to inhibit the response to a loud startling stimulus. Impaired GPIAS following tinnitus induction has been shown in a number of species, as well as in humans with tinnitus. Reduced detectability of the gap was originally thought to be caused by the tinnitus 'filling' the gap, but there have been suggestions that another mechanism is involved. Preliminary work in humans measuring the eye blink reflex responses showed gap detection deficits in tinnitus subjects, but the underlying mechanisms of this effect were unclear (1). The eye blink response is not specifically related to the auditory system and consequently has a relatively long latency (>40ms) that is subject to attentional modulation.

We have developed a variation of the GPIAS method in which we measure GPIAS in guinea pigs using the reflex pinna movement. The post-auricular muscle reflex (PAMR) is the human analogue of the pinna reflex and may represent a route for developing an objective tinnitus test. The PAMR is a short-latency (10-12ms) response that involves two or three synapses in the brainstem and is more tightly linked to auditory input and less susceptible to attentional modulation. However, gap-induced pre-pulse inhibition (PPI) of the PAMR has not previously been demonstrated.

In the present study, we measured gap-induced PPI of the PAMR in 45 normal-hearing subjects. This was a group of young participants (18 – 30 years old) who did not have chronic tinnitus. PAMR responses were recorded simultaneously with the eye blink reflex electromyographically with surface electrodes placed over the insertion of the post-auricular muscle to the pinna. Gap detection was evaluated against a 1 kHz pure tone background, presented monaurally to the right ear at 70 dB SPL, and startling stimuli comprising very brief broadband noise bursts presented at 105 dB SPL. The embedded gaps ranged from 20-100ms long with the position of the gaps ranging from 20-500ms from the end of the gap to the onset of the startle stimuli. Eye direction has been shown to have a dramatic effect on the amplitude of the PAMR reflex (2) and we confirmed this for most subjects. We also investigated the effect of gap position and gap duration on the degree of PPI. The data indicate that the PAMR is susceptible to gap-induced PPI and that the optimal parameters for inducing PPI vary between individuals. Future studies will establish whether deficits in PPI using the PAMR are characteristic of subjects with tinnitus.

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P60: Treatment of acute salicylate-induced tinnitus with TNF-α blocker in an animal model.
Liu, T.C., Chang-Wei Huang D. (National Taiwan University Hospital, Taiwan)

Objectives
Salicylate-induced tinnitus was known to augment TNF-α gene expression in the cochlea of mice. We assumed this pro-inflammatory cytokine may directly induce tinnitus or via modulating the NMDA receptor. Therefore, we tried to observe treatment outcome of TNF-α blocker and its interaction with NMDA receptor.

Methods
Thirty 3-month-old male C57BL/6 mice were randomly divided into TNF-α blocker treatment group (n=15) and saline-treated control group (n=15). ABR were performed before and after study to record hearing threshold. 5-days Active avoidance task training was performed first and the tinnitus score was determined. Tinnitus baseline test was measured 1-hour before intraperitoneal injection of 300mg/kg sodium salicylate. Two treatment strategies were as followed: 30mg/kg TNF-α blocker (Enbrel) or saline administration 1-hour after salicylate injection. Then, tinnitus score test was repeatedly performed immediately and for consecutive 2 days after treatment. Eventually, mice were euthanized to determine the geneexpression level of TNF-αR1/2 and NR2B in cochlea.

Results
Enbrel may significant decrease salicylate-induced ABR hearing threshold shift. The tinnitus score (saline/Enbrel) were significant decreased on day2 and day3. The relative quantification gene expression for TNF-αR1/2 to β-actin was significantly decreased in treatment group. Moreover, TNF-αR2 had dominant gene expression to TNF-αR1 in control group. One the other hand, NR2B and DREAM protein gene expression were also significantly decreased in treatment group.

Conclusions
TNF-α blocker revealed reduction of salicylate-induced acute tinnitus in animal model. TNF-αR2 played more dominant role than TNF-αR1. Finaly, the NMDA receptor is also modulated by TNF-α blocker.

P61: Behavioral animal model for tinnitus-related distress.
Lauer A., Larkin G., Jones A., May B.J. (Johns Hopkins University, Baltimore, Maryland, USA)

The relationship between tinnitus and psychological distress has been contemplated for decades. Many studies report increased prevalence of anxiety and depression in tinnitus sufferers, and these negative emotional states likely increase perceived tinnitus annoyance. The underlying mechanisms of the negative emotional responses to tinnitus remain poorly understood because tinnitus and anxiety can be challenging to characterize in animal models. The causality of preexisting psychological profiles in the development of tinnitus-related distress is also poorly understood because the emotional state of patients prior to development of tinnitus can be difficult to establish retrospectively. Furthermore, hearing loss itself is associated with increased anxiety and depression, and it is difficult to disentangle the independent psychological consequences of tinnitus and hearing loss in patients experiencing both disorders. We have addressed these important questions in laboratory rats using two common anxiety screening assays: the open field test of exploratory activity and the social interaction test. In the first set of experiments designed to validate the behavioral tests, open field exploration and social interaction were reduced in rats exposed to acute anxiogenic conditions, salicylate injections, and monaural sound trauma

compared to controls. In the second set of experiments, monaurally sound-exposed animals were tested for tinnitus using a conditioned lick suppression procedure and screened for anxiety. Tinnitus-positive rats showed high anxiety phenotypes in the open field test, whereas tinnitus-negative rats showed low anxiety phenotypes. In contrast, both tinnitus-positive and tinnitus-negative rats showed reduced social interactions. These results identify that the open field test as a selective measure of tinnitus-related distress, whereas reduced social interaction test performance may reflect the consequences of hearing loss. This new animal model will facilitate future studies of the structural and functional changes in the brain's auditory and emotion pathways underlying tinnitus-related distress, as well as development of novel interventions to ameliorate or prevent negative emotional responses to tinnitus.

P62: The short-term effects of predictable and unpredictable surf-like sounds on tinnitus adaptation.

Durai M[1]., Searchfield G.D[1, 2]. ([1]Section of Audiology, School of Population Health, University of Auckland, New Zealand, [2]Centre for Brain Research, The University of Auckland, New Zealand)

Traditional psychoacoustic and physiological models of tinnitus to date tend to adopt a reductionist approach in which perceptual characteristics of tinnitus are studied in isolation. The Adaptation Level Theory (ALT) model (Searchfield, Kobayashi& Sanders, 2012) provides a more holistic approach to tinnitus perception, by proposing an ecological framework where interaction between the individual with their environment can potentially alter tinnitus magnitude and distress. The adaptation level (AL) is the body's internal anchor or reference point, which can change according to context, modelled as the weighted mean of 3 components: 1) the focal component (tinnitus), 2) background or contextual stimuli and 3) residual individual factors including certain personality traits, emotions or states (including depression and anxiety), previous experiences/memory of the tinnitus, prediction and physiological arousal level.

The first empirical assessment of this ALT model examined the individual effects and interactions of contextual noise levels and personality traits on tinnitus audibility and distress outcomes. An interaction between the personality traits of social closeness, positive emotionality, stress reaction and negative emotionality and contextual noise effects on tinnitus was observed, consistent with the model. In this study we investigate prediction as a residual factor for tinnitus adaptation.

Study Design

The effect of amplitude-modulated sound therapy stimuli on tinnitus was investigated, using sounds masking tinnitus at either predictable or unpredictable intervals. The study consisted of 2 parts. 1. A short-term adaptation experiment. Loudness level matches and rating scales for loudness and distress were obtained at a silent baseline and at the end of three counterbalanced 30 minute exposures –, silence, predictable and unpredictable sounds. 2. A qualitative two-week sound therapy feasibility trial. Participants took home a digital music player with the test stimuli for two weeks and were interviewed at the end of the trial. Study sample: Twenty-three individuals with chronic tinnitus participated in Part 1, seven individuals randomly selected using a number generator participated in Part 2. Results: Self-reported tinnitus loudness for the unpredictable sound was significantly lower than baseline ratings after acute exposure. Tinnitus annoyance ratings for the unpredictable condition were significantly lower than baseline; changes following the predictive sound condition were also significant but the effect was smaller. The feasibility trial identified participant preferences for sounds varied, of those participants who obtained benefit from the sound trial, the majority preferred unpredictable compared to predictable sounds. Conclusions: Sound therapy stimuli in which tinnitus is made audible at unpredictable intervals may lead to greater reduction in tinnitus outcomes,

than when audible at predictable intervals. The feasibility trial highlighted that natural, non-static (e.g. environmental) sounds may be preferred over computer generated sound, and user-friendly devices with manual volume controls may be better for administering sound therapy

P63: Evidence in support of shared route to sound annoyance and emotional distress for bothersome tinnitus and misophonia.

Kowalkowski K.L[1, 2]., Lavens A[1]., Sidwell A[1]., Krumbholz K[1].([1]MRC Institute of Hearing Research, Nottingham, UK, [2] Otology and Hearing Group, Department of Clinical Neuroscience, School of Medicine, University of Nottingham, UK)

It is estimated that 1-2% of adults with tinnitus in the UK have bothersome tinnitus, defined as tinnitus that is distressing and impacts their quality of life. It is this subgroup of tinnitus patients that present with the greatest clinical need.

The degree to which tinnitus is bothersome has been shown not to correlate well with the psychoacoustic properties of the phantom sound itself, and so it has been proposed that other factors are more important in determining the bothersomeness of an individual's tinnitus and its impact on their lives. Pre-existing anxiety and poor wellbeing at tinnitus onset are thought to be predictive factors for distress (Holgers et al. 2000, 2005), as well as cognitive deficits including resource limitations in working memory and attentional control, negative emotional processing bias and negative tinnitus appraisal (Andersson and McKenna 2006). Personality traits such as neuroticism are also implicated as contributing factors (McCormack et al 2014).

Misophonia, like bothersome tinnitus, is a condition in which specific perceived sounds can result in high levels of emotional distress. Here, we present key data from our population survey of 380 individuals with suspected clinical misophonia, as measured by an online version of the A-MISO-S diagnostic questionnaire, to show that the emotional and functional consequences of misophonia manifest in ways highly similar to bothersome tinnitus: irritation, anxiety, worry, sleep problems, cognitive difficulties such as reduced concentration and an inability to focus attention away from the bothersome sound are key symptoms of both conditions. There is also evidence for autonomic arousal in both bothersome tinnitus and misophonia (Van der Loo et al 2008, Edelstein et al 2013) suggesting that chronic bothersome tinnitus acts as a stressor (Herbert et al 2009). It has previously been proposed that misophonia and bothersome tinnitus may be causally related.

Lawrence McKenna proposed a cognitive behavioural model to help explain how emotional distress due to tinnitus may arise in some individuals and not others (Handscombe et al 2015). This work draws on previous models for emotional distress arising from conditions such as insomnia and chronic pain, and provides us with scientifically testable hypotheses for how a diverse set of implicated factors fit together to generate something as complex and individualised as tinnitus distress. Both thematic analysis of our population survey responses, and a scoping review of the misophonia literature field suggest the McKenna model may also be applicable to misophonia, with negative automatic thoughts (e.g., believed interference with social or cognitive functioning), safety behaviours (such as avoidance using masking sounds), selective attention and monitoring, distorted perception and unwanted autonomic arousal presenting as key themes.

We conclude with data from our second online misophonia study, in which we invited 200 individuals from our first study to complete in-depth questionnaires to test a cognitive behavioural model of misophonia based on McKenna's tinnitus model. We hope that an increased understanding of the shared routes to sound annoyance and emotional distress will help to inform more effective cognitive behavioural therapies for both conditions.

P64: The consequences of tinnitus and tinnitus severity on cognition: a cross sectional study.
Mohamad N., Hall D.A., Hoare D.J. (NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK)

People with tinnitus anecdotally report difficulties in mental concentration, and psychological treatments for tinnitus include advice on concentration difficulties and how to manage them. Empirical behavioural evidence for an effect is somewhat limited, but there is some support that tinnitus interferes with executive attention, and mixed support that it impairs working memory and selective attention. However, a number of methodological issues in previous studies limit confidence in their estimates. We proposed a putative model of the complex inter-relationships between tinnitus, cognition (working memory, selective attention, sustained attention, and switching attention) and confounding factors as a basis for hypothesis testing. The model was tested in a large cross-sectional study of adults (n=200) using a battery of behavioural and questionnaire measures of cognitive performance and potential confounding factors (hearing handicap, global psychological distress, and fluid intelligence). A structural equation modelling technique with SmartPLS software was adopted for analysis of the empirical data. Findings demonstrate significant negative relationships between tinnitus severity and all four cognitive components of interest, as well as between hearing handicap and working memory. Fluid intelligence showed an influence on the relationship between tinnitus severity and working memory performance. In contrast, the other confounding factors (hearing handicap and global psychological distress) did not show significant effects. The effects of tinnitus severity on different components of cognition may prove to support a new therapeutic target for tinnitus management.

P65: Targeting Tinnitus-Related Neural Plasticity by Optogenetic Silencing.
Gold J.R[1]., Nodal F.R[1]., Furness D.N[2]., King A.J[1]., Bajo V.M[1]. ([1]University of Oxford, Department of Physiology, Anatomy & Genetics, Oxford, UK, [2]Keele University, Department of Life Sciences, Keele, UK)

Subjective tinnitus is thought to derive from maladaptive neuroplasticity that occurs following hearing impairment. However, the underlying structural and functional mechanisms remain unresolved. Our aims were to develop a model of trauma-induced tinnitus, putatively instigated by a lesion of the spiral ganglion (SG), and to explore the perceptual changes, and their physiological correlates, that developed post-insult. In particular, we wished to determine whether primary auditory cortex played a causal role in mediating these changes. Our animal of choice was the ferret (Mustelid putorius furo), which possesses a hearing range overlapping that of humans; a complex, gyrencephalic cortical architecture; and is ethologically reliant on auditory cues.

Auditory temporal processing is known to be impaired in tinnitus and following hearing loss. We thus tested ferrets and humans on a gap-in-noise detection task that relies on accurate encoding of temporally modulated sounds (Gold et al., 2015). Ferrets displayed robust gap-detection performance, with sensitivity that varied with the frequency content of the acoustic carrier noise. Compared with ferrets, human subjects displayed lower thresholds but equivalent stimulus-type sensitivity, confirming that the ferret is a relevant model of auditory temporal processing.

To investigate hearing-loss-related neuroplasticity, ferrets underwent a partial, unilateral lesion of the SG that replicates aspects of tinnitus-related otopathology, which we confirmed anatomically. Behaviourally, some ferrets displayed temporal processing impairments, and others showing post-lesion adaptation. By recording auditory brainstem responses (ABRs), we found evidence for plasticity over time with improvements in lesion-diminished late-wave (IV) amplitudes. Interestingly, the presence of pre-lesion shorter latencies and higher amplitudes of waves I and IV was

significantly correlated with post-lesion behavioural impairment. This suggested that animals may be physiologically predisposed towards adaptation/maladaptation.

Electrophysiological recordings from auditory cortical cells showed evidence for lesion-related central neuroplasticity that correlated with each animal's behavioural phenotype. In particular, behaviourally-impaired animals displayed relative hyperactivity and neural synchrony enhancements in their spiking responses, compared with un-impaired animals and unlesioned controls. Anatomical examination of the central auditory system revealed enhancement of nitric oxide synthase expression in ferrets with lesion-induced hearing loss. In contrast, cortical expression changes in activity-regulated cytoskeleton-associated protein (Arc) were specifically related to the behavioural phenotype.

Lastly, we examined whether gap-detection behavioural changes were underpinned by post-lesion cortical neuroplasticity. The optogenetic protein Archaerhodopsin-T was expressed bilaterally in auditory cortical neurons of SG-lesioned ferrets, allowing suppression of neural activity during behaviour. Remarkably, contralesional cortical suppression selectively induced improvements in the performance of animals with post-lesion temporal processing impairments, and vice-versa. The mechanistic basis for these effects putatively derives from a significant enhancement in the gap-detection capabilities of cortical neurons observed electrophysiologically during optogenetic suppression. Together, these results suggest that primary auditory cortex plays an important role in mediating deafferentation-related neuroplasticity, suggesting possible strategies for rescuing the maladaptive processing potentially responsible for tinnitus in humans.

Reference

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Available interventions

P66: Individualized rTMS: a proof-of-concept study in chronic tinnitus.

Kreuzer P.M[1 3]., Poeppl T.B[1, 3]., Vielsmeier V[2, 3]., Langguth B[1, 3]., Schecklmann M[1, 3]. ([1]University of Regensburg,Department of Psychiatry and Psychotherapy, University of Regensburg, Germany, [2]Department of Otorhinolaryngology, University of Regensburg, Regensburg, Germany, [3]Interdisciplinary Tinnitus Center of the University of Regensburg, Regensburg, Germany)

Background

Prefrontal and temporoparietal repetitive transcranial magnetic stimulation (rTMS) in chronic tinnitus showed significant but only moderate effectiveness with high inter-individual variability in treatment response. This study was designed to proof the feasibility of an individualized fronto-temporal rTMS paradigm.

Methods

During the first session of our standard two-week rTMS setting we applied different protocols to the left and right temporoparietal and dorsolateral prefrontal cortex (DLPFC) in 25 tinnitus patients. In each protocol 200 pulses (except for 1Hz frequency containing 50 pulses) were applied at frequencies of 1Hz, 5Hz, 10Hz, 20Hz, cTBS, sham (continuous theta burst stimulation). Patients reporting immediate tinnitus reduction were treated

in an individualized manner applying a combined protocol consisting of the most effective frontal and the most effective temporoparietal stimulation protocol. Those patients who did not improve after the test session were treated with a standard fronto-temporoparietal protocol.

Results
Almost half of the patients (12 out of 25) reported immediate tinnitus reduction in the test session. In this group the mean pre-to-post-treatment amelioration in the tinnitus questionnaire was 8.6±8.9 whereas the improvement was only 1.5±8.5 in those patients who did not respond to the test session. Treatment outcome remained stable over a follow-up period of ten weeks.

Discussion
Individualized rTMS was shown to be feasible and effective in chronic tinnitus and might provide a basis for a "tailored" application of rTMS in tinnitus and other neuropsychiatric disorders.

P67: A proof-of-concept study on the combination of repetitive transcranial magnetic stimulation and relaxation techniques in chronic tinnitus.
Kreuzer P.M[1, 3]., Poeppl T.B[1, 3]., Bulla J[2]., Schlee W[11, 3]., Lehner A[1, 3]., Langguth B[1, 3]., Schecklmann M[1, 3]. ([1]University of Regensburg, Department of Psychiatry and Psychotherapy, University of Regensburg, Germany, [2]Department of Mathematics, University of Bergen, P.O. Box 7800, 5020 Bergen, Norway, [3]Interdisciplinary Tinnitus Centre of the University of Regensburg, Regensburg, Germany)

Background
Interference of ongoing neuronal activity and brain stimulation motivated this study to prove the concept of a combined treatment approach integrating repetitive transcranial magnetic stimulation (rTMS) and relaxation techniques in patients with chronic tinnitus.

Methods
Forty-two patients received rTMS consisting of ten sessions of high-frequency left dorsolateral prefrontal cortex followed by low-frequency left temporo-parietal cortex stimulation in this one-arm proof-of-concept study. During low-frequency stimulation patients listened to different kinds of relaxation audios selected according individual preferences (classical music; instructions to muscle or breath relaxation, imaginary journey or hypnosis). Variables of interest were tinnitus questionnaires, tinnitus numeric rating scales, depressivity, and quality of life. Results were compared to results of historical control groups having received the same rTMS protocol (active control) and sham treatment (placebo) without relaxation techniques.

Results
Drop-outs and adverse events were low. Responder rates (reduction in tinnitus questionnaire (TQ) score by at least 5 points ten weeks after treatment) were 44.7% in the study, 27.8% in the active control group, and 21.7% in the placebo group, differing between groups on a near-significant level. Combination of rTMS and relaxation showed higher amelioration in the tinnitus handicap inventory questionnaire (THI) in contrast to rTMS alone. Deepness of relaxation during rTMS and selection of active relaxation vs. passive listening to music predicted larger reductions in the TQ-score. All remaining secondary outcomes turned out non-significant.

Discussion
Combining rTMS and relaxation techniques has proven to be a safe, feasible and promising approach to enhance rTMS treatment effects in chronic tinnitus.

P68: Cochlear implantation in tinnitus patients with sudden unilateral hearing loss.
Fabijanska A., Fronczak P., Lorens A., Skarżynski H. (Institute of Physiology and Pathology of Hearing, Warsaw, Poland)

Introduction
Sudden sensory-neural hearing loss is usually assiociated with severe, debilitating tinnitus. In patients with profound or severe hearing loss hearing aids are not able to provide sufficient amplification to supress tinnitus. Contralateral routing of signal devices usually also fail in tinnitus alleviation.

Aim of the study
Retrospective analysis of 35 patients with tinnitus and sudden unilateral sensory-neural hearing loss (profound or severe) who received cochlear implants from July 2014 to August 2015 in our center.

Results
Subjective reduction of tinnitus intensity was observed in 28 patients. In 6 patients tinnitus remained unchanged. In 1 patient tinnitus was temporarily worsened after the operation, but returned to its usual level four months after activation of the procesor. We did not observed any case of persistent tinnitus worsening in this group as well as any severe post-operative complications.

Conclusions
Cochlear implantation seems to be an effective and safe method of treatment for tinnitus patients with sudden unilateral sensory-neural hearing loss who did not responded to standard pharmacotherapy and hyperbaric oxygen therapy and should be regarded as a treatment of choice for patients with profound or severe hearing loss.

P69: The treatment of chronic tinnitus with sLORETA neurofeedback.
Güntensperger D.G[1]., Meyer M.M[1]., Kleinjung T.K[2]. ([1]Neuroplasticity and Learning in the Healthy Aging Brain (HAB LAB), Institute of Psychology, University of Zurich, Switzerland, [2]Department of Otorhinolaryngology, Head and Neck Surgery, University of Zurich, Switzerland)

Despite extensive research no suitable treatment could yet be discovered to effectively cure tinnitus. However, neurofeedback and especially its spatially improved version tomographic neurofeedback (ToNF) can be seen as a highly promising form of therapy in this regard.

Many studies working with electroencephalography (EEG) and magnetoencephalography (MEG) could find tinnitus specific patterns of brain activity in temporal areas, specifically in the primary auditory cortex (Lorenz et al., 2009; Meyer et al., 2014; Moazami-Goudarzi et al., 2010; Weisz et al., 2007). While usually the slower delta- and the faster gamma- oscillations appear to be abnormally increased, alpha-waves tend to be significantly suppressed for tinnitus sufferers. It could already be shown that normalizing of these unfortunate activity patterns with neurofeedback leads to significant improvements of tinnitus symptoms (Dohrmann et al., 2007; Hartmann et al., 2013).

Combining the source estimation algorithm sLORETA with neurofeedback in the software Cygnet (EEGInfo) we will investigate the efficiency of ToNF in the treatment of chronic tinnitus. Over the course of 15 weeks participants will use neurofeedback to train an increasing of their resting-state alpha

activity, while at the same time trying to down-regulate the amount of delta power in the auditory cortex. With the goal of including 52 patients in the training while for the first time using a 31-channel neurofeedback system with source localization this project can be seen as highly innovative in tinnitus research. Furthermore, pre and post resting-state EEG recordings (immediately after and 3 months after completion of trainings) always combined with a multitude of psychological and health-related questionnaires and audiometric testing will help to evaluate treatment success in general and disentangle subgroups with differing progress and benefit from the planned protocol. This project can be seen as a first step towards the long-term goal of identifying different forms of subjective tinnitus and developing individually tailored neurofeedback protocols for each of these subtypes.

P70: Manualisation and feasibility study of audiologist-delivered counselling for tinnitus: protocol.

Taylor J[1]., Thompson D[1]., Hall D[1]., Stockdale D[2]., Walker D-M[3]., McMurran M[4]., Featherstone D[5]., Casey A[6]., Hoare D.[1] ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]The British Tinnitus Association, Sheffield, UK, [3]Health Sciences, University of Southampton, Southampton, UK, [4]Division of Psychiatry & Applied Psychology, University of Nottingham, Nottingham, UK, [5]Clitheroe Therapies Clinic, Clitheroe, UK, [6]School of Life & Health Sciences, Aston University, Birmingham, UK)

Background

Chronic tinnitus is a common incurable condition often associated with depression, anxiety, insomnia and reduced quality of life. Within National Health Service (NHS) audiology, tinnitus is treated using a number of recommended interventions but there is no standard protocol for deciding on a first line approach. Sound therapy and patient education are widely available but counselling is only available in less than half of audiology departments and there is no agreed standard for what constitutes tinnitus counselling. There is substantial evidence from systematic reviews for the clinical benefit of counselling for tinnitus delivered by clinical psychologists or psychiatrists, but no studies have sufficiently evidenced the NHS model of tinnitus care where face-to-face counselling is delivered by audiology professionals. This remains an important unanswered question given that specialist tinnitus care is increasingly becoming the domain of the audiologist

Aims

To manualise and then evaluate the feasibility of audiologist-delivered counselling for tinnitus patients

Methods and analysis

Following Medical Research Council recommendations for evaluating complex interventions, a scoping review has been conducted of all potential relevant practice guidelines and educational material relating to counselling for tinnitus. Combined with expert clinical and patient opinion, a comprehensive set of tinnitus counselling components will be generated. This will form the basis of a Delphi survey of patients (n=20) who have experienced tinnitus counselling and specialist audiologists (n=20) who are trained in counselling and consult tinnitus patients, to establish consensus on the essential core attributes of tinnitus counselling.

These elements will be incorporated into a manualised care protocol which, following training in a dedicated workshop, will be delivered by three experienced audiologists across three different sites. Patients (n=30) will be randomly allocated to receive either 1) standard care from an audiologist who has not received any counselling training or 2) specialised care from an audiologist trained to deliver the counselling components of the manualised intervention.

The feasibility and acceptability of the counselling package will be evaluated post-treatment via qualitative interviews with participating patients and clinicians, and completion of quantitative outcome measures by patients and treatment fidelity questionnaires by clinicians.

Conclusions
The potential for the counselling intervention to proceed to a definitive randomised controlled trial will be assessed via compliance with the manual, willingness to be randomised, number of eligible participants, rate of recruitment, retention and collection of outcome measures. This research offers an important first step to an evidence-based, costed, standardised and accessible approach to tinnitus care.

Ethics
The above study is subject to pending NHS approvals.

P71: Regional Tinnitus Networks – Tinnitus Communities of Practice.
Carr D., Stockdale D. (British Tinnitus Association, Sheffield, UK)

Introduction
A community of practice is any group of people whose members have a common interest in a subject, problem or goal; through collaboration, negotiation and sharing of ideas, they find solutions and new ideas (Wenger, 1998). When people think of a learning opportunity, they often think of a formal training course or conference presentation. Most people will think of a transfer of knowledge from a teacher to a learner. Research shows that much human knowledge is passed along through participation with coworkers in everyday activities (Brown, Collins & Duguid, 1989; Machíes, 2004).

Method
Using an Action Research Methodology and based on an existing East of England network created by David Baguley the BTA are developing regional tinnitus networks for NHS professionals that reflect local needs and reflect the unique nature of what is happening in each region. Using post event evaluations and follow up questionnaires one month after meetings together with one to one interviews we are able to provide some initial feedback on the difference that Regional Tinnitus Networks as Communities of Practice are making to NHS professionals.

Results and outcomes
100% of professionals attending network meetings state that it worthwhile.
94% of professionals identify that a primary benefit of meeting is the opportunity to share experiences.
Top six themes identified are:
Case study discussions
Different approaches of different clinics/individuals
Sharing research and answering the 'So what?' question by applying research findings to patients
Sharing pathways - triage and outcome measures
Products, claims, research behind them
Psychological aspects of tinnitus
From the initial meetings some practical outcomes have resulted including:

Increased communication about the variety of patient journeys through the NHS
Creation of new services for tinnitus patients
Sharing of experiences in supporting tinnitus patients with complex needs
Improved understanding of hearing aid products
Opportunities to rethink use of THI and TFI questionnaires
Developing new online services for tinnitus patients

Discussion
Whilst acknowledging the limited data available, results indicate that attending a Community of Practice can be beneficial for the professional development of audiologists treating tinnitus patients. What is learnt is driven by learners and their own needs rather than being decided by the teacher. Learning is informal and developed through mutual engagement and recognises the shared experiences expertise in each region.

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P72: Holistic Attitude in Tinnitus Treatment.
Estola M.K. (Honkaharju Hospital, Imatra, Finland)

Tinnitus is one of the most common complains. It might be a very slight sensation or drive the patient crazy. The symptoms are individual as the whole tinnitus itself. That's why we have to choose a right and individual treatment for every patient.

First part in treatment is proper examination, hearing measurement and in some cases x-ray or magnetic imaging. Explaining the results to the patient is one part of treatment.

Some people have benign paroxysmal postural vertigo and for them I always correct that first. They get more balance and some of them get rid of their tinnitus as well. It is the easiest and most beneficial way to start because correcting imbalance helps treating the muscles too.

One third of my tinnitus patients get benefit from muscular treatment. I have used trigger point injections and stretch and spray technic for more than 20 years. It is a technic written by Travell and Simons in the book Trigger point manual. Then I found kinesio taping and it works nicely for some of my patients and is easy and cheap. The newest treatment in my palette is fascial manipulation. It is a treatment invented by Luigi Stecco in Italy and it is used mostly for muscular pain and restriction. I use only the upper body points of fascial manipulation. It helps more if it is combined to trigger point injections. I try to work more with physical therapists to find more points in other parts of body and maybe get more permanent cure from tinnitus.

If the hearing is impaired we have to check that too. Correcting hearing by hearing aids is beneficial in two ways: it might relieve the tinnitus by itself and secondly it helps to regain the ability to hear and so it can relieve stress caused by misunderstanding. If hearing aids are not working we try a masker or other background sound.

For some people I use hypnosis treatment. We try to find calm and nice place in the patient's mind and either ask the tinnitus to leave outside of the mind or we try to mask in in the imagination to the background noise. The noise might be a street or forest or lakeside, where the patient feels herself or himself comfortable. They might use the imaginary feeling to do self-hypnosis later on.
If the patient is working in a noisy place, we have to inform the employee to correct either the surroundings or move the patient to a more suitable working place.

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P73: Tinnitus and hyperacusis therapy in a UK National Health Service audiology department: Patients' evaluations of the effectiveness of treatments.
Aazh H. (Royal Surrey County Hospital, Surrey, UK)

Objective
To assess patients' judgements of the effectiveness of the tinnitus and hyperacusis therapies offered in a specialist UK National Health Service audiology department.

Design
Cross-sectional service evaluation questionnaire survey.Patients were asked to rank the effectiveness of the treatment they received on a scale from 1 to 5 (1=no effect, 5=very effective).

Study sample
The questionnaire was sent to all patients who received treatment between January and March 2014 (n=200) and 92 questionnaires were returned.

Results
The mean score was greatest for counselling (Mean=4.7, SD=0.6) followed by education (Mean=4.5, SD=0.8), cognitive behavioural therapy (Mean= 4.4, SD= 0.7) and hearing tests (Mean= 4.4, SD=0.9). Only 6% of responders rated counselling as 3 or below. In contrast, bedside sound generators, hearing aid and wideband noise generators were rated as 3 or below by 25%, 36%, and 47% of participants, respectively.

Conclusion

The most effective components of the tinnitus and hyperacusis therapy interventions were judged to be counselling, education and CBT.g

P74: Combined amplification and sound generation for tinnitus: Scoping review.
Tutaj L[3]., Sereda M[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and hearing group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, UK, [3]Division of Audiology, Faculty of Health and Life Sciences, De Montfort University, Leicester, UK)

In most cases tinnitus is accompanied by some degree of hearing loss. Current tinnitus management guidelines recognise the importance of addressing hearing difficulties, with hearing aids being a common option. Sound therapy is the primary and preferred mode of audiological tinnitus management and refers to a wearable sound generator or hearing aid. Combination instruments provide a further option for those with an aidable hearing loss, as they combine amplification with a sound generation option.

A scoping review is being conducted to establish current knowledge around combined amplification and sound generation for tinnitus (combination devices and wireless streaming) including clinical practice, candidacy, fitting, efficacy, acceptability and patients' preferences. The review will also identify gaps in the current knowledge and explore possible research directions. Data were gathered using a systematic methodology consisting of following steps: 1) identifying potentially relevant records; 2) selecting relevant records; 3) collecting data; 4) collating, summarising and reporting the results.

An extensive search using twenty different electronic databases covered peer-reviewed and non-peer-reviewed publications, industry and professional articles, theses, conference presentations and registered clinical trials. These search strategies returned 5959 records. Duplicate records (n=2781) were excluded. Overall 163 records were retained after title/abstract review. It is estimated that around 70 records in scope will form the full set of records for data charting. A large proportion of records look at the combination device use and efficacy in the context of broader tinnitus management programmes (e.g. Tinnitus Retraining Therapy, Progressive Tinnitus Management, Tinnitus Masking, Zen Therapy).

P75: 84 over 84 consecutive patients with predominant tone tinnitus successfully treated with principles of sound wave cancellation.
Choy D., Fioretti A.F., Ludovici C.L. Zukerman Brain science and neuroscience, Columbia University, New York, USA)

Predominant tone tinnitus appeared in the Egyptian, Grecian, and Chinese medical literature; and for 6000 years has had no effective rx. There are 52 million moderate to severe sufferers in the U.S., 8 documented suicides in Portland, Oregon, and 1 billion patients worldwide. Constructive invention requires unorthodox thinking, and a dash of luck. I was trained in internal medicine and oncology @ Columbia, and had no contact with Otolaryngology. What am I doing at a tinnitus meeting? Together with 2 Italian colleagues, I was able to stop tinnitus in 84/84 consecutive pts with an average drop of 8.8 db averaging 33 months. I hold 17 patents in fields outside of tinnitus: Aeroplast, a spray-on dressing for survivors in atomic attack, the first laser knife, ultrasound imaging, coronary artery laser angioplasty, coronary angiogenesis by i.a. fgf infusion, a lvad with an intraventricular balloon assist device, multiple hearts in barosaurus and squid (lancet), percutaneous laser disc decompression in >8000 cases, and a textbook. A Robert Padden, with herniated discs, successfully treated twice, asked me to cure his "tinnitus" It was my first contact with "tinnitus." Since tinnitus will continue despite severing the 8th n, it had to be in the brain. I thought I had to manipulate the db and pitch, and at the time, only Agilent had a

physics lab machine to control db, pitch, and vibration plane. With one of these machines I had Padden self-assess his db, and pitch, and treated him for 1 hour. No effect. Two days later, his 20 year tinnitus disappeared, and lasted 10 years until his death from cancer in 2010. Hence the title: Padden-Choy procedure. Where was the luck? By chance I had landed on his plane of vibration! FDA approval was awarded in 2003. The 1 x a week by every 3 weeks x 6db (50%) produced 61% success rate ww. Then a patient from Texas called: Do I need to stay in NYC for 3 weeks? Very quickly, I answered "No, I'll treat you Monday, Wednesday, Friday - 4 days!" The success rate rose to 81% Luck! 61 to 81% when I shortened the rx period! What if I further shortened it to Monday, Tuesday, Wednesday, 3 days in a row? This was only single blind! At 2 months I could no longer wait for a full 6 months! My assistant told me: 20 out of 20! Finally 60 patients showed a full 60 and responded, falling 12.6 db; Dr Fioretti ; 15 pts, 8.9db, ludovico 4/4 8.7 db. 84/84 tells the whole story! We will not claim 100%!

P76: Acoustic coordinated reset neuromodulation tinnitus therapy based on the concept of the equivalent rectangular bandwidth.

Tass P.A[1, 2, 3]., Qian R[4]., Popelka G[5]. ([1]Institute of Neuroscience and Medicine - Neuromodulation (INM-7), Jülich Research Center, Jülich, Germany, [2]Department of Neurosurgery, Stanford University, Stanford, CA, USA, [3]Department of Neuromodulation, University of Cologne, Cologne, Germany, [4]DESYNCRA Technologies Inc., London, UK, [5]Department of Otolaryngology - Head and Neck Surgery, Stanford University, Stanford, CA, USA)

Primary tinnitus is associated with abnormal neuronal synchrony. Acoustic coordinated reset (CR) neuromodulation is a model-based stimulation technique, designed to specifically counteract abnormal neuronal synchrony by desynchronization. According to computational studies, CR stimulation induces a reduction of the rate of coincidences and, mediated by synaptic plasticity, an unlearning of abnormal synaptic connectivity.

As shown in a proof of concept study in 63 patients with chronic subjective tinnitus, acoustic CR stimulation leads to a significant clinical improvement associated with a decrease of tinnitus-related abnormal neuronal synchrony and a decrease of abnormal interactions between different brain areas. The CR-induced tinnitus relief was confirmed by two observational studies in 200 and 66 patients.

CR stimulation employs a sequential phase reset of different, interacting subpopulations involved in a synchronization process. Based on computational studies (as well as pre-clinical studies in the field of CR deep brain stimulation for motor disorders) it is known that for a given stimulation intensity the spacing between adjacent stimulation sites is crucial for the desynchronizing outcome. In the tinnitus context, hearing impairment-associated changes of tuning curves and, hence, auditory filters are relevant.

So far, acoustic CR neuromodulation employed a standard template defined by frequencies at ratios relative to the audiologically determined pitch match of the tinnitus frequency. In contrast, in this study we use the concept of the equivalent rectangular bandwidth (ERB) to design qualitatively different variants of CR tone arrangements characterized by hearing impairment-adjusted ERB overlap characteristics. To this end, we extended the basic ERB formula (for normal hearing) by incorporating hearing impairment-induced ERB broadening (for up to 50 dB HL) in accordance with previously published human data. We developed software that calculates CR tones with pre-defined ERB overlaps and adjustments for hearing threshold. We use this approach to re-evaluate previously determined clinical data in order to determine ERB overlap parameters associated with optimal clinical benefit. Our results provide testable hypotheses for improved CR tone arrangements that will be evaluated in forthcoming studies.

P77: Acute effects and acute after-effects of acoustic coordinated reset neuromodulation tinnitus therapy.

Adamchic I[1]., Toth T[1]., Hauptmann C[1]., Meister H[2]., Walger M[2, 3]., Langguth B[4, 5]., Klingmann [6]., von Wedel H[2]., Tass P.A[31, 7, 8]. ([1]Institute of Neuroscience and Medicine–Neuromodulation, Jülich Research Center, Jülich, Germany, [2]Jean-Uhrmacher-Institute for Clinical ENT-Research, University of Cologne, Cologne, Germany, [3]Department of Otorhinolaryngology, Head and Neck Surgery, Audiology and Pediatric Audiology, University of Cologne, Cologne, Germany, [4]Department of Psychiatry and Psychotherapy, University of Regensburg, Regensburg, Germany, [5]Interdisciplinary Tinnitus Center, University of Regensburg, Regensburg, Germany, Pharmaplex bvba, Wezembeek-Oppem, Belgium, [7]Department of Neurosurgery, Stanford University, Stanford, USA, [8]Department of Neuromodulation, University of Cologne, Cologne, Germany)

Primary tinnitus is associated with abnormal neuronal synchrony. Acoustic coordinated reset (CR) neuromodulation is a model-based stimulation technique, designed to specifically counteract abnormal neuronal synchrony by desynchronization. In a proof of concept study in 63 patients acoustic CR neuromodulation (with four tones centered around the tinnitus frequency within less than an octave) led to a pronounced acute and long-lasting tinnitus symptom reduction. In contrast, noisy CR-like stimulation (with tones narrowly spaced, but more remote from the tinnitus frequency, and random selection of treatment tones for each stimulation cycle) caused acute, but no long-lasting symptom relief. Accordingly, in this study we analyzed whether both stimulation protocols differed with respect to their acute effects and acute after-effects. In addition, we hypothesized that detuned CR stimulation (with fivefold slower stimulus repetition rate and stimulation tones far apart from the tinnitus frequency) has minimal or no effect on the tinnitus intensity and on oscillatory brain activity.

We measured acute effects and acute after-effects in a single-blind, single application, cross over study in 18 patients with chronic tonal tinnitus by administering three different stimulation protocols: acoustic CR neuromodulation, noisy CR-like stimulation and detuned CR stimulation as control stimulation. We measured visual analogue scale and spontaneous EEG activity pre-, during- and post-stimulation.

The three stimulation types - standard CR neuromodulation, noisy CR-like stimulation and detuned CR stimulation - differed with respect to their effect on tinnitus loudness, annoyance and the oscillatory brain activity. Acoustic CR neuromodulation caused the longest significant reduction of delta and gamma oscillatory activity in the auditory cortex region after cessation of stimulation. The noisy CR-like stimulation and the detuned CR stimulation showed changes in the oscillatory activity that differed both in strength and in time course of the changes caused by acoustic CR neuromodulation. This qualitative difference indicates that acute electrophysiological after-effects as assessed by EEG might provide a biomarker for further optimization of stimulus parameters of acoustic CR therapy, such as tone spacing and distance to tinnitus frequency. In addition, our results indicate that the detuned CR stimulation might be used as placebo/sham stimulation.

P78: Validation of a Mobile Device for Acoustic Coordinated Reset (CR®) Neuromodulation Tinnitus Therapy.

Hauptmann C[1, 2]. Wegener A[1, 2]., Poppe H[3]., Williams M[2, 4]., Popelka G[5]., Tass P.A[1, 6, 7]. ([1]Institute of Neuroscience and Medicine - Neuromodulation (INM-7), Jülich Research Center, Jülich, Germany, [2]DESYNCRA Technologies Ltd., London, UK, [3]Lifestream Creations GmbH, München/Bremen, Germany, [4]The Tinnitus Clinic Ltd., London, UK, [5]Department of Otolaryngology, Stanford University, Stanford, CA, USA, [6]Department of Neurosurgery, Stanford University, Stanford, CA, USA, [7]Department of Neuromodulation, University of Cologne, Cologne, Germany)

Sound-based tinnitus interventions utilize a variety of acoustic signals that include broad-band noise with subjectively adjusted bandwidths, environmental sounds, spectrally shaped music and a host of other stimuli, generally not specified in detail. These signals are presented via consumer devices or hearing aids.

Acoustic Coordinated Reset (CR®) Neuromodulation therapy for tinnitus has unique and more stringent requirements compared to all other sound based tinnitus interventions. These include precisely-specified tones (frequency, level and duration) based on accurate characterization of tinnitus pitch and effective delivery of patient-controlled daily therapy signals outside of the clinic. We evaluated an approach to accommodate these requirements that adapts a consumer mobile device to implement a new automated pitch matching process, patient-controlled signal delivery and outcomes recording. The evaluation included laboratory measurements of five devices and two usability studies in 30 symptomatic and 15 healthy subjects.

The acoustic characteristics of the mobile devices were nearly identical across devices and indicated high quality signals that easily met requirements. The new automated pitch matching method was validated with the mean pitch measure the same as that of a traditional manual pitch matching method (t-test, $p < 0.05$). More importantly, the variability of the automated pitch matching method was much less (f-test, $p < 0.05$) than the manual pitch matching method. After a short initial training, all subjects were able to use the mobile device effectively and to perform the required tasks without further professional assistance. We concluded that mobile devices are able to reliably and accurately deliver the required acoustic therapy signals and can be used to optimize the delivery of Acoustic Coordinated Reset (CR®) Neuromodulation therapy for tinnitus with a valid, reliable and accurate pitch matching procedure.

P79: Acoustic Coordinated Reset (CR®) Neuromodulation for the Treatment of Tonal Tinnitus.

Hauptmann C[1, 2]. Qian R[2]., Williams M[2, 3]., Haller M[3, 5]., Tass P.A [1, 4, 5]. ([1]Institute of Neuroscience and Medicine - Neuromodulation (INM-7), Jülich Research Center, Jülich, Germany, [2]DESYNCRA Technologies Ltd., London, UK, [3]The Tinnitus Clinic Ltd., London, UK, [4]Department of Neurosurgery, Stanford University, Stanford, CA, USA, [5]Department of Neuromodulation, University of Cologne, Cologne, Germany)

Primary tinnitus has a severe negative influence on the quality of life of a significant portion of the general population. Acoustic Coordinated Reset (CR®) Neuromodulation is designed to induce a long-lasting reduction of tinnitus symptoms [1,2]. To test Acoustic Coordinated Reset (CR®) Neuromodulation as a treatment for chronic, tonal tinnitus under real–life conditions, several clinical trials were commissioned in the last years [2-4].

In a randomized controlled trial and two observational studies more than 300 patients were treated and a statistically and clinically significant reduction of tinnitus symptoms as measured by TQ, THQ, TBF-12 and VAS was observed [2-4].

In the first randomized controlled proof of concept trial (RESET), which reported therapy outcomes in 63 subjects, baseline TQ scores were reduced by 28.8% ($p<0.01$) after 12 weeks of therapy [2]. In a large scale observational trial (RESET REAL LIFE), with a study population of 200 patients, a reduction of 37.9 % ($p<0.01$) was recorded, with respect to TBF-12 scores, after 12 months of therapy [3]. At the London based Tinnitus Clinic 61 patients were studied and THQ scores significantly improved by 19.4% after 22-26 weeks of therapy [4]. These findings are supported by data obtained from field use. This collection of data demonstrates that Acoustic Coordinated Reset (CR®) Neuromodulation is a safe and well accepted therapy for patients.

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P80: Tinnitus and hyperacusis therapy in a UK National Health Service audiology department: Patients' evaluations of the effectiveness of treatments.

Aazh H. (Royal Surrey County Hospital, Surrey, UK)

Objective
To assess patients' judgements of the effectiveness of the tinnitus and hyperacusis therapies offered in a specialist UK National Health Service audiology department.

Design
Cross-sectional service evaluation questionnaire survey.Patients were asked to rank the effectiveness of the treatment they received on a scale from 1 to 5 (1=no effect, 5=very effective).

Study sample
The questionnaire was sent to all patients who received treatment between January and March 2014 (n=200) and 92 questionnaires were returned.

Results
The mean score was greatest for counselling (Mean=4.7, SD=0.6) followed by education (Mean=4.5, SD=0.8), cognitive behavioural therapy (Mean= 4.4, SD= 0.7) and hearing tests (Mean= 4.4, SD=0.9). Only 6% of responders rated counselling as 3 or below. In contrast, bedside sound generators, hearing aid and wideband noise generators were rated as 3 or below by 25%, 36%, and 47% of participants, respectively.

Conclusion
The most effective components of the tinnitus and hyperacusis therapy interventions were judged to be counselling, education and CBT.g

P81: Tinnitus support groups - a survey of their effectiveness.

White L., Wray N.M. (British Tinnitus Association, Sheffield, UK)

Introduction
In around 1% of adults, tinnitus may affect quality of life. Access to reliable information, ongoing support and reassurance are key elements in the management and treatment of tinnitus. Tinnitus support groups can play a role in the delivery of these functions.

The British Tinnitus Association (BTA) maintains a network of over 60 tinnitus support groups around the UK. However, we have not previously undertaken any research to evaluate the effectiveness of tinnitus support groups.

Method
The BTA distributed a survey to all of the support groups in the BTA network and to all BTA members in Autumn 2014 designed to assess how attendance at a support group meeting has impacted on the individual's experience and management of tinnitus, general wellbeing and quality of life. We received 100 responses from people who had attended a support group meeting.

Results
After attending a support group:
85% of respondents felt it had helped them with their tinnitus
78% of respondents reported an improved ability to manage their tinnitus
98% of respondents gained a sense of reassurance
94% of respondents experienced an improvement in emotional wellbeing
82% of those surveyed reported an improved relationship with family and friends
94% respondents reported a reduction in feelings of isolation

Discussion
Whilst acknowledging the limited data available, these results indicate that attending a support group can be beneficial for some people with tinnitus in terms of their general wellbeing and emotional health, as well as their ability to understand and manage the condition itself.

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P82: Use of Slow Cortical Potential Neurofeedback in chronic tinnitus treatment.
Milner R., Lewandowska M., Ganc M., Ciesla K., Niedzialek I., Skarzynski H. (World Hearing Center, Institute of Physiology and Pathology of Hearing, Kajetany/Warsaw, Poland)

The study is the first to demonstrate outcomes of Slow Cortical Potential (SCP) Neurofeedback training in chronic tinnitus. A 50-year old male who had suffered from tinnitus for 8 years participated in training. He learned how to self-regulate SCPs and change the cortical excitability threshold of his own brain. It was assumed that this method would attenuate the abnormal tinnitus-related brain activity, as well as improve the clinical state of the patient. The results of the SCP Neurofeedback training were evaluated with use of a number of research tools, including a detailed clinical interview, the Tinnitus Functional Index, measurement of tinnitus characteristics with an in-house software program *Tinnitus* and quantitative electroencephalography analysis (qEEG). It was found that the SCP Neurofeedback training had a positive effect on tinnitus perception and the patient reported reduction of its loudness and pitch. Positive changes have also been demonstrated in several domains of patient's daily life. Most apparent

improvements were present with respect to quality of sleep, the ability to relax as well as cognitive, auditory and social aspects of daily functioning. The qEEG analysis revealed that the behavioral improvement was accompanied with beneficial changes in the patient`s resting state brain activity. After the SCP training, the power of different brain waves in Delta, Theta, Alpha and Beta ranges were close to normal in brain regions (mainly in the left hemisphere) reported as crucial in tinnitus generation.
The present case study, therefore, indicates that SCP Neurofeedback training may improve numerous tinnitus-related symptoms and can be considered a promising method for tinnitus treatment.

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P83: Understanding user reactions and interactions with an internet-based intervention for tinnitus self-management: A mixed methods process evaluation.

Greenwell K[1]., Sereda M[1]., Coulson N[2]., Hoare D[1]. (NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [1] University of Nottingham, Nottingham, UK)

Introduction
Internet-based interventions have the potential to reduce the disparity in access to psychological support that people with tinnitus currently experience. However, we have little understanding on how people with tinnitus use and react to these interventions. This research will explore users' reactions to and interactions with the Tinnitus E-Programme, an internet-based intervention for the self-management of tinnitus which is currently available online.

Methods
Two parallel mixed methods studies were carried out with two different populations. Study 1 used an online survey to gather past and current users' views of the programme (N = 30). In Study 2, 13 new programme users took part in an interview and completed a relaxation log to explore how well they were able to enact the skills they learnt in their everyday lives. Thematic analysis and descriptive statistics were used to analyse the qualitative and quantitative data, respectively.

Results
Overall, findings suggest that the programme was acceptable to its target population. In Study 1, 90% of users reported that the programme had benefited them. Users in both studies particularly valued the education about tinnitus and its management, relaxation skills training and cognitive restructuring training. Usage of tools to self-monitor levels of tinnitus distress and the online support group was variable and less acceptable to users. Participants appreciated being able to work flexibly with the programme and engaging with the materials 'offline'. The relaxation log data implies that some users found it difficult to meet the daily relaxation goals.

Discussion
Findings suggest that acceptability was high among the target group. They also highlighted some key areas for improvement. Mainly, enhancing usability and user autonomy and removal of underutilised components. Following Yardley et al.'s (2015) person-based approach, findings will inform the common guiding principles for future intervention optimisation work.

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P84: A new combination hearing aid for tinnitus management: feasibility of evaluation, usability and acceptability.

Sereda M[1, 2]., Davies J[3]., Hall D.A[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, [2]Otology and hearing group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, UK, [3]Division of Audiology, Faculty of Health and Life Sciences, De Montfort University, Leicester, UK)

Introduction
Sound therapy is the primary and preferred mode of audiological tinnitus management and refers to a wearable sound generator or hearing aid. Recent innovations in hearing aid technology have seen the arrival of combination devices: hearing aids with built-in sound generators. Combination devices offer amplification and masking sound for when a patient needs amplification for a hearing loss and also additional sound to reduce the perception of tinnitus.

Methods
The current study retrospectively analysed the data collected as part of an exploratory study to examine the feasibility of conducting a clinical trial on the clinical efficacy of combination devices for tinnitus. Eight experienced combination device users (mean age 67.25 years) wore a pre-market version of the Oticon Alta with Tinnitus Sound Generator for two weeks. They were asked to try four different programmes (amplification only; amplification and sound generation with manual volume control; the same with level steering; amplification with nature sound) in different listening situations. Open-ended and closed questionnaires explored the issues around participant recruitment, acceptability, programme preferences in different self-nominated listening situations, usability and compliance.

Results
Findings from these data enable the following recommendation to be made: 1) For optimal recruitment future studies should consider extending the inclusion criteria to current conventional hearing aid (amplification only) users or those who do not currently use any devices to manage their tinnitus; 2) The candidacy criteria and outcome measures should be tailored according to the intended mechanism of action of the sound used; 3) The acceptability and role of different sounds in providing tinnitus relief should be investigated alongside efficacy; 4) The fitting protocol should be sufficiently flexible to accommodate individual needs and preferences; 5) A service evaluation to explore common practices and differences between UK clinics should be conducted.

Discussion
Flexibility of fitting according to individual needs and preferences calls for more pragmatic clinical trial design.
The study was funded by Oticon A/S.

P85: Objective tinnitus due to myoclonus - can counselling help?

Lim J.J[1]., Wai Y.H[1]., Lu P.K[1]., Koh D.S[1, 2, 3]. ([1]Changi General Hospital, Singapore, [2]PAPRSB Institute of Health Sciences, University Brunei Darussalam, Brunei, [3]Saw Swee Hock School of Public Health, National University Health System, National University of Singapore, Singapore)

An 11 years old boy, presented at our tinnitus counseling clinic with a history of bilateral clicking tinnitus for 4 years. The clicking tinnitus was heard continuously and could be heard by others who were close to his ear region. The tinnitus became more intense and rapid when triggered by factors such as noisy environments, vigorous exercises and when feeling unwell. The child was distressed as it affected his daily life and school activities. He previously had a tonsillectomy two years ago when he was about 9 years old. There was no clicking tinnitus post-operatively for a year but after a bout of fever, the clicking tinnitus recurred.

On examination, the clicks were objectively heard by examiner, and appeared to be loudest behind each ear. No visible movements of the tympanic membrane were noted. Direct examination of soft palate showed contractile movements of the soft palate. Fiberoptic nasopharyngoscopy confirmed synchronised contraction of the Eustachian tube opening together with palatic myoclonic movements bilaterally. Pure-tone audiometry were within normal limits (<20dB HL bilaterally) and both ears had a type A tympanograms. Magnetic resonance imaging of the brain and internal auditory meatus indicated no abnormal findings. The ENT surgeon suggested that for this case of palatal and middle ear myoclonus, counselling would be helpful. Surgical intervention could be performed when the tinnitus become unbearable.

We explained the nature of the palatal and middle ear myoclonus to the patient and his mother and reassured them that the sound will not cause major harm. We educated both mother and child on self-help coping strategies such as sound strategies, distraction activities and relaxation techniques. One month after counselling, the mother reported the child was happier and learning to accept his tinnitus as a normal sound. The child was also able to identify specific trigger factors such as being unwell and examination stressors, which changed his clicking tinnitus to a different pitch.

While the treatment of myoclonus can include medication (e.g. carbamazepine or anxiolytics), botulinum injections or resection of the affected muscles, counselling of patients is often beneficial in the treatment of objective tinnitus. Counselling is helpful after initial diagnosis, as well as for management of residual tinnitus after medical or surgical intervention.

P86: ---Poster withdrawn---

P87: Electroacupuncture therapy on different types of tinnitus patients based on objective audiologic evaluation.

Wang T-C[1]., Lin C.D[1,2]., Huang C.H[3]. Tsai M.H[1, 2].([1]Department of Otolaryngology-Head and Neck Surgery, China Medical University Hospital, Taiwan, [2]School of Medicine, China Medical University, Taichung, Taiwan, [3]Department of Acupuncture, China Medical University Hospital, Taiwan)

Acupuncture has been used to treat tinnitus for a long time. Up to now, all we know about tinnitus are far less than what we don't know. Patients who suffer from tinnitus but have no response to the common therapies are turning to complementary or alternative medical therapies, such as acupuncture. There is not enough evidence for supporting acupuncture as a treatment option recommend by otolaryngologists. This study aims to assess the efficacy of electroacupuncture in tinnitus combing hearing loss.

This study compares two groups with real electroacupuncture and sham acupuncture. We recruited persons with a history of chronic tinnitus and combining mild to moderate hearing loss. In the study, the patients will be randomly assigned into two groups according to a computer-generated randomization list and assessed prior to treatment. Then they will receive 24 acupuncture treatments in 8 consecutive weeks and undergo a 4-week-follow-up period. The administration of acupuncture follows the guidelines for clinical research on acupuncture (WHO Regional Publication, Western Pacific Series Number 15, 1995), and is performed double-blind by physicians well-trained in acupuncture. The measures of outcome include the subjective symptoms scores by questionaires and objective clinical examinations on audiology.

P88: Patient and clinician experiences about the impact of tinnitus on post-operative assessments in cochlear implant clinics.

Corner C[1, 2]., Kitterick P.T[1, 2]., Pierzycki R.H[1, 2]. ([1]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK, UK, [2]Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK)

Objectives

The impact of tinnitus on cochlear implant (CI) programming appointments was explored in a mixed-methods study. The study addressed three questions prompted by the literature on the clinical experience of managing CI patients: (1) What aspects of programming appointments are more difficult to conduct due to tinnitus?; (2) If used, what specific strategies are considered to be most effective for dealing with these difficulties; (3) Is there a need for specific programming guidelines for CI recipients presenting with tinnitus?

Methods

The study used semi-structured interviews with clinicians and a survey of adult CI patients. The interviews were conducted with six CI audiologists working across two large UK implant centres. The interviews included questions in three broad areas mirroring the study objectives. The surveys were sent out to 400 CI patients of the Nottingham Auditory Implant Programme and asked patients whether they felt their tinnitus affected the programming appointments when their implant was first activated, at 6 to 12-month follow-up, and during their most recent appointment. Interviews and free text sections of the survey were analysed thematically using an inductive approach.

Results

All clinicians felt that setting the lower stimulation limits for CI electrodes (threshold levels) was the aspect of programming most affected by tinnitus. The two main strategies employed to overcome this were redirecting the patient's attention and using specific methods to enable completing aspects of programming within the appointment. Despite difficulties with establishing threshold levels in patients with tinnitus, clinicians felt that little would be gained from arranging longer or additional appointments. Instead, they unanimously agreed that increasing the amount of hearing therapy for the patient would bring more benefit. Although four of the six clinicians thought that some guidance on programming with tinnitus would be useful, a recurring theme was that practice is highly dependent on individual patient needs and so flexibility and experience are essential. Notably, all clinicians were of the opinion that implantation often suppresses tinnitus and that those benefits outweigh the difficulties that can arise during programming appointments.

To date, 57 patients have responded to the survey (14.2% response rate). Approximately 50% of patients expressed an opinion about whether or not their tinnitus interfered with appointments. Among those that did, 37% felt that their tinnitus interfered during CI activation appointment, 34% at

appointments between 6 to 12 months after activation, and 29% at the most recent appointments. The analysis of the free text sections also identified many tinnitus-related issues that were in close alignment with those identified in the clinician interviews.

Conclusions
While tinnitus does not interfere with implant programming in a majority of patients, the present results suggest that tinnitus can have disruptive effects in some patients and in particular for the estimation of threshold levels. Clinicians appear to have developed strategies to achieve a satisfactory programming result in spite of these difficulties. Guidelines may be useful and acceptable as long as they do not diminish the role of clinical experience in CI programming.

Epidemiology & modelling

P89: Watchful waiting and tinnitus: a systematic review and meta-analysis.
Phillips J[1, 2]., McFerran D[1, 2]., Hall D.A[3]., Hoare D[3]. ([1]Norfolk & Norwich University Hospitals NHS Foundation Trust, Norwich, Norfolk, UK, [2]Colchester Hospital University NHS Foundation Trust, Clolchester, UK, [3]NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK)

Introduction
Part of the counselling provided to tinnitus patients by tinnitus practitioners involves reassurance that both the perception of the tinnitus sounds and the emotional impact of tinnitus will improve in time. However, although this may indeed be true, the data to both support the validity of this statement and quantify any improvement in symptoms has not yet been comprehensively synthesised from the literature. The primary aim of this study was to quantify the change in tinnitus self-report that occurs during watchful waiting.

Methods
A systematic literature search was conducted using CINAHL, PsycINFO, EMBASE, ASSIA, PubMed, Web of Science, Science Direct, and EBSCO Host, and the search terms 'tinnitus AND waiting OR wait* OR waiting-list OR watchful OR observation'. This was supplemented with hand searches. Studies were included if they reported a participant group who had repeated measures on a tinnitus measurement questionnaire but who received no intervention between measures, typically waiting list or non-interventional control groups. Data were extracted independently by two authors and synthesised using meta-analytic techniques. Percentage of change and standard mean difference effect sizes were calculated for the reported time interval.

Results
Twenty-five studies, involving 977 participants with tinnitus but receiving no intervention, were suitable for inclusion. The watchful waiting period varied from 1-52 weeks, with an average of 12 weeks. Across all studies there was a decrease in tinnitus questionnaire score of 2.3%, equating to a statistically significant small mean within-group effect size (Hedges' g = 0.13). The size of effect appeared to be affected by time; at an average interval of 8 week Hedges' g = 0.16, at 16 weeks it was 0.12, and at longer average intervals it was 0.04.

Discussion

Participants in research studies generally demonstrate an improvement in self-reported tinnitus severity scores over time despite receiving no intervention. This provides statistical evidence that tinnitus does indeed improve over time. However, this effect is highly variable across individuals. Effects also seem to decrease when there is a longer interval between measurements. This is likely a limitation of the measurement instruments.

P90: Computational model of tinnitus from the cochlea to the dorsal cochlea nucleus.

Gault R[1]., McGinnity T.M[1, 2]., Coleman S[1]. ([1]Ulster University, Coleraine, Londonderry, Northern Ireland, [2]Nottingham Trent University, Nottingham, UK)

Computational models of tinnitus have been able to illuminate the potential underlying mechanisms which generate the phantom sound. However to date computational models of tinnitus have focused on a localised segment of the auditory system with no detailed models of the cochlea included. A detailed model of cochlear processing would make it possible to experiment with a variety of complex sound stimuli in order to investigate their effects on the underlying mechanisms of tinnitus. This work presents a new firing rate model of tinnitus that incorporates a detailed model of the cochlea and the early stages of the auditory periphery, including the dorsal cochlear nucleus. The model of the cochlea is based on previous work by Zilany et al. [1] and incorporates an audiogram function to approximate the inner and outer hair cell impairment factors needed to model the cochlear processing for a given audiogram. The auditory nerve fibres provide input to a network of model neurons, replicating the behaviour of the dorsal cochlear nuclei, which uses homeostatic plasticity to modulate the synaptic gain. In regions of hearing loss the gain adaption generates hyperactivity within the auditory system as seen in other tinnitus models [2]. Masking devices used in tinnitus treatment often contain white, pink or red noise. These masking sounds provide auditory stimulus for this new tinnitus model and their efficacy of subduing the increase in auditory gain is accessed. This work builds upon previous tinnitus models by including a model of the cochlea thus allowing for the investigation of the effects of complex sound stimuli on the underlying mechanisms of tinnitus. This model replicates basic tinnitus behaviour. By fitting the model to a tinnitus sufferer's audiogram it is hoped that the model can be used to suggest the most beneficial sound therapy for the tinnitus sufferer.

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P91: Investigating the Non-Monotonic Relation between Cochlear Damage and Central Hyperactivity with a Computational Model.

Schaette R. (UCL Ear Institute, London, UK)

The development of tinnitus can be linked to hearing loss in the majority of cases, but it has remained unclear why hearing loss not always leads to tinnitus. In animal studies it has been shown that cochlear damage through exposure to noise or ototoxic drugs generates elevated spontaneous firing rates in the dorsal and ventral cochlear nuclei, the inferior colliculus, and the auditory cortex. As this neuronal hyperactivity has been linked to behavioural signs of tinnitus, it is regarded as a potential neural correlate of tinnitus. Moreover, animal and modelling results indicate that the degree

of hyperactivity may be proportional to the hearing threshold increase, suggesting that more severe cochlear damage might be more likely to cause tinnitus.
However, the relation between cochlear damage and hyperactivity could be non-monotonic. In a mouse model, we have recently found that noise exposure that only causes "hidden hearing loss" can lead to a stronger increase of spontaneous firing rates in the inferior colliculus than a more severe exposure causing permanent elevation of hearing thresholds (Hesse et al., 2015). Moreover, there is also a nonlinear relation between cisplatin-induced hair cell loss and hyperactivity in the dorsal cochlear nucleus (Kaltenbach et al., 2002): hyperactivity was proportional to the degree of outer hair cell loss for low doses of cisplatin that did not cause inner hair cell loss, whereas additional inner hair cell loss decreased hyperactivity.

Here we use a computational model to investigate the relation between cochlear damage and neuronal hyperactivity in the central auditory system. The model is based on the assumption that in attempting to stabilize neuronal activity following hearing loss, homeostatic plasticity elevates neuronal response gain in the central auditory system, thereby generating increased spontaneous firing rates through over-amplification of spontaneous activity. With the model, we explored a multi-dimensional parameter space of damage parameters spanning the degree of auditory nerve fibre (ANF) deafferentation, the pattern of deafferentation (i.e. low, medium and high spontaneous ANFs), the degree of hearing loss (threshold increase), and the degree of hair cell loss.

The model results indicate that the non-monotonicities in the relation between cochlear damage and neuronal hyperactivity might be due to different degrees of deafferentation of ANFs with high spontaneous firing rates and/or different degrees of loss of inner hair cells: both these types of cochlear damage decrease the overall spontaneous activity of the auditory nerve, which effectively reduces the "substrate" for generating hyperactivity through over-amplification of spontaneous activity, and therefore decreases neuronal hyperactivity. The same degree of elevation of hyperactivity can thus be generated by different types of cochlear damage, and trajectories exist through the "cochlear damage space" where more damage can even lead to a reduction in spontaneous neuronal firing rates in the central auditory system. Some specific patterns or configurations of cochlear damage might then be more likely to lead to tinnitus than others, offering an explanation why hearing loss not always leads to tinnitus.

P92: Neurofunctional Tinnitus model: Cognitive model of tinnitus development from neutral phantom sound to clinical distress.
Toostani I.G.[1], Zana Y. [2], Delbem A.C.B. [1,3], Sani S.S. [4], Ekhtiari H. [5], Sanchez T.G. [6,7] ([1] USP - Interunidades Bioengenharia (EESC/FMRP/IQSC), Universidade De São Paulo, São Carlos, SP, Brazil; [2]Universidade Federal do ABC, Cognitive and Complex Systems Unit, São Paulo, Brazil; [3] USP-Institute of Mathematics and Computer Science, Universidade De São Paulo, São Carlos, SP, Brazil; [4] WHO research- World Hearing Organization, San Jose, CA, USA; [5]ICSS - Iranian Institute for Cognitive Sciences Studies, Tehran, Iran; [6]USP-Faculdade de Medicina da Universidade de São Paulo, SP,Brazil; [7]Instituto Ganz Sanchez, São Paulo, Brazil.)

Our knowledge about tinnitus physiopathology has improved in the last decades, but we still lack information about the main mechanisms that lead a neutral phantom sound to transform in tinnitus distress. Non-causal association of clinical distress with neutral phantom sound specifications can be explained by the brain cognitive evaluation conditioning processes On the other hand, cognitive and emotional appraisal emerge as reactions to the differences between the information stored in memory and the actual information.
We aim to present the Neurofunctional Tinnitus Model (NTM) to fill in the gaps about tinnitus distress. NTM cognitively hypothesizes that: A) patients have no intuitive understanding of tinnitus signal; thus, the risk of negative appraisal increases. One of the crucial causes of appraisal is the patient's hypochondriac impression of neutral phenomena [1-3], like the fear of the unknown. B) Negative symptoms related to tinnitus emerge during a stage

when tinnitus is neutral and there is an Evaluative Conditioning (EC) learning procedure. When presented in association with a negative or positive Unconditioned Stimulus (US), EC can change the liking of the cognitive-emotionally neutral Conditioned Stimulus (CS). Such change is the retained response to the previously neutral stimulus [4].
The model projects that the pathways of tinnitus distress start with convergence of CS and US pathways in prefrontal cortex (PFC), leading to plasticity of ventromedial prefrontal cortex (VMPFC) and lateral prefrontal cortex (LPFC), as well as medial geniculate nucleus (MGN) and lateral nucleus of amygdala (LA) from thalamic and cortical processing regions in the sensory systems that process the CS (Auditory system) and US (cognitive-emotional mechanism). The MGN projects into auditory cortices. It also receives inhibitory input from thalamic reticular nucleus (TRN). The LA then connects with the central nucleus of amygdala (CE) directly and also by the way of other amygdala regions. Outputs of the CE then control the expression of fear responses and related autonomic nervous system (e.g., heart rate) and endocrine (pituitary adrenal hormones) responses. We present empirical evidence from using electrophysiology, neuroimaging, brain lesion and behavioral methods to strengthen the Neurofunctional tinnitus model. This model represents an advance in our understanding of clinically-significant tinnitus symptoms and might eventually help to improve current treatments.

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P93: Decision support system can improve accuracy and time efficacy evaluation of tinnitus psychoacoustic parameters.

Toostani I.G[1]., Jalilvand H[2]., Delbem A.C.B[1,3]., Sanchez T.G[4,5]., ([1]USP - Interunidades Bioengenharia (EESC/FMRP/IQSC), Neurocognitive Engineering Lab, Universidade De São Paulo, São Carlos, Brazil, [2]Shahid Beheshti medical Sciences University, Department of Audiology, School of Rehabilitation Sciences, Iran, Tehran, [3] USP- Institute of Mathematics and Computer Science, Universidade De São Paulo, São Carlos, Brazil, [4]USP-Faculdade de Medicina da Universidade de São Paulo, SP,Brazil; [5]Instituto Ganz Sanchez, São Paulo, Brazil)

Introduction

Psychoacoustic measurements of tinnitus is one of the relevant outcomes to evaluate the benefit of several types of tinnitus treatments. Determining the tinnitus pitch and loudness using the audiometer is often a difficult and imprecise task. Moreover, it is also time demanding because the examiner can only give the patient two different sound stimuli at a time to be compared with his own tinnitus pitch, what sometimes makes patients tired and unsure about the best comparison. So, in order to be faster and accurate, it would be recommended to develop new ways of testing psychoacoustic measurements

Objective

To find an interactional intelligent algorithm in order to help clinicians to determine the tinnitus pitch match and loudness.

Methodology

We are developing the machine learning process to project patient's audiological data to predict the tinnitus pitch. In the present pilot stage, pitch has been classified into high (>3000Hz) and low (<3000Hz) frequency in each ear.

The model was developed in MTLAB and WEKA by several well-known classification approaches, especially Naïve Bayesian, logistic transform function and decision trees J48(DTJ48). We trained our classifier with the data of 817 patients belonging to tinnitus centers in Tehran, Iran and São Paulo, Brazil. This is part of a running multicenter project about Multidisciplinary Tinnitus Rehabilitation (MTR). Such data include a) pure tone audiometry from 250 to 8000Hz, b) speech tests, and c) tympanometry in both ears independently. We applied 10 fold cross-validation to have better training and prevent over-fitting of data in all applied methods.

Results and Conclusions
Naïve Bayesian, logistic transform function and DTJ48 respectively reaches to 76, 78.5 and 84.8% of accuracy. DTJ48 illustrated the fastest and better performance to apply for real-time algorithm for future approach as well. The next step is to obtain more precision for tinnitus pitch matching and improve the algorithm for future activities.

P94: A 'precision' model of tinnitus.
Sedley W.[1], Gander P.E.[2], Kumar S.[1, 3], Griffiths T.D.[1, 3] ([1]Newcastle University, Newcastle, UK, [2]University of Iowa, Iowa, USA, , [3]University College London, London, UK)

Tinnitus predominantly results from peripheral hearing loss, though in many cases this is mild, and many cases of hearing loss do not develop tinnitus. Theoretical mechanisms largely fall into four groups, proposing that tinnitus is generated by either: deranged nerve firing in the auditory periphery; enhanced gain subcortically due to deafferentation; hyperpolarised thalamic burst firing; cortical deafferentation leading to perceptual filling in from memory. Presently, all of these mechanisms are supported by some evidence, though none provides a complete account, and there are fundamental incompatibilities between them. This new model uses the computational quantity of 'precision', within a Bayesian inference framework, to unite these mechanisms into a single comprehensive account of tinnitus, which can potentially explain several unsolved paradoxes in tinnitus research, and makes testable hypotheses about future investigation and treatment.

Preclinical interventions

P95: Comparison the long-term effect of positioning the cathode in tdcs in tinnitus patients.
Rabau S[1, 2]., Shekhawat G.[23, 4]., Aboseria M[5]., Van Rompaey V[1, 2]., Bikson M[5]., Van de Heyning P[1, 2]. ([1]Faculty of Medicine, Campus Drie Eiken, University of Antwerp, Antwerp, Belgium, [2]University Department of otorhinolaryngology and Head & Neck surgery, Antwerp University Hospital, Edegem, Belgium, [3]Section of Audiology, University of Auckland, New Zealand, [4]Centre for Brain Research, University of Auckland, New Zealand, [5]Department of Biomedical Engineering, The City College of the City University of New York, New York, NY, USA)

Transcranial direct current stimulation (tDCS) is one of the methods described in the literature to decrease the perceived loudness and experienced distress of tinnitus. However, the main effect is not clear and the amount of responders is variable. The objective of the present study was to investigate the effect of the placement of the cathode on the outcome measurements.

Patients considered for the trial were chronic non-pulsatile tinnitus patients with a Tinnitus Functional Index (TFI) score that exceeded 25. The anode was placed on the right dorsolateral prefrontal cortex (DLPFC). In the first group 'bifrontal' cathode was placed on the left DLPFC. While in the second group 'shoulder' the cathode was placed on the shoulder. Each patient received 2 sessions tDCS every week and in total 8 sessions. Evaluations took place at the first visit on the ENT-consultation, at the start of therapy, after 8 sessions of tDCS and at last the follow-up visit took place after 84 days of the start of the therapy. Subjective outcome measurements such as TFI and Visual Analogue Scales of loudness (VAS) were administered in every patient.

No significant differences were found for tinnitus loudness and the experienced distress between the placement of the cathode. Also, no significant overall effect was found between the four test moments. In the bifrontal group 16% and in the shoulder group 8.4% of the subjects showed a clinical significant improvement of more than 13 points. 56% in the bilateral group and 37.8% in the shoulder group showed an improvement less than 13 points on the TFI. We can conclude that the placement of the cathode doesn't change the outcome of tDCS. Further research should rule out what is causing the variability of responders and the parameters that can improve the long-lasting effect of tDCS.

P96: The influence of ear electrical stimulation on EEG in tinnitus patients – A Pilot Study.
Mielczarek M., Michalska J., Olszewski J. (Department of Otolaryngology, Laryngological Oncology, Audiology and Phoniatrics, Medical University of Lodz, Poland)

The application of electrical stimulation of the ear in tinnitus treatment started in the 70's of XX century. At first invasive, then non- invasive electrical stimulations of the hearing organ had been used in tinnitus treatment. When invasive techniques were used (transtympanal stimulations of the round window, promontorium or via cochlear implant) the results appeared more satisfactory comparing to non-invasive stimulations (of the mastoid, tympanic membrane or when stimulating electrode was dipped in external acoustic canal filled with saline). Nowadays electrical stimulation is used as a test to predict post-operative profits before cochlear implantation. During non-invasive extratympanic ear stimulation (via ball-shaped electrode dipped in external ear canal in saline) sound perception is considered an evidence of acoustic nerve excitation (proving in the same time it's restored function). Despite different forms of non-invasive electrical stimulations, the actual mechanism in which it influences tinnitus remains unclear.

The aim of the study was to determine how/whether electrical stimulation influences brain activity, and to determine whether change in tinnitus after electrical stimulation was associated with a change in brain activity recorded in EEG.

Material and methods
The material of the study was a group of 12 tinnitus patients (6 patients with unilateral, and 6 - with bilateral tinnitus, 6 females and 6 males). Before the beginning of the study, ENT examination, hearing tests, and radiological diagnostics were performed. Pathology in the external and/or the middle ear, as well as central nervous system disorders (e.g. epilepsy) were excluding criteria. Patients who reported tinnitus in the head, not in ears, were also disqualified from the research.

Electrical stimulation was performed with the use of a custom made device supplied with 4 batteries of 1.5 V. The external ear canal was filled with saline solution. The active, silver probe – was immersed inside external ear canal, avoiding contact with the skin of the canal. The passive electrode was placed on the forehead after skin abrasion. Direct rectangular negative current was applied via the active electrode. The voltage was constant and equals 3V. In all the cases stimulating frequency was 250Hz, the intensity ranged from 0.14 to 1.08 mA, and was applied according to patient's sensation.

The EEG recording (Deymed QEST 32) was performed before and after electrical stimulation. Patients was asked to assess the intensity of tinnitus in visual analogue scale before and after electrical stimulation.

Results
the authors compared EEG recordings before and after electrical stimulations. The assessment was performed with regard to the effect of electrical stimulation on tinnitus.

Conclusions
As the peripheral hearing organ is the most probable site of tinnitus origin, peripheral extra- or cochlear electrical stimulations seem to be a reason-based management. On the other hand the literature describes alterations at cortical and subcortical level which justify the therapy aimed at neuromodulation.

P97: Acute effect of transcutaneous vagus nerve stimulation (tVNS) on tinnitus related mental stress as measured by heart rate variability (HRV) test.
Lehtimäki J[1]., Ylikoski J[1]., Szibor A[2]., Hyvärinen P[2]., Ylikoski M[2]., Aarnisalo A[2]., Mäkitie A[2]. ([1]Helsinki Ear Institute, Helsinki, Finland, [2]Department of Otolaryngology-Head and Neck Surgery, University of Helsinki, Helsinki, Finland)

Background
The main problem of patients with disturbing moderate or severe tinnitus is tinnitus related mental stress (TRMS), that is associated with imbalance of the autonomous nervous system (ANS) and reduced parasympathetic activity. Therefore, the optimal treatment of TRMS would be by tropotrophic means such as biofeedback, yoga, cognitive behavioral therapy and relaxing music, which all aim at activation of the parasympathetic system. As vagal nerve is responsible for the parasympathetic function its stimulation might be an additional and novel possibility to maintain balance in ANS. Conventionally, vagal nerve stimulation (VNS) has been performed to treat severe epilepsy and depression with an implanted electrode. VNS as an invasive procedure is however, not suitable for tinnitus treatment. It has been recently shown by functional MRI, MEG and EEG recordings that transcutaneous VNS (tVNS) of the auricular branch of the vagus nerve (ABVN) activates the central vagal pathways in a similar way as an implanted VNS. We have previously shown in a magnetoencephalography study, that tVNS modulates auditory N1m –responses in the auditory cortex.

Patients and Methods
We analyzed ANS function by testing heart rate variability (HRV) in 64 tinnitus patients immediately before and after a 20-60 min tVNS stimulation.

Results

The pretreatment HRV recording showed reduced parasympathetic activity in about three quarters (73%) of patients. Active tVNS significantly increased variability of R-R intervals in 75% of patients and HRV-age was decreased in 78% of patients. Either the variability of R-R intervals was increased or the HRV-age decreased in 95% of the patients. These results indicate a shift in ANS function toward parasympathetic predominance. tVNS caused no major morbidity and heart rate monitoring during the tVNS treatments showed no cardiac or circulatory effects (e.g. bradycardia) in any of the patients.

Conclusion
This study shows that tVNS seems to increase HRV and thus parasympathetic activity which is desirable in conditions characterized by enhanced sympathetic nervous system activity, such as TRMS. May be the most important strategic goal for successful tinnitus therapy, is to diminish tinnitus related mental distress. Even more importantly, tVNS showed no morbidity in our series.

P98: Daily transcranial random noise stimulation of the temporal cortex in chronic tinnitus.
Schecklmann, M., Kreuzer P.M.K., Poeppl T.B.P., Langguth B.L. (University of Regensburg, Department of Psychiatry and Psychotherapy, Germany)

Background
Hyper-activity and hyper-synchronicity of auditory areas are involved in the pathology of chronic tinnitus. Transcranial random noise stimulation (tRNS) – a non-invasive electric brain stimulation method – was recently shown to be able to reduce tinnitus loudness and distress after single sessions in big samples and after daily sessions of tRNS in one small sample. For the first time, we investigate the tolerability and efficacy of daily sessions of tRNS in a bigger sample of chronic tinnitus.

Methods
In this one-arm study, thirty patients receive high-frequency tRNS of the left and right temporal cortex consisting of ten daily sessions. Efficacy variables of interest are tinnitus questionnaires, tinnitus numeric rating scales, depressivity, and quality of life. Tolerability variables of interest were side effects (standardized questionnaire) and neuropsychological tests for attention and working memory. Results will be compared to results of a historical control group having received repetitive transcranial magnetic stimulation with the same treatment scheme (ten stimulation days, same number of visits).

Results
The trial is registered (ClinicalTrials.gov identifier: NCT01965028). The last visit will be done in January 2016. First clinical impression shows good tolerability and clinical efficacy in a proportion of patients. For the conference we will present the completed statistical analyses.

Discussion
We will discuss putative mechanisms of action of tRNS such as de-synchronizing hyper-active auditory areas.

P99: Effect of Modulation of the Frontostriatal Gating System Using Transcranial Direct Current Stimulation on Tinnitus Perception.
Maudoux A[1, 2]., Turkeltaub P.E[3, 4]., Rauschecker J.P[2]. ([1]OtoRhinoLaryngology Head and Neck Surgery Department, CHU Sart Tilman Hospital, University of Liège, Belgium, [2]Laboratory of Integrative Neuroscience and Cognition, Department of Neuroscience, Georgetown University Medical Center,

Washington, USA, [3]Cognitive Recovery Laboratory, Department of Neurology, Georgetown University Medical Center, Washington, USA, [4]Research Division, MedStar National Rehabilitation Hospital, Washington, USA)

Background
Tinnitus is defined as a perception of sound in the absence of external auditory stimuli. Despite its prevalence, tinnitus pathophysiology remains poorly understood. We have previously proposed (Rauschecker et al., Neuron 2010 - TICS 2015) that tinnitus perception arises only if two conditions are met: (1) a tinnitus signal is being generated within the auditory system, and (2) this uninformative signal fails to be suppressed by a cortico-striatal limbic network encompassing ventromedial prefrontal cortex (vmPFC) and nucleus accumbens (NAc) ("gating theory").

Methods
In our current study, we have chosen to test this model using a combination of transcranial direct current stimulation (tDCS) and functional magnetic resonance imaging (fMRI). In a randomized, doubleblind, shamcontrolled cross-over design, chronic tinnitus subjects were submitted to 15 minutes of 2-mA tDCS anodal stimulation of the vmPFC and cathodal stimulation of the right dorsolateral prefrontal cortex (dlPFC). Participants were scanned at baseline and after each of the tDCS sessions. The locations of anode and cathode were based on a recent study showing that this noninvasive direct stimulation of prefrontal cortex can induce neural activity in the distally connected ventral midbrain, with a direct behavioral effect on an attractiveness rating task (Chib et al., Transl Psychiatry, 2013). Using this stimulation protocol we aimed to target regions of the gating system, such as the prefrontal region and the NAc.

Our primary outcome measure was a change in tinnitus intensity and/or distress assessed with a Visual Analog Scale. We were also looking at how tDCS stimulation modified the pleasantness rating of a series of affective auditory stimuli.

The fMRI session comprised a resting-state acquisition (3T Siemens TIM Trio, TR = 1500 ms, duration = 8 min) and a sparse-sampling acquisition (3T Siemens TIM Trio, TR = 12000ms, TR delay = 10500 ms) during which sounds from the International Affective Digitized Sounds database were presented (Stevenson et al., Behav Res Methods 2008).

Results
Preliminary results are based on the analysis of the first 12 subjects (8 males, mean age 49, mean tinnitus duration 13.13 years). Our resting-state functional connectivity analyses indicate that tDCS anodal stimulation of the vmPFC and cathodal stimulation of the right dlPFC does modify the activity in, and connectivity pattern between, regions of our gating network. When looking at individuals' ratings, tDCS does decrease the tinnitus loudness in five subjects. However, the Wilcoxon signed rank test with continuity correction shows that there is no significant difference before and after treatment ($p = 0.2837$). We show that inter-individual differences in baseline VTA and NAc functional connectivity patterns might explain why some subjects responded to tDCS and why some did not. Additionally, tDCS seems to increase participants' appraisals of sound pleasantness. Our preliminary fMRI results suggest that this might be achieved through a modification of thalamic activity/connectivity patterns.

P100: M1 targeted vagus nerve stimulation-new therapeutical approach for chronic tinnitus?
Bojić T[1]., Senćanski M[2]., 2 Perović V.R[2]., 2 Glišić S[2].([1]Institute of Nuclear Sciences Vinča,University of Belgrade, Laboratory of Radiobiology and Molecular Genetics, Belgrade, Serbia, [2]Institute of Nuclear Sciences Vinča University of Belgrade, Center for Multidisciplinary Research, Belgrade, Serbia)

Chronic tinnitus is characterized by neuroplastic changes of auditory cortex. Promising method for therapy of chronic tinnitus is vagus nerve stimulation (VNS) combined with auditory stimulation [1]. The principle of VNS is reversal of pathological neuroplastic changes of auditory cortex towards physiological neural activity and synchronicity. VNS mechanism of action in chronic tinnitus patients is the muscarinic neuromodulation of auditory cortex by the activation of nc. basalis Maynerti [1]. Also, VNS has substantial number of negative effects like invasiveness, bradycardia and gastrointestinal side effects.

The aim of this study is to propose potential pharmaceutics that would improve neuromodulatory effects of VNS and change its protocol toward less intense vagal stimulation and diminution of VNS side effects.
The working hypothesis is that M1 receptors have dominant role in the neural plasticity of auditory cortex[2]. VNS unselectively activates both muscarinic and nicotinic receptors in CNS and periphery. Our idea is that alosteric agonists of M1 receptors could improve specificity and selectivity of neuromodulatory effect of VNS on auditory cortex of chronic tinnitus patients even in the circumstances of lower acetylcholine brain concentration.

We performed in silico screening of drug space using EIIP/AQVN filter [3]and selected 50 drugs as candidates for allosteric modulators of muscarinic receptors. Further filtering of these compounds by means of 3D QSAR and docking revealed 3 approved drugs as the most promising candidates for chronic tinnitus therapy. These drugs should be further evaluated by biological tests and clinical trials.

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P101: Treatment of intractable tinnitus by neurostimulation of the cochlear nerve: long-term evaluation of 11 patients.

van den Berge M.J.C[1]., Stienstra J[1]., Free R.H[1]., van Dijk P[1]., van Dijk J.M.C[2]. ([1]University Medical Center Groningen, Department of Ear-, Nose- and Throat Surgery, Groningen, The Netherlands, [2]University Medical Center Groningen, department of Neurosurgery, Groningen, The Netherlands)

Background: Tinnitus may lead to severe impairment of quality of life. Currently, no satisfying treatment modality for severe tinnitus is available. Neurostimulation of the neural auditory tract for the treatment of tinnitus is being extensively investigated. Our center has experience with electrical stimulation of the cochlear nerve using a cuff electrode for more than a decade. We aimed to investigate the effect of neurostimulation of the cochlear nerve for intractable, unilateral tinnitus.

Methods

Between 2001 and 2013, 11 patients with severe, unilateral, intractable tinnitus and ipsilateral severe hearing loss wereimplanted with a cuff electrode around the cochleovestibular nerve. Pre- and postoperative Tinnitus Handicap Inventory (THI) scores and audiometric values (i.e. pure tone audiometry) were collected. Treatment success was defined as satisfactory usage based on patients' self-assessment.

Results
The mean age at implantation was 56.6±5.6 years and the mean duration of tinnitus at the time of intervention was 8.2±5.7 years. The preoperative THI score was 71±18 points. Over a median follow-up of 25 months, the mean reduction of THI score was 25±26 points. Treatment success was demonstrated in six patients (55%). In these patients, neurostimulation did not lead to disappearance of tinnitus, but to transformation into a more bearable sound. In the remaining five patients (45%) the neurostimulator was not successful. In six patients (55%), hearing loss had increased after surgery and in one patient persistent vertigo occurred after surgery.

Conclusion
Although the neurostimulator resulted in substantial reduction of THI in a small majority of patients, tinnitus did not disappear in any patient and there was a high complication rate. Therefore we conclude that neurostimulation with a cuff electrode around the cochleovestibular nerve is currently not recommended as a treatment for tinnitus. More research is needed to further evaluate whether other approaches, such as cochlear implantation, are more effective in tinnitus reduction.

P102: Otogenic causes of tinnitus.
Djeric D. (Clinic for Otorhinolaryngology and Maxillofacial Surgery, Clinical Centre of Serbia, Medical Faculty University of Belgrade, Serbia)

Tinnitus is commonly defined as hearing a sound in absence of external sounds. Tinnitus may be caused due to various problems in different part of the hearing system.The outer ear problem as ear wax, foring body, infection, trauma, tumour), can results in tinnitus. Middle ear disease may cause tinnitus. These include common disease as middle ear inflammatory process with or without cholesteatoma, than less comon (trauma, otosclerosis, tumours), Also, cause of tinnitus may be due to muscle spasms of the tiny muscles in the middle ear. Most subjective tinnitus originates due to inner ear changes and various diseases. Damages and loss of sensory cells caused by different factors (trauma, infection, medication, age) may be associated with tinnitus.

The purpose of our presentation is to report our experiences in diagnosis and treatment of patients with a different otogenic origin of tinnitus. Appling a new concept in diagnosis of tinnitus we found we found various pathologic process in the ear

P103: The effects of bilateral nucleus accumbems lesions on acoustic trauma-induced tinnitus in rats: A Preliminary Analysis.
Zheng Y[1, 2, 3]., Reid P[1, 2, 3]. ([1]Department of Pharmacology and Toxicology, School of Medical Sciences, University of Otago, New Zealand [2]Brain Health Research Centre, University of Otago, [3]Brain Research, New Zealand)

Background
Chronic tinnitus is experienced by about 10% of the population and produces many detrimental effects on the quality of life. There are very limited treatment options, mainly due to a lack of understanding of the underlying mechanisms. Imaging studies in tinnitus patients revealed activity and connectivity changes in both auditory and non-auditory neural networks, including thise associated with reward, novelty and aversive conditions, such as the nucleus accumbens (NAc). This suggests that activation of the awareness region(s) of the brain may bew necessary for the conscious perception of phantom sound, i.e., tinnitus. In the present study, we tested whether bilateral lesions of the NAc after the consolidation of acoustic trauma-induced tinnitus would affect tinnitus perception in a rat model.

Materials and Methods
Male Wistar rats were divided into 4 groups: 1) sham (i.e., no acoustic trauma); 2) sham with NAc lesions; 3) acoustic trauma-exposed exhibiting tinnitus; and 4) acoustic trauma-exposed exhibiting tinnitus with NAc lesions. The acoustic trauma consisted of a 16 kHz, 115 dB pure tone delivered unilaterally for 1 h under anaesthesia and the animals were tested behaviourally for psychophysiological evidence of tinnitus using a conditioned lick suppression paradigm at 1 month post-exposure. Following the confirmation of tinnitus, the animals in the NAc lesion group underwent stereotaxic surgery under isoflurane anaesthesia. Bilateral NAc shell lesions were made by 3 injections of 0.09 M NMDA at the following coordinates: AP 1.6, ML ±0.9, at DV -7.5 (0.2 µl), DV -6.9 (0.1 µl) and DV -6.2 (0.1 µl). Tinnitus peception was re-evaluated again at 2 - 3 weeks post-lesion.

Results
Acoustic trauma caused a significant immediate increase in the auditory brainstem response (ABR) thresholds in the exposed animals. Fourteen out of 30 acoustic trauma-exposed animals displayed behavioural signs of tinnitus. Preliminary analysis showed that bilateral NAc shell lesions did not significantly alter tinnitus perception in rats. However, conclusions cannot be made until further analysis correlating tinnitus perception with the accuracy and extent of the NAc lesions is done.

P104: Ginkgo biloba extract EGb 761® improves noise trauma induced hearing loss and tinnitus in an animal model.
Krauss P., Tziridis K., Buerbank S., Schilling A., Schulze H. (Experimental Otolaryngology, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany)

Noise induced hearing loss (NIHL) is a common disease in modern societies and may lead to maladaptations within the auditory system that finally results in subjective tinnitus. Several technical and pharmacological interventions have significantly reduced symptoms, however they usually do not restore normal hearing.

In a previous study (Tziridis et al., 2014) we were able to demonstrate that pretreatment with Ginkgo biloba extract EGb 761® significantly reduces NIHL and tinnitus development in our animal model, the Mongolian gerbil (Meriones unguiculatus). However, the practical potential of a prophylactic treatment against NIHL and tinnitus is limited to a small group of individuals, e.g. those who are prone to severe but unpredictable noise exposure, such as soldiers or construction workers.

Therefore, we here tested if application of EGb 761® has beneficial effects after the formation of permanent NIHL and tinnitus. To this end we monitored the effects of EGb 761® on noise trauma-induced changes in signal processing within the auditory system of our animals by behavioral (acoustic startle response, ASR) and electrophysiological approaches (auditory brainstem responses, ABR). EGb 761® was applied daily for three weeks, starting one week after noise trauma. We found that – in contrast to vehicle treatment – EGb 761® administration (100 mg extract per kg body weight, oral application) led to a restoration of hearing thresholds back to pre-trauma conditions. In addition, all animals that displayed behavioral signs of subjective tinnitus showed improvement of tinnitus symptoms. Moreover, 7 of 9 animals showed complete relief of tinnitus during the time of EGb 761® treatment. Nevertheless, in all except one of these animals tinnitus reappeared after the end of EGb 761® treatment, while auditory thresholds remained restored.

A detailed analysis of ABR responses revealed that EGb 761® treatment did not simply change auditory processing back to pre-trauma conditions, but led to subtle changes of ABR wave amplitude and latency at different levels of the auditory pathway, with an overall increase of response strength for low stimulus intensities and a decrease at high intensities. The functional relevance of these changes may be the observed improvement of hearing thresholds while at the same time suppression of responses to high stimulus intensities may point to a global inhibitory mechanism that counteracts tinnitus.

Tziridis K, Korn S, Ahlf S, Schulze H (2014) Protective effects of Ginkgo biloba extract EGb 761 against noise trauma-induced hearing loss and tinnitus development. Neural Plast 2014:427298.

P105: Efficacy of customized filtered sound for tinnitus relief: a randomized controlled trial.

Kam A.C.S[1]., Sung J.K.K[2]., Lee T[3]., Wong T.K.C[2]., van Hasselt C.A[2]. ([1]Department of Special Education & Counselling, The Hong Kong Institute of Education, Hong Kong, [2]Department of Otorhinolaryngology, Head & Neck Surgery, The Chinese University of Hong Kong, Hong Kong[3]Department of Electronic Engineering, The Chinese University of Hong Kong, Hong Kong)

Purpose of study

The objective of this study was to assess the efficacy of two sound therapy approaches, 1) customized tinnitus frequency notched sound therapy and 2) customized sound therapy.

Methods

This was a randomized controlled trial. Thirty-one subjects, who had continuous tinnitus for a minimum of 6 months, participated in the study. They were randomized prospectively into 3 groups: 1) customized tinnitus frequency notched sound therapy (CNS); 2) customized sound therapy (CS); and 3) no treatment control group (NT). After 6 months of therapy, immediate outcomes were compared using the 1) Chinese Tinnitus Handicap Inventory, 2) Chinese Tinnitus Questionnaire, 3) self-rated visual analogue scale on tinnitus loudness, and 4) tinnitus loudness matches measured psychoacoustically.

Results

The Chinese Tinnitus Questionnaire score was significantly lowered in the CNS and CS group as compared to the NT group. There was no significant difference in the score reduction between the CNS and CS group. No significant difference was observed among all three groups in psychoacoustic measures.

Conclusion

Preliminary results suggest that both the customized sound therapy and customized tinnitus frequency notched sound therapy are effective for tinnitus relief.

P106: Amplitude modulated sounds for tinnitus relief.

Neff P[1]., Schlee W[3]., Meyer M[2]. ([1]University of Zurich, Zurich, Switzerland, [2]Neuroplasticity and Learning in the Normal Aging Brain (HAB LAB), University of Zurich, Zurich, Switzerland, [3]Department of Psychiatry and Psychotherapy , University of Regensburg , Regensburg, Germany, [4]Interdisciplinary Tinnitus Clinic, University of Regensburg , Regensburg, Germany)

Lowered EEG alpha activity in tinnitus patients has been shown in many studies. Rhythmic neuromodulation in the alpha frequency could lower tinnitus symptoms as shown by rhythmic transcranial magnetic stimulation (Müller et al., 2013) and a single study applying 10 Hz binaural beats (David et al., 2010). These approaches entrained endogenous neural oscillations by rhythmic external stimuli. Sinusoidally amplitude modulated (SAM) „monaural" sound stimuli produce an optimal entrainment as shown in recent studies including one applying intracranial EEG recordings (Becher et al., 2015). In addition, EEG alpha activity could be trained with neurofeedback in other studies.

The ongoing multicenter study aims at testing the feasibility of SAM stimuli in tinnitus suppression and related changes in oscillatory patterns. Different carrier sounds (pure tones at frequencies in or around the tinnitus pitch, low frequencies,noise types and music) are sinusoidally amplitude modulated with 10 Hz or individual alpha frequency (IAF) and presented continuously to the participants. Low-frequency carrier sounds are deemed especially promising for patients with hyperacousis. At this stage, efficacy in tinnitus suppression and perceptual valence of the sounds are primarily tested. Secondarily, EEG is recorded testing the alpha entrainment and measuring possible further correlates of the tinnitus suppression. A comprehensive clinical, audiometric and tinnitus assessment is performed following TRI guidelines. Furthermore, it is planned to test the approach longitudinally in real life application with the end goal of developing an app with sound stimulation.

Preliminary data showed a transient decrease in tinnitus loudness after AM stimulation in 7 of 12 patients (2 patients with no change, 1 patient terminated participation, and 2 patients with non-tonal tinnitus). The data was gathered applying VAS for loudness and distress in Zurich after 5 minutes of stimulation and a health change item after 3 and 6 minutes respectively in Regensburg. Repeated sessions with a single subject showed test-retest reliability: the AM stimuli in the tinnitus frequency produced a complete tinnitus suppression of up to 3 minutes (2:46, 3:05) after 6 minutes of stimulation compared to 1 minute (0:56, 1:00) with an unmodulated control carrier sound. Beyond that, EEG recordings (n=3) comparing baseline activity to 1 minute post-stimulation activity showed a significant increase in the entrained alpha frequency over bilateral temporofrontal electrodes after 5 minutes of stimulation ($p<0.05$).

The preliminary data shows an effect of tinnitus suppression as well as persisting entrainment of EEG alpha activity. A relation between both phenomena has to be systematically tested. Furthermore, contrary to rhythmic transcranial electric stimulation ((r)TES) stimulating most of the neurons under the stimulation site, it is unclear if the entrained oscillations stem from relevant neuronal assemblies and therefore can contribute to tinnitus suppression. Nevertheless, auditory AM stimulation seems feasible due to its harmless non-invasive nature and ease of application.

In conclusion, the approach seems promising and compatible for mobile application. Joint use with other neuromodulation techniques like neurofeedback and TES could increase treatment efficacy reciprocatively.

P107: Effect of a selective p38 MAPK alpha inhibitor on the amplitude of the inferior colliculus's evoked potential response after auditory damage induced by acoustic trauma in rats.

Cosnier-Pucheu S.C.P[1]., Larroze-Chicot P.L.C[2]., Marie A.M[1]., Cazals Y.C[2].,Norena A.N[2]., Alam J.A[3]. ([1]Cilcare, Montpellier, France, [2]University of Aix-Marseille, Marseille, France, [3]EIP Pharma, LLC, ~cambridge, Massachusetts, USA)

Mitogen-activated protein kinase (MAPK) is an important intracellular transduction system involved in physiological processes such as cell growth, differentiation and apoptotic cell death. P38 MAPK pathways are strongly stimulated by inflammatory cytokines and environmental stress including oxidative stress. Several publications suggested that MAPK is involved in damage of cochlear OHC, induced by cisplatin ototoxicity or acoustic overexposure. A recent study showed that the early effects of acoustic trauma, that eventually result in permanent damage to auditory system leads to a transient activation of BDNF and MAPK in the inferior colliculus (IC) (Maeda, 2013 ; Meltser I, 2010). The effects of acoustic trauma in the IC is of particular interest because of its possible involvement in the generation of hyperacousis and tinnitus (Berger, 2015). Another study showed that these inhibitors decreased dose-dependently the auditory threshold shift and outer hair cell loss induced after acoustic trauma (Tabuchi K., 2010).

Based on these results, the objective of this study was to assess the effect in rats of a selective small molecule inhibitor of the alpha isoform of p38 MAPK (Alam, 2015), when administered by oral route, on auditory nerve (CAP and inferior colliculus (IC)) evoked potentials. Adult Long Evans rats were used, electrodes were implanted chronically at the lateral base of the ventral cochlear nucleus to measure the CAP of the auditory nerve, and in the colliculus. Measures were recorded at frequencies of 2, 4, 6, 8, 10, 12, 16, 20, 26, and 32 kHz from 90 to 10 dB SPL in 10 dB steps. Normality of evoked responses was checked at the beginning of the experiments for all animals and each animal served as its own reference. Then rats anesthetized with isoflurane, were exposed to a bilateral acoustic trauma of 1 hour, at 120dB sound pressure level (SPL), with a two-octave noise band (4-16kHz) for a vehicle group (n=9), two groups treated at 1.5mg/kg and 4.5mg/kg (n=10/group) and a non-exposed group (sham, n=11). Post acoustic trauma evoked responses were measured after 3, 7, 10, 14 and 16 days. The investigated compound was administered twice daily from day 8 post-trauma and during 7 days.

The noise exposure produced approximately a 20 to 30 dB transient CAP threshold shift measured 24 hours after the noise exposure in all exposed groups. After 3 days, the threshold values returned to their baselines. An increase of the IC evoked potential amplitude was observed at 6kHz and was significant at day 3 and day 14 compared to the values observed in sham rats. Both doses of the p38 MAP kinase inhibitor reduced somewhat the amplitude increase of the IC response at 6kHz, but the effect did not reach statistical significance.

In conclusion, this first reported study of a selective p38 MAP kinase inhibitor after acoustic trauma indicates that the approach might provide some protection against inferior colliculus alterations induced by such trauma. However determination of its therapeutic potential requires further studies. The observed effects might be significant for hyperacousis and tinnitus treatment.

P108: Does tDCS influences latency or amplitude of event-related potentials?

Rabau S[1, 2]., Van Rompaey V[1, 2]., Van de Heyning P[1, 2].
([1]Faculty of Medicine, Campus Drie Eiken, University of Antwerp, Antwerp, Belgium, [2]University Department of otorhinolaryngology and Head & Neck surgery, Antwerp University Hospital, Edegem, Belgium)

Background

The last year, neuromodulation techniques such as transcranial direct current stimulation (tDCS) are described more and more in the literature to treat symptoms as loudness and distress caused by tinnitus. The effect of tDCS on tinnitus is still unclear and various effects are described in the literature. Knowing the physiological process of tDCS can maybe explain the inter-subject variability. In the present study, we will investigate the impact of tDCS on Event-Related potentials (ERP).

Methods
Fifteen normal hearing female subjects (median age: 26 years) without tinnitus received a single tDCS-session (anode placed on right dorsolateral prefrontal cortex and cathode placed on left shoulder). Event-related potentials (ERP) were measured immediately before and after the tDCS session. To investigate the impact of tDCS on latency and amplitude of ERP, a Wilcoxon signed rank test was performed.

Results and conclusion
Although the literature reports that a single session tDCS can have a positive short-term effect on tinnitus, no statistically significant difference ($p>0.05$) was found on latency and amplitude of pre and post-ERP. On the right side an effect was found for wave N1 and P2, but after post hoc testing this effect disappeared. However, previous research showed that tDCS could alter cortical-subcortical activation and connectivity (Lapenta et al., 2014*), no clear effect of tDCS on physiology was found in the present study.

Reference
*Lapenta O.M., Sierve K.D., de Macedo E.C., Fregni F. & Boggio P.S. 2014. Transcranial direct current stimulation modulates ERP-indexed inhibitory control and reduces food consumption. Appetite, 83, 42-48.

P109: Potential of IGF-1 for restoration of synaptic contacts between inner hair cells and spiral ganglion neurons.
Nakagawa T., Asaka N., Kita T., Tona R., Yamamoto N., Ito J., Omori K. (Kyoto University, Kyoto Prefecture, Japan)

Recently, degeneration of synaptic contacts between inner hair cells (IHC) and spiral ganglion neurons (SGN) has been gained considerable attention as an initial pathological change in a various type of hearing loss, and a trigger of tinnitus associated with noise-induced hearing loss. Previously, we performed a clinical trial of topical IGF-1 therapy for sudden sensorineural hearing loss. Hearing recovery in patients treated with IGF-1 showed delayed onsets, which is difficult to explain only by protection of cochlear cells by IGF-1. We speculated that any regenerative processes could be involved in mechanisms for delayed on-set of hearing recovery and slow and gradual hearing recovery observed in patients treated with IGF-1. We hypothesized that IGF-1 has effects to promote regeneration of synapses between inner hair cells and spiral ganglion neurons.

Cochlear explants of postnatal day-2 mice were used. To induce degeneration of IHC-SGN synaptic contacts, NMDA and kainate was applied to culture media, which reduced a number of IHC-SGN synaptic contacts, but not that of IHC or SGN. After exposure to NMDA and kainate, cochlear explants were maintained in culture media supplemented IGF-1 at various concentrations for 48 h. Immunohistochemistry for CtBP2 and PSD95 was used for labeling of IHC-SGN synaptic contacts. IGF-1 showed a dose-dependent effect for an increase of synaptic contacts, indicating IGF-1 effects on restoration of IHC-SGN synaptic contacts. In consequence, inhibition of IGF-1 associated cellular signaling pathways was investigated. Results indicated that the PI3K/Akt was involved in IGF-1 effects on restoration of IHC-SGN synaptic contacts. These findings suggest that IGF-1 has an effect for promotion of regeneration of IHC-SGN synaptic contacts.

P110: Regional gray matter changes in patients with recent-onset tinnitus induced by music therapy.

Grapp M.[1], Krick C.M.[2], Argstatter H.[1], Plinkert P.K.[3] ([1]German Center for Music Therapy Research (Victor Dulger Institute) DZM, Heidelberg, Germany, [2]Department for Neuroradiology, Saarland University Hospital, Homburg, Germany, [3]University Hospital for Ear, Nose, and Throat, University of Heidelberg, Heidelberg, Germany)

Background

Neuroimaging studies of tinnitus indicate the involvement of wide-spread brain networks for perception, attention, memory, and emotional aversive processes. Moreover, gray matter alterations in auditory brain areas seem to play a crucial role in tinnitus genera-tion and chronification.
Therefore, for patients with recent-onset tinnitus a music therapeutic intervention according to the 'Heidelberg Model of music therapy' was evaluated as a complementary treatment option if initial medical treatment only brought minimal or no improvement. This treatment approach strives for an integration of strategies to manage the psychological condition and to possibly reverse the underlying neuronal reorganization. The specific interventions were expected to be able to intervene at an early stage in those neuronal processes leading to a chronic manifestation of the tinnitus symptom.

Objectives

The primary objective of this study was to investigate the corresponding neural correlates of the reduction in subjective perceived tinnitus distress observed immediately after the treatment. As in previous studies tinnitus distress was highly related to structural gray matter loss in auditory areas, we expected neural correlates of the therapy effect to be most prominent within these regions.
Methods: Treatment was applied to n = 20 patients with recent-onset tinnitus (treatment group, TG) and n = 22 healthy active controls without tinnitus (active control group, AC). Additionally, n = 22 untreated patients with recent-onset tinnitus served as an untreated comparison group (passive control group, PC). These patients received music therapy at a later date.The neuro-music therapy was carried out as manualized short term music thera-peutic treatment lasting for ten consecutive 50-minutes sessions of individualized therapy. Therapy takes place in the German Center of Music Therapy Research in Heidelberg on five consecutive days (from Monday to Friday) with two therapy sessions per day. Before and after the treatment week, high-resolution MRT scans were obtained for each subject. Changes in individual tinnitus-related distress were assessed by the German version of the tinnitus questionnaire.

Results

The therapeutic intervention led to a significant decrease of tinnitus-related distress in TG compared to PC. Structural gray matter (GM) increase in TG compared to PC was found within the following three clusters: precuneus, medial superior frontal areas, and auditory cortex. The therapy-like procedure in AC also elicited GM increases in precuneus and frontal regions when contrasted with PC. Comparison between structural effects in TG versus AC was calculated within the mask for general GM changes (contrast between TG and PC) and yielded GM increase in right Heschl's gyrus, right Rolandic operculum and medial superior frontal regions.

Conclusions

It could be shown that the music therapy according to the Heidelberg Model was able to reveal rapid improvements in subjective tinnitus distress. These therapeutic effects were also reflected in structural gray matter changes in auditory regions as well as in areas of the default-mode and attention network.

P111: A Balanced Randomised Placebo Controlled Double-Blind Study to Investigate the Efficacy and Safety of AUT00063 versus Placebo in Subjective Tinnitus: Protocol for a Phase IIa Trial

Hall D.A. [1], Ray J.[2], Watson J.[1], Millar B.[1], Grant A.[3], Large C.[3], Harris P.[3] ([1]National Institute for Health Research (NIHR) Nottingham Hearing Biomedical Research Unit, Ropewalk House, 113 The Ropewalk, Nottingham, UK, [2]Department of Ear, Nose and Throat Surgery, Royal Hallamshire Hospital, Sheffield, UK, [3]Autifony Therapeutics Limited, Imperial Incubator, Level 1 Bessemer Building, Imperial College London, UK)

Reduced activity at certain sites in the brain (called "voltage-gated potassium channels") has been linked to hearing problems, like age-related loss of hearing or tinnitus (a 'ringing' or buzzing noise in the ears). AUT00063 is an experimental new medicine that has been developed to improve the action of these specific channels and so treat the brain component of these hearing problems. The main purpose of this study is to try to demonstrate an improvement in the severity of tinnitus after 28 days of treatment with the study medicine or the placebo (dummy drug which does not contain the medication). The first participant was recruited in November 2014, and recruitment will continue at 18 UK sites throughout 2015, with a target sample size up to 152. A clinically relevant interpretation of tinnitus severity relates to the functional impact of tinnitus on daily activities and is measured as a primary outcome using the Tinnitus Functional Index. Secondary outcomes consider the effect on tinnitus loudness. Safety and efficacy will be determined by looking at a number of assessments (physical examinations, blood sampling, hearing assessments, questionnaires, etc.) and in case of any serious medical event during the study. A safety follow-up will be conducted after the treatment period.

Here we present the clinical trial design, and discuss some of the design and implementation challenges that we have had to overcome. The study is co-funded by a UK government-backed Biomedical Catalyst award. ClinicalTrials.gov Identifier: NCT02315508.