

ID: 100

Abstract Submissions

Keywords: fMRI, distress, Bayesian brain, nucleus accumbens, free energy principle

Predictive-brain mechanisms of phantom perception pathology

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Among recent innovations in tinnitus research, the application of Bayesian brain theory has proven especially promising, treating phantom perception as part of the brain's strategy to resolve the uncertainty resulting from sensory deafferentation. The involvement of reward-processing regions such as nucleus accumbens is however an unresolved paradox in tinnitus, a disorder that features a neutral percept and presents with distressful symptoms in roughly one in five cases. Here, I specifically examine the role of nucleus accumbens in cases of chronic, distressful tinnitus. I present two separate experiments to this end: (1) a within-subjects, block-design fMRI experiment comparing patients' responses to auditory stimuli at their tinnitus frequency versus control-frequency stimuli; (2) a resting-state fMRI experiment comparing tinnitus patients to healthy controls. While nucleus accumbens is reportedly involved in processing both positive and negative affect, I show that its involvement in cases of distressful tinnitus is dissociable from the effect of tinnitus-related distress itself, which correlates instead with functional connectivity in subgenual anterior cingulate cortex and the amygdala. I conclude that the tinnitus percept is merely an incidental byproduct of the large-scale neuroplastic changes made to resolve the persistent negative reward prediction error that results from hearing loss, per Bayesian brain theory. Tinnitus-related distress is likely a learned reaction to that percept specifically and not related to the broader error resolution mechanism, thus eliminating the apparent paradox of nucleus accumbens' role in tinnitus pathology.

ID: 102

Abstract Submissions

Keywords: dynamic connectivity, distress, sLORETA, EEG, tinnitus

Distress-dependent temporal binding of regions encoding disorder-specific and disorder-general behavioral manifestations of phantom percepts

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Background: Tinnitus is the perception of a phantom sound in the absence of an external auditory stimulus characterized by a specific sensory component i.e. loudness and a non-specific affective component i.e. distress. Tinnitus is hypothesized to be a maladaptive compensation to a prediction error generated between compromised bottom-up information and top-down prediction of the upcoming stimulus. Although a wealth of information is available about the relationship between these behavioral correlates and changes in static functional connectivity (FC), its relationship with dynamic changes in network connectivity is yet unexplored.

Objective: The aim of the current study is to investigate changes in the flexibility and specificity of time-varying functional connectivity in tinnitus and its relation to loudness and distress.

Methods: We calculate a measure called temporal variability of functional connectivity from the source-localized resting state EEG of 151 tinnitus patients and 125 controls using an overlapping and non-overlapping sliding window.

Results and discussion: In low distressed patients, no relationship between temporal variability and loudness or distress was observed, demonstrating a resilience in temporal binding. However, highly distressed patients exhibited increased temporal variability in FC with increasing loudness percept in the primary auditory cortex and parahippocampus and a decreased temporal variability in FC and increasing distress percept in the parahippocampus.

Conclusion: Thus, in tinnitus, the sensory specific component exhibited increased variability in FC, possibly related to a Bayesian search for updating deafferentation-based missing information, whereas the decreased variability in the parahippocampus related to the non-specific distress possibly reflecting a more hard-wired, i.e. less adaptive, contextual processing.

ID: 103 / Session 20: 1

Abstract Submissions

Keywords: Innovation, Tinnitus, Research design, Yachting

Throwing the ball further: What tinnitus research can learn from Team New Zealand's winning of yachting's Americas Cup.

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Winning yachting's Americas cup and curing tinnitus are no small feats. Both were goals of Emirates Team New Zealand's (ETNZ) principal, and founder of the Tinnitus Research Initiative, Matteo de Nora. The first goal was achieved in 2017 after many years of trying; the later goal remains unattained. Tinnitus research may not seem to share much in common with yachting, but in order to win the world's oldest sporting trophy ETNZ faced financial, technical and methodological issues not dissimilar to the challenges we face in tinnitus research. ETNZ's victory was not based on incremental improvements in design and performance, but instead a philosophy of "throwing the ball out as far as we can and see if we can get to it". While scientific method and funders favor safe, or proven, research we may miss opportunities to rapidly advance our field if we do not take risks. This talk will use ETNZ as a sporting analogy for how we can change the tinnitus research space by emboldening researchers to take greater risks. Four themes for success will be explored; innovation, risk, persistence and people.

ID: 104 / Session 3: 1

Abstract Submissions

Keywords: Tinnitus, cognitive behavioral therapy, treatment, hyperacusis

Efficacy of treatment for tinnitus based on cognitive behavioral therapy in an inpatient setting: a 10-year retrospective outcome analysis

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ABSTRACT

AIM: Tinnitus is a phenomenon with a high prevalence in the general population, leading to high levels of suffering. It is a symptom that can present itself comorbidly with a variety of psychiatric and medical illnesses. We established a treatment of tinnitus, which is based on a multimodal approach including a specific cognitive-behavioral therapy (CBT) method in an inpatient setting. This approach includes education on tinnitus, applying coping strategies and techniques of relaxation, directed attention and music therapy. We aim to evaluate the efficacy of this treatment approach.

MATERIAL / METHODS: We included retrospective data of 268 patients that underwent tinnitus treatment throughout the ten-year existence of the treatment program. We assessed routine clinical data pre and post treatment with parameters concerning tinnitus-distress, hyperacusis and psychological well-being. To determine these variables we used validated instruments including the Tinnitus Questionnaire (TQ), Questionnaire on hypersensitivity to sound (QHS), Brief Symptom Inventory (BSI) and the Beck Depression Inventory (BDI). Questionnaires were implemented before and after the treatment program.

RESULTS: Patients showed highly significant reduction in all of the implemented questionnaires. Reduction of TQ, the primary outcome measure, was 15.39 points (SD 21.88) from 35.72 to 20.32 ($p < 0.001$). The QHS showed a reduction from 18.98 down to 12.26, which equals 6.72 points (SD 8.23; $p < 0.001$). Moreover, psychological strain was also reduced with high significance, as illustrated in reduction of BSI and BDI with all examined subsets; reduction in BSI from 49.63 to 25.21 points (24.41, SD 26.88; $p < 0.001$) and BDI from 16.89 to 9.41 points (7.47, SD 8.76; $p < 0.001$).

DISCUSSION: The multimodal treatment program for tinnitus, including a specific CBT method proves to be a highly effective means of significantly reducing not only tinnitus and hyperacusis, but also distress related to tinnitus. It also offers patients preservation of symptom reduction. Furthermore it also enables considerable reduction of concomitant psychiatric symptoms such as depression.

CONCLUSIONS: Our results underline the necessity of intensive and multimodal approaches to the treatment of tinnitus.

ID: 105 / Session 1: 1
Abstract Submissions
Keywords: vagus nerve

A Prospective Randomized Double-blind Controlled Clinical Study Using Vagus-Nerve Stimulation Paired with Tones for the Treatment of Tinnitus

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Introduction: Chronic tinnitus is a debilitating condition that significantly interferes with quality of life of the individual. Several counseling and sound-based therapies have been developed to help some patients manage tinnitus symptoms. However, many patients with chronic tinnitus continue to remain refractory to treatments. Based on preclinical studies, we developed a therapy in which vagus nerve stimulation was paired with tones over several weeks. The hypothesis was that this paired stimulation would decrease tinnitus symptoms by decreasing the pathological plasticity associated with tinnitus.

Methods:

Subjects with chronic refractory tinnitus were enrolled in the study. 30 were implanted with a VNS device, consisting of an implantable pulse generator and lead. The lead was wrapped around the cervical vagus nerve in a surgery performed by an otolaryngologist. Subjects were randomized to receive either VNS paired with tones or unpaired VNS (control) for six-weeks. Subjects performed the therapy at home for 2.5 hrs/day. All subjects received paired VNS after the 6-week randomized phase.

Results:

The device was used on 96% of days with good compliance. Adverse events included incision pain, hoarseness, and coughing and in one situation, a fractured electrode lead. Two patients had partial vocal cord paralysis lasting longer than 6-weeks that slowly improved over time. At the end of 6 weeks, the paired VNS group showed a significant improvement on the Tinnitus Handicap Inventory (THI) (-17.7%; 95% confidence interval, -28% to -7.3%, p=0.0012) compared to the control group (-7.3%; 95% confidence interval, -27.5% to 12.7%, p=0.1561). There was no significant difference between the two groups at this time-point (between-group difference, 10.3 %; 95% confidence interval, -10.49 % to 31.12 %, p =0.3393). Fifty percent of the subjects in the paired VNS group exhibited clinically meaningful improvements in their tinnitus compared to 28% in controls at 6 weeks, based on the THI questionnaire. At one-year follow-up, 50% of participants had a clinically meaningful response to the treatment (47% reduction on the THI). Furthermore, we observed that patients who had a hissing quality to their tinnitus and/or blast-induced tinnitus did not respond as well to the therapy. It is possible that a different pairing paradigm may be required for this subset of individuals or it is possible that the therapy may not work in all patients, given the heterogeneity and varied pathophysiologic mechanisms associated with tinnitus.

Conclusion:

VNS is feasible and safe in adults with chronic tinnitus. Further studies will help tease out the various subgroups and sensitivity to treatment. The study will provide information for a larger study that will support regulatory approval in the US.

ID: 108 / Session 4: 2

Abstract Submissions

Keywords: tinnitus, depression, amygdala, functional connectivity, resting-state fMRI.

Amygdala functional disconnection with the prefrontal-cingulate-temporal circuit in chronic tinnitus patients with depressive mood

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Purpose: Chronic tinnitus is often accompanied with depressive symptom, which may arise from aberrant functional coupling between the amygdala and cerebral cortex. To explore this hypothesis, resting-state functional magnetic resonance imaging (fMRI) was used to investigate the disrupted amygdala-cortical functional connectivity (FC) in chronic tinnitus patients with depressive mood.

Materials and Methods: Chronic tinnitus patients with depressive mood (n=20), without depressive mood (n=20), and well-matched healthy controls (n=23) underwent resting-state fMRI scanning. Amygdala-cortical FC was characterized using a seed-based whole-brain correlation method. The bilateral amygdala FC was compared among the three groups.

Results: Compared to non-depressed patients, depressive tinnitus patients showed decreased amygdala FC with the prefrontal cortex, anterior cingulate cortex and angular gyrus as well as increased amygdala FC with the postcentral gyrus and lingual gyrus. Relative to healthy controls, depressive tinnitus patients revealed decreased amygdala FC with the superior and middle temporal gyrus, anterior and posterior cingulate cortex, and prefrontal cortex, as well as increased amygdala FC with the postcentral gyrus and lingual gyrus.

Conclusions: The current study identified for the first time abnormal resting-state amygdala-cortical FC with the prefrontal-cingulate-temporal circuit in chronic tinnitus patients with depressive mood, which will provide novel insight into the underlying neuropathological mechanisms of tinnitus-induced depressive disorder.

ID: 109

Abstract Submissions

Keywords: tinnitus, effective connectivity, limbic system, functional connectivity, resting-state fMRI.

Altered effective connectivity network of the limbic system in chronic tinnitus

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Purpose: The phantom sound of tinnitus is believed to be triggered by aberrant neural activity in the central auditory pathway, but since this debilitating condition is often associated with emotional distress and anxiety, these comorbid symptoms likely arise from maladaptive functional connections to limbic structures such as the amygdala and hippocampus. To test this hypothesis, we used resting-state functional magnetic resonance imaging (fMRI) to identify aberrant effective connectivity of the amygdala and hippocampus in tinnitus patients and determine the relationship with tinnitus characteristics.

Methods: Chronic tinnitus patients (n=26) and age-, sex-, and education-matched healthy controls (n=23) were included. We used Granger causality analysis (GCA) utilizing the amygdala and hippocampus as seed regions to investigate the directional connectivity and the relationship with tinnitus duration or distress.

Results: Relative to healthy controls, tinnitus patients demonstrated abnormal directional connectivity of the amygdala and hippocampus, including primary and association auditory cortex, and other non-auditory areas. Importantly, scores on the Tinnitus Handicap Questionnaires were positively correlated with increased connectivity from the left amygdala to the left superior temporal gyrus ($r=0.570$, $p=0.005$), and from the right amygdala to the right superior temporal gyrus ($r=0.487$, $p=0.018$). Moreover, enhanced effective connectivity from the right hippocampus to the left transverse temporal gyrus was correlated with tinnitus duration ($r=0.452$, $p=0.030$).

Conclusions: Our results show that tinnitus distress is strongly correlated with enhanced effective connectivity that is directed from the amygdala to the auditory cortex. The longer the phantom sensation, the more likely acute tinnitus becomes permanently encoded (chronic) by memory traces in the hippocampus.

ID: 110

Abstract Submissions

Keywords: tinnitus, cerebellum, functional connectivity, resting-state fMRI.

Aberrant resting-state cerebellar-cerebral functional connectivity underlying chronic tinnitus

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Purpose: The chronic subjective tinnitus may arise from aberrant functional coupling between the cerebellum and cerebral cortex. To explore this hypothesis, we used resting-state functional magnetic resonance imaging (fMRI) to illuminate the functional connectivity network of the cerebellar regions in chronic tinnitus patients and controls.

Methods: Resting-state fMRI scans were obtained from 28 chronic tinnitus patients and 29 healthy controls (age, sex and education well-matched) in this study. Cerebellar-cerebral functional connectivity was characterized using a seed-based whole-brain correlation method. The resulting cerebellar functional connectivity measures were correlated with each clinical tinnitus characteristics.

Results: Chronic tinnitus patients demonstrated abnormal functional connectivity between the cerebellum and several cerebral regions, including the superior temporal gyrus (STG), middle temporal gyrus, parahippocampal gyrus, fusiform gyrus, inferior occipital gyrus, and precentral gyrus. The enhanced connectivity between the left cerebellar Lobule VIIb and right STG was positively correlated with the Tinnitus Handicap Questionnaires (THQ) score ($r=0.533$, $p=0.003$). Furthermore, the increased connectivity between the cerebellar vermis and right STG was also associated with the THQ score ($r=0.473$, $p=0.009$).

Conclusions: Chronic tinnitus patients have disrupted cerebellar functional connectivity to selected cerebral brain regions which is associated with specific tinnitus characteristics. Resting-state cerebellar-cerebral functional connectivity disturbances may play a pivotal role in neuropathological features of tinnitus.

ID: 112 / Session 2: 1

Abstract Submissions

Keywords: auditory brainstem response, prepulse inhibition of the auditory startle response, rodents, cochlea, hearing loss

Tinnitus development is associated with synaptopathy of inner hair cells in Mongolian gerbils

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Human hearing loss is often accompanied by comorbidities like tinnitus. This perception of phantom sounds without external stimulation is affecting up to 15% of the adult population and can lead to psychological disorders like depression. Animal studies in rodents could show that tinnitus may not only be a result of hearing loss due to cochlear hair cell damage but can also be a consequence of synaptopathy at the inner hair cells already induced by moderate sound traumata (hidden hearing loss).

In this study we investigate the synaptopathy previously shown in mice in our animal model, the Mongolian gerbil, and relate it to behavioral signs of tinnitus in this species. Tinnitus was induced by a mild monaural acoustic trauma leading to a monaural noise induced hearing loss in the animals quantified by auditory brainstem response audiometry. Behavioral signs of tinnitus percepts were detected by measurement of pre-pulse inhibition of the acoustic startle response in a gap-noise paradigm in about two-thirds of the animals. 14 days after trauma the cochleae of traumatized and non-traumatized ears were isolated and inner hair cell synapses were counted within several spectral regions of the cochlea. Inner hair cell synaptopathy was only found in animals with behavioral signs of tinnitus, independent of type of hearing loss. On the other hand, animals with apparent hearing loss but without behavioral signs of tinnitus showed a reduction in amplitudes of auditory brainstem response waves I/II (cochlear nerve and dorsal cochlear nucleus) but no significant changes in the number of synapses at the inner hair cells. We conclude – in line with the literature – that hearing loss is caused by damage to the inner and / or outer hair cells but that the development of tinnitus, at least in our animal model, is closely linked to synaptopathy at the inner hair cells.

ID: 113 / Session 11: 1

Abstract Submissions

Keywords: dorsal cochlear nucleus (DCN), Zwicker tone, computational model, auditory nerve

Stochastic Resonance Controlled Upregulation of Internal Noise after Hearing Loss as a Putative Cause of Tinnitus-Related Neuronal Hyperactivity

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Subjective tinnitus is generally assumed to be a consequence of hearing loss. In animal studies it has been demonstrated that acoustic trauma induced cochlear damage can lead to behavioral signs of tinnitus. In addition it was shown that noise trauma may lead to deafferentation of cochlear inner hair cells even in the absence of elevated hearing thresholds, and it seems conceivable that such hidden hearing loss may be sufficient to cause tinnitus.

Numerous studies have indicated that tinnitus is correlated with pathologically increased spontaneous firing rates and hyperactivity of neurons along the auditory pathway. It has been proposed that this hyperactivity is the consequence of a mechanism aiming to compensate for reduced input to the auditory system by increasing central neuronal gain, a mechanism referred to as homeostatic plasticity (HP), thereby maintaining mean firing rates over longer timescales for stabilization of neuronal processing.

Here we propose an alternative, new interpretation of tinnitus-related development of neuronal hyperactivity in terms of information theory. In particular, we suggest that stochastic resonance (SR) plays a key role in both short- and long-term plasticity within the auditory system and that SR is the primary cause of neuronal hyperactivity and tinnitus. We argue that following hearing loss, SR serves to lift signals above the increased neuronal thresholds, thereby partly compensating for the hearing loss. In our model, the increased amount of internal noise - which is crucial for SR to work - corresponds to neuronal hyperactivity which subsequently causes neuronal plasticity along the auditory pathway and finally may lead to the development of a phantom percept, i.e. subjective tinnitus. We demonstrate the plausibility of our hypothesis using a computational model and provide exemplary findings in human patients that are consistent with that model.

ID: 114 / Session 13: 1

Abstract Submissions

Keywords: Tinnitus, Residual Inhibition, Minimum Masking Level, Psychoacoustics

A new method for assessing masking and residual inhibition of tinnitus

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Purpose: While masking and residual inhibition (RI) may provide diagnostic and prognostic valuable information, these measures are rarely performed in clinics, as they are not adapted to clinical constraints. In this context, we devised a new method to assess these measures. The main goal of the present study was to validate this new method. **Methods:** The new method used an acoustic sequence made of pulsed acoustic stimulation of fixed duration and inter-stimulus interval. Firstly, the level of the stimulus was raised until the tinnitus was masked during the stimulus presentation (measurement of the minimum masking level - MML). Secondly, the level of the stimulus was raised further (from the MML) until tinnitus is suppressed during the silence interval between the acoustic pulses. A total of 68 participants with continuous tinnitus (either unilateral or bilateral) including large variety of hearing loss configurations were tested in two different sites with two different teams: Marseille (n=34) and Lyon (n=34). Different parameters such as the stimulation duration (1 sec, 3 sec and 5 sec) and frequency of the center noise were tested. **Results:** Overall, tinnitus masking was obtained in at least one condition for all of the 64 tinnitus patients tested except one (98.5%) and some level of residual inhibition was obtained for 59 participants (86.7%). In terms of stimulation durations, the 3 and 5 seconds stimulations provided both, optimal masking and inhibition, compared to the 1 sec stimulation. The RI was found stronger (lower MRIL from this new approach) within the frequency region close to the tinnitus frequency. **Conclusions:** Our study confirms that, from this new approach, MML and MRIL can be easily, quickly and reliably obtained from a wide variety of patients displaying different hearing loss configurations such as presbycusis, flat hearing loss and even normal hearing. More so, this approach allows the categorization of tinnitus patients into different sub-groups based on the properties of their MRIL. Thus, MRIL may provide crucial prognostic information on clinical approaches based on acoustic stimulation and could even be used as a treatment approach.

ID: 115 / Session 3: 2

Abstract Submissions

Keywords: Tinnitus; Insomnia; Sleep; CBT; psychological therapy

Cognitive Behavioural Therapy for Insomnia in Tinnitus

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Introduction

Sleep disturbance affects 50-70% of chronic tinnitus patients and poor sleep may lead to greater distress. Yet there is little research into sleep management in tinnitus and few treatment studies specifically address insomnia. There is a strong evidence base that CBT for insomnia (CBTi) is an effective treatment for sleep disturbance when it presents both as a primary problem and when it is co-morbid with other physical (and mental) health problems, for example, chronic pain.

Method / techniques

Patients with chronic and distressing tinnitus and significant sleep disturbance were offered CBTi. The specifics of the CBT intervention are described, including sleep restriction, stimulus control, psychoeducation, applied relaxation, cognitive restructuring and worry management. Outcome measures included Insomnia Severity Index and sleep diaries, tinnitus distress (Tinnitus Questionnaire – TQ) and psychological distress (CORE-OM, GAD7 and PHQ9).

Results / outcome

Results are reported from two different sources: (1) A Single Case Experimental Design in individual-delivered CBTi and (2) From 20 patients completing group-delivered CBTi within routine care. Results demonstrate that patients completing both group and individual treatment showed a significant improvement in sleep measures.

Discussion / conclusion

Converging evidence from single-case experimental design and routine evaluation suggests that CBTi can offer real improvements for patients with chronic tinnitus and sleep disturbance. Considering the paucity of research into the management and treatment of sleep problems in tinnitus, this evidence is an important addition to our understanding and treatment of insomnia in tinnitus. The authors are now undertaking a Randomized Controlled Trial for CBTi in a tinnitus population, and we will give a brief overview of this to demonstrate how we plan to further assess the efficacy of CBTi compared to existing standard interventions.

ID: 116

Abstract Submissions

Keywords: Noise-induced tinnitus, objective assessment, Auditory Brainstem Response, Empirical Mode Decomposition

Empirical Mode Decomposition of the auditory brainstem response as objective tool for tinnitus assessment

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Amplitudes and latencies of the auditory brainstem response (ABR) have been previously proposed for the search of objective cues of tinnitus. However, although slight differences have been found for impaired and control groups, these differences are not significant enough for diagnosing purpose. A finer technique of processing ABR waveforms is proposed here, which shows quantitatively significant differences between impaired and control subjects. The technique, based on the Empirical Mode Decomposition (EMD) of the ABR, has been applied to click elicited ABR waveforms of Long Evans rats with normal hearing (control group) and noise-induced tinnitus (impaired group). The average ellipse of the control rats group is calculated from the mean and standard deviations of the (tc,fc) centres of the spectrogram of the IMF1s. Results show that the centres of the IMF1 of the tinnitus rats are significantly far of this average ellipse of the control rats.

ID: 118 / Session 8: 3

Abstract Submissions

Keywords: cochlear migraine, tinnitus, hearing loss

Cochlear migraine: proposal for a new diagnosis

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Vestibular migraine (VM) is a common cause of recurrent episodic vertigo and is accompanied by migraine-related symptoms. In the last 30 years of practice in otology and neuro-otology, we have encountered patients presenting with long-term, unilateral, fluctuating hearing loss with aural fullness and tinnitus who never developed vertigo or experienced only mild dizziness that did not meet the strict criteria for VM. Moreover, these patients reported migraine-related symptoms and family histories. Therefore, we coined a new term, "cochlear migraine (CM)," for such patients. The literature supports the view that migraine can damage the cochlear portion of the inner ear via neurovascular mechanisms alone.

We have encountered a number of possible CM patients with similar clinical features and treatment outcomes, and we will describe a representative case in this report.

We propose that patients should fulfill the following criteria for a diagnosis of CM. The major ones include recurrent or fluctuating unilateral sensorineural hearing loss (low frequency or all frequencies) without vertigo or mild dizziness that does not meet the criteria for VM or MD along with aural fullness in the affected ear. Minor clinical features include aura before hearing loss; concomitant tinnitus; family history of migraine-related disorders; previous history of migraine headaches, chronic headaches, or unilateral neck stiffness (on the side of the hearing loss); photo or phonophobia; motion sickness; visual motion intolerance; and sensitivity to atmospheric pressure changes.

We speculate that CM may initially present or be diagnosed as sudden deafness because of the sudden onset of hearing loss. However, after a longer follow-up, when some atypical changes in hearing such as fluctuation or deterioration are observed, a diagnosis of CM should be considered. It is possible that many CM cases are initially misdiagnosed as sudden deafness. In reality, migraine has been found to be a risk factor for sudden deafness. While definite diagnostic criteria and clinical characteristics are not presently defined with scientific rigor in this report, we believe that CM does exist and is a common cause of chronic tinnitus and hearing loss.

ID: 119 / Session 16: 4

Abstract Submissions

Keywords: tinnitus, salicylate, K⁺-Cl⁻ co-transporter gene, Na-K-Cl co-transporter gene, spirulina

Expressions of ion co-transporter genes in salicylate-induced tinnitus and treatment effects with Spirulina

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Background: Although the activity of tinnitus-related ion co-transporter are known, their mRNA expressions has seldom been reported. We aimed to investigate the mRNA expressions of tinnitus-related ion co-transporter genes, and treatment effects of Spirulina.

Methods: The mRNA expressions of K⁺-Cl⁻ co-transporter (KCC2) and Na-K-2Cl co-transporter 1 (NKCC1) genes in the cochlea and brain of mice were evaluated after tinnitus was induced by intraperitoneal injection of salicylate. The effects of spirulina water extract on these gene expressions were investigated.

Results: Compared to the control group, the tinnitus scores increased significantly, however, the salicylate-induced tinnitus could be reduced significantly by spirulina water extract. The tinnitus group had higher of borderline significance mRNA expression of KCC2 gene in the cochlear, significantly higher in the temporal lobes and in the frontal lobes. Meanwhile, compared to the tinnitus group, the spirulina group had significantly lower mRNA expression of KCC2 gene in the cochlear, temporal lobes, frontal lobes and parahippocampus/hippocampus. However, the NKCC1 mRNA expression was not significantly different between three groups in the cochlea and these brain areas.

Conclusion: Salicylate-induced tinnitus might be associated with increased mRNA expression of KCC2 gene, but not with mRNA expressions of NKCC1 gene in the cochlear and some tinnitus-related brain areas. Spirulina reduced the expression of KCC2 genes in salicylate-induced tinnitus.

ID: 120 / Session 19: 2

Abstract Submissions

Keywords: tinnitus, sleep disturbances, sleep apnea, population, case-control study.

Risk of tinnitus in patients with sleep apnea: a nationwide, population-based case-control study

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Objective: To investigate the risk of tinnitus in patients with sleep disturbance or sleep apnea.

Methods: We identified 21,798 middle-aged and elderly patients with otolaryngologist- diagnosed tinnitus between January 1, 2000 and December 31, 2012 from the Longitudinal Health Insurance Database 2000 of the Taiwan National Health Insurance Research Database. A total of 108,990 controls were also identified from the same database based on frequency matching on 10-year age interval, sex, year of index date of the cases. Diagnoses of sleep disturbance (ICD-9-CM codes 780.50, 780.52, 307.4) and sleep apnea (ICD-9-CM codes 780.51, 780.53, 780.57) in the cases and controls prior to the index date were assessed. The risks of tinnitus in patients with sleep disturbance and sleep apnea were separately evaluated with multivariate logistic regression analyses.

Results: The mean age of the total 130,788 patients was 59.8 years and 47% of them were males. The risk of tinnitus was higher in patients with sleep disturbance compared to those without the condition (adjusted odds ratio=1.16, 95% confidence interval [95% CI]=1.12–1.20) and the risk of tinnitus was higher in patients with sleep apnea compared to those without the condition (adjusted odds ratio=1.47, 95% CI=1.26–1.72).

Conclusion: In this population-based, case-control study, the risk of tinnitus was found to be significantly higher among middle-aged and elderly Taiwanese patients with sleep disturbances, especially with sleep apnea.

ID: 121

Abstract Submissions

Keywords: tinnitus, bibliotherapy, manual, anxiety, depression

The use of a small manual as a therapeutic approach to tinnitus patients: some results

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The therapeutic approach to tinnitus patients is difficult for their great heterogeneity, and the individual aspects of each patient complaint's.

The approaches to the psychological aspects tend to be carried out through cognitive-behavioral strategies, which are, sometimes, time consuming for the patient. A small book or manual, which is considered for several authors as an important tool for the success of therapeutic program, and a good tool itself for some patients, could improve the therapeutic approach.

The objectives of this study were: a) develop a manual with information on tinnitus and strategies to deal with them and; b) evaluate their effectiveness in the management of tinnitus discomfort, and to decrease depression and anxiety of patients with tinnitus complaints, and also c) cross this results with other psychological variables, as self-efficacy, coping, optimism and social support.

For this purpose, we have two groups: the intervention group (IG: N = 27), which, in addition to usual care provided at the ENT department of Military Hospital of Porto (Portugal), was also provided with the previously developed manual and the respective instructions for use, and the comparison group (CG: N = 31) who received only the usual care. The pre- and post-intervention assessments were conducted using questionnaires, and Tinnitus Handicap Inventory as reference evaluation.

The values obtained in relation to the perception of the manual's utility (M = 5.81) are moderate such as those found in the literature. The low education level of the sample can be one of the aspects that could explain this result.

Additionally, the individuals of the IG showed a decrease in the intensity of tinnitus, and some decrease in anxiety and depression compared to CG individuals. The THI shows also an improvement in the IG tinnitus perception.

Concerning the other variables, we found an improvement in the self-efficacy perception, and a slight increase in optimism.

This results must be confirmed with a larger sample, and with the use of other therapies. We also propose the use of similar material with hearing loss, hyperacusis or dizziness, to realize their efficacy also with this complaints.

ID: 122

Abstract Submissions

Keywords: chronic, subjective tinnitus, tailor-made notched music, treatment

Chronic subjective tinnitus therapy using tailor-made notched music training

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Background : Chronic tinnitus is a disease that deserves attention and study, because to this date there is no standard cure. The generation and maintenance of tinnitus are assumed to be based on maladaptive functional cortical reorganization. Listening to modified music, which contains no energy in the range of the individual tinnitus frequency, can inhibit the corresponding neuronal activity in the auditory cortex. Based on this assumption, a novel treatment for tonal tinnitus - tailor-made notched music training (TMNMT) - has been introduced and was tested in this clinical trial.

Methods: A randomized controlled trial in parallel group design was performed in a double-blinded manner. We included 30 participants with chronic, tonal tinnitus assigned to either a classical TMNM (treatment group) or an normal music group (control group), who listened to music for two hours a day for three months. Our primary outcome measures were the Tinnitus Handicap Inventory (THI) and Visual Analog Scales (VAS) measuring perceived tinnitus loudness, awareness, distress and handicap. Participants rated their tinnitus before and one month, two months and three months during the training.

Results: There was no difference between the primary outcome measures by THI and VAS before treatment. The mean score of tinnitus loudness, awareness, distress and handicap in the treatment group was significantly reduced as compared to those of the control group during the one month, two months and three months of treatment.

Conclusion: Chronic tinnitus patients who underwent TMNM therapy showed improved THI and VAS scores, particularly the emotional score of the THI. TMNM therapy is a effective treatment for chronic subjective tinnitus.

ID: 123 / Session 18: 4

Abstract Submissions

Keywords: Cochleara Implant, Tinnitus, Hearing Loss

Cochlear Implantation for Tinnitus in Subjects with Hearing Loss

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Aim:

Cochlear implants (CIs) have been reported as a standard method to rehabilitate severe-to-profound sensorineural hearing loss, hence improve speech and language significantly. In some studies, cochlear implantation also has its role in reduce tinnitus. The aim of this study is to present our experience in tinnitus management with cochlear implantation in patients with both tinnitus and asymmetrical hearing loss.

Material and Methods:

Subjects with profound hearing loss with tinnitus were recruited in this study . All subjects underwent implantation of a multichannel CI. The device was switched on 1 day after cochlear implantation. A visual analog scale (VAS) , The Hospital Anxiety and Depression Scale (HADS) and the Tinnitus Questionnaire(Tinnitus Handicap Inventory, THI) were administered before implantation (within 1 day prior to surgery) and 1 day, 1 week, 2 weeks, 1 month, 3 months after the operation. The scores of the questionnaires were analyzed by paired T test.

Results

The structural interview revealed that all patients (7/7) still wear their CI seven days a week after cochlear implantation. Given the relative small sample size, quantitative data are presented as median and range (minimum and maximum).

The data presented above demonstrate a consistent reduction in tinnitus loudness with electrical stimulation via a CI in all of our subjects. In our study, tinnitus reduced significantly after 2 weeks of the first-matching and this condition remained stable in further follow up periods, which is consistent with other recent studies. Another finding was that the THI,VAS and HADS scores were all increased one day after the operation, we hypothesize that is related to the post-operative stress and discomfort.

Conclusion:

Significant reduction of tinnitus was noted after the initial matching and remained stable after then. Further study with larger population is needed to validate the long-term scenario of tinnitus reduction, and the effect of daily performance over time as well.

ID: 124 / Session 3: 3

Abstract Submissions

Keywords: CBT, implementation, stepped-care, effectiveness trial

CBT for tinnitus: successful replication of a stepped care approach

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Background

A previous randomised controlled trial (RCT) of specialised stepped care CBT treatment demonstrated significant reductions in the severity and interference experienced by individuals suffering from tinnitus (a common audiological symptom frequently likened to a ringing or buzzing in the ears) (Cima et al., 2012). A replication and external validation study was conducted in order to examine whether this specialised CBT treatment could be implemented within a different existing audiological rehabilitation practice in The Netherlands and also successfully achieve similar levels of effectiveness.

Method

An uncontrolled, prospective intervention study was conducted between March 2014 and December 2016 at an audiological rehabilitation centre in Eindhoven, The Netherlands. A total of 925 adult participants suffering from tinnitus were included in an intention to treat analysis.

Outcome measures included patients': levels of tinnitus related distress and interference (Tinnitus Questionnaire, Tinnitus Handicap Inventory); catastrophizing (Tinnitus Catastrophizing Scale); fear (Fear of Tinnitus Questionnaire); quality of life (Health Utilities Index), and affect (Hospital Anxiety and Depression Scale). Data was collected at baseline, and three, eight and 12-months after baseline (total trial time: 12 months).

Psychologists, physical therapists and audiologists underwent training in the specialised treatment prior to the trial commencing and received regular supervision and coaching throughout to promote treatment fidelity. The stepped-care CBT treatment is tailored to patients' needs; those with relatively mild tinnitus distress receive only Step 1 of the treatment and only those with more severe interference also receiving Step 2. Step 1 involves individual psychological and audiometric assessment respectively, a group based education session and a case-by-case interdisciplinary treatment plan discussion. Step 2 involves group based CBT treatment ranging from 12 to 22 sessions (dependent on severity and hearing impairment) with a main focus on exposure with use of mindfulness based methods tailored to tinnitus, physical and relaxation exercises.

Results

Intention to treat, multilevel regression analyses indicated ($p < .01$) improvements on all outcome measures at all time points after controlling for tinnitus severity and duration, age and sex.

Discussion

Results indicate that overall, patients who received the specialised stepped care CBT program for tinnitus, reported similar levels of improvement as those in the earlier RCT. The absence of a control group represents the major limitation of the study. All sessions were video- and audio-recorded to enable a treatment fidelity check with the analyses of protocol adherence and treatment contamination in process. Results of the treatment fidelity analyses will be reported in the near future.

Conclusion

Specialised stepped care CBT for tinnitus appears to be effective at reducing tinnitus severity and interference in activities of daily living when implemented under "real world" conditions. Wider implementation of this specialised treatment program is likely to be successful without compromising effectiveness and has the potential to be included in future standard treatment protocols for tinnitus.

ID: 125 / Session 7: 1

Abstract Submissions

Keywords: Auditory cortex, cortical plasticity, lateral inhibition, tinnitus, music, MEG

Cortical plasticity induced by unimodal and multimodal training in tinnitus patients

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The generation and maintenance of tinnitus is assumed to be based on maladaptive functional cortical reorganization. Listening to modified music, which contains no energy in the range of the individual tinnitus frequency, can inhibit the corresponding neuronal activity in the auditory cortex. Music making has been shown to be a powerful stimulator for brain plasticity, inducing changes in multiple sensory systems. Using magnetoencephalographic (MEG) and behavioral measurements we evaluated the cortical plasticity effects of two months of (a) active listening to (unisensory) vs. (b) learning to play (multisensory) tailor-made notched music in non-musician tinnitus patients. Taking into account the fact that uni- and multi- sensory training induces different patterns of cortical plasticity we hypothesized that these two protocols will have different affects. Only the active listening (unisensory) group showed significant reduction of tinnitus related auditory activity and an increase in the activity of a tinnitus-coping related posterior parietal area. These findings indicate that active listening to tailor-made notched music induces greater neuroplastic changes in the maladaptively reorganized cortical network of tinnitus patients, while additional integration of other sensory modalities during training reduces these neuroplastic effects.

ID: 126 / Session 8: 1

Abstract Submissions

Keywords: tinnitus, cognitive, model, qualitative

“My goodness, that really does actually sum it up:” tinnitus patients’ and therapists’ perspectives on the cognitive model of tinnitus distress

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Introduction and Aims

The cognitive model of tinnitus distress (McKenna et al., 2014) proposes that tinnitus becomes and is maintained as a problem due to a cycle of interaction between negative thoughts, beliefs, emotions, selective attention, safety behaviour and distorted perception. As well as informing the development of psychological therapy for tinnitus, the model has potential for use as a therapeutic tool to help patients understand their problems with tinnitus better. Tinnitus education is a key component of many types of tinnitus therapy and yet little is known about how helpful patients find it to have a tinnitus model explained to them. The aim of this qualitative study was to explore patients’ and therapists’ perspectives on the cognitive model of tinnitus distress.

Methods

There were two groups of participants. The first was made up of 11 tinnitus patients (8 women and 3 men) who had been attending a mindfulness- based cognitive behavioural therapy for tinnitus course, at which the cognitive model had been explained to them using a diagram. Ages ranged from 29 to 70 and tinnitus duration from 10 months to 50 years. A semi-structured interview was conducted with each participant, in which they were invited to discuss the model in relation to their personal experience with tinnitus. The second group was made up of five experienced tinnitus therapists. They took part in a focus group in which they were invited to discuss the model from a clinical perspective. All interviews and the focus group were audio recorded, transcribed and coded by two independent coders using thematic analysis. Codes were compared and discrepancies resolved through discussion.

Results

Therapists regarded the model as over-complicated, while all the patients found the model quite easy to understand, bar a few confusions over terminology. All participants felt that the model reflected their own experience with tinnitus to a substantial degree and people identified particularly strongly with the idea of negative thoughts increasing tinnitus distress. Some patients and some therapists felt that parts of the experience of tinnitus were missing from the model or not depicted accurately and there were differing views about whether one’s perception of tinnitus loudness might be distorted. Opinions also differed about whether or not understanding the model is in itself a helpful step towards successful tinnitus management, and therapists preferred alternative methods of explaining tinnitus

Conclusion

All patients in this study found the cognitive model understandable and broadly reflective of their experience, but therapists had reservations about using it in appointments. Further investigation into its usefulness as a therapeutic tool is recommended.

MCKENNA, L., HANDSCOMB, L., HOARE, D. & HALL, D. 2014. A scientific cognitive behavioral model of tinnitus: novel conceptualizations of tinnitus distress. *Frontiers in Neurology*, 5.

ID: 127

Abstract Submissions

Keywords: tinnitus, cognitive, model, path analysis

Systematic Evaluation of a Cognitive Model of Tinnitus Distress using Path Analysis

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Aim

The cognitive model of tinnitus distress (McKenna, Handscomb et al. 2014) is a theoretical model which describes the interaction between thoughts, emotions, behaviour and attention that may cause tinnitus to become, and be maintained as, a distressing problem. This project set out to construct testable versions of this theoretical model and assess how well these fit data obtained from people with tinnitus.

Material and methods

A survey was compiled from existing questionnaires which provided measures of each separate construct within the model. This was made available online and on paper. Members of the public with tinnitus were recruited from a volunteer database and from tinnitus organisations. The survey was completed by 342 adults who reported varying degrees of overall tinnitus distress. Factor analysis of all the questionnaires was carried out and 12 different versions of the cognitive model were created based on questionnaire results, existing literature and theory. These were then tested using path analysis.

Results

A satisfactory factor structure was found for all questionnaires and the resulting 15 factor scores were used in path analysis. All of the path models constructed were at least an acceptable fit to the data (RMSEA <0.080). The two best fitting models had comparable fit indices (model 1: RMSEA = 0.063, CFI = 0.984, TLI = 0.969; model 2: RMSEA = 0.057, CFI = 0.993, TLI = 0.981). They differed primarily in the placement of tinnitus magnitude, which was a product of attention in model 1, but an exogenous variable in model 2. Additionally, model 1 included tinnitus control beliefs while model 2 did not.

Conclusions

The predictions made by the cognitive model of tinnitus distress were supported by the questionnaire data obtained in this study, and it is to be recommended as a solid foundation for psychological therapy for tinnitus. Questions remain as to the role of beliefs in tinnitus distress and as to whether and to what degree perceived magnitude is influenced by psychological processes.

Reference:

McKenna, L., L. Handscomb, D. Hoare and D. Hall (2014). "A scientific cognitive behavioral model of tinnitus: novel conceptualizations of tinnitus distress." *Frontiers in Neurology* 5.

ID: 129

Abstract Submissions

Keywords: control groups, tinnitus distress, psychopathology profiles

THE NECESSITY OF CONTROL GROUPS WITH PSYCHIATRIC DISORDERS IN TINNITUS RESEARCH

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Introduction

In previous research tinnitus patients were often compared to healthy controls or other otological patients. This assumes that those two groups differ only in one aspect – the presence of tinnitus. On the other hand, patients with high tinnitus distress are often excluded from tinnitus studies due to high comorbidity with psychiatric disorders, making it impossible to generalise the research outcomes to the whole tinnitus-population. Here, we examine the psychiatric profiles of 4 groups, i.e. mild tinnitus distress, severe tinnitus distress, healthy controls and psychiatric controls.

Methods

A total of 136 participants took part in this study (37 tinnitus patients with mild distress, 24 tinnitus patients with severe distress, 42 healthy controls and 33 psychiatric inpatient controls with depression and/or anxiety disorders). The group allocation was performed with the German version of the Tinnitus-Questionnaire and the SKID-I-Interview. Assessment of the psychiatric profile was done with various standardised clinical questionnaires such as BDI-II, HADS, HAM, SLC-90-R and SOMS-2. To avoid type I-error inflation by multiple comparisons, we performed explorative discriminant analyses to identify group profiles indexed by psychiatric measures.

Results

In our analysis we were able to identify two discriminant factors which were able to explain more than 90 % of the group variance. The first factor explains 60.4 % of the variance, and discriminates all groups but severe tinnitus patients from psychiatric controls. The second factor explains additional 30.3% of group variance, and enables us to discriminate between psychiatric controls and both tinnitus groups, but not between mild and severe tinnitus distress. Results also showed consistently high discrimination of the healthy control group from all other groups.

Discussion

Our findings indicate considerably high rates of psychopathology in tinnitus patients, which are comparable to a psychiatric controls with manifest depression and/or anxiety disorders. Most importantly, our results indicate that the psychopathology profiles have to be taken into account even if patients with mild tinnitus distress are being compared with healthy controls. Moreover, severe tinnitus distress and psychiatric controls are similarly affected regarding standardised psychiatric measures. Therefore, for the investigation of patients with severe tinnitus distress the use of a psychiatric control group recommends itself. Such an approach would finally allow us to include all tinnitus patients and to capture the whole width of the phenomenon in future research.

ID: 130 / Session 13: 2

Abstract Submissions

Keywords: prediction, treatment, distress

PREDICTION OF THERAPY SUCCESS IN CHRONIC TINNITUS

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Introduction

Despite the development of diverse tinnitus treatments, the prediction of success proved to be difficult. We present data from a large group of chronic tinnitus patients that received a 5 day interdisciplinary day care treatment (JITT, Ivansic et al. 2017).

In line with psychiatric findings, we found in an earlier study that an early change as fast response to minimal treatment predicts later treatment success. In the current study we investigated this further, we searched for the best regression model to predict early change, the change by treatment and how treatment prediction could be improved.

Method

The sample consisted of 446 patients that were treated according to JITT. Treatment outcome was defined by change in score of German version of the Tinnitus-Questionnaire between screening day (T0), start (T1) and end (T2) of treatment, as well as for follow ups at T3 (25 days after T1) and T4 (6 months after T2).

The total of 28 predictive variables came from four domains of interest: Demographics, tinnitus-related variables, strain variables and otological comorbidity. We conducted an exhaustive search of all possible linear regression subsets of those variables using the leaps-Package in R.

Results

The prediction of early change was best modelled (adj. $R^2 = .19$) with eight variables from tinnitus-related, strain and otological-comorbidity domains. Across analyses, these variables appear stable. In comparison, the prediction of treatment outcome from T1 to T4 was less successful (adj. $R^2 = .11$) resulting in a model with eight variables from all domains of interest with age and gender being the most stable ones. Only two variables for prediction of early change and response to treatment overlapped, i.e. PHQ-15 somatic symptoms and tinnitus distress at T0.

To account for heterogeneity, the sample was divided into quartiles regarding tinnitus severity at T0. Performing similar analyses as described above improved the explained variance within subgroups (e.g. change from T1 to T4: adj. $R^2 = .31$ for patients with moderate tinnitus). The subgroup whose treatment success was hardest to predict was the group with most severe tinnitus (adj. $R^2 < .1$).

Discussion

Even though we used a rather large sample and performed an exhaustive search of regression models, the prediction of treatment outcome remains difficult for tinnitus patients. The improvement of the prediction in subgroups supports the assumption that heterogeneity is one reason for this difficulty. From a statistical viewpoint we feel safe to say that a larger sample would not increase the explained variance. Early change seems to rely on different mechanisms than response to treatment, as indicated by the sparse overlap of predictors. It is yet an open question why treatment success is so hard to predict in patients with severe tinnitus distress. We assume that they are either a particularly heterogeneous group and/or suitable variables to describe this group were not measured. Taken together, it appears that the heterogeneity of tinnitus is still a driving question even if therapies are successful. To predict therapy success the various stages of treatment have to be taken into account.

ID: 131

Abstract Submissions

Keywords: 5-HTTLPR polymorphism, ANS function, sleep quality, chronic subjective tinnitus

5-HTTLPR Polymorphism affects Sleep Quality and Autonomic Function among Chronic Subjective Tinnitus Patients

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Objectives: Anxiety and sleep disturbance are common in chronic tinnitus. Serotonin transporter (5-HTT)-linked polymorphic region (5-HTTLPR) polymorphism is a well-known risk factor for anxiety. For adult subjects with chronic subjective tinnitus, we investigated the influence of 5-HTTLPR functional polymorphisms on autonomic nerve system (ANS) function and sleep quality.

Methods: Adult patients with subjective tinnitus were recruited. Duration of tinnitus complaint was required to be at least 6 months. Subjects with hearing impairment and known diagnosed insomnia and mood disorders were excluded. Objective assessments included over-night polysomnography and ANS function test (Cold Pressor Test). Subjective questionnaire assessment was Tinnitus Handicap Inventory (THI). 5-HTTLPR and rs25531 polymorphisms of SLC6A4 gene were determined by polymerase chain reaction-restriction fragment length polymorphism analysis. Because S and LG carriers express lower levels of 5-HTT, we divided 5-HTTLPR polymorphisms into two groups, low-functional (S/S, S/LG, LG/LG: hereafter S+) and high-functional (S/LA, LG/LA, LA/LA: hereafter L+), for data analysis.

Results: Forty tinnitus patients and 40 control subjects without tinnitus were analyzed. Total score of THI among tinnitus group was significantly higher ($p < 0.05$). For the group with 5-HTTLPR S+ genotype, higher tinnitus severity was significantly correlated to sympathetic hyperactivity and longer sleep latency, individually ($p < 0.05$). Unfortunately, there was only a significantly correlation between tinnitus severity and increase in heart rate occurred in Cold Pressor Test among subjects with 5-HTTLPR L+ genotype.

Conclusion: For subjects with low functional genotype of 5-HTTLPR polymorphism, the associations of tinnitus severity with ANS function and sleep quality were significant.

ID: 132 / Session 16: 2

Abstract Submissions

Keywords: gene set enrichment analysis, genome-wide association study, heritability, oxidative stress, phenotype, serotonin, tinnitus

A pilot Genome-wide Association Study identifies potential metabolic pathways involved in tinnitus

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Introduction. A Genome-Wide Association Study (GWAS) on age-related hearing impairment (ARHI), the most common form of hearing impairment in the elderly, was previously carried out. A highly polygenic character of ARHI was shown, with no major genes involved (Fransen et al., 2014). In this dataset, 18% of the participants reported to perceive 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. Tinnitus is perceived by approximately 15% of the population. The contribution of genes on the development of tinnitus is still under debate as heritability estimated range from 11% to 40% in literature. In the current study, the tinnitus phenotype was retrospectively tested for association with the genome-wide single-nucleotide polymorphism (SNP) data from the ARHI population obtained in the previous study.

Methods. The current study performed a pilot Genome Wide Association Study (GWAS) into tinnitus, in a small cohort of 167 independent tinnitus subjects, and 749 non-tinnitus controls, who were collected as part of a cross-sectional study. After genotyping, imputation and quality checking, the association between the tinnitus phenotype and 4 000 000 SNPs was tested followed by gene set enrichment analysis.

Results. None of the SNPs reached the threshold for genome-wide significance ($p < 5.0e-8$), with the most significant SNPs, situated outside coding genes, reaching a p-value of $3.4e-7$. By using the Genetic Analysis of Complex Traits (GACT) software, the percentage of the variance explained by all SNPs in the GWAS was estimated to be 3.2%, indicating that additive genetic effects explain only a small fraction of the tinnitus phenotype. Despite the lack of genome-wide significant SNPs, evidence was found for a genetic involvement in tinnitus. Gene set enrichment analysis showed several metabolic pathways to be significantly enriched with SNPs having a low p-value in the GWAS. These pathways are involved in oxidative stress, endoplasmatic reticulum (ER) stress and serotonin reception mediated signalling.

Conclusions.

These results are a promising basis for further research into the genetic basis of tinnitus, including GWAS with larger sample sizes and considering tinnitus subtypes for which a greater genetic contribution is more likely.

ID: 133

Abstract Submissions

Keywords: tinnitus, neuromodulation, transcranial direct current stimulation, high-definition transcranial direct current stimulation, treatment

Effects of electrical stimulation in tinnitus patients: a comparison between t-DCS with two different electrode placements and HD t-DCS

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Aim. There is currently no effective therapy available for all tinnitus patients. Maladaptive plastic changes and altered activity in the auditory and prefrontal cortex underlie the tinnitus percept. Concerning transcranial direct current stimulation (t-DCS) as a treatment for tinnitus, contradictory results have been reported in literature. The present study compares t-DCS using two different electrode placements with high-definition t-DCS (HD t-DCS) in terms of their therapy effects. HD t-DCS is a recent technique that limits the broad excitation patterns of t-DCS by using smaller electrodes.

Material and methods. The first retrospective part of the study compares two t-DCS electrode placements. 39 patients receive bifrontal t-DCS (DLPFC), another 39 patients receive the alternative t-DCS positioning (SO-LTA), where the electrodes are placed at the right supraorbital area (SO) and the left temporal area (LTA). The second prospective part of the study administers HD t-DCS at the right dorsolateral prefrontal cortex (DLPFC) in 17 patients. The therapy effects are determined by the tinnitus functional index (TFI), visual analogue scale (VAS), hyperacusis questionnaire (HQ), tinnitus questionnaire (TQ) and hospital anxiety and depression scale (HADS) filled out at three visits: pre-therapy, post-therapy and follow-up.

Results. The first part of the study shows a highly significant improvement determined with the TFI in both tDCS groups (DLPFC: $p=0.002$; SO-LTA: $p=0.007$). In 33% of the tinnitus patients a decrease of 13 points or more on the TFI from the pre-therapy visit to the follow-up visit is apparent, indicating a clinically significant improvement. The effect of t-DCS on the HQ or VAS over time is not significant in both groups (DLPFC HQ: $p=0.71$; DLPFC VAS: $p=0.49$; SO-LTA HQ: $p=0.31$; SO-LTA VAS: $p=0.06$). The two groups do not show differences on the outcomes measurements (TFI: $p=0.16$; HQ: $p=0.85$; VAS: $p=0.06$). The second part of the study shows a significant improvement determined with the TFI ($p=0.047$). In 35% of the tinnitus patients a clinically significant improvement is apparent. Furthermore, there is a significant improvement on the anxiety subscale of the HADS after HD t-DCS ($p=0.049$).

Discussion. The TFI scores decrease significantly in the patients who receive t-DCS and HD t-DCS, with respectively 33 and 35% showing a clinically significant improvement. The two electrode placements for t-DCS do not differ in their therapy effect. The lack of a sham group forms a limitation in the current study.

Conclusions. Electrical stimulation with t-DCS and HD t-DCS improves significantly the TFI scores of patients with chronic tinnitus.

ID: 135

Abstract Submissions

Keywords: Misophonia, tinnitus, hyperacusis, selective attention, auditory processing

Evaluation of selective attention in patients with misophonia.

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University of São Paulo / Instituto Ganz Sanchez, Brazil;

INTRODUCTION: Misophonia is characterized by the aversion to very selective sounds, which evoke a strong emotional reaction. It has been inferred that misophonia, alike tinnitus, is associated with increased connectivity between auditory and limbic systems. Individuals with bothersome tinnitus may have impairment of selective attention, but it has not yet been studied in misophonia.

OBJECTIVE: to evaluate a sample of misophonic subjects and compare it to two control groups, one with tinnitus and another with asymptomatic individuals, regarding the selective attention.

METHODS: we evaluated 40 normal-hearing participants who were included in 3 groups: 10 with misophonia (MG), 10 with tinnitus (without misophonia) (TG) and 20 asymptomatic (without tinnitus and misophonia) (AG). In order to evaluate the selective attention, the Brazilian Portuguese version of the Dichotic Sentence Identification (DSI) Test was applied to MG, TG and AG. Then, we adapted the conventional DSI test with a combination of two competitive sounds: a chewing sound (a common trigger of misophonia) and white noise (a common type of annoying tinnitus), using each one at a time. Afterward, the DSI test was applied 3 times to all participants of the 3 groups following a randomized order of 1:1.

RESULTS: In the DSI test with chewing sound, the average of correct responses was lower for subjects of MG when compared to AG ($p=0.027$) and TG ($p=0.002$). In the conventional DSI test and in DSI test with white noise, no significant difference was observed at the average of correct responses in the 3 groups ($p\geq 0.452$).

CONCLUSION: Participants of Misophonia Group showed an impairment of their selective attention when they were concomitantly exposed to sounds that commonly trigger the condition.

ID: 136

Abstract Submissions

Keywords: Misophonia, tinnitus, hyperacusis, heredity, autosomal dominant inheritance

Familial misophonia or Selective Sound Sensitivity Syndrome: evidence for autosomal dominant inheritance?

Tanit Ganz Sanchez, Fulvia Eduarda Silva

University of São Paulo / Instituto Ganz Sanchez, Brazil;

Introduction: Misophonia is a recently described, poorly understood and neglected condition. It is featured by strong negative reactions of hatred, anger or fear when subjects have to face some selective and low level repetitive sounds. The most common ones that trigger such aversive reactions are those elicited by the mouth (chewing gum or food, popping lips), the nose (breathing, sniffing, and blowing) or by the fingers (typing, kneading paper, clicking pen, drumming on the table). Previous articles have cited that such individuals usually know at least one close relative with similar symptoms, suggesting a possible hereditary component.

Objective: to describe a family with 15 members having misophonia, detailing their common characteristics and the pattern of sounds that trigger the symptoms.

Method: All 15 members agreed to give us their epidemiological data, and 12 agreed to answer a specific questionnaire about their symptoms, specific trigger sounds, main feelings and attitudes adopted by each participant.

Results: The 15 members belong to three generations of the family. Their age ranged from 9 to 73 years (mean 38.3 years; median 41 years) and 10 were females (66.7%). Analysis of the 12 questionnaires showed that 10 subjects (83.3%) developed the first symptoms during childhood or teenage. The mean annoyance score on the Visual Analogue Scale from 0 to 10 was 7.3 (median 7.5). Individuals reported hatred/anger, irritability and anxiety in response to sounds, and faced the situation asking to stop the sound, leaving/avoiding the place and even fighting. The self-reported associated comorbidities were anxiety (91.3%), tinnitus (50%), obsessive-compulsive disorder (41.6%), depression (33.3%), and hypersensitivity to sounds (25%).

Conclusion: The high incidence of misophonia in this particular familial distribution suggests that it might be more common than expected and raises the possibility of having an autosomal dominant inheritance.

ID: 137 / Session 18: 1

Abstract Submissions

Keywords: Single-sided deafness, tinnitus, cochlear implantation, 10 years follow-up

Cochlear Implantation as a Long-Term Treatment for Ipsilateral Incapacitating Tinnitus in Subjects with Unilateral Hearing Loss up to 10 years.

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

SUBJECTS: 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). The SSD group comprises subjects with contralateral normal hearing (i.e. air conduction pure tone average (PTA_{0.5, 1, 2 and 4kHz}) ≤ 30 dB HL) and the AHL group subjects with contralateral mild to moderate hearing loss (i.e. air conduction PTA_{0.5, 1, 2 and 4kHz} > 30 dB HL).

METHODS: 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 VAS_{tinnitus 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 CI_{ON} and the CI_{OFF} 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. It appeared that in all subjects but one CI switch-on is the first act when rising and CI switch-off is the last act before bedtime. 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 CI_{OFF} condition and improved to 23,5 (12-39) in the CI_{ON} condition in the SSD group.

CONCLUSION: This is the first study to report on LT results in a large number of UHL CI users, up to 10 years. 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.

ID: 138 / Session 7: 2

Abstract Submissions

Keywords: tinnitus, comorbidity, limbic system, voxel based morphometry

BRAIN STRUCTURAL CHANGES IN CHRONIC TINNITUS – THE PROBLEM OF PSYCHIATRIC COMORBIDITY

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Introduction

A large number of studies evidenced that tinnitus is not only a sensory phenomenon, but that it affects also cognitive and emotional processes. Regarding the latter, the high comorbidity of tinnitus with psychiatric disorders such as depression and anxiety, spoke for itself. On the neuronal level this is reflected in neuroimaging studies addressing structural and functional changes demonstrating involvement of limbic structure. Nevertheless, psychiatric symptoms are often an exclusion criterion for participation. Due to the high comorbidity with tinnitus, this very often results in exclusion of patients with severe tinnitus. We investigated grey matter changes measured with voxel based morphometry (VBM) in four groups: patients with mild tinnitus distress, patients with severe tinnitus distress, healthy controls and psychiatric inpatient controls. This approach allows us to describe structural changes in a 2x2 design and thus to assess main effects and interactions.

Methods

A total of 125 participants took part in this study (30 patients with mild tinnitus distress, 29 patients with severe tinnitus distress, 40 healthy controls and 26 psychiatric inpatient controls). The group allocation was performed using the German version of the Tinnitus-Questionnaire and the SKID-I-interviews. Psychiatric patients were recruited from consecutive admissions with depressive and/or anxiety disorders. For the T1-weighted measures a standard quadrature head coil and an axial 3-dimensional magnetization prepared rapid gradient echo (MP-RAGE) sequence (TR 2300ms, TE 2.07ms, α 9°, 192 contiguous sagittal slices, in-plane field of view 256 mm, voxel resolution 1 × 1 × 1 mm; acquisition time 5:21 min) was used on a 3 Tesla Siemens Prisma fit system. The CAT12 toolbox implemented in SPM12 was employed for VBM analyses.

Results

Confirming earlier results in a hypothesis-based analysis, comparison of patients with mild tinnitus distress and healthy controls revealed significantly smaller grey matter volumes (GMV) for patients in anterior and posterior cingulate as well as parahippocampal gyri. The 2x2 ANOVA evidenced for the main effect “tinnitus vs. no-tinnitus” decreased GMV in tinnitus patients ($p < 0.001$, uncorrected), mainly in left parahippocampal and fusiform gyri, as well as right inferior parietal gyrus and precuneus. The main effect “psychiatric symptoms vs. no psychiatric symptoms” revealed only differences between groups in very small clusters. Only one cluster exceeded the expected cluster size of 158.37 with a size of $k = 260$ and was located in right superior temporal gyrus. No interaction effects were found.

Discussion

We replicated earlier evidence for structural grey matter changes in mild tinnitus patients compared to controls. Importantly, we also demonstrate an involvement of the left parahippocampal and fusiform gyri, as well as right inferior parietal gyrus and precuneus. These changes are independent from the presence of psychiatric symptoms. The lack of interaction effects argues, in our view, for largely independent effects of tinnitus and psychiatric symptoms on structural brain changes.

ID: 139 / Session 6: 1

Abstract Submissions

Keywords: outcome domains; clinical trials; methodology; standards

INTERACTIVE CONSENSUS WORKSHOP FOR THE COMIT'ID STUDY: INTERNATIONAL CONSENSUS ON CORE OUTCOME DOMAINS FOR EARLY-PHASE CLINICAL TRIALS OF SOUND-, PSYCHOLOGY-, AND PHARMACOLOGY-BASED INTERVENTIONS TO MANAGE CHRONIC SUBJECTIVE TINNITUS IN ADULTS: THE COMIT'ID STUDY

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Background: The reporting of outcomes in clinical trials of subjective tinnitus indicates that many different tinnitus-related complaints are of interest to investigators, from the perceptual attributes of tinnitus (e.g. loudness) to psychosocial impacts (e.g. quality of life). Even when considering one type of intervention strategy for subjective tinnitus, there is no agreement about what is critically important for deciding whether a treatment is effective. The main purpose of this observational study is therefore to develop Core Outcome Domain Sets for the three different intervention strategies (sound, psychological, and pharmacological) for adults with chronic subjective tinnitus that should be measured and reported in every clinical trial of these interventions (even if they are not one of the primary outcomes). This workshop invites all those interested in this topic to share their views on the recommendations arising from the COMIT'ID study ('Core Outcome Measures in Tinnitus: International Delphi').

Methods: The 'Core Outcome Measures in Tinnitus: International Delphi' (COMIT'ID) study used a mixed methods approach for achieving consensus, designed with input from healthcare users, clinical experts and a trialist. Healthcare users, healthcare practitioners, clinical researchers, commercial representatives and funders all participated in online Delphi surveys (over 650 participants, from over 30 countries) and face-to-face meetings (over 55 participants). For transparency, our methods have been published ahead of the analysis (Fackrell et al., 2017).

Results: Findings will be summarised for three independent studies; one for each intervention. In each case, the Delphi surveys reduced a long list of over 60 candidate outcome domains to those 20 or so considered by all stakeholder groups to be important and critical. The subsequent meetings reduced these down to a maximum of 6. Some were common to more than one intervention strategy (e.g. 'tinnitus intrusiveness'), others were deemed to be specific to just one intervention strategy (e.g. 'negative thoughts and beliefs'). This workshop invites active participation to discuss the findings; with the aspiration to obtain TRI and TINNET endorsement for the recommendations.

Discussion: This COMIT'ID study seeks to improve future tinnitus research by creating an evidence-based consensus about minimum reporting standards for outcomes in clinical trials of a tinnitus intervention. The output will be a core set of important and critical outcomes to be measured and reported in all clinical trials. Endorsement and dissemination will be crucial for promoting uptake across the community.

Funding: We acknowledge support from NIHR Nottingham Hearing Biomedical Research Unit, NIHR Nottingham Biomedical Research Centre, British Tinnitus Association, Action on Hearing Loss, and European Cooperation in Science and Technology (COST) Action (BM1306).

Reference: Fackrell K, Smith H, Colley V, Thacker B, Horobin A, Haider HF, Londero A, Mazurek B, Hall DA (2017) Core Outcome Domains for early phase clinical trials of sound, psychology-, and pharmacology-based interventions to manage chronic subjective tinnitus in adults: the COMIT'ID study protocol for using a Delphi process and face-to-face meetings to establish consensus. *Trials* 18(1): 388.

ID: 140 / Session 14: 1

Abstract Submissions

Keywords: Patients; lived experience; plain language

INVOLVING MEMBERS OF THE PUBLIC IN THE COMIT'ID STUDY (CORE OUTCOME MEASURES IN TINNITUS: INTERNATIONAL DELPHI)

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Background: Tinnitus is a complex audiological condition affecting many different facets of everyday life. Clinical trials of tinnitus interventions measure and report outcomes inconsistently and this hinders direct comparison between study findings. To address this problem, an ongoing project is developing a Core Outcome Set; an agreed list of outcomes to be measured and reported in all future trials. Part of this process uses a consensus methodology ('Delphi' survey), whereby all relevant stakeholders identify important and critical outcomes from a long list of candidate outcome domains. This article addresses a gap in the patient involvement literature by describing and reflecting on our involvement of patients to create a meaningful long list of candidate outcomes.

Methods: Two Public Research Partners with lived experience of tinnitus reviewed an initial list of 124 domains over two face-to-face workshops. With the Study Management Team, they were asked to interpret each candidate outcome domain and generate a plain language description. Following this, the outcome names and descriptions underwent an additional lay review by 14 patients and 5 clinical experts, via an online survey platform.

Results: Insights gained from the workshops and survey feedback prompted substantial, unforeseen modifications to the long list. These included the reduction of the number of domains (from 124 to 66) via the exclusion of broad concepts and consolidation of equivalent outcome domains or domains outside the scope of the study. Reviewers also applied their lived experience of tinnitus to bring clarity and relevance to outcome names and plain language descriptions.

Conclusions: Patient involvement was an integral and transformative step of the study design process. Patient involvement was impactful because the online Delphi survey was successful in recruiting and retaining participants, and there were many comments about a positive participatory experience. We highlight seven general features of our approach which fit with general principles of good patient involvement. These can benefit other Core Outcome Set developers.

Funding: We acknowledge support from NIHR Nottingham Hearing Biomedical Research Unit, NIHR Nottingham Biomedical Research Centre, British Tinnitus Association, Action on Hearing Loss, and European Cooperation in Science and Technology (COST) Action (BM1306).

CORE OUTCOME DOMAINS FOR EARLY-PHASE CLINICAL TRIALS OF SOUND-, PSYCHOLOGICAL-, AND PHARMACOLOGICAL-BASED INTERVENTIONS TO MANAGE CHRONIC SUBJECTIVE TINNITUS IN ADULTS: PROTOCOL FOR USING A DELPHI PROCESS AND FACE-TO-FACE MEETINGS TO ESTABLISH CONSENSUS

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Infante Santo - Nova Medical School, Portugal.; ⁵Consultation Acouphène et Hyperacousie, Hôpital Européen G. France.;

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Background: The reporting of outcomes in clinical trials of subjective tinnitus indicates that many different tinnitus-related complaints are of interest to investigators, from perceptual attributes of the sound (e.g. loudness) to psychosocial impacts (e.g. quality of life). Even when considering one type of intervention strategy for subjective tinnitus, there is no agreement about what is critically important for deciding whether a treatment is effective. The main purpose of this observational study is, therefore to, develop Core Outcome Domain Sets for the three different intervention strategies (sound, psychological, and pharmacological) for adults with chronic subjective tinnitus that should be measured and reported in every clinical trial of these interventions. Secondary objectives are to identify the strengths and limitations of our study design for recruiting and reducing attrition of participants, and to explore uptake of the core outcomes. This poster describes the study protocol [Fackrell et al., 2017].

Methods: The 'Core Outcome Measures in Tinnitus: International Delphi' (COMIT'ID) study will use a mixed-methods approach that incorporates input from health care users at the pre-Delphi stage, a modified three-round Delphi survey and final consensus meetings (one for each intervention). The meetings will generate recommendations by stakeholder representatives on agreed Core Outcome Domain Sets specific to each intervention. A subsequent step will establish a common cross-cutting Core Outcome Domain Set by identifying the common outcome domains included in all three intervention-specific Core Outcome Domain Sets.

Discussion: The COMIT'ID study aims to develop a Core Outcome Domain Set that is agreed as critically important for deciding whether a treatment for subjective tinnitus is effective. Such a recommendation would help to standardise future clinical trials worldwide and so we will determine if participation increases use of the Core Outcome Set in the long term.

Funding: We acknowledge support from NIHR Nottingham Hearing Biomedical Research Unit, NIHR Nottingham Biomedical Research Centre, British Tinnitus Association, Action on Hearing Loss, and European Cooperation in Science and Technology (COST) Action (BM1306).

Trial registration: This project has been registered (November 2014) in the database of the Core Outcome Measures in Effectiveness Trials (COMET) initiative.

Reference: Fackrell K, Smith H, Colley V, Thacker B, Horobin A, Haider HF, Londero A, Mazurek B, Hall DA (2017) Core Outcome Domains for early phase clinical trials of sound, psychology-, and pharmacology-based interventions to manage chronic subjective tinnitus in adults: the COMIT'ID study protocol for using a Delphi process and face-to-face meetings to establish consensus. *Trials* 18(1): 388.

ID: 142

Abstract Submissions

Keywords: Heterogeneity; subtyping; review; standardisation

A REVIEW OF THE CURRENT FRAMEWORKS FOR SUBTYPING TINNITUS – SYNTHESIZING EVIDENCE TOWARDS A GLOBAL CONSENSUS

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Background: There are numerous proposed categorizations of tinnitus, both classical and more recent. However, current algorithms are often very complex and can be impractical to apply in everyday clinical practice. To date, a standard classification system for tinnitus remains elusive. To achieve that, all current classifications must be evaluated, as well as all recent scientific and clinical evidence regarding tinnitus.

One major tinnitus categorization parameter is 'objective' and 'subjective'. In the first case, the sound has an objective source, while in the second case, which is the most common, it can only be subjectively perceived by the patient [1, 2]. Tinnitus can also be categorized on the basis of other characteristics such as triggering factors, the affected side, its temporal characteristics and its quality [1]. Another classification parameter is 'endogenous' and 'exogenous' tinnitus, or a combination of the two [3]. Endogenous tinnitus can be characteristically masked and can be further subdivided into low tone, middle tone and high tone tinnitus. Exogenous tinnitus is associated with an external sound and cannot easily be masked. More recent categorizations, based on the possible etiologic mechanisms, emphasize the importance of evaluating the involvement of the auditory system [1, 4], the involvement of the somatosensory system [1, 4], or the presence of psychopathological disorders [4]. Many other categorizations have been proposed such as based on the perceived tinnitus severity as reported by patients [4].

Methods and Conclusions: The overall goal of this ESIT project is to define meaningful subtypes of tinnitus and to develop an agreed categorisation system in adults. In this poster, we will report a comprehensive review of the literature to identify the frameworks that have been proposed so far. We will analyse this information by conducting a synthesis of those frameworks and by identifying similarities and differences. This work will be the first step towards developing a global subtyping framework.

Funding: This project is funded through the Marie Skłodowska-Curie Innovative Training Network scheme: European School for Interdisciplinary Tinnitus Research (ESIT, H2020-MSCA-ITN-2016).

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ID: 143

Abstract Submissions

Keywords: idiopathic sudden sensorineural hearing loss, speech discrimination score, cochlear migraine

Poor speech recognition in idiopathic sudden sensorineural hearing loss: Implication of the relationship to Cochlear migraine.

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¹Kuang Tien General Hospital, Taiwan; ²National Taiwan University Hospital, Taiwan;

Objectives/Hypothesis

To assess possible poor speech discrimination score (SDS) after idiopathic sudden sensorineural hearing loss (ISSNHL).

Methods

We reviewed speech audiometry of 77 patients with unilateral sudden hearing loss and normal hearing in the contralateral ear. The inclusion criteria were a hearing threshold decrease of 30 dB or more in at least three contiguous frequencies occurring within 3 days, idiopathic causes and follow up more than 3 months after the hearing impairment. Audiometry of 51 patients fulfilled the criteria. Another 32 patients was bilaterally symmetric sensorineural hearing loss. The findings of pure-tone average (PTA) and SDS were compared among the two groups.

Results

The rates of speech recognition mismatch in ISSNHL patients was 66.7%. Besides, contralateral PTA fluctuation(35.3%) and recurrent ipsilateral hearing loss(5.9%) were also noted in this study.

Conclusion

The results of the present study suggested speech recognition mismatch and hearing fluctuation after some idiopathic sudden sensorineural hearing loss. These findings may be because of the effects cochlear migraine.

ID: 144 / Session 17: 1

Abstract Submissions

Keywords: Cochlear Migraine, Tinnitus, dCM, pCM

Cochlear Migraine and Chronic Tinnitus

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Migraine is a chronic and progressive neuroinflammatory disease that usually result in episodic somatosensory manifestations. Many patients present to Otolaryngologist as fluctuating hearing loss (HL) or refractory chronic tinnitus with a previous diagnosis of migraine. From the clinical observation in the Neuro-otologic Special Clinics, we propose a new category in migraine - cochlear migraine (CM) - to define those with unstable hearing or chronic tinnitus associated with migraine.

Vestibular migraine (VM) is used to describe vestibular dysfunction related to migraine. It is the most common cause of vertigo in our 25 years Vertigo Clinic, but still underdiagnosed in this field.

The clinical presentation of CM varies a lot due to the fact of neurogenic disorder. The classifications and the diagnostic criteria of CM will allow more identification to it.

The proposed CM classifications included six patterns:

1. Fluctuating HL
2. Sudden HL
3. Acute tinnitus with mild HL (< 30 dB)
4. Asymmetrical HL
5. Chronic tinnitus with poor habituation
6. Progressive unilateral HL

We will also present the diagnostic criteria of CM:

1. definite cochlear migraine (dCM)
2. probable cochlear migraine (pCM)
3. suspected cochlear migraine (sCM)

The foundational theory of CM in chronic tinnitus is very important. We will present this new theory in its process of chronic tinnitus and its possible pathophysiology. CM, the neurogenic inflammatory model, could resolve the varied clinical hearing problems that could be chronic, fluctuating and even progressive. The altered top-down processing theory of CM would make a great breakthrough in managing chronic tinnitus patients.

ID: 145

Abstract Submissions

Keywords: tinnitus, hearing loss, presbycusis

Relationship between tinnitus and hearing loss – taking presbycusis as an example

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Many clinical studies have shown that hearing loss is one of the main causes of tinnitus. As an Audiologist, when I was in the clinical hearing aids fitting, but found that patients with Chronic tinnitus tinnitus, probably only one percent, the rest of the patients don't suffer from tinnitus.

This study collected 50 patients, 28 males and 22 females with an average age of 79 years. The hearing of these patients are bilateral symmetrical sensorineural hearing loss (binaural difference <10dB), and the exclusion of sudden deafness, otosclerosis, ski-slope hearing loss, taking ototoxic drugs, and dizziness. Also collect the degree of hearing loss and SDS average.

The results show that in 50 patients, the real symptoms of chronic tinnitus only five patients, accounting for 10% of the overall. Hearing loss around 41 to 50 dB, the average SDS is 83.5%; around 51 to 60 dB, the average of SDS is 76.9%; around 61 to 70 dB, the average of SDS is 71.8%; around 71 to 80 dB, the average of SDS is 69.5%. From the conclusion that tinnitus may not only just caused by hearing problems, but other causes.

ID: 147 / Session 12: 1

Abstract Submissions

Keywords: chronic tinnitus, Cochlear Migraine, HRT

Menopausal Hormone replacement therapy for chronic tinnitus in migraine patient: a preliminary study

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Chronic tinnitus is highly prevalent among the **migraine** patient. As **menopause** approaches, estrogen fluctuate and decline likely trigger migraine attack. Therefore, we want to evaluate the result of **HRT in chronic tinnitus in the migraine group control**.

We review chronic tinnitus last year with laboratory data confirmed menopause stage collected since the end of 2016. Low dose HRT [**0.625/0.3125 mg Conjugated Estrogens with 5 mg Medroxyprogesterone Acetate daily or Conjugated Estrogens- only**] would prescribed for the patients. The severity of tinnitus is assessed by Tinnitus Handicapped Inventory (THI) [0~100 points], and the loudness was assessed by Visual Analog Scale (VAS) [0~10 points]. Patients with vertigo/dizziness, conductive hearing loss, or retrocochlear lesion are excluded.

26 migraine patients (average age 54.7 years old) randomly choose in Vertigo & Tinnitus Clinics Center in Taiwan were analyzed. Average initial **THI, VAS scores was 61.2 and 7.5 point**. And average THI and VAS scores decreased to **14.1 and 2.8 point** after 3 months course HRT. 14 patients with atypical hearing loss show surprising result in the hearing back and tinnitus improved condition after 3 month low dose HRT treatment. Low dose HRT significantly lessen their chronic tinnitus condition in the migraine patients during menopause status in our study. **Sleep architecture changed, the prefrontal cortex positive processing, and a potential steady hormone level** are the possible benefit of HRT in this study. Furthermore, asymmetrical mild hearing loss in migraine patients in one or consecutive tone may require more attention to the possible unstable hearing loss improved. The improved result of 14 migraine cases imply the association with unstable hearing loss and neurogenic inflammation in the cochlear system of migraineur. Cochlear migraine, the neurogenic inflammatory process in peripheral or central, result in varied atypical hearing loss clinical presentation. Low dose menopausal HRT, the strategy both in prevention and protection, show a quiet satisfied result in chronic tinnitus control, especially in the sensitive migraine group.

ID: 148

Abstract Submissions

Keywords: ABR, Tinnitus, Empirical Mode Decomposition

**Looking for differences in the Auditory Brainstem Response of tinnitus and non-tinnitus subjects:
Preliminary results in humans**

PEDRO COBO, MARIA CUESTA

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The auditory brainstem response (ABR) has been previously used for the search of possible abnormalities in tinnitus subjects. However, although small differences have been found in the latencies and amplitudes of the ABR waves of impaired and control groups, the present research literature evidences that these differences are slight [Milloy *et al.*, Auditory Brainstem Responses in Tinnitus: A Review of Who, How, and What? *Front. Aging Neurosci.* 9: 237, 2017]. A finer processing technique of ABR in rodents, based on the combination of time-frequency analysis and features extraction is proposed here to provide the objective cues of the occurrence of tinnitus. The main aim of this work is to present preliminary results on the application of this technique to a cohort of 82 human subjects categorized in control (62) and tinnitus (20) groups. Participants have been distributed in age and sex subgroups. Hearing Loss and ABR of each participant have been measured. Individual features extracted from the ABRs of each tinnitus participant are compared with the average features of the corresponding age and sex matched control subgroup.

ID: 149 / Session 12: 2

Abstract Submissions

Keywords: Tinnitus retraining therapy, Cognitive Behavioral Therapy, Eye Movement Desensitization Reprocessing, Event-related potentials

The value of Eye Movement Desensitization Reprocessing in the treatment of tinnitus

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Abstract

Aim: To date, no effective pharmacologic treatment is available for chronic, subjective tinnitus. Current therapy forms most often provide psychotherapeutic treatment which are intended to train the patient how to deal with the tinnitus sound. Recent studies have shown that Tinnitus Retraining Therapy (TRT) significantly improves the quality of life for tinnitus patients. Furthermore, several studies have reported that cognitive behavioral therapy (CBT) relieves a substantial amount of distress by changing dysfunctional cognitions. When the tinnitus causes a great interference with daily functioning, these treatment methods are not always sufficiently effective. Recent insights show that Eye Movement Desensitization Reprocessing (EMDR) is a highly effective therapy for medically unexplained symptoms such as chronic pain and phantom pain. In scientific research, tinnitus is compared to phantom limb pain. Starting from tinnitus as a phantom percept we therefore want to show that the operating mechanisms of EMDR also may be an effective treatment method for patients with subjective tinnitus.

Methods and Materials: Patients with subjective, chronic, non-pulsatile tinnitus will be randomized in two treatment groups: TRT and CBT versus TRT and EMDR. Evaluations will take place at baseline before therapy, at the end of the treatment and 3 months after therapy. The score on the Tinnitus Functional Index (TFI) will be used as the primary outcome measurement. Secondary outcome measurements will be the Visual Analogue Scale of Loudness (VAS), Tinnitus Questionnaire (TQ), Hospital Anxiety and Depression Scale (HADS), Hyperacusis Questionnaire (HQ), psychoacoustic measurements and Event-related potentials (ERP).

Results: The objective is to evaluate whether the bimodal therapy TRT and EMDR can provide faster and/or more relief from the annoyance experienced in chronic tinnitus patients' daily lives compared to the bimodal therapy TRT and CBT. This is to our knowledge the first prospective, randomized, controlled, clinical trial with blind evaluator that uses TRT and EMDR as a treatment for tinnitus. To date, patient recruiting and treatment has started. The end date of study will be June 2019.

Conclusion: EMDR could be an important therapy for patients with tinnitus who experience a great decrease in their quality of life. EMDR has shown promising results for the treatment of phantom limb pain. Therefore, we hypothesize that EMDR also may be an effective treatment method for patients with subjective, chronic tinnitus. Tinnitus viewed from the perspective of a trauma, more specifically in the auditory and limbic regions, leads to the need for effective information processing. The development of new neural networks could be generated through EMDR. Bilateral stimulation promotes the plasticity of the brain causing neural networks to be adjusted. In the literature, only limited data can be found in a few case studies where EMDR treatment is performed on tinnitus patients. These scarce data however provide insufficient insights concerning the mechanisms and the EMDR treatment. This randomized-controlled study trial addresses the issues concerning the effectiveness of EMDR in persons suffering from tinnitus.

ID: 150 / Session 2: 2
Abstract Submissions

Keywords: "tinnitus assessment in animal models"

A new statistical approach for the evaluation of gap-prepulse inhibition of the acoustic startle reflex (GPIAS) for tinnitus assessment

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An increasingly used behavioral paradigm for the objective assessment of a possible tinnitus percept in animal models has been proposed by Turner and coworkers in 2006. It is based on gap-prepulse inhibition (PPI) of the acoustic startle reflex (ASR) and usually referred to as GPIAS. As it does not require conditioning it became the method of choice to study neuroplastic phenomena associated with the development of tinnitus. Nevertheless, it is still controversial if GPIAS is really appropriate for tinnitus screening, as the hypothesis that a tinnitus percept impairs the gap detection ability ("filling-in interpretation") is still questioned. Furthermore, a wide range of criteria for positive tinnitus detection in GPIAS have been used across different laboratories and there still is no consensus on a best practice for statistical evaluation of GPIAS results. Current approaches are often based on simple averaging of measured PPI values and comparisons on a population level without the possibility to perform valid statistics on the level of the single animal.

We here present a new statistical approach to overcome the methodological limitations of GPIAS. In a first step we show that ASR amplitudes are not normally distributed. Next we estimate the distribution of the measured PPI values by exploiting the full combinatorial power of all measured ASR amplitudes. We demonstrate that the PPI values are approximately lognormally distributed, allowing for parametrical testing of the logarithmized values and present a new statistical approach allowing for a valid and reliable statistical assessment of PPI changes in GPIAS.

ID: 151

Abstract Submissions

Keywords: tinnitus distress, in silico analysis, information spectrum method, pharmacotherapy, autonomic nervous system

Novel in silico insights for potential treatment of chronic tinnitus distress - combined therapy of glutamate receptor antagonists with creatine supplementation

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Tinnitus is defined as the perception of phantom sound. Approximately 10-15% of general population experience it during the life time and around 7 million experience it as a chronic debilitating state. Up to 25% of tinnitus patients experience a considerable distress which, finally, results with 2-4% of population impaired in their quality of life (1).

Functional neuroanatomy of tinnitus distress points on anterior cingulate cortex (ACC) as one of the most important hubs of central autonomic network that participates in this phenomenon (1). ACC is of hall mark importance in many similar pathophysiological states like anxiety (2), social anxiety disorder (3) and experimentally induced panic (4). Neurochemistry of ACC region shows that glutamate, glutamine and creatine ratio (Glu+Gln/Cr) positively correlates with the total anxiety scores (2), implying that glutamate and creatine metabolism probably play an important role in tinnitus distress genesis.

Nutraceuticals (nutritional supplements) database generated through DrugBank was screened using an electrostatic-ion interaction potential (EIIP) / average quasi-valence number (AQVN) filter to find the most promising candidate glutamate receptor antagonists. After further filtering of selected molecules by docking, amino acids threonine, glutamine, tyrosine, citrulline and tryptophan were proposed as best candidate molecules for further evaluation.

Since all identified aminoacids and creatine have transport mechanisms on blood brain barrier our rational is that the combined proposed amino acid/creatine supplementation might give positive results in the treatment of tinnitus distress syndrome.

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Tinnitus and REM sleep incompatibility-a pathophysiological milestone for unraveling functional neural networks overlap**Tijana Bojić¹, Zoran Matic², Stefan Mandić-Rajčević³, Mirjana Platiša⁴, Aleksandar Kalauzi⁵**

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REM sleep, known as a dream state, is a puzzling state of vigilance (1), whose insufficiency is an early sign of neurodegenerative diseases (2). REM sleep is reciprocally incompatible with chronic tinnitus: tinnitus is not perceived during a REM sleep (3) and vice versa-in chronic tinnitus patients the amount of REM sleep is notably diminished (4). Since pathophysiological substrate of tinnitus is still unknown, this reciprocal undoing of REM sleep and tinnitus speaks in favor of alternative use of common neural networks, as it is the case with REM sleep and thermoregulatory system (5). The identification of common neural hubs of REM sleep and tinnitus provides new data and potential new loci that can be identified as crucial for inhibition of tinnitus perception and as such, treated with invasive and noninvasive neuromodulation (6).

On the basis of the literature data we performed the comparative analysis of the most acknowledged theories of tinnitus (7, 3) and REM sleep (8, 9) neural networks and proposed a framework for the overlap of critical hubs.

Our analysis confirmed that majority cortical areas that are inhibited during REM might be critical for tinnitus absence in REM sleep. These areas, like auditory cortex, parietal cortex and DLPFC should be targeted by noninvasive treatment methods that would inhibit their activity (i.e. rTMS,6).

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ID: 153

Abstract Submissions

Keywords: Event-related potentials, tinnitus, neuromodulation, high-definition transcranial direct current stimulation, treatment

Event-Related Potentials before and after HD tDCS in tinnitus patients

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Aim. There is currently a lack of objective measurements to evaluate the effects of therapeutic interventions in tinnitus patients. Maladaptive plastic changes and altered activity in the auditory and prefrontal cortex are shown in tinnitus patients. Event-related potentials (ERPs) can provide more insight into the brain processing, as the amplitude represents the extent to which neural resources are allocated to cognitive processes and the latency relates to the time course of these processes. The present study explores the value of ERPs in the evaluation of high-definition transcranial direct current stimulation (HD tDCS) in tinnitus patients.

Material and methods. This study compares ERPs before and after HD tDCS treatment at the right dorsolateral prefrontal cortex (DLPFC) in 22 tinnitus patients. The ERP measurement consists of a classical oddball task in which frequent standard stimuli of a 1 kHz pure tone (80% probability) and infrequent stimuli of a 2 kHz pure tone (20% probability) are presented. The patients have to push a button on a remote control each time the target stimulus is heard. During this task, the electrical brain activities are recorded using a 32-channel electroencephalography system. In addition to this objective measurement, the therapy effects are determined by use of questionnaires: the tinnitus functional index (TFI), visual analogue scale (VAS), hyperacusis questionnaire (HQ), tinnitus questionnaire (TQ) and hospital anxiety and depression scale (HADS).

Results. The results of this study will be presented at the congress.

ID: 154

Abstract Submissions

Keywords: electric stimulation, tinnitus suppression, mastoid, ear canal, tympanic membrane

SAFE AND EFFECTIVE TINNITUS TREATMENT BY NON-INVASIVE ELECTRIC STIMULATION: CHARACTERIZING THE EFFECT OF ELECTRODE MONTAGES, SITES, AND STIMULATION PARAMETERS ON AUDITORY PERCEPTION

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Electric stimulation can be potentially a safe and effective option for tinnitus treatment. Cochlear implantation has been shown to suppress tinnitus but its invasive nature and resulting damage to the normal cochlear structure limit its usage to only tinnitus sufferers who also have significant hearing loss. Non-invasive or minimally-invasive electric stimulation offers the most desirable treatment option for the majority of tinnitus sufferers who still have significant hearing and want to preserve that hearing. Although this promising approach has been investigated for nearly 200 years, neither its safety nor effectiveness is established at present. We believe the first step toward establishing non-invasive electric stimulation as a safe and effective tinnitus treatment option is to identify a set of stimulation locations and parameters that can reliably produce primarily auditory perception, with minimal side effects and tolerable non-auditory sensations.

Methods. We used two tools to guide the search for such a set of stimulation parameters. The first tool was a human head electric model that can simulate current flow from the scalp surface to the deep brain. The second tool used the cochlear implant telemetry to experimentally measure the amount of current that enters the cochlea in response to non-invasive electric stimulation. Based on the modeling and telemetry data, we selected 2 electrode montages, 3 active electrode sites, and a wide range of safe stimulation parameters. The 2 montages included placing an active electrode near a site on one ear while placing a 2.3x3 cm silver-chloride plate return electrode on either the forehead or the contralateral mastoid. The 3 active sites near the ear included the ipsilateral mastoid where the same silver-chloride plate electrode was placed, the ear canal where a gold-foil-wrapped-foam tip electrode was inserted, and the tympanic membrane where a saline-soaked wick electrode was positioned. The parameters for 500-ms charge-balanced sinusoidal or pulsatile stimuli included current varying from 0 to 2 mA, and frequency from 5 to 10,000 Hz. We systematically measured electric impedance for these stimulation configurations and evaluated their perceptual consequences.

Results. Systematic data from 5 normal-hearing subjects show a relatively weak electrode montage effect but strong active electrode site and stimulus frequency effects. Stimulus frequencies from 5 to 100 Hz more often produced visual perceptions, namely white flashes; frequencies from 100 to 1000 Hz produced auditory perception including tonal and complex sounds; all frequencies were able to produce a wide range of tactile sensations from mild tingling to vibration, pressure, stinging, prick, burning, and even pain. Auditory thresholds decreased systematically from the plate electrode placed on the ipsilateral mastoid to the tiprode in the ear canal to the wick electrode on the tympanic membrane. Preliminary data show that some sets of electric stimulation could suppress tinnitus and even produce auditory sensation in deaf individuals.

Conclusions. Non-invasive electric stimulation is capable of producing auditory perception with minimal or tolerable adverse sensations. Electrode montages, sites and stimulation parameters need to be optimized for safe and effective treatment of tinnitus.

This work was funded by NIH 5 R01 DC015587.

ID: 155

Abstract Submissions

Keywords: tinnitus, vestibular symptoms, quality of life, listening effort

The connection between listening effort and quality of life in patients with chronic tinnitus and vestibular disorders

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Introduction. Chronic tinnitus can result in comorbid distressing symptoms, of which one is related to impaired concentration attributable to difficulties with speech understanding in various listening conditions (Andersson et al., 2002; Tyler & Baker, 1983). Therefore, tinnitus has been linked with cognitive interference (e.g. Andersson et al, 1999; Tyler & Baker, 1983). An exploratory study in normal-hearing young adults with chronic leisure noise-induced tinnitus revealed that listening effort was significantly higher in the tinnitus group compared to a control group (Degeest et al., 2017). These results suggest that the cognitive reserve is reduced in persons with tinnitus so that speech understanding may become more effortful for them. Furthermore, coexisting disorders in patients with chronic tinnitus may include vertigo or balance disorders. As with patients with chronic tinnitus, a common symptom of vestibular disorders is the experience of difficulties with cognitive skills such as concentration (Hanes and McCollum, 2006). For both patients with chronic tinnitus and patients with vestibular disorders, difficulties with cognitive skills such as concentration may negatively affect the quality of life (e.g. Tyler and Bakers, 1983; Hanes and McCollum, 2006). It would be interesting to perform more extensive cognitive testing in a subpopulation of patients with chronic tinnitus and vestibular disorders in order to explore if cognition, and more specifically listening effort, is disturbed and whether this has a cumulative negative effect on their quality of life. Hence, the present study was an exploratory study aimed at examining the connection between listening effort and the quality of life in patients with chronic tinnitus and vestibular disorders.

Method. Subjects with chronic subjective non-pulsatile tinnitus consulting an ENT-specialist between September 2016 and February 2018 will be included in the study. First, hearing status is evaluated using tympanometry and tonal audiometry. Second, a tinnitus analysis is performed. Third, a vestibular test battery is administered including oculomotor tests, rotational test, caloric test and vestibular evoked myogenic potential. Furthermore, a dual-task paradigm will be used to evaluate listening effort in different listening conditions. A primary speech-recognition task and a secondary memory task are performed both separately and simultaneously. Finally, subjective measures of the impact of tinnitus and vestibular disorders on daily functioning are administered using the Tinnitus Handicap Inventory, the Tinnitus Functional Index and the Dizziness Handicap Inventory. The amount of listening effort as well as the results of the questionnaires will be compared with a group with tinnitus but without vestibular disorders and a group without tinnitus and without vestibular disorders.

Results. Data collection is still ongoing and will be finalized by time of the conference. All results will be analyzed and presented.

Conclusion. Based on previous research regarding listening effort in patients with chronic tinnitus (Degeest et al., 2017), it is expected that patients with tinnitus and vestibular disorders expend more listening effort compared to a group with tinnitus but without vestibular disorders. Besides, it may be expected that tinnitus in combination with vestibular disorders may interfere more with daily activities, leading to a greater impact on the quality of life.

ID: 156

Abstract Submissions

Keywords: tinnitus, non-otologic risk factors, epidemiology

Identifying non-otologic risk factors for tinnitus: a systematic review

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Aim: The origin of tinnitus is usually linked to a mechanism implying some form of auditory deprivation, giving rise to a deafferentation phenomenon, inducing neuronal activity changes on a more central level due to neuroplasticity, resulting in the tinnitus percept. However, tinnitus patients without apparent hearing loss exist and on the other hand, a large number of patients with hearing loss show no tinnitus. This indicates the possible significant involvement of non-otologic factors in tinnitus development. Identification of these factors could be meaningful to select patients at risk and/or treat concomitant non-otologic comorbidities of influence on the tinnitus complaint. Multiple studies have been conducted to analyze different tinnitus risk factors, but to our knowledge, they have never been merged and systematically described. The current systematic review aimed at systematically assembling, analyzing and describing the literature with regard to non-otologic risk factors for tinnitus.

Material and Methods: A systematic review was conducted, following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (Liberati et al., 2009). The Medline, Embase and Web of Science databases were systematically searched by two independent reviewers for eligible articles, using the search terms "Tinnitus/epidemiology"[Mesh] AND (Cross-sectional OR Cohort) for Pubmed and 'Tinnitus AND Epidemiology AND (Cross-sectional OR Cohort)' for Embase and Web of Science. Only cohort or cross-sectional studies were included, investigating prevalence and incidence of tinnitus and association with one or more risk factors. Studies considering only otologic risk factors were excluded, and only articles in English, French or Dutch were selected. There were no restrictions on publication status, date of publication or tinnitus characteristics. After study selection, data were extracted and assessed for quality and risk of bias.

Results: Initial screening of titles and abstracts revealed 37 eligible records, of which 28 were included in the systematic review after full text screening and application of in- and exclusion criteria. All possible non-otologic risk factors were extracted from the included articles and clustered into demographic, cardiovascular, dietary, psychological, musculoskeletal, endocrine and infectious disease. Because of the heterogeneous study populations and low number of uniform studies per risk factor, a primary narrative systematic review was conducted. All important risk factors will be discussed, and possible clinical or research implications will be presented.

Conclusion: This study systematically reviews all relevant non-otologic risk factors for tinnitus, thereby describing its possible influence and significance. These results could help clinicians in finding a lead towards tinnitus management in patients without significant otologic disease, or with concomitant important non-otologic comorbidities. These risk factors can also help future researchers towards further exploration of tinnitus generating mechanisms, other than or complementary to the classical pathway of auditory deprivation.

ID: 157 / Session 4: 3

Abstract Submissions

Keywords: tinnitus, resting state EEG, residual inhibition, microstates, attention

Resting state EEG microstate in tinnitus patients

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Aim: Recent Aim: Recent pathophysiological models postulate that tinnitus can be associated with dysfunctions of central nervous system networks, referred to as a 'tinnitus network', involving auditory as well as non-auditory brain regions. More specific, hemodynamic neuroimaging studies previously reported abnormal functional connectivity between specific (auditory) brain areas accounting for tinnitus perception, and non-overlapping brain regions associated with psychological and cognitive symptoms. It is thereby primordial to only isolate the neuronal correlates responsible for tinnitus generation, and distinguish them from other unspecific brain changes involved in the disrupted auditory processing by concomitant hearing loss or hyperacusis. 'Residual inhibition' (RI) could be applied in these experimental paradigms as a method to transiently suppress tinnitus, without any interference by acoustic stimuli during data acquisition (as in auditory evoked paradigms). This resting state EEG study aims at exploring state dependent changes in cortical/neural processing, between a 'tinnitus-suppressed' status and a 'tinnitus' status, while keeping all other experimental factors comparable between these two conditions. This is done by using advanced topographic analysis of the EEG data i.e. microstates.

Material and Methods: The EEG study was preceded by an extensive pilot study, testing duration and reproducibility of the RI response in 32 tinnitus patients with a (partial) positive response on RI testing. Subsequently, 3 groups of 10 age-, gender-, hearing- and tinnitus duration-matched subjects (tinnitus patients with RI-positive and -negative response respectively, and controls without tinnitus) were invited to participate in a resting state 128-channel EEG RI paradigm, consisting of 4 blocks of 5 trials. In each trial, a masking white noise (WN) or a non-masking narrow band noise (NBN) centered at 500 Hz was presented for 1 minute, followed by 80s resting state, in order to allow data acquisition during tinnitus suppression (RI after WN) or presence (after NBN), followed by recuperation. Each block was followed by tinnitus rating on the spot and a pause.

Results: As our pilot study showed a very good reliability for RI over four test moments on the immediate and short term (ICC (3,4) = 0.871), RI could be successfully used in the main EEG experiment. Preliminary EEG results obtained in 9 responsive tinnitus patients and matched controls without tinnitus, confirm that the topographical variance at rest, irrespective of the actual tinnitus state, was best explained by four dominant and different microstates, as previously validated in healthy controls (Britz et al., 2010). Crucially, two microstates showed reliable changes: there was a relative change in topographic distribution of the 'auditory' and the 'visual' microstate after specific auditory stimulation, independent from tinnitus manipulation and different for tinnitus and controls. EEG data analysis of the remaining subjects over the 3 study groups is still ongoing.

Conclusion: Resting state EEG experiments using RI as tinnitus suppression, could give insight into central neuronal functional connectivity alterations in tinnitus patients in a situation without (external) acoustic interference. EEG data indicate that transient dynamic interaction involving auditory and visual cortical network could underlie aberrant auditory processing in tinnitus patients compared to controls.

ID: 158 / Session 3: 4

Abstract Submissions

Keywords: CBT, systematic review, Cochrane, efficacy

Is CBT for tinnitus effective? A progress report on a new Cochrane systematic review

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Background

It has been nearly eight years since the previous Cochrane systematic review reported that cognitive behavioural therapy (CBT) is an effective intervention for reducing the adverse psychosocial effects of chronic bothersome tinnitus. Results from other reviews and meta-analyses have reached similar conclusions. Additionally, reviews report that the perceived loudness of the tinnitus sound is not altered by CBT. Since these reviews, recent randomised controlled trials of CBT have been conducted and Cochrane systematic review standards and methods have been refined. In this new Cochrane review we use tinnitus reactivity as the primary outcome of interest as it is arguably more likely to be directly affected by CBT than the perceived psycho-acoustic quality of the tinnitus sound.

Method

The Cochrane ENT Information Specialist conducted an extensive search of a wide range of databases (e.g. Medline) for randomised controlled trials of CBT for adults with chronic subjective tinnitus. This review used an inclusive definition of CBT recognising it as an umbrella term that refers to a wide range of intervention components that are labelled or considered "CBT" or are part thereof. Two authors independently conducted all steps of the process of study selection, data extraction, and assessment of risk of bias.

Results and Discussion

Available results from the literature search will be presented in addition to analyses of the effectiveness of CBT compared with: wait-list control, audiological care, tinnitus retraining therapy, or another experimental control condition. Sub-group analyses will be performed to examine the effects that CBT-type or specific CBT-treatment element has, as well as the mode of CBT-delivery, i.e. whether treatment is offered to a group of patients simultaneously or to the individual, whether it was delivered in person or as part of an E-health intervention, and whether the effectiveness of CBT depends upon the discipline providing CBT. Results from this systematic review on the effectiveness of CBT for tinnitus, will help inform treatment and service related decisions for patients, healthcare providers and policymakers.

ID: 159 / Session 13: 3

Abstract Submissions

Keywords: Questionnaire, methods, translation

A GOOD PRACTICE GUIDE FOR TRANSLATING AND ADAPTING HEARING-RELATED QUESTIONNAIRES FOR DIFFERENT LANGUAGES AND CULTURES

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Objectives To raise awareness and propose a good practice guide for translating and adapting any hearing-related questionnaire to be used for comparisons across populations divided by language or culture, and to encourage investigators to publish detailed steps.

Design From a synthesis of existing guidelines, we propose important considerations for getting started, followed by six early steps: 1) Preparation, 2&3) Translation steps, 4) Committee Review, 5) Field testing, and 6) Reviewing and finalising the translation.

Results Across these six steps, 22 different items are specified for creating a questionnaire that promotes equivalence to the original by accounting for any cultural differences. Published examples illustrate how these steps have been implemented and reported, with shared experiences from the authors, members of the International Collegium of Rehabilitative Audiology (ICRA) and TINnitus research NETwork (TINNET).

Conclusions A checklist of the preferred reporting items is included to help researchers and clinicians make informed choices about conducting or omitting any items. We also recommend using the checklist to document these decisions in any resulting report or publication. Following this step-by-step guide would promote quality assurance in multinational trials and outcome evaluations but, to confirm functional equivalence, large-scale evaluation of psychometric properties should follow.

This project is supported by the International Collegium of Rehabilitative Audiology (ICRA) and TINnitus research NETwork (TINNET). By the time of the TRI2018 conference it will have been published in the *International Journal of Audiology* (open access).

ID: 160 / Session 8: 5

Abstract Submissions

Keywords: Frustration, Disablement, Intra-individual variability, Modulation, Goal-directed behaviours

Modulating individual frustration: a new approach to tinnitus management?

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Recent studies investigating moment-to-moment variability in tinnitus annoyance (Probst et al. 2017; Schlee et al. 2016; Wilson et al. 2015) have opened new perspectives for understanding tinnitus-induced disablement. They suggest that intra-individual variability may be considered as a paradigm shift in tinnitus research, which has been mainly focused hitherto on inter-individual differences (Dauman et al 2015). The current presentation will show the main findings of a qualitative study on intra-individual variability in tinnitus annoyance (Dauman et al 2017). In-depth interviews were conducted by a clinical psychologist to investigate the perception of tinnitus-induced disablement in a small group of ageing individuals (12 participants, aged 56-79). Data analysis (i.e. grounded theory) revealed the experience of frustration as being a core issue in participants' daily struggle with the condition, extending the scope of their daily living of chronic tinnitus. Frustration has been identified as the experience of being unable to achieve one's goal or to change a situation according to one's desire. Frustration is of special interest in a goal-directed, behavioural approach to individual-environment interactions. Just as tinnitus does, frustration may vary from moment-to-moment depending on the challenges the individual has to face in his/her social and physical environment. Our findings suggest that tinnitus-induced disablement varies according to the degree of frustration sensed by the individual experiencing the inability to achieve his/her goal (or to change a given situation). The more intense the participants' frustration was, the more intrusive and disabling the tinnitus became. Implications of this hypothesis will be described and illustrated using three main supporting categories related to tinnitus frustration: "Losing body ownership", "Lacking perspectives", and "Overcoming conflictuality". We use these findings to establish a substantive theory of tinnitus tolerance that promotes an active, disciplined and individualized approach to tinnitus-induced disablement. This model, which is designed to be implemented in the clinical dialogue with the patient, highlights pathways from sustained suffering to reduced annoyance (i.e. emerging tolerance) with their behavioural characteristics. It accounts for difficulties the participants experienced from an unchanging pattern of annoyance over time. Furthermore, it identifies a set of new attitudes toward oneself and others that tinnitus tolerance would entail. Preliminary findings from an ongoing study involving younger and working participants will be added to the model, contributing to enlighten occupational-related issues and interpersonal conflictuality in relationship to tinnitus frustration. In clinical practice, it is a well-known observation that many tinnitus-affected patients fear that their tinnitus will increase with time and thus become unbearable owing to the lack of control over the condition. A goal-directed behavioural perspective enables the clinician to introduce frustration as an underlying experience for moment-to-moment variability in tinnitus annoyance. It helps in empowering patients with a sense of control over their condition, assigning to modulation of frustration a perspective of improvement that is distinguishable from, and perhaps more reliable than, mere moderation of unspecified tinnitus interference. Eventually, modulation of frustration may reveal why achievable and meaningful activities are an effective way to better tolerate the constant presence of tinnitus via lessened obstacles to goal-directed behaviours.

ID: 161 / Session 9: 2
Abstract Submissions

Keywords: music, relaxation, stress management, resting state network, noise cancellation system

The power of music for restoring the compromised noise-cancellation system – influence of two different, music based relaxation techniques

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AIM:

An impaired activity of the brain's resting-state network (RSN), is held responsible for the tinnitus-associated distress. Therefore, mindfulness-based interventions and relaxation trainings are part of many tinnitus centered treatments.

The Heidelberg Neuro-Music Therapy (HNMT) consists of active auditory trainings modules but also incorporates music-based relaxation. HNMT has proven to effect a considerable improvement of tinnitus distress by a one-week short-term treatment. Imaging results revealed an augmented activity in RNS after HNMT. The current trial compares the impact of two different music based interventions (vibroacoustically induced relaxation (VR) and music guided imagination (MI)). We suppose that music based relaxation induces altered states of consciousness (ASC) and enables patients to effectively restore their compromised neuronal noise-cancellation system.

METHODS:

MI conditions use pre-recorded, soothing musical pieces as tension releasing stimulus by combining the music with positive mental images. VR uses a body monochord (string instrument with 21 chords tuned to one base tone producing rich overtones). 53 patients suffering from chronic tinnitus received eight 15-minute-sessions of either MI or VR as part of their 5-day HNMT. By midweek, a "filter training" using tinnitus-similar external stimuli superposing the relaxing sounds was implemented.

Perception of tinnitus loudness and grade of relaxation/tension were assessed by visual analogue scales (VAS) before and after each intervention, additionally the patients could rate their subjective appraisal of the interventions on a VAS. The overall tinnitus distress was assessed by the Tinnitus Questionnaire before and after HNMT.

RESULTS:

Data were processed using multivariate statistics. Generally, TQ scores declined from before (TQ=32,5 ± 15,3) to after HNMT (TQ=26,0 ± 13,7). Subjective loudness ratings decreased while patients reported increasingly higher grades of relaxation. Additional external sound (filter training) initially result in greater tinnitus loudness and slightly reduced relaxation but the patients reactions are progressively less affected. These results do not depend on the kind of music based intervention, VR and MI are equally effective. However, in comparison with MI, VR is rated as more pleasing and has a higher potency than MI to temporarily eliminate tinnitus perception.

DISCUSSION:

Both VR and MI are effective in inducing relaxation. Monochord sounds used in VR are very rich in overtones, foster ASC and allow for frequent temporary tinnitus deletion. The advantage of MI is its better everyday suitability. Both interventions have ecological validity since the patients gradually manage to control their reactions towards the tinnitus and one can assume that the treatment with HNMT initiated a reorganization procedure with opposite direction to the tinnitus effects.

CONCLUSIONS:

Music based relaxation techniques promote both mental and physical regeneration and alleviate tinnitus saliency. Depending on the patients' preferences, MI and VR are complementary interventions and form an integral part of the HNMT. However, relaxation as single intervention seems to be insufficient and should be integrated in a more complex treatment regime.

ID: 162 / Session 19: 3

Abstract Submissions

Keywords: tinnitus, anxiety, outcome measurement, feedback

Self-reported attributions of multimodal treatment improvement in patients with chronic tinnitus

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Background: Numerous outcome domains have been used in assessing treatment efficacy for adults with tinnitus (Hall et al. 2016). However, few studies have investigated patient-reported, subjective factors contributing to perceived treatment benefit.

Method: One-hundred and fifty adults with tinnitus completed a course of multimodal intensive tinnitus therapy (MITT; Seydel et al., 2015). Pre- and posttreatment self-report measures assessed tinnitus impact, perceived stress, and the presence of symptoms associated with depression, anxiety, OCD, and somatoform or eating disorders. At posttreatment, participants further completed a feedback measure assessing therapeutic relationships with members of the multidisciplinary team, satisfaction with the MITT programme components, and subjectively perceived mechanisms of treatment change. **Results:** Patients attributed treatment improvement to intervention-focused, social and structural factors. **Conclusions:** Outcomes from self-report and feedback measures highlight the importance of patients' views in assessing treatment benefit and informing multimodal treatment programmes.

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ID: 163

Abstract Submissions

Keywords: Tinnitus, Hyperacusis, oxidative stress metabolism, mineral imbalance, spectrophotometry evaluation

Impact of oxidative stress metabolism and imbalance of Ca/Mg, Ca/P, K/Na index ratios in perception of tinnitus and other inner ear disorders.

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Background: There are several theories regarding pathophysiological mechanisms involved in tinnitus and hyperacusis as an inner ear disease. Authors discuss errors in the regulating processes of amplification of hearing cells. Other theories about the disorder are based upon central sound processing at subcortical level. There are also discussions about the role of certain substances that could activate neurotransmitters that could increase both nervous system cell activity and sound perception.

A prospective study from the last two years in a group of patients who were suffering from several inner ear disorders (Tinnitus and other auditory co-disorders) have been evaluated in relation to their oxidative stress metabolism and as well as their oligoelements unbalance status.

An initial test based on spectrophotometry was used to evaluate both, their trace intracellular mineral reserves, level of oxidation stress and toxic metals before starting any tinnitus therapy or treatment. Spectrophotometry is based on the principle of absorption, transmission or reflection of light by the chemical compounds over a certain wavelength range.

Materials and method: The data concerns individuals who visited our Clinic for a variety of complaints. Over a total base data of 900 patients, all those with inner ear disorders were evaluated by spectrophotometry. This test is a non-invasive hand measurement taken in situ. The measurement is taken directly by a portable spectrometer (OligoScan Technology) connected on-line to Network Web of the Lab Provider's computer server. Patient's physiological data is entered and Patient's hand dermis is scanned by spectroscopy.

Results: Data Base Analysis shows an extremely high statistical correlation in nearly all the tinnitus patient group with deficiency/excess in certain minerals and potential toxic metal poisoning. Minerals have a key role in the proper functioning of our body cells. Thus a daily intake of nutritional supplements is essential to maintain a healthy condition since the human body is unable to synthesize these nutrients itself.

The report shows that certain changes observed in index variables (Ca/P, Ca/Mg, K/Na and others..) in tinnitus & hyperacusis disorders in patients have a statistically significant effect involved in improving the symptoms when patients are treated globally.

Conclusion: A way to detect deficiency/excess in minerals and potential toxic metal poisoning may be a useful tool to evaluate health condition in tinnitus patients.

Oligoscan (TM) technology may be used by all medical professionals and tinnitus specialists allowing for rapid and pain free analysis of mineral metabolism.

The results confirm that Tinnitus & Hyperacusis as a disorder is more susceptible to a bad cochlear homeostasis condition together with a previous unbalance of certain minerals. This imbalance probably also has a large impact on damage or disease in age-related neurodegenerative processes.

ID: 164

Abstract Submissions

Keywords: Tinnitus, Assessment, Client-centred, Goal planning

The Client Orientated Scale of Improvement in Tinnitus (COSIT)

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Background: A goal planning method widely used in aural rehabilitation is the Client Oriented Scale of Improvement. A modified version of the COSI has been used to identify tinnitus treatment goals and outcomes **Objective:** The aims of this study were to identify treatment goals in a clinic sample, and ascertain the convergent validity of the COSIT to 3 widely used standardized questionnaires. **Research design:** A retrospective evaluation of client treatment goals using thematic analysis and correlational analysis of secondary research data comparing the COSIT to Tinnitus Handicap Questionnaire, Tinnitus Handicap inventory and Tinnitus Functional Index. **Study Sample:** 122 adult patients and research participants attending the University of Auckland Hearing and Tinnitus Clinic. **Results:** Specific treatment goals were categorized into 11 themes. The most common treatment goals (>10% of responses) were: 1. Reducing tinnitus' effects on Hearing 2. Improved wellbeing and being less depressed. 3. Coping with or controlling the tinnitus. 4. Managing the effect of the environment (context) on tinnitus. 5. Improving sleep. 6. Understanding tinnitus. Individuals differed in their complaints and priorities for treatment. The COSIT showed moderate convergent validity with the THQ, THI and TFI indicating that the total scores measured similar constructs. **Conclusions:** The COSIT is a pragmatic method for determining tinnitus treatment goals and priorities in a format that should be familiar to audiologists.

ID: 165

Abstract Submissions

Keywords: Tinnitus, Stress, Cortisol.

Tinnitus and stress.

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Tinnitus is an auditory phantom perception of sound in absence of any external source. The prevalence of tinnitus is between 10 and 15 and it can be severe and affect the ability to lead a normal life in 0.5% of the population (Baguley et al., 2013). Tinnitus is associated with otological and non-otological disorders and risk factors; hearing loss, ototoxic medication, diabetes mellitus, and depression are examples. Stress is another risk factor that is believed to be associated with tinnitus and it can be the event that stimulate the response, a transaction between the body and the environment, or a bio-physiological response. Stress response is mediated by activation and inhibition of several axes and pathways. the main axis activated is the hypothalamus-pituitary-adrenal (HPA) axis and its end effector is the cortisol. Exposure to chronic stressors elevates cortisol level and causes adverse health effects.

It has become evident that stress can modulate tinnitus (Baigi et al., 2011). Also, the severity of tinnitus and level of stress are correlated. Exposure to stressors, occupational stressors for example , increases the prevalence of tinnitus. This is possibly due to the effect of cortisol on the cochlea and/or central auditory and non-auditory structures. To date, the evidence that supports this relationship is based on results from animal studies, cross-sectional, and few prospective studies. When the level of cortisol was studied, salivary and/or blood/plasma cortisol concentration were mostly used. These sampling techniques have their own drawbacks that might affect the results. In addition, these techniques measures the instantaneous cortisol secretion in response to stressor. Therefore, the direction of the relationship has not been established. Measuring the cortisol retrospectively by using hair from patients with tinnitus and correlate the results with self-reported measures of stress and may resolve this question.

The aim of this project is to determine if stress-related cortisol secretion plays a role in the pathogenesis of tinnitus and/or in modulating tinnitus to become bothersome. In order to achieve this aim, scoping of the relevant literature is ongoing to describe the relationship between tinnitus and stress in adult human. Next, a systematic review will examine the strength of the correlation between the psychological and bio-physiological measures of stress used in tinnitus patients. The findings of these reviews will be used to refine the methodology of the final step; a longitudinal study. The study objective is to correlate between hair cortisol concentration and self-reported measures of stress in tinnitus patients and controls.

The importance of investigating the relationship between stress and tinnitus, especially bothersome tinnitus, and the role of cortisol can be summarized in two points. First, understanding the role of cortisol and stress in the pathophysiology of tinnitus, and helping decision makers to prioritise the intervention and treatment programmes in patients with tinnitus.

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ID: 166 / Session 15: 1

Abstract Submissions

Keywords: TAT, hearing aid, sound therapy

Tinnitus Activities Treatment – hearing aids and sound therapy

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We tested Tinnitus Activities Treatment in two parallel studies in patients with and without hearing aids. Within each study, tinnitus patients were randomly assigned to one of three groups; counseling, counseling plus binaural noise generators set to completely mask the tinnitus, or counseling plus binaural noise generators with a low-level of partial masking. The Tinnitus Handicap Questionnaire was used as the primary measure. Additionally, measurements were made with the Tinnitus Primary Functions Questionnaire, tinnitus loudness and the minimum masking level.

In those that did not use hearing aids; in the counseling group, 8 of 22 patients benefited significantly (with THQ score decreases ≥ 20), in the total mask group, 8 of 13 patients benefited, and in the partial mask group, 8 of 24 patients benefited from the treatment. The average decrease in the handicap questionnaire was 15% for the Counseling group, 25% for the total mask group, and 14% for the partial mask group. In those who did use hearing aids; in the counseling group, 5 of 16 patients benefited significantly, in the total mask group, 3 of 14 patients benefited, and in the partial mask group, 6 of 13 patients benefited from the treatment. The average decrease in the handicap questionnaire was 12% for the counseling group, 13% for the total mask group, and 16% for the partial mask group. No significant average differences among groups were observed.

We conclude that Tinnitus Activities Treatment, with or without sound therapy, can be effective for some, but not all, patients with and without hearing aids.

ID: 167

Abstract Submissions

Keywords: tDCS, neuromodulation

The Adjunctive Role of Bifrontal Transcranial Direct Current Stimulation in Patients with Severe Tinnitus Distress

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Objectives:

Treatment effect by bifrontal transcranial direct current stimulation (tDCS) for tinnitus is debatable. We aimed to assess the evaluate the treatment effect of bifrontal transcranial direct current stimulation (tDCS) in tinnitus.

Material and methods:

From January to December 2016, patients who complained of non-pulsatile subjective tinnitus were enrolled in this study. Patients who agreed to tDCS treatment were allocated to study groups; the others were control group. For study group, patients underwent counseling and bifrontal tDCS (F4: anode, F3: cathode) with a 1.5mA of direct current during 20 minutes per session. For control group, counseling, sound therapy such as sound generator or hearing aids, and/or medication were used. Epidemiologic characteristics, questionnaires including tinnitus handicap inventory (THI) and Beck depression inventory (BDI), visual analogue on the tinnitus loudness, awareness, annoyance, and effect on life by tinnitus (VAS; 0-10) was documented at initial visit and once per month.

Results:

Twenty-six patients underwent tDCS treatment, and the control group was 44. Patients who were younger, longer duration of tinnitus, higher THIs and higher VAS score agreed to tDCS treatment. THI improvement 20 or more was significantly higher in study group ($p=0.010$). In catastrophic handicap (THI: 78-100) and moderate handicap (THI: 38-56), the ratio of study group was higher than control group ($p=0.026$). For patients with mild handicap (THI: 18-36), no one showed improvement in study group. For tinnitus subtype, patients with combined tinnitus showed significant improvement after treatment, irrespective of treatment method. The numbers of tDCS session were not correlated with change in THI score ($p>0.05$). Logistic regression analysis revealed that the initial THI score was independently associated with THI improvement. However, tDCS treatment was not significant factors for recovery.

Conclusion

tDCS seems to be one of the adjunctive treatments for tinnitus by reducing, not tinnitus loudness, but tinnitus distress in patients having moderate handicap or more.

ID: 168

Abstract Submissions

Keywords: music therapy, fMRI, resting state network, precuneus, relaxation

Neuro-Music Therapy restores Resting-State Network in Tinnitus Patients

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Abstract

AIM: Suffering from tinnitus causes mental distress in most patients. An impaired activity of the brain's resting-state network (RSN), is held responsible for the tinnitus-associated distress. The compact Heidelberg Neuro-Music Therapy (HNMT) has proven to effect a considerable improvement of tinnitus distress by a one-week short-term treatment. The current study intended to measure the related activity levels in RSN before and after the therapy by means of functional MRI (fMRI).

MATERIAL AND METHOD: The RSN activity was estimated by analyzing the task-negative activation during long inter-trial intervals in a word recognition task. The RSN level was evaluated twice, before and after a one-week study period, in 18 treated tinnitus patients (TG), 21 passive tinnitus controls (PTC), and 22 active healthy subjects (AC), respectively. During the study week the participants from TG and AC were treated with HNMT, whereas PTC patients did not receive any tinnitus-specific treatment. Tinnitus distress was assessed by the Tinnitus Questionnaire TQ (German version).

RESULTS: The HNMT application over 5 days resulted in a significant decrease in TQ-scores by 17.7 (SD 13.6) TQ scale points in the TG group while in PTC the TQ score did not significantly change over the observation period of one week.

Imaging results revealed an augmented activity in RSN (especially in PCC/precuneus, LP, and MPF) in the TP group but not the PTC group. The treated patients TG exhibited also a rising RSN activity compared to the "treated" healthy participants AC. This result signified the additional tinnitus-related effects among participants with identical HNMT experience.

DISCUSSION: The enhancement of the RSN activity in the precuneus was correlated with a reduction in psychological tinnitus distress as induced by the HNMT.

The localization of increased activity in the precuneus area corresponds with previous finding of structural increase in GM by HNMT. One can assume that the treatment with HNMT initiated a reorganization procedure with opposite direction to the tinnitus effects.

CONCLUSIONS:

The convergence of functional and structural effects in the precuneus confirmed the role of RSN in tinnitus and its relationship to changes in tinnitus-related distress by means of tinnitus treatment.

ID: 169

Abstract Submissions

Keywords: tinnitus, hearing, sampling, ageing, reading

Tinnitus: Hearing, Seeing, Ageing and Sampling - Can they all be Connected?

Peter James Hampton

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My previous talk and posters at tinnitus conferences have looked at the possibility of tinnitus originating as a result of reduction of an internal sampling frequency due to outer hair cell (OHC) damage in the organ of Corti (OC).

Could tinnitus provide a method for estimating the efficiency of sampling and processing of environmental information from other sensory inputs such as sight?

The maximum rate at which the cochlear amplifier's OHCs can operate in mammals is about 25 kHz so it is quite possible that sampling is taking place in the cochlea at a frequency somewhat lower than this. A range of 20 - 24 kHz for a sampling frequency, f_s , would be above human hearing but below the cochlear amplifier's frequency limit.

The first row of OHCs nearest to the inner hair cell row may provide such a sampling signal, f_s , in normal hearing, but if cells in this row suffer damage, then OHCs in the second, third or (partial) fourth rows may come into play. These would have to operate at sub-harmonics $f_s/2$, $f_s/3$ or $f_s/5$. Whilst f_s is inaudible to humans, the sub-harmonics may well be heard through cross-talk and give rise to tinnitus with components at one or more of these frequencies.

The consequences of sampling audio at sub-harmonics of f_s are that templates in the brain for a particular sound may still be used but the probability of detecting that sound in a given time may be reduced to 1/2, 1/3 or 1/5. To put another way, the time taken to identify a sound may go up by 2, 3 or 5 times. Localisation of sounds will also take proportionately longer. Unless large numbers of OHCs in each row suffer damage the overall reduction in sampling rate will be less than the ratios given above.

OHC damage is likely to occur only in certain parts of the cochlea, and with age-related hearing loss this will be particularly in the areas of the OC with higher characteristic frequencies (CFs). Over time the OHC damage increases to lateral fibres with lower CFs through increased 'wear and tear'.

Long-term tinnitus sufferers with age-related high frequency hearing loss hear progressively lower tinnitus frequency components, less of the high frequency sibilants like 's' and 't' and become less able to quickly localise sounds. Consequently their ability to multi-task is reduced and they may concentrate more and more on sounds and speakers directly in front of them, where they can synchronise speech with mouth movements as additional visual clues.

The visual system in tinnitus sufferers may then follow the auditory system by focusing longer on subjects in the centre of the field of view rather than the periphery. Gaze is less likely to be so frequently diverted and less visual information from the environment perceived without head movement. If visual information is being sampled at a lower than usual rate then more mistakes will also be made in reading text, without re-reading, and in recognizing objects placed in unusual orientations.

ID: 170

Abstract Submissions

Keywords: Tinnitus Alleviation Therapy, self-healing power, tinnitus Coach

Tinnitus Alleviation Therapy for the practitioner and as an online course

Maria Holl

Praxis Maria Holl, Aachen, Germany;

Psychosomatic disorders are only partially accessible by purely verbal psychotherapy methods. The Tinnitus Alleviation Therapy by Maria Holl closes the gap which exists in regard to many psychosomatic disorders, namely that between the theoretical knowledge about the disorder and the helpless despair felt by those who suffer from it.

The Tinnitus Alleviation Therapy (TAT) was devised by Maria Holl to help activate the patient's self-healing powers through a unique synthesis of psychotherapy, self-massage and her knowledge of ancient Chinese medicine that activates the body's energy system or chi thereby increasing the self-esteem and stabilizing the self-confidence of the patient.

Presentation of the therapy and its unique approach.

Therapeutic elements:

1 Slow gymnastics with the special focus to ground and center the patient. This part is based on elements of a modern body-oriented psychotherapy in the tradition of Bioenergetic analysis by Alexander Lowen. It is designed for the patient who lives a normal life in modern society.

2 Self-massage following the approach as taught by Dr. med Ita Wegmann, which emphasizes the importance to influence the watery part of the body through a special method of massage.

3 Energetic balancing, restructuring and regeneration according to Taoist healing methods.

The Tinnitus Alleviation Therapy gives the patient a tool to master the noises and their accompanying symptoms with approximately 15-30 minutes of exercise every day.

It is a first success for the patients when the sounds change through the exercises and inner peace and hope re-emerge. This usually happens after 4-6 weeks of practice.

Accompanying symptoms such as sleep disorders, anxiety and depressive states are treated and managed by the patient at the same time.

All elements of the Tinnitus Alleviation Therapy (TAT) are not only available through traditional therapy sessions but also in a modern training tool, the online course "Tinnitus Coach". The online course enables the tinnitus sufferers to treat their tinnitus independently using educational films and an accompanying book with exercises at any time. An intervention of a therapist is only necessary when required. The tinnitus sufferer is given the opportunity to resolve the tinnitus without being dependent on a therapist through the online course. Through the independent training the affected persons find a new access themselves for a self-determined life.

ID: 171 / Session 15: 2

Abstract Submissions

Keywords: combination aids, recommended procedure, sound therapy

Recommended procedure for fitting combination aids: Delphi review

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According to a recent British Tinnitus Association service evaluation 74% of UK audiology clinics can offer combination hearing aids. However, our recent UK wide survey of clinicians indicated that number of people with tinnitus fitted with combination aids varies greatly between clinics and fitting protocols are far from standardised. Several areas of considerable variability in practice have been highlighted including: i) candidacy, ii) level of sound, iii) type of sound/s used, iv) adjustments, v) laterality of fitting, vi) programmes used, vii) recommended use per day. One reason for those differences is the lack of current UK tinnitus management guidelines and lack of any clear recommendations about candidature and prescription options for combination hearing aids.

The British Society of Audiology Tinnitus and Hyperacusis Special Interest Group (SIG) is currently developing a recommended procedure for fitting combination aids for tinnitus in adults with the view to support parity of clinical practice. This document will be based on clinical expertise and clinical consensus amongst panel of expert comprising UK hearing professionals.

To identify clinical consensus we used a validated method for health research called a 'Delphi review'. Thirty six members of the expert panel filled in a series of online questionnaires. In the first questionnaire they were asked to answer general open-ended questions about current practice concerning fitting combination aids for patients with tinnitus. A draft version of the open-ended questionnaire was developed based on information from the UK-wide survey of clinical practice regarding combination aids. The questionnaire went through the consultation process with members of the Tinnitus & Hyperacusis SIG and changes implemented. The topics included i) candidacy, ii) fitting practices, iii) procedures, and iv) comments. Following questionnaires were developed applying thematic analysis of the open-ended responses and comprised a series of closed questions. Expert panel members indicated how much they agree with certain statements and agreement was measured for each of the statements.

We identified those topics where there was consensus and those where consensus was not reached. The areas where consensus was reached informed recommended procedure for fitting of combination aids for tinnitus and hearing loss. The areas where there was no consensus directly inform new research questions.

ID: 172 / Session 14: 4

Abstract Submissions

Keywords: combination aids, recommended procedure, users survey, sound therapy

Combined amplification and sound generation devices for tinnitus: survey of users expectations and experiences

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In response to variability in UK clinical practice regarding candidacy and fitting of combination hearing aids, and the absence of standard recommendations about candidature and prescription options, the British Society of Audiology Tinnitus and Hyperacusis Special Interest Group (SIG) is currently developing a recommended procedure for fitting combination aids for tinnitus in adults. It is important to incorporate patients' views into this process. This will equip clinicians to take a more patient centred approach.

A draft version of the survey was developed by the members of the Tinnitus & Hyperacusis SIG including clinicians, researchers and patient representative. The survey questions were then reviewed by lay people with tinnitus who wear combination aids or consider wearing one and questions were amended based on the feedback. The online survey accounted expectations of patients with tinnitus regarding combination aids and explored patients' experiences using combination aids including: perceived benefit for tinnitus, managing multiple programmes, choosing right programmes/sounds for different everyday situations, managing volume control, and utilising wireless streaming options. The survey was opened to current and past combination aid users as well as non-users who considered using combination aids. The survey was delivered to participants using Survey Monkey and comprised open and closed questions.

Closed questions were analysed in SPSS using descriptive statistics, including frequencies, means and standard deviations. Qualitative data from the open questions were analysed using thematic analysis.

Better understanding of patients' expectations and experiences will inform counselling and more individualised care. The results of this survey will directly inform the British Society of Audiology recommended procedure for candidacy and fitting of combination hearing aids.

ID: 173 / Session 18: 2

Abstract Submissions

Keywords: single sided deafness; tinnitus; Cochlear implant; binaural hearing

TINNITUS OUTCOMES IN COCHLEAR IMPLANTED PATIENTS WITH TOTAL SINGLE-SIDED DEAFNESS: A MULTICENTRIC STUDY

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Objectives

Recent studies reported successful reduction of tinnitus after cochlear implantation (CI) in most CI users, but the mechanisms of this reduction and the amount of improvement remain largely unknown. The present study assessed the effect of CI electrical stimulation on tinnitus in patients with unilateral tinnitus related to a total single-sided deafness (SSD).

Methodology

Twenty-five subjects with ipsilateral SSD of sensorineural origin and presenting a severe tinnitus, unresponsive to usual treatments were enrolled to receive a CI. After CI activation, a continuous white noise stimulation was delivered by the CI during the first month and a conventional CI stimulation thereafter. Outcomes were monitored after 1 month of white noise stimulation and at 3, 6 and 12 months of standard CI use. Tinnitus loudness and annoyance were measured with a Visual Analog Scale (VAS) and tinnitus distress and quality of life were evaluated with tinnitus questionnaires (THI, TRQ and STSS) at each visit.

Results

After one year of CI treatment, a significant decrease of subjective tinnitus was observed in 23 patients (92%). The tinnitus questionnaires revealed a positive effect of CI stimulation with a reduction of THI (76.0 ± 7.1 vs. 29.5 ± 19.8), TRQ (56 ± 17.3 vs. 22 ± 19.2) and STSS scores (12.8 ± 2 vs. 8.3 ± 4.5). The results tend to underline the importance of a meaningful stimulation reflecting everyday sounds, rather than a more peripheral and un-meaningful stimulation. The outcomes were unfortunately not positive for all patients: one patient withdrew from the study because of a lack of improvement and another withdrew because of an increase of tinnitus.

Conclusion

Cochlear implantation is an efficient treatment option, allowing a decrease of subjective tinnitus sensations in patients with single sided deafness. Further rehabilitation programs and optimizing treatments for this population could ease the acceptance and increase the benefit of this solution.

ID: 174

Abstract Submissions

Keywords: Auditory steady-state response, Tinnitus

Steady-state Auditory Evoked Fields in Normal Subjects and Tinnitus Patients

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Aim:

Auditory steady-state response (ASSR) can be measured using electro-encephalography (EEG) and magnetoencephalography (MEG), referred to as steady-state auditory evoked potential (SSAEP) and steady-state auditory evoked field (SSAEF), respectively. However, the signal level of SSAEP and SSAEF are weak so that signal processing technique is required to increase its signal-to-noise ratio. In this study, a complementary ensemble empirical mode decomposition (CEEMD)-based approach is proposed in MEG study and the extraction of SSAEF has been demonstrated in normal subjects and tinnitus patients.

Material and methods:

Ten subjects (5 normal and 5 tinnitus patients) were studied. The auditory stimulus was designed as 1 kHz carrier frequency with 37 Hz modulation frequency. Two channels in the vicinities of right and left temporal areas were chosen as channel-of-interests (COI) and decomposed into IMFs. The spatial distribution of each IMF was correlated with a pair of left- and right-hemisphere spatial templates. IMFs with spatial distributions highly correlated with spatial templates were identified using K-means and those SSAEF-related IMFs were used to reconstruct noise-suppressed SSAEFs.

Results:

The current strengths estimated from CEEMD processed SSAEF showed neural activities greater or comparable to those processed by conventional filtering method. Both the normal and tinnitus groups showed the phenomenon of right-hemisphere dominance. The mean current strengths of auditory-induced neural activities in tinnitus group were larger than the normal group.

Discussion:

ASSR induced by repetitive auditory stimulus is commonly used for audiometric testing. Human ASSR has been reported as an effective tool for the measurements of hearing loss in adults and children, Anesthesia level, and tinnitus. Since the SNR in ASSR signal is weak, it usually requires average over a large amount of epochs for noise suppression. A complementary ensemble empirical mode decomposition (CEEMD)-based approach may be up to the task.

Conclusions:

The present study proposes an effective method for SSAEF extraction. The enhanced SSAEF in tinnitus group echoes the decreased inhibition in tinnitus's central auditory structures as reported in previous studies.

ID: 175 / Session 10: 1

Abstract Submissions

Keywords: Stimulation Methods, rTMS, CBT, Insomnia

Combining rTMS and CBT for Effective Treatment of Tinnitus and Insomnia - A Case Report

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We present the case of a 53-year-old male patient, who had been suffering from symptoms of decompensated and chronified tinnitus for four years, most likely caused by work stress. In addition, the patient developed comorbid decompensated insomnia. Because of potential bidirectional connections between tinnitus and sleep disorders, an interdisciplinary approach to treatment was chosen. The treatment plan we developed consisted of ten sessions of repetitive transcranial magnetic stimulation (rTMS) for tinnitus, followed by ten sessions of cognitive behavioral therapy (CBT) for tinnitus and insomnia. We used the Tinnitus Questionnaire (TF) to assess tinnitus severity, the Beck Depression Inventory (BDI-II) for depressive symptoms, as well as the WHO Well-being Index (WHO-5) for subjective well-being. Improvements could be achieved with regard to everyday functioning, as the patient went from decompensated and severe to clinically negligible TF scores, from minimal to no depressive symptoms, and from just above critical to above average well-being. Combining equipment-based and psychological approaches to treatment proved successful in this case. We conclude that a combination of rTMS and CBT may be considered as an effective treatment for chronic tinnitus and comorbid sleep disorders.

ID: 176

Abstract Submissions

Keywords: rTMS, Parameters, Literature Review

Conflicting Results: A Literature Review of Parameters utilized by Previous rTMS Research in Tinnitus

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Abundant research investigated the effects of a non-invasive brain stimulation tool called repetitive transcranial magnetic stimulation (rTMS) as a promising treatment option in patients with chronic tinnitus. However, there is a lack of sham-controlled trials and results are very heterogeneous. For instance, Folmer and colleagues (Folmer et al., 2015) were able to show a significant effect of a sham-controlled 1 Hz rTMS protocol applied over the auditory cortex on the improvement of tinnitus severity. In contrast, a recent published multi-center randomized sham-controlled trial from Landgrebe et al. (2017) could not report any improvements as a consequence of rTMS even by investigating a larger sample. It was discussed in subsequent letters to the editors that differences in sample size and characteristics, outcome measures, stimulation sites and TMS devices might be responsible for conflicting results. The used TMS devices differ in direction of current flow by default which was shown to be critical for induction of neuroplasticity. The aim of this review is to examine previous research concerning rTMS for tinnitus to identify possible factors, e.g., TMS device, sample size or primary outcome parameters, which might be crucial for an effect of rTMS on tinnitus.

References:

Folmer, R. L., Theodoroff, S. M., Casiana, L., Shi, Y., Griest, S. & Vachhani, J. (2015). Repetitive Transcranial Magnetic Stimulation Treatment for Chronic Tinnitus. A Randomized Clinical Trial. *JAMA Otolaryngol Head Neck Surg*, Vol. 141, No. 8, 716-722.

Landgrebe, M., Hajak, G., Wolf, S., Padberg, F., Klupp, P., Fallgatter, A. J., . . . Langguth, B. (2017). 1-Hz rTMS in the treatment of tinnitus: A sham-controlled, randomized multicenter trial. *Brain Stimulation*, <http://dx.doi.org/10.1016/j.brs.2017.08.001>.

ID: 177

Abstract Submissions

Keywords: Endolymphatic Hydrops, defined Vestibular Migraine, Tinnitus, Dizziness, Vertigo

Clinical and demographic description of tinnitus's characteristics on patients with Endolymphatic Hydrops and Defined Vestibular Migraine at Hospital Británico 2013- 2016 : Retrospective study

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Introduction: Vestibular migraine and endolymphatic hydrops have reported a world prevalence between 0.3 - 56%. Otologic and vestibular symptoms have been described as present in both diseases, however tinnitus's characteristics for those patients with both pathologies had not been described. This study analyzes the tinnitus's features on a sample of patients with Defined Vestibular Migraine and Endolymphatic Hydrops in an Otolaryngology Unit.

Methods: Retrospective study which includes a non- consecutive sample of 53 patients diagnosed with Vestibular Migraine and Endolymphatic Hydrops. Inclusion criteria were patients with both diagnoses presented as comorbid according to American Academy of Otolaryngology and International Headache Society's criteria, with tinnitus reported on Pure Tonal Audiometry and Tinnitus's measurement from January 2013 to January 2016. Chi- Square and U-Mann Whitney test were used for statistical significance. ($p < 0.05$)

Results: This study showed a mean age of 44.4 years old. Women were the most affected population. 85% of patients described tinnitus as unilateral and 81% indicated this symptom lasting more than 6 months. Men between 40 to 80 years old were the most affected population with fluctuant tinnitus, in whom 500 and 1000 Hz were the most affected frequencies in patients with sensorineural hearing loss and low frequencies involvement ($p = 0.035$). In women, between 20 to 70 years old, with same audiological involvement as men, fluctuant tinnitus presented 250 and 500 Hz as main affected frequencies ($p = 0.008$).

ID: 178 / Session 11: 2

Abstract Submissions

Keywords: tinnitus, flocculus, gaze-modulated, TFI

THE RELATION BETWEEN FLOCCULUS VOLUME AND TINNITUS CHARACTERISTICS SUGGESTS A MEDIATING ROLE OF THE FLOCCULUS

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Many patients who underwent surgical removal of a cerebellopontine angle tumor, describe hearing tinnitus. This surgery often involves manipulation of the flocculus, in order to access the tumor. Based on an animal model, the flocculus has been implicated in tinnitus (Brozoski et al., 2007, *Hear Res* 228, 168-179). Also, it has been suggested that the flocculus is involved in gaze-modulated tinnitus (Chen et al., 2017, *Hear Res* 349, 208-222). Possibly, the surgical procedure or the presence of the tumor causes atrophy of the flocculus. We tested whether atrophy of the flocculus on the surgery side is related to tinnitus characteristics, in particular to gaze-modulation of tinnitus. A questionnaire was sent out to 70 patients that underwent tumor surgery. The questionnaire was completed by 51 patients, of which 36 (71%) hear tinnitus. In 29 of these 36 patients (81%), the tinnitus was modulated by eye gaze. For 34 patients, of which 25 experienced tinnitus, post-op CISS T2 MRI scans were available to measure the volume of the flocculus on each side. Flocculus volumes were not significantly different between patients with and without tinnitus. In the patients with tinnitus, the flocculus volume on the surgery side and the contralateral side were correlated with the tinnitus functionality index (TFI, ipsilateral to the surgery: $R=0.52$, $p<0.01$; contralateral: $R=0.43$, $p=0.03$). In the patients with gaze-modulated tinnitus, the ipsi-to-contralateral flocculus volume ratio was smaller than in patients where tinnitus was not modulated by eye gaze ($t=3.3$, $p<0.01$). These results suggest that the flocculus may not be causal in tinnitus generation. Rather, once tinnitus is present the flocculus may mediate the severity of tinnitus.

ID: 179 / Session 11: 3

Abstract Submissions

Keywords: tinnitus, salicylate, inferior colliculus

The tinnitus-inducing agent salicylate has a direct effect on neural activity in the inferior colliculus

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High doses of sodium salicylate have been shown to induce tinnitus in humans and animals. Salicylate reportedly increases spontaneous firing rates of neurons in the inferior colliculus (IC) (Jastreboff & Sasaki, 1986), although it is currently unclear whether these effects are mediated up-stream of the IC, or within the IC itself. We addressed this question by comparing the effects of systemic and locally applied salicylate on neuronal activity in the IC.

Ten pigmented guinea pigs (350-650 g) were anaesthetised (urethane 1g/kg i.p., fentanyl 0.3 mg/kg i.p. and midazolam 5mg/kg i.m.) implanted with a microdialysis probe and a single shank 32-channel recording electrode in the right IC. Spontaneous and sound-evoked multiunit activity was recorded at sites through the IC at baseline and after salicylate administration. In 7 animals the microdialysis probe was perfused with artificial cerebrospinal fluid (aCSF) throughout, following a baseline period of recording, salicylate was administered systemically (200mg/kg) by i.p. injection. In the other 3 animals the microdialysis probe was perfused with aCSF during baseline recording followed by aCSF containing salicylate at increasing concentrations (0.1mM (2h), 1mM (2h) and 10mM (1h)).

Following systemic injection of salicylate, spontaneous activity remained unchanged for the first three hours, but then increased rapidly to more than double six hours post salicylate administration. In contrast, local delivery of salicylate into the IC reduced spontaneous activity in a time/concentration-dependent manner.

During the first two hours following the systemic salicylate injection, frequency response areas (FRAs) showed a reduction in driven activity on the low frequency side of the characteristic frequency (CF). At later time points, an increase in driven activity was observed across the entire FRA, but was most prominent in the high frequency regions resulting in an increase in the CF.

Local administration of salicylate, via the microdialysis probe, also increased the driven activity across the FRA again resulting in an increase in CF. However, the local administration did not lead to a reduction in driven activity at lower frequencies. It was notable that neither mode of application of salicylate altered the minimum threshold for driven responses.

These results confirm previous findings that systemic administration of salicylate increases spontaneous and sound-driven activity. Since salicylate applied locally in the IC decreased rather than increased spontaneous activity, we conclude that the elevation of spontaneous firing by systemic salicylate is mediated upstream of the IC. Similarly, the initial effect of systemic salicylate in reducing sound-driven activity in a frequency-selective manner was not mirrored by locally applied salicylate and hence likely originates elsewhere. However, the finding that both locally applied and systemic salicylate increased sound driven activity across the FRA and raised the CF, suggests that these effects are, at least in part, elicited directly within the IC. We conclude that salicylate, in addition to its previously reported effects on the hair cells in the cochlea, also has a direct effect on neurons in the IC.

Supported by a Flexigrant from Action on Hearing Loss

ID: 180 / Session 15: 3

Abstract Submissions

Keywords: Sleep stages, Polysomnography, Sound stimulation

IMPACT OF SOUND STIMULATION AT DIFFERENT SLEEP STAGES IN PATIENTS WITH TINNITUS

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Sound mimicking tinnitus applied during sleep has been demonstrated that decreases the tinnitus intensity in patients suffering idiopathic tinnitus^(1,2). Furthermore, we have studied the impact of sound stimulation on the power spectrum and the coherence of the electroencephalographic waves during sleep, starting to learn about the electrophysiological mechanisms that underlie the decrease in the intensity of the tinnitus⁽³⁾. Taking into account these results and the well known fact that each sleep stage has different roles in learning process, the objective of this research was to analyze the impact on the tinnitus intensity with sound stimulation in the different stages of sleep, separately.

Eleven patients suffering idiopathic tinnitus (6 females, 5 males; between 32 and 69 years old; tinnitus evolution between 6 months and 20 years) participated in this study. All the patients presented binaural tinnitus. The spectral characteristics of the perceived sound were a combination of bandpass noise and pure tones in four patients; a combination of pure tones was referred by 4 and a pure tone alone by 3. The stage of sleep in which each patient was stimulated was selected at random; 4 patients were stimulated in the Stage N2 (sleep stage characterized by spindles), 4 in Stage N3 (sleep with slow waves) and 3 in REM sleep (stage with Rapid Eye Movements). Patients were recorded with a complete Polysomnography, for sleep stages diagnosis (from 10pm to 6am). A researcher monitored the patient and performed online diagnosis of sleep stages by which the patient is passing, and put on and off the sound according to the protocol in the corresponding sleep stage. The tinnitus intensity was measured 10 times throughout the day prior to stimulation and was compared, and statistically analyzed (paired *Student t-test*), with the tinnitus intensity in the next day.

All patients stimulated at stage N2 showed statistically significant decrement in the tinnitus intensity the day after stimulation, while nobody stimulated at the stage N3 showed changes in intensity and only one out of three stimulated during REM sleep had changes. The results show that the N2 sleep stage would be the sleep stage that interacts with the auditory processing networks, reducing tinnitus intensity. These results are coincident with the previous results that showed more changes in power spectra and coherence in electroencephalographic waves in N2 sleep stage when there is sound stimulation⁽³⁾. There is not background in the literature of the impact of sound on sleep in patients with tinnitus, so these results are the first step in the interpretation of the mechanisms underlying the improvement in tinnitus.

(1) Pedemonte et al. Tinnitus treatment with sound stimulation during sleep. *The International Tinnitus Journal*, 16: 37-43,2010.

(2) Drexler et al. Impact of reduction of tinnitus intensity on patients' quality of life. *International J Audiol.*, 55(1):11-9, 2016.

(3) Pedemonte et al. The Impact of Sound on Electroencephalographic Waves during Sleep in Patients Suffering From Tinnitus. *Sleep Sci.* 7: 143-151,2014.

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ID: 182 / Session 15: 4

Abstract Submissions

Keywords: Tinnitus, hearing aids, hearing training

Usage of hearing aids in chronic tinnitus patients within the day-care-therapy in Tinnitus Center Jena

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Introduction

More than 80% of patients with chronic tinnitus suffer from hearing loss and the tinnitus frequency is usually within the range of the greatest hearing loss. Chronic tinnitus patients report frequently problems with speech comprehension, especially in noise, even if they have normal hearing. Therefore many patients avoid noise-intensive surroundings, which can lead to social isolation and increase tinnitus perception. The targeted increase of sensory input could be achieved by hearing aids fitting.

Method

In addition to ENT counseling, psychological and physiotherapeutic therapy, chronic tinnitus patients were binaurally fitted with hearing aids as part of the 5-day day tinnitus therapy. The hearing aids should be worn for 3.5 weeks all day. In addition, all patients received auditory speech-in-noise training for 1 h per day. Following parameters were recorded digitally by the hearing aid software during the therapy: total wearing time in hours, average wearing time per day and the proportion of the acoustic environment in which the hearing aids were worn (speech at rest, speech in noise, noisy environment, music, car driving, quiet surroundings).

Results

Altogether we gathered the wearing properties of 248 our patients. Chronic tinnitus patients wore hearing aids 6.31(±3.8) hours a day. The distribution of surroundings in which hearing aids were worn was as follows: 22.06% of the time the hearing aids were used to hear speech at rest, 7.4% for speech in noise, in 7.06% in noisy environment, in 1.58% while listening to music, 5.5% while driving a car and in 56.4% in quiet surroundings.

We divided the patients in subgroups according to their hearing level (WHO grades of hearing impairment) and used Kruskal-Wallis test for independent samples to investigate if the wearing properties of hearing aids depend on grade of hearing impairment. There were no significant differences between the different WHO grades of hearing impairment regarding time of wearing hearing aids per day nor regarding surroundings in which hearing aids were worn.

Conclusion

With this data we can show that in the framework of a hearing training which is embedded in a day-care tinnitus-therapy, hearing aids have a broad acceptance by chronic tinnitus patients and were worn in potentially unpleasant environments (e.g. noisy environment) as well. Additionally this data showed that vary between different groups of WHO grades of hearing impairment so that we can unconditionally recommend hearing aids for the therapy of hearing problems in chronic tinnitus patients.

ID: 183

Abstract Submissions

Keywords: tinnitus, tinnitus burden, coping

Tinnitus burden and coping

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Abstract

Background: Tinnitus is the perception of sound without an external stimulus. A large part of the adult population experiences this symptom but only a small percentage is bothered by it. The wide variety of the burden that tinnitus causes suggest that possibly coping or other psychological factors influence the experienced burden.

Objective: To investigate the relationship between tinnitus severity and different coping strategies. Also the correlation between tinnitus severity, psychological characteristics and quality of life is investigated.

Study design and setting: Prospective, cross-sectional, tertiary referral center, University Medical Center Utrecht, the Netherlands.

Subjects and method: 321 consecutive chronic tinnitus patients were evaluated by the tinnitus care group Utrecht from 6-2007 till 11-2012 using a structured diagnostic protocol. The patients completed multiple tinnitus questionnaires (THI, TQ, THQ) and psychological, coping and quality of life questionnaires (SCL-90-R, CISS, SF-36).

Results: emotional-oriented coping and distraction-orientated coping strategies were significantly correlated with tinnitus severity. Tinnitus severity had also a significant positive correlation with anxiety, agoraphobia, hostility and sleeping problems in all used tinnitus questionnaires. A significant negative correlation between quality of life and tinnitus severity was found.

Conclusion: Chronic tinnitus patients with higher tinnitus severity scores demonstrate the use of other coping strategies and psychological characteristics than the patients with lower tinnitus severity scores. Patients with a higher tinnitus severity also have a lower quality of life. This information could be useful to select tinnitus patients who need different support to handle with the burden their tinnitus causes.

ID: 184

Abstract Submissions

Keywords: tinnitus, mental health, personality, depressive symptoms

Tinnitus and mental health

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Background: Tinnitus is the perception of sound in the absence of an external stimulus affecting 8-25% of the population. Only a small percentage of patients with tinnitus perception however, is bothered by it and evidence on the relationship between tinnitus and personality characteristics and depressive symptoms is indistinctive. A better understanding of this association can be helpful to tailor treatment options for an individual patient suffering from tinnitus.

Objective: The aim of this study was to assess the scientific evidence for the association between tinnitus burden and 1) depressive symptoms 2) personality characteristics.

Data sources: PubMed, Embase and The Cochrane Library databases.

Research methods: Databases were searched for tinnitus burden, depressive symptoms and personality characteristics and all synonyms in two separate searches. Title, abstract and full-text of retrieved articles were screened for eligibility. Directness of evidence and risk of bias were assessed. For the included articles, study characteristics and outcome data were extracted.

Results: We will describe the study selection and summarize the outcome stratified by outcome measurement of studies exploring the relation between tinnitus burden, depressive symptoms and personality.

Conclusion: We conclude on the basis of this literature review that some personality traits may be associated with the experienced burden due to tinnitus perception. Secondly, there seems to be a relation between tinnitus burden and depressive symptoms.

ID: 185

Abstract Submissions

Keywords: tinnitus, prevalence, prediction, tinnitus burden

The incidence of tinnitus and prediction of tinnitus harm

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Aim: The exact incidence of tinnitus in the general population is hard to study. Studies assessing tinnitus incidence usually have a high risk of selection bias and generally do not assess the general public. It is well known that there is a wide variety of the experienced tinnitus burden. Those individuals who experience the highest burden and start consuming health care are not identified yet. Therefore the aim of our study is to (1) assess the incidence of tinnitus in the general Dutch population, and (2) to develop a prediction model to identify those tinnitus patients who experience a high tinnitus burden and are in need for medical care for their tinnitus complaints.

Methods: This is a stepwise study. In the first step, data will be collected among members of the Dutch Health Care Consumer Panel of the Netherlands institute for health services research (NIVEL). The Dutch Health Care Consumer Panel consists of more than 10.000 citizens aged 18 years or older in the Netherlands who voluntarily, after invitation by NIVEL, participate in surveys on diverse topics in health care. A sample of 2500 panel members representative for the general adult population in the Netherlands in terms of age, gender and social economic states (SES) will be selected. Baseline characteristics about SES, age and gender are available for the NIVEL panel. The members of the panel will be asked to answer the Tinnitus Health Inventory (THI) in order to assess their tinnitus burden.

In the second step of the study the Dutch general Practitioners database will be used to assess the health consumption and demographic data of individuals with tinnitus attending a general practitioner.

In the third and last step of the study we will assess those individuals with tinnitus visiting a tertiary clinic. Differences in characteristics between those three groups will be used to develop a prediction model assessing the distinction between patients having tinnitus with and without everyday harm from their tinnitus.

The study will start in 2018, during the conference we will describe the study protocol in detail.

ID: 186 / Session 17: 3

Abstract Submissions

Keywords: Presbycusis, GRM7, NAT2, tinnitus, markers, comorbidities.

Biomarkers of presbycusis and tinnitus in a Portuguese older population

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Introduction: Presbycusis or age-related hearing loss (ARHL) is a ubiquitous health problem. It is estimated that it will affect up to 1.5 billion people by 2025. In addition, tinnitus occurs in a large majority of cases with presbycusis. Glutamate metabotropic receptor 7 (*GRM7*) and N-acetyltransferase 2 (*NAT2*) are some of the genetic markers for presbycusis.

Objectives: To explore patterns of hearing loss and the role of *GRM7* and *NAT2* as possible markers of presbycusis and tinnitus in a Portuguese population sample.

Materials and Methods: Tonal and speech audiometry, tinnitus assessment, clinical interview, and DNA samples were obtained from patients aged from 55 to 75 with or without tinnitus. *GRM7* analysis was performed by qPCR. Genotyping of single nucleotide polymorphisms (SNPs) in *NAT2* was performed by PCR amplification followed by Sanger sequencing or by qPCR.

Results: We screened samples from 78 individuals (33 men and 45 women). T allele at *GRM7* gene was the most observed (60.3% T/T and 33.3% A/T). Individuals with a T/T genotype have a higher risk for ARHL and 33% lower risk for tinnitus, compared to individuals with A/A and A/T genotype, respectively. Being a slow acetylator (53%) was the most common *NAT2* phenotype, more common in men (55.8%). Intermediate acetylator was the second most common phenotype (35.9%) also more frequent in men (82.6%). Noise exposed individuals and individuals with 'high frequency' hearing loss seem to have a higher risk for tinnitus. Our data suggests that allele AT of *GRM7* can have a statistically significant influence towards the severity of tinnitus.

Conclusion: For each increasing year of age the chance of HL increases by 9%. The risk for ARHL was not significantly associated with *GRM7* neither *NAT2*. However we cannot conclude from our data whether the presence of T allele at *GRM7* increases the odds for ARHL or whether the A allele has a protective effect. Genotype A/T at *GRM7* could potentially be considered biomarkers of tinnitus severity. This is the first study evaluating the effect of *GRM7* and *NAT2* gene in tinnitus.

ID: 187 / Session 4: 4

Abstract Submissions

Keywords: Dynamic Range Adaptation, Tinnitus

AUDITORY EVOKED MAGNETIC FIELD SIGNATURES OF DYNAMIC RANGE ADAPTATION OF SOUND LEVEL CODING IN TINNITUS PATIENTS AND HEALTHY CONTROLS.

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U Heidelberg, Germany;

Introduction

Across natural settings, the level of acoustic signals varies over the range of approximately 120-140 dB. The dynamic range of auditory system neurons is much smaller, typically between 20 and 40 dB. Animal studies show that the auditory system handles the conflict between sensitivity and accuracy arising from this mismatch by dynamically adjusting the response range of single neurons. Here we investigate (1) if dynamic range adaption of sound level coding may be demonstrated in steady-state auditory evoked magnetic field recordings and (2) if dynamic range adaptation is altered in tinnitus.

Methods

In the first study, the steady-state auditory evoked magnetic field was recorded in healthy subjects. An amplitude-modulated tone with a 40 Hz modulation frequency was presented continuously. Every 2000 to 2200 ms the stimulus changed in level. The difference between levels was 18 dB and the transition ramp duration was either 500 ms or 125 ms. The steady-state response (SSR) was recovered by bandpass filtering. A spatiotemporal minimum norm estimation (MNE) distributed source model was computed to account for the response. Mean source amplitude was determined for seven auditory cortex fields (TP, PP, HG, HS, PT, STG, STS). Source envelope amplitude and phase were computed using the Hilbert transform. Both intra- and interhemispheric phase coherence was computed among the seven cortical fields for a succession of overlapping time windows.

In the second study, the SSR was recorded in tinnitus sufferers and healthy controls. The stimulus protocol was identical to the one used in the first study. Only the 125 ms ramp was presented. Patients and controls were individually matched (yoked control design) for age, sex, side of stimulated ear, and audiogram. Patients completed the German version of the tinnitus questionnaire (TF). All subjects completed a measure of auditory sensitivity (GÜF) and the German hyperacusis questionnaire (HQ). Patients earned higher scores on these tests than healthy controls.

Results

The first study demonstrated a response amplitude overshoot effect following ascending ramps and an amplitude undershoot effect after descending ramps. Phase coherence was correlated with response amplitude, but attained its maximum value significantly later after ascending ramps and its minimum value significantly later after descending ramps. In the second study, the response amplitude overshoot effect was weaker and the undershoot effect was stronger in patients than healthy controls. Phase coherence of the response to low-level stimulus segments was stronger in patients. The post-amplitude overshoot delay of the phase coherence maximum, while present in controls, was absent in patients.

Discussion

The overshoot and undershoot effects observed in both the first and the second study fit the hypothesis of dynamic range adaptation. Dynamic range adaptation may be the result of collaborative action of several auditory cortex fields. The difference between patients and controls suggests that dynamic range adaptation is compromised in tinnitus. The temporal evolution of phase coherence in the wake of stimulus level transitions suggests that phase coherence mirrors both excitatory and inhibitory processes. The inhibitory component may be deficient in patients.

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ID: 188 / Session 13: 4

Abstract Submissions

Keywords: hearing disorder, text mining, computational predictive medicine, patient reported outcome

What do tinnitus and hyperacusis patients complain about? A Machine-Learning approach.

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Tinnitus and hyperacusis are common auditory symptoms that may become incapacitating in a sub-group of patients who thereby seek medical advice. In most of the cases the available treatment options remain palliative and do not aim at the total disappearance of the condition. The subjective characteristic of these distorted auditory perceptions and the lack of objective measurement tool makes the initial diagnosis challenging and so the outcome measurement after intervention. To date, these assessments essentially rely upon medical interviews, psychoacoustic measurements and validated questionnaires. But all these measurement tools suffer the limitation of being medically driven. As regards to their symptoms, an in depth and systematic analysis of patients' natural narratives would permit to gain knowledge on the patients-centered domains of interest. This could allow developing more efficient therapeutic strategies and more suited measurement tools. In this work, we propose a non-supervised Machine Learning approach to the analysis of patients' verbatim. Using a variant of the Latent Dirichlet Allocation (LDA) algorithm we expect to reveal what are the key symptoms and issues that tinnitus or hyperacusis patients are actually complaining about. We present the feasibility and the preliminary results of such a method by applying it to data extracted from a freely accessible Internet forum (TinnitusTalk.com). Using statistical tools and machine learning technics we are able to identify the most frequent items in patients' talks. Furthermore, we can decompose, with no prior knowledge, the patients' forum posts into 15 different topics and measure their relative importance regarding the patients' complains and considerations. Future directions and research topics emerging from this innovative algorithmic analysis of patient data in the field of tinnitus-hyperacusis are finally discussed.

ID: 189 / Session 1: 4

Abstract Submissions

Keywords: neurofeedback, frequency bands, plasticity, treatment

Treating Chronic Tinnitus with Neurofeedback

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Due to recent neurophysiological studies, subjective tinnitus has been associated with a change of ratio between differential EEG frequency modulations. While usually the slow delta- and the faster gamma- oscillations appear to be abnormally increased, alpha waves tend to be significantly suppressed for tinnitus sufferers, presumably in auditory regions. Application of neurofeedback treatment aiming for reversing these pathological activity patterns has formerly been proven successful for tinnitus treatment. In this project, we aim at replicating these earlier findings on the one hand while also investigating a newer more elaborated tomographic neurofeedback approach using EEG source estimation on the other. In an extensive and well controlled clinical study, 50 patients with chronic tinnitus took part in 15 weekly neurofeedback training sessions as well as substantial pre-, post and follow-up testing. First results indicate that tinnitus symptoms measured by standard tinnitus questionnaires prior and after the training period improved significantly over the course of the training and participants succeeded in altering their brain activity accordingly. What is more, these changes remain constant when measured 3 and 6 months after the completion of training. Neurofeedback can thus be considered a highly promising form of therapy in the treatment of chronic tinnitus.

ID: 190 / Session 16: 3

Abstract Submissions

Keywords: Tinnitus, hearing impairment, clinical pilot study, audiometry, fMRI

Identification of functional and molecular biomarkers in mildly hearing impaired subjects with and without tinnitus

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Tinnitus is as a symptomatic malfunction of our hearing system, where phantom sounds are perceived without acoustic stimulation.

In recent years we have developed a fingerprint for tinnitus using a combination of behavior animal models for tinnitus and electrophysiological as well as molecular approaches in the peripheral and central auditory system. The characteristic features that distinguished equally hearing impaired animals with and without tinnitus are described through a failure to centrally maintain sound sensitivity after peripheral deprivation selectively in tinnitus animals (Knipper et al 2013, Prog. Biology; Rüttiger et al 2013, Singer et al 2013).

Here we present a clinical pilot study in hearing-impaired subjects with and without tinnitus that aimed to test our hypotheses in humans. We use audiometric measurements, the analysis of body fluids, and functional magnetic resonance tomography (fMRI). The results of this first pilot study in humans are discussed in the context of previous findings gained in animals.

ID: 191 / Session 14: 3

Abstract Submissions

Keywords: Cure, strategy, innovative, collaboration

Tinnitus Cure Map

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The British Tinnitus Association (BTA) is the United Kingdom's leading tinnitus charity, offering support to people with tinnitus, providing educational resources and funding tinnitus research projects. The BTA has recently undergone a restructuring exercise, resulting in the creation of a corporate Vision of "a world where no one suffers from tinnitus." Pivotal to that aim is working towards an ultimate cure for tinnitus. As part of that aspiration the BTA has instituted a series of strategic work streams, one of which is specifically aimed at achieving a cure.

The first step in this process has been to take stock of what has been achieved to date and what current research is being conducted. To try and identify areas where gaps in our knowledge are hampering progress, the BTA Cure Team has developed a mind map that synthesises the current tinnitus research world. It is hoped that by being able to see where our knowledge is deficient we can more effectively apportion research resources. This should also help to ensure that research funding is not directed towards areas that have already been fully explored.

ID: 192 / Session 12: 3

Abstract Submissions

Keywords: Tinnitus, questionnaires

Tinnitus outcome measures after a brief multidisciplinary intervention

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Introduction: Tinnitus is a multi-faceted phenomenon which is often correlated with psychological co-morbidity. It appears that successful treatments improve - perceived - tinnitus severity as well as associated or underlying emotional distress. However, few studies use outcome measures that are sensitive to assessing such change. The present talk reports data from two clinical samples to assess 1) whether several applied outcome measures are sensitive to assessing change following a brief multidisciplinary intervention and 2) which tinnitus-related measure might be best used in the presence of psychological co-morbidity.

Method:Sample 1: Two hundred-twenty nine patients with subjective tinnitus completed a short-term, 7-day intervention ("Modified multimodal tinnitus retraining therapy"). Data were assessed at pre and posttreatment and comprised eight measures assessing tinnitus (TQ, THI, TFI), anxiety and depression (HADS, ADS), quality of life (SF36), stress (PSQ), and a screening of psychiatric comorbidities (ISR). Sample 2: Three-hundred and thirteen patients were assessed using four measures focusing on tinnitus (TQ), depression (ADS), stress (PSQ) and psychiatric comorbidity (ISR).

Results:At posttreatment, significant and reliable improvement occurred across all outcome domains emphasizing the efficacy of short-term treatment. Tinnitus questionnaires differed in capturing change in psychological co-morbidities.

Conclusion: Multimodal interventions should assess both tinnitus and psychological co-morbidities. The THI appears to change in both tinnitus-related and associated symptomatology. Additional measures might be used to further differentiate clinical and psychological outcome domains.

ID: 193 / Session 1: 2

Abstract Submissions

Keywords: rTMS, non-invasive brain stimulation, duration, stimulation frequency

Current state and perspectives of repetitive transcranial magnetic stimulation in chronic tinnitus

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Multisite repetitive transcranial magnetic stimulation (rTMS) interferes with pathological activity and neuroplasticity in auditory and prefrontal cortex. So far results of rTMS trials are highly heterogeneous with small effect sizes. Approaches to increase treatment effects are increase of treatment duration and high stimulation frequency. Here we investigate the feasibility and efficacy of a multisite intervention with four treatment arms (two vs. four weeks of treatment and low vs. high frequency stimulation). Patients can choose treatment duration by own choice. Stimulation frequency (combined high-frequency dorsolateral prefrontal (unilateral) and low frequency temporoparietal (bilateral) stimulation vs. combined high frequency dorsolateral prefrontal (unilateral) and high frequency temporoparietal (bilateral) stimulation) is randomized. The study is registered at clinicaltrials.gov (NCT02653547). We expect completion of the recruitment (n=80) on December 2017 and of the analysis on February 2018.

ID: 194 / Session 11: 4

Abstract Submissions

Keywords: Tinnitus, tonotopic mapping, tonotopy, neural plasticity, hearing loss

Tinnitus and cortical tonotopic maps

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Clinical hearing loss, associated with neural plasticity, increases the chances of developing tinnitus, the perception of a sound in the absence of an external source. The specific plastic changes that are involved in tinnitus remain elusive. A striking feature of the auditory cortex is its tonotopic organization. Several studies have suggested a relation between hearing-loss-induced tonotopic reorganization and tinnitus. However, recent research has shown that the tonotopic organisation of tinnitus patients without hearing loss is not significantly different from that of normal hearing participants without tinnitus (Langers et al. 2012). We now focus on tinnitus patients with high-frequency sensorineural hearing loss to determine if any characteristics in the tonotopic maps are detectable that can be attributed to tinnitus.

In this study we use functional magnetic resonance imaging (fMRI) to gain insight in the association between tonotopic reorganization, hearing loss and tinnitus. In particular, we look into the changes of the tonotopic maps as a consequence of tinnitus and hearing loss. Three groups of participants were included: a tinnitus and hearing loss group, a hearing loss only group and a normal hearing control group. Pure tone stimuli were presented in the MRI

scanner as the attention of participants was controlled by a non-related visual task. The loudness of the stimuli was matched across frequencies, within each participant.

A preliminary analysis showed that tonotopic maps of the bilateral auditory cortices could be created, with opposing frequency gradients high-low-high in the posterior to anterior direction.

Tonotopic maps in hearing impaired participants with and without tinnitus, respectively, were similar to those observed in normal hearing subjects (e.g. Langers et al 2012). Further analysis will show whether maps differ between the participant groups.ab

ID: 195 / Session 12: 5

Abstract Submissions

Keywords: Treatment, plasticity, crossover study, double-blinded

Auditory-somatosensory stimulation desynchronizes brain circuitry to reduce tinnitus, Part II

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Background: A majority of tinnitus subjects are able to modulate their tinnitus by moving or applying pressure to their head or neck, so called, 'somatic' tinnitus (Levine, Am. J. Otolaryngol 1999). This ability is mediated, at least in part, by the dorsal cochlear nucleus (DCN), which integrates auditory and somatosensory information (Koehler and Shore, J. Neurosci 2013). DCN circuitry is altered in tinnitus to produce hypersynchrony and heightened spontaneous firing rates in output neurons (Wu et al, J. Neurosci 2016). Pairing auditory- with somatosensory stimuli can induce long-term increases or decreases in firing rates and synchrony in these neurons, depending on the precise timing of the bimodal intervals (Wu et al, J. Neurosci. 2016). By presenting bimodal intervals that depressed firing rates and synchrony, we were able to decrease physiological and behavioral evidence of tinnitus in animals (Part I; Marks et al, Sci. Transl. Med. 2017). Here, we extend these findings to a human population.

Methods: Twenty human subjects with constant, bothersome somatic tinnitus were recruited to participate in a double-blinded, sham-controlled, cross-over study. Subjects were randomly assigned to sham (auditory only) or active (bimodal auditory-somatosensory) stimulation treatment at the start of the trial. Somatosensory stimulation was achieved by cup-electrodes placed on the face or neck. Using a take-home device, treatments consisted of 30 minutes per day of auditory only (sham) or bimodal (auditory-electric) stimulation for four weeks. After a four-week washout period, the alternate treatment was provided (Group One: Sham to Active; Group Two: Active to Sham). Throughout the sixteen-week study, subjects completed the Tinnitus functional Index (TFI) and loudness matching tasks to monitor their tinnitus on a weekly basis.

Results: Bimodal but not unimodal stimulation resulted in significant reductions in loudness matching (8.04 ± 1.33 dB; $P=5.5e-5$) and total TFI score (7.33 ± 0.956 TFI Units; $P=6.14e-5$), with ten of the subjects showing greater than a 13 point reduction in their TFI scores. Reductions in loudness were found to correlate with reductions in TFI (LME; $\beta = 0.169 \pm 0.058$, $T=2.94$, $P=0.0035$). Neither group demonstrated significant demographic or hearing-related differences.

Conclusion: Bimodal auditory-somatosensory stimulation alters tinnitus circuitry to alleviate tinnitus in human subjects and could be a safe and effective treatment for a large number of tinnitus patients.

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ID: 196 / Session 12: 4

Abstract Submissions

Keywords: Tinnitus, STDP, treatment, Plasticity, LTP/LTD

Auditory-somatosensory stimulation desynchronizes brain circuitry to reduce tinnitus, Part I

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Introduction: Spike-timing-dependent plasticity (*stdp*) theoretically regulates neural synchrony by modulating connectivity via synaptic strength adjustment (eg, Tass and Popovych, Biol. Cybern 2012). Dorsal cochlear nucleus (DCN) fusiform cells, putative tinnitus generators, exhibit the *in vivo* equivalent of *stdp*: stimulus-timing-dependent plasticity (STDP). Enhanced long term potentiation (LTP: persistent increase in synaptic strength) and diminished long term depression (LTD) (Koehler and Shore, J. Neurosci. 2013) likely result in hypersynchrony and underpin the neural basis of tinnitus. If enhanced LTP triggers tinnitus, then shifting STDP towards LTD and de-synchrony, could reverse tinnitus (Marks et al, Sci. Transl. Med 2017).

Methods: Guinea pigs were exposed to unilateral narrow band noise (1/2 octave, centered at 7 kHz, 97 dB SPL) for two hours to induce temporary threshold shifts. Tinnitus was assessed with gap-prepulse inhibition of acoustic startle paradigm (Turner et al, APA PsychNET 2006). A bimodal stimulus paradigm consisting of somatosensory stimuli (via transdermal stimulating electrodes placed dorsal to the cervical vertebrae) presented within 20 ms of 40 dB SL sounds matching the tinnitus spectra. Animals were treated with this bimodal stimulus daily for 20 minutes for four weeks concurrently with biweekly tinnitus assessments. Following bimodal treatments, single unit recordings were obtained using electrodes placed into the DCN fusiform cell layer after ketamine/xylazine anesthesia. Responses were analyzed for neurons with best frequencies ranging from 4 kHz to 32 kHz. Neural synchrony was assessed via spike train cross-correlation.

Results: Bimodal stimulation with an interstimulus interval targeting the LTD window reversed STDP timing rules and synchrony in fusiform cells and reduced behavioral evidence of tinnitus.

Conclusion: The results suggest that non-invasive, long-term alteration of DCN neural activity through bimodal stimulation can be utilized to alleviate tinnitus in humans (Part II; Marks et al, Sci. Transl. Med 2017). Further, *stdp* plays a fundamental role in regulating neural synchrony, providing a framework for treating diverse disorders of aberrant neural synchrony.

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(SES)

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ID: 197

Abstract Submissions

Keywords: tinnitus, olanzapine

An open pilot study to evaluate efficacy and safety of olanzapine to treat tinnitus

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Introduction: Many neuronal circuits are supposed to be involved in tinnitus pathophysiology, including dopaminergic and serotonergic ones. Olanzapine is an anti-psychotic drug that acts as a D2 and 5HT_{2A} antagonist at mesolimbic and pre-frontal pathways. Method: Fifteen tinnitus patients screened, 5 mg daily olanzapine for 12 weeks, outcomes measured with THI and CGI. Results: Twelve patients completed the trial. THI (mean +/- SD) = 53.1 +/- 32.0 at screening, 38.2 +/- 28.3 final (paired t test = 2.3, $p = 0.04$); CGI = 8 patients improved. Mild side effects in 2 patients. Discussion: Dopamine and serotonin neuronal pathways may be an interesting target to treat tinnitus. Unlike other anti-psychotic drugs, olanzapine side effects are mild with 5 mg per day dosage. Conclusion: Olanzapine may be an alternative to treat tinnitus. Randomized trials are needed to confirm its potential.

ID: 198

Abstract Submissions

Keywords: tinnitus, ERPs, P300

Event Related Potentials as a Possible Tool to Objectively Measure the Effects of Tinnitus Treatment: Preliminary Data

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Tinnitus is a difficult symptom to evaluate, because it involves an individual reaction factor and its measurement and treatment is still done subjectively, being evaluated by questionnaires and visual-analog scales.

The aim of this study is to verify if the long-latency evoked potentials, especially the P 300, present changes in their latency and amplitude that can measure, together with THI (Tinnitus Handicap Inventory) questionnaire and VAS (Visual Analog Scale), the benefits of pharmacological treatment.

Method: Seventy-seven individuals with tinnitus complaints will be selected and randomly assigned to 7 groups of drugs previously studied for tinnitus treatment, and will be evaluated by VAS, THI and long-latency auditory potentials in three moments: pre-medication, immediately after the end of treatment and after a wash out period.

Preliminary Data: Up to this moment, a significant variation in the parameters N1L ($p = 0.012$) and P300 AMP ($p = 0.050$), and also in THI ($p < 0.0001$), VAS for Volume ($p = 0.0007$) and VAS for Distress ($p < 0.0001$) scores over time was observed in 47 ears with tinnitus was observed, according to Friedman's ANOVA.

ID: 199

Abstract Submissions

Keywords: Neuroinflammation, microglia, cochlear nuclei, choroid plexus, cochlear damage

Neuroinflammatory responses in choroid plexus and dorsal cochlear nuclei after unilateral cochlear damage

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Cochlear nuclei, the first CNS station of auditory pathways, are located on the surface of the fourth ventricle, and therefore are largely covered by an ependymal layer rather than by pia. In other structures, ependyma has been shown to be very permeable to liquor factors and even to blood-derived cells entering the CSF by crossing the choroid plexus epithelium. This trafficking is strongly modulated by inflammation. Cochlear destruction is known to elicit a clear inflammatory response in the VCN, whereas little is known in the DCN, which is thought to be involved in tinnitus onset. The aim of our study is to assess the possible involvement of inflammation in the mechanisms leading to tinnitus onset.

Given that macrophages are a central player in inflammatory reactions, we investigated the changes of DCN-related Iba1+ macrophages and microglia after unilateral cochlear destruction in the rat. Young Wistar male rats (40-90 days) were used.

A week after cochlear destruction, disorganized clusters of Iba1+ cells appeared at the ipsilateral DCN surface facing the 4th ventricle, especially at contact sites with the choroid plexus and cerebellum, whereas less evident changes were seen in the contralateral DCN, where changes mainly consisted in the formation of rod microglial trains at the ependymal surface. An increase in ring-shaped and the appearance of occasional dystrophic microglia was also observed in the ipsilateral DCN. This was very different from responses in VCN, where microglia density uniformly increased in the ipsilateral nucleus, and did not change appreciably in the contralateral one. When looking at DCN 30 days after cochlear destruction, microglial density and distribution were not significantly different from control.

In the choroid plexus, Iba1+ macrophages displayed interesting changes after cochlear destruction. In all conditions tested, macrophages were strongly clustered, with local density within plexus branches varying more than tenfold. No clear asymmetries were observed in density distribution between sides. However, one week after cochlear destruction, macrophage populations residing in the branches in close apposition to the DCN were often continuous with the DCN population. Macrophages could be discriminated from microglia due to their lack of expression of P2Y12R. Moreover, both at 7 and 30 days, macrophages in the choroid plexus became prevalently associated to the outside of the epithelium (epiplexus cells), whereas in control condition they were mostly located inside the epithelial barrier (stromal macrophages). At 30 days, choroid plexus epithelium (labeled by transthyretin) showed morphological changes as well, becoming thinner and delimiting a larger and less uniform lumen, similar to what was observed in spinal cord injury.

When blocking microglial activation with minocycline, DCN microglial density increase due to damage was blocked, but choroid plexus was not similarly affected.

These data suggest that the response of the Iba1+ population after cochlear damage includes contribution from both local microglia and choroid plexus-derived factors and cells. The present work suggests that the DCN, in addition to integrating nonauditory context nerve signals with auditory stimuli, also integrates immune factors crossing its ventricular surface, possibly in order to differentiate physiological and pathological stimulation patterns.

ID: 200

Abstract Submissions

Keywords: Meniere's syndrome, arterial hypotension

Arterial hypotension in Meniere's Syndrome

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Arterial hypotension in Meniere's Syndrome

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BACKGROUND:

The classic symptoms of Ménière's Disease (MD) are fluctuating hearing loss (frequently in low frequencies), low pitch tinnitus, fullness in the ear, and episodic spinning vertigo which could last from twenty minutes to two or three hours.

When it is secondary to another disorder it is called Ménière's Syndrome and there is a long list of possible causes, including hypothyroidism, hyperinsulinaemia, genetic mutations and more.

Ménière's disease happens when a person has Ménière's Syndrome (MS) and the cause cannot be identified – idiopathic, in other words.

This means the more inquisitive a doctor is looking for underlying cause, the less diagnosis for Meniere's Disease will be made.

Also, there is a part of the world's population who suffer from Chronic hypotension. The percentage of healthy people with low blood pressure hasn't been identified yet.

We found in our anamnesis that patients with meniere syndrome frequently also report having arterial hypotension.

TYPE OF STUDY: Prospective Prevalence Study

AIM OF STUDY:

The objective of this work was to find out what is the incidence of arterial hypotension in patients diagnosed with Meniere's disease, compared with healthy people without meniere's disease who attended an annual routine health checkup.

PATIENT POPULATION:

The first group enrolled were a cohort of mainly urban dwelling Argentinian subjects, either employees or spouses of employees of a major national bank. A total of 200 subjects were studied.

The second group of patients comes from an Otolaryngology outpatient Hospital Service diagnosed with MD, who were asked to keep a daily vertigo diary to document MD episodes (2015–2016).

A total of 60 persons (59% female) around the age of 56 years were included. The total follow-up time was 270 days. They experienced on average 10.3 episodes during the observational period. Low blood pressure was significantly associated with vertigo onset risk.

METHODS

Both groups of subjects had an ambulatory blood pressure monitor fitted which they wore for 24 hours straight.

The subjects also filled out a detailed lifestyle questionnaire and kept an activity diary.

Results:

49% of the people in the group without Meniere syndrome presented hypotension, while 68% of patients with Meniere's syndrome did as well.

Individual hypotensive values were more frequently found in women (63%), and occurred in a group of individuals with a distinct body habitus, specifically thin subjects with a low creatinine levels suggesting a smaller muscle mass.

The hypotensive profile in these subjects was associated with a low risk cardiovascular profile, were of a lower weight and were less likely to have a family history of hypertension or vascular disease, but they did have a greater prevalence of Meniere Syndrome.

CONCLUSION

Hypotension is common in the general population, and specially in people with Meniere's Syndrome.

ID: 201 / Session 2: 3

Abstract Submissions

Keywords: tinnitus, monkey, startle, ABR, salicylate

A Tinnitus Model in Nonhuman Primates

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Tinnitus, the most common hearing disorder characterized by a phantom perception of sound (i. e. constant sensation of ringing), impairs the quality of life of millions, making it a current concern for Public Health. Animal models are necessary for a better understanding of its pathophysiology and ultimately for the development of evidence-based therapy. Currently, studies are increasingly criticizing validity of existing animal models used in tinnitus research, especially with regard to their transferability to human tinnitus patients. Rodents are commonly used as animal models; however, they hardly exhibit prefrontal structures (i. e. , ventromedial prefrontal cortex, vmPFC). Our previous studies in three independent cohorts of human tinnitus patients revealed that the vmPFC plays a crucial role and undergoes significant volume loss in tinnitus patients. We assume that the morphological changes in the vmPFC disable top-down inhibition from this structure to auditory centers, thus preventing normally available suppression of the tinnitus signal. Given that the vmPFC is highly developed in nonhuman primates, we aimed to establish a tinnitus model in rhesus monkeys (*Macaca mulatta*).

Tinnitus was determined by using a non-acoustic startle paradigm. Eye blinks were monitored by recording electromyographic (EMG) activity in response to air-puffs as startle stimuli, preceded by short auditory stimuli varying in frequency and intensity. The tones were adjusted according to the animals' hearing thresholds, which were determined by frequency-specific Auditory Brainstem Response (ABR) recordings. In this pilot study, one monkey was tested at its baseline, at a reversible tinnitus level (after administration of salicylate, 150 mg/kg), and at a follow-up level. In order to ensure translation of the results to humans, a sample of human tinnitus patients and of matched control subjects without tinnitus underwent the same testing paradigm. Preliminary results suggest that the preceding tone facilitates the eye blink response as long as it is reliably perceived. A larger sample of animals and patients will reveal whether the tinnitus frequency is reflected by a lack of eye blink facilitation at the condition of the specific preceding tone, thus mimicking the tinnitus. The use of a non-acoustic startle stimulus is advantageous since it is free from acoustic interference and is less aversive (especially for patients with hearing issues like tinnitus and hyperacusis).

ID: 202

Abstract Submissions

Keywords: Resting state, fMRI, connectivity, replicability

Replicability of Resting State Networks in Tinnitus Patients

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Resting state functional connectivity studies of tinnitus using fMRI have become popular in recent years. While this tool has the potential to identify invariant biomarkers of tinnitus useful for developing objective diagnostics, results of resting state studies of tinnitus have produced variable and inconsistent results. In the current study, we directly assess the replicability of resting state networks of tinnitus patients by scanning participants twice, with scan dates separated by exactly 1 week. Data for 47 tinnitus patients and 22 controls were collected. Of those, 8 tinnitus patients and 6 controls were active duty service members and veterans recruited from the Wilford Hall Ambulatory Surgical Center (WHASC) in San Antonio, Texas. The remaining 39 tinnitus and 16 control participants were civilians recruited at the University of Illinois (UIUC). At UIUC, the PTA was 23.12 ± 10.66 for the tinnitus group and 12.34 ± 9.74 for the controls. At WHASC, the PTA for tinnitus participants was 14.88 ± 6.52 , and for controls, it was 11.53 ± 5.48 . More control participants are currently being collected at both sites to better match hearing thresholds across groups. The Tinnitus Functional Index (TFI) was used to assess tinnitus severity at both sites. TFI scores at UIUC ranged from 1.2 to 69.6, with an average of 25.79 ± 18.00 at the first scan and 22.44 ± 17.73 . Similarly, at WHASC, TFI scores ranged from 11.2 to 48.4, with an average of 26.65 ± 13.21 at the first scan and 24.57 ± 9.37 at the second. We focused our analysis on three main resting state networks: the default mode, dorsal attention, and auditory networks. Standard preprocessing was performed using SPM12, followed by a seed-to-voxel analysis using the Conn toolbox. When controlling for the effect of site of data collection, no significant differences were found in a whole-brain connectivity analysis for any of the networks examined while controlling for data collection site, as assessed using a two-way analysis of variance. Replication analyses were performed following the Conn analysis. Fisher-transformed correlation coefficients assessing within-network connectivity were examined, and values for the first scan were plotted against the values of the second scan to visualize replicability. The plots revealed good replicability for control and tinnitus participants at both UIUC and WHASC. Differences in correlations across scans in the tinnitus patients did not demonstrate a clear relationship with differences in TFI scores; note that for all but one participant, differences in TFI score across scans did not alter the clinical category of the patients. This suggests that the neural correlates of tinnitus as determined by resting state connectivity may be impervious to the day-to-day changes in TFI. Further, control participants demonstrated similar connectivity variability. We are investigating correlations between these connectivity changes and variations in mood as a possible explanation for the discrepancies. However, our results thus far suggest that resting state functional connectivity in tinnitus patients is a reliable measure and therefore a useful tool in studying the heterogeneous tinnitus patient population.

ID: 203 / Session 13: 5

Abstract Submissions

Keywords: Tinnitus, biomarker, hearing loss, genetic

Evidence for biological markers in tinnitus: A systematic review

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Introduction: Biological markers are an emerging field in the area of Otology. Once identified, they may provide a means of determining the time-course or most effective treatment for an individual with tinnitus, presbycusis or any other otologic disease or impairment. Potential tinnitus biomarkers include mutations in mitochondrial DNA, chromosomal mutations, proteins, hormones, immunoglobulin, cytokine, interleukin, vitamins.

Purpose: To evaluate what biological factors are predictive of subjective tinnitus and tinnitus severity. The protocol is registered at PROSPERO: CRD42017070998.

Methods: We conducted a systematic search employing CINAHL, PsychINFO, EMBASE, ASSIA, PubMed, Web of Science, Science Direct, and EBSCO Host, using the search terms:tinnitus* AND gene* OR protein OR hormone OR immunoglobulin OR enzyme OR cytokine OR interleukin OR lipid OR vitamin OR marker.The initial search was complemented by scanning reference lists from relevant systematic reviews and the included primary studies; citation searching of the included primary studies using Web of Science; and hand searching the last six months of key otology journals.

Inclusion criteria: Human subjects with subjective tinnitus. Searches were limited to articles in the English language, published in peer reviewed journals.

Exclusion criteria: Animal studies, objective tinnitus, Ménière's disease, Otosclerosis, Chronic otitis media, history of oncology and chemotherapy, ototoxic drugs intake, autoimmune diseases, neurodegenerative or demyelinating disease.

Results: All stages of the study were carried out by at least two members of the review team. The titles and abstracts of the studies identified through the initial search has yielded 3801 records, after removal of duplicates and exclusion based on defined criteria 79 records were selected and the full text articles was requested.

Data were extracted using a data extraction form which was developed for purpose and piloted prior to its use. Any disagreements were resolved through discussion or consultation with the third member of the review team. Extracted data included participant information (demographics, baseline characteristics, sample size), country, control, study design, research question, tinnitus characteristics (type of sound, constancy, severity [measure used]), genes and/or biological factor assessed, and key data and findings, conclusions.

Pooled estimates (or narrative synthesis) of the association between biological factors and presence or severity of tinnitus from individual studies will be presented.

ID: 204

Abstract Submissions

Keywords: presbycusis, tinnitus, morphometry, fMRI

Morphometric and functional changes in the auditory brain in patients with presbycusis and tinnitus

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Presbycusis and tinnitus are two of the most common hearing related pathologies. Although both presumably originate in the inner ear, there are several reports about their central components. The onset of presbycusis coincides with the highest appearance of the tinnitus (between 60-70 years of age).

The aim of our project is to identify age and tinnitus related changes within the auditory system and associated structures.

A group of patients with presbycusis and tinnitus, another group with presbycusis only and a group of young controls underwent extensive audiological examination to characterize degree of the hearing loss and tinnitus. MR morphometry and event related fMRI were examined with 3T MR system. For MR morphometry cortical reconstruction and volumetric segmentation were performed with the aim to evaluate surface, volume and thickness of the grey matter. fMRI was performed under following acoustic conditions: speech, speech in babble noise, babble noise, speech like sounds. Speech and speech in babble noise were also coupled with congruent or incongruent visual stimulation.

Morphometric analysis showed clear age related changes within the Heschl gyrus and planum temporale (a decrease of thickness and surface). Similar findings (changes in thickness) were also present in the parahippocampal gyrus and anterior insula. The thickness and surface changes within the planum temporale were related to tinnitus, too. fMRI displayed age related differences within the Heschl gyrus and planum temporale, that also showed effects of lateralization. The results of morphometric as well as functional analysis are at present time in the process of final evaluation.

ID: 205

Abstract Submissions

Keywords: Tinnitus, ARC therapy, BDNF, NT-3

ARC synaptic adaptation therapy a new treatment for the tinnitus

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Tinnitus is a more common problem, and it's because how big impact in our life is stress, lack of right diet and physical activity that protect us from sudden and progressive hearing loss. Our nervous system seems to have a problem with losing something very fast rather than progressively. And it can be a major factor also in tinnitus patients due to very fast electric stimulation lost from cochlear hair cells. If not only to fast losing of the hair cell is a major factor for tinnitus generated but also a lack of right Neurotrophic protein level such as BDNF, NT-3 we understand how tinnitus pathology is complex and much more associated with neuroscience and neurobiology than with the audiology. The beginning of tinnitus pathology begins in the range of audiology science but ends strictly in neuroscience. Our clinical trial shows that not only we should focus on what has been damage regarding what why have lost during the hearing loss (hair cell, ribbon synapses or auditory nerve fibers) but also we should diagnosis how nervous system react after losing the input. Everything begins from the inner ear cells, but we should also determination what type of change already have made the nervous system in the structure of (synapses and neurons). There is growing evidence that not only is important what has been damage but also how fast it was damaged; this means that the time of losing something is a major factor for increase the excitability of the nervous system neurons. And a progressive losing in every type of sensory deprivation looks like the best strategy. Arc synaptic adaptation therapy as a first clinical treatment can reduce the tinnitus. And it's because it uses similar process which appears during the progressive hearing loss. If the nervous system sees reduced stimulation in time he can predict and distinguish between progressive hearing loss that is natural process and present in strategy that the nervous system can adapt to it and sudden hearing loss that is not often a natural way of losing sensory input.

ID: 206

Abstract Submissions

Keywords: Immunohistochemistry, Auditory cortex, Parvalbumin, NMDA receptors, nNOS

The distribution of cell and neurotransmitter markers in the auditory cortex of rats in a tinnitus model

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Changes in cortical gamma oscillations have been reported in tinnitus in humans, however, the nature of their contribution to the tinnitus percept is controversial (Sedley et al. 2012). In an *in vitro* study, Rentisi et al. (this meeting) report a reduction in the peak frequency of kainate induced gamma activity in auditory cortex in rats with tinnitus. Fast spiking GABAergic parvalbumin interneurons are necessary for the generation of gamma oscillations, and NMDA receptors reportedly influence the frequency of hippocampal gamma oscillations (Mann and Mody, 2009). We therefore hypothesised that the expression of parvalbumin and GluN1 (an obligatory subunit of the NMDA receptor) may be altered in tinnitus.

We used immunohistochemistry to examine the expression of parvalbumin and GluN1, in rats with tinnitus. We also examined neuronal nitric oxide synthase (nNOS) which has been reported to be upregulated in other auditory areas in tinnitus.

Long Evans rats were acoustically over exposed (16 kHz at 115 dB SPL, 2 hours) with the left ear plugged and subsequently tested for tinnitus with the gap-pre-pulse inhibition of the acoustic startle (GPIAS) paradigm. Rats with reduced inhibition of acoustic startle at one or more test frequencies were deemed to be 'tinnitus' rats. Controls were unexposed.

Exposed and control rats were deeply anaesthetised with sodium pentobarbital and transcardially perfused with 4% paraformaldehyde. Brains were cryoprotected with 30% sucrose and 30µm coronal sections were cut using a microtome. Primary antibodies targeting parvalbumin, GluN1 and nNOS were applied to free floating sections and detected using fluorophore-linked secondary antibodies. Labelling was visualised with a Nikon A1 confocal microscope. ImageJ and Matlab were used for quantitative image analysis. Comparisons were made between the right and left auditory cortices and between tinnitus and control rats.

Parvalbumin labelled somata were mainly located in the middle cortical layers, whilst GluN1 labelling was evenly distributed across the cortex and was mostly somatic. Cell bodies labelled for nNOS were most densely distributed in the superficial and deep layers of the auditory cortex. Neuropil throughout the cortex showed nNOS labelling. In 'tinnitus' and control rats, the number of cells in the auditory cortex expressing either nNOS or parvalbumin did not differ between left and right hemispheres. Similarly, no consistent differences were observed between hemispheres in mean brightness of labelling for parvalbumin, nNOS and GluN1. The pattern and degree of labelling in 'tinnitus' rats was also not different to that in control rats.

These results suggest that changes in gamma oscillations observed *in vitro* in this tinnitus model in rat are not reflected in immuno-labelling for parvalbumin, GluN1 or nNOS in the auditory cortex.

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ID: 207 / Session 19: 4

Abstract Submissions

Keywords: speech perception, speech in noise, central hearing, tinnitus distress

Speech Perception in Tinnitus and its Relations to Distress, Hearing Abilities, and Higher-Order Processes

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Individuals suffering from tinnitus often complain about difficulties regarding speech comprehension, especially in advanced listening situations. Underlying mechanisms are unknown and highly under-investigated. In this study we examined a sample of individuals suffering from chronic, subjective tinnitus (n=30, age range 30-50 yrs.), who underwent comprehensive audiometric (pure tone audiometry, suprathreshold audiometry, speech in noise performance) and behavioural testing (standard tinnitus questionnaires). They performed a phoneme discrimination task embedded in an oddball paradigm, while neurophysiological data were recorded. Thereby, we aimed at investigating, if difficulties are already existent in elementary speech processing at the phoneme level. In particular, we addressed the issue at what level speech perception is hindered and whether peripheral or central hearing deficits account for it. The analysis of behavioural and audiometric data showed no indications of peripheral hearing loss and mild-moderate symptoms of tinnitus distress. Due to our data tinnitus distress negatively correlates with speech in noise performance, while there were no relations with peripheral or central hearing abilities. Participants reached generally high accuracy in the phoneme discrimination task. The analysis of behavioural data even revealed a positive effect of tinnitus distress on accuracy in the difficult condition. In the easier conditions tinnitus distress was related with longer reaction times. The neurophysiological data analysis showed positive effects of tinnitus distress and tinnitus duration on the N2 peak in the easier conditions. No effects were found for tinnitus parameters on the P3 component. A post-hoc mediation analysis revealed the effect of tinnitus distress on reaction times to be fully mediated by the N2 peak. Our results indicate that reported speech in noise difficulties are related to tinnitus distress and exist also in absence of a peripheral or central hearing loss. Tinnitus distress appeared to benefit the detection of slight phonetical variations, but prolonged the reaction to stronger variations. The mediation effect of the N2 might represent an over-sensitivity to variations in the auditory domain and a waste of resources spend on their classification. For a better understanding of reported speech in noise difficulties, its relation to tinnitus distress should be further explored in more detail especially regarding the role of cognitive processes (inhibition, attention).

ID: 208 / Session 7: 3

Abstract Submissions

Keywords: Tinnitus; hearing loss; electroencephalography

Hearing loss may induce tinnitus by strong auditory memory and increased vigilance: a qEEG study on the relationship between hearing loss and tinnitus

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AIM: Peripheral hearing loss (HL)-induced changes in the central auditory system is a prerequisite for the generation of subjective tinnitus. However, there are cases with considerable amount of HL without any development of tinnitus and this question on the differences between HL with or without tinnitus with regard to the cortical activity has never been addressed. In this regard, we compared resting-state quantitative electroencephalography (rs-qEEG) findings between the HL with tinnitus (HL-T) group and with no tinnitus (HL-NT) group to reveal cortical activity differences between the two.

MATERIAL / METHODS: Sixty-one HL-NT subjects were enrolled prospectively, and 61 HL-T subjects were selected from our database. The hearing thresholds were strictly matched between the two groups, and only subjects with low distress level (grade 1 or 2) were enrolled for the HL-T group. Rs-qEEG was measured in all included subjects and compared between the 2 groups with regard to source-localized activity and functional connectivity.

RESULTS: As compared with the HL-NT group, the HL-T group showed increased activity in the parahippocampus (PHC) for the beta 2 and 3 frequency bands and in the inferior parietal lobule (IPL) for the gamma band. Also, the HL-NT group showed increased connectivity between the PHC and the auditory cortex (A1) as compared with the HL-T group.

DISCUSSION: The PHC is an area where auditory memory is stored, and the IPL is an area that has circuit-breaker activity and makes a subject vigilant when an external stimulus is presented. In this regard, HL may induce tinnitus when auditory memory is strong enough to generate phantom auditory perception and the circuit-breaker activity of the IPL is high enough to make the subject with HL vigilant.

CONCLUSIONS: Based on the current study, HL may induce tinnitus if the PHC-based auditory memory is strong enough to generate tinnitus and the circuit-breaker activity of the IPL is high enough to make the subject with HL vigilant.

EXPLORATORY CLINICAL TRIAL FOR A NEW BIMODAL NEUROMODULATION TREATMENT FOR TINNITUS: POSITIVE RESULTS FROM 326 TINNITUS PATIENTS

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Over the past decade, there have been a wide range of novel and scientifically-based approaches for treating tinnitus. These treatments have spanned invasive implants, customized sound therapies, noninvasive neuromodulation using electricity or magnetic fields, and alternative methods interacting with the cognitive and affective components of tinnitus. Although clinical findings across these different approaches have been encouraging, there still exists uncertainty as to which patients can benefit from specific treatments and the lack of properly powered and blinded randomized clinical trials to demonstrate treatment efficacy. Towards these needs, we worked together with experts in the tinnitus field to design an initial clinical trial in a large number of tinnitus patients to explore the therapeutic effects of bimodal neuromodulation, consisting of customized tongue and sound stimulation with our CE-marked device (MBT). A previous open label pilot study demonstrated the ability of this technology to significantly improve tinnitus across 44 patients. To explore the effects of different MBT stimulation parameters (PS1, PS2, PS3) in various subgroups of tinnitus patients, we performed a clinical trial in 326 subjects with three treatment paradigms. Treatment was delivered for 12 weeks with a take-home device and tinnitus outcome measurements were performed at several time points before, during and after treatment (up to 12 months post-treatment). The patients across two clinical sites were randomized to the three treatment arms. Patients, investigators and statisticians were all blinded to those treatment arms. Pre-specified outcome measures included the Tinnitus Handicap Inventory (THI) and the Tinnitus Functional Index (TFI). Other tinnitus, cognitive, affective, health, safety and demographic information were collected from the patients throughout the study. Within-group statistical analyses were conducted with paired t-tests between scores at baseline and final treatment, and were based on a per-protocol analysis estimand. Overall, all three MBT paradigms resulted in statistically and clinically significant improvements in tinnitus during treatment for THI (PS1: 14.6 points, $p < 0.0001$; PS2: 14.2 points, $p < 0.0001$; PS3: 13.8 points, $p < 0.0001$) and TFI (PS1: 13.6 points, $p < 0.0001$; PS2: 13.6 points, $p < 0.0001$; PS3: 13.2 points, $p < 0.0001$). There were also no reported safety issues and the study achieved a high treatment compliance (85% of enrolled subjects). Significant therapeutic effects occurred within the first 6 weeks of treatment and continued for many patients for more than 6 months after termination of treatment. Initial analyses suggest that specific MBT parameters may be more effective in certain subgroups of tinnitus patients, including those with reduced sound tolerance or with the ability to modulate their tinnitus with somatic manipulations, and requires further investigation. These findings provide encouraging and critical information for guiding a multi-site confirmatory clinical trial. Protocols and data associated with these clinical trials will be published and made available to our collaborators within the scientific and clinical communities to foster greater efforts towards finding more consistent and effective treatments for tinnitus (e.g., clinical trial protocol details are published in *D'Arcy et al., BMJ Open* 7(10):e018465, 2017).

Efficacy and Safety of AM-101 in the Treatment of Acute Inner Ear Tinnitus – A Double-Blind, Randomized, Placebo-Controlled Phase III Study

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Objectives: Acute cochlear injury has been shown to trigger tinnitus mediated by aberrant NMDA receptor activity. AM-101 (esketamine hydrochloride otic gel) is a small molecule NMDA receptor antagonist under clinical development for the intratympanic treatment of acute inner ear tinnitus. The double-blind, randomized, placebo-controlled phase III trial "TACTT3" sought to confirm the efficacy and safety of AM-101 during the acute stage and to explore the breadth of the therapeutic window for this type of intervention.

Methods: In total, the trial enrolled 741 patients suffering from persistent tinnitus after traumatic cochlear injury (acoustic trauma, blast trauma, middle ear surgery, inner ear barotrauma, tympanic membrane trauma) or otitis media. 373 of them were enrolled within the first three months from tinnitus onset (acute stage) and 368 were enrolled three to twelve months from onset (post-acute stage). Patients were randomized to receive three intratympanic doses of either AM-101 0.87 mg/mL or placebo over 3 to 5 days. Follow-up visits were on Days 10, 35 and 84. The improvements in the Tinnitus Functional Index (TFI) and in subjective tinnitus loudness captured on a 10-point numerical rating scale from baseline to Day 84 were alternate primary efficacy endpoints. The secondary efficacy endpoints included the improvement in tinnitus annoyance, the TFI sleep subscore and the patient global impression of change in tinnitus severity. For the acute stage, confirmatory statistical testing was performed for the entire population as well as for two pre-specified subgroups. For the post-acute stage, statistical analyses were exploratory. The primary safety endpoint was the incidence of clinically meaningful hearing deterioration from baseline to Day 35.

Results: Efficacy outcomes will be analysed for statistical significance and clinical relevance compared to placebo / natural recovery and compared with previous clinical outcomes. Further, outcomes in patients treated during the acute stage will be compared with those treated during the post-acute stage. Preliminary data show that the study drug and the administration procedure were well tolerated.

Conclusions: The study shall demonstrate whether AM-101 has the potential to become the first-in-class compound for pharmacologic treatment of acute inner ear tinnitus and provide further insights into the progression of tinnitus from the acute to the chronic state.

Untangling the relationship between tinnitus and hyperacusis: What are the problems reported by patients with a primary complaint of hyperacusis.

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Objectives

Tinnitus is associated with a wide variety of problems. In a recent study, 18 different problem domains were reported by 678 tinnitus patients and of these, the most commonly reported problems were fear, constant awareness, and annoyance (Watts et al., 2016). Tinnitus is often comorbid with hyperacusis (decreased sound tolerance to ordinary environmental sounds). More than 40% of adult patients with a primary complaint of tinnitus experience hyperacusis and 86% of adult patients with a primary complaint of hyperacusis experience tinnitus (Jastreboff & Jastreboff, 2000). Whilst priorities for hyperacusis are currently being established (Fackrell et al., 2017), the James Lind Alliance prioritisation for tinnitus established that research should prioritise addressing 'the link between tinnitus and hyperacusis?' (Hall et al., 2013). In order to progress this avenue of work, we first need to establish from a clinical perspective what problems arising from hyperacusis are being reported most often.

Methods

This was a retrospective analysis of an anonymised clinical dataset from 355 patients who experience hyperacusis and attended a single commercial tinnitus and hyperacusis treatment centre in the UK between 1997 and 2017. Of this number, 319 patients also reported experiencing tinnitus. Responses to the clinical interview question 'Why is hyperacusis a problem?' were coded and collated in problem domains using content analysis.

Results

Thirty-five potential domains of hyperacusis-associated problems have been identified, including impact on work activities, isolation and being different from others. The most commonly reported were fear, pain, avoidance and impact on quality of life.

Conclusion

Numerous problem domains are associated with hyperacusis. In comparison to the problem domains reported for tinnitus, there are a number of problems that seem to be uniquely associated with hyperacusis above tinnitus and vice versa. Fear however was the commonly reported problem for both tinnitus and hyperacusis. Researchers and clinicians alike need to be mindful of this and future research priorities should address this issue.

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ID: 212 / Session 2: 4

Abstract Submissions

Keywords: behavioral tinnitus identification, GPIAS, mGluRs, Eglumegad

Cross-validation of Two Tinnitus Screening Approaches in Mice

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Background

Research projects that focus on identification of neurobiological mechanisms underlying tinnitus typically compare tinnitus-positive and tinnitus-negative experimental animal groups. Therefore, accurate animal classification is the foundation for all investigations. Currently, there are two commonly used but conceptually different approaches to screen animals for tinnitus-like behavior: operant conditioning methods and gap-induced inhibition of the acoustic startle reflex. Typically, only one of the methods is used to assign animals to experimental groups. However, cross-validation of the outcomes obtained by these two approaches is of paramount importance due to concerns which challenge the validity of tinnitus assessment methods. Therefore, the aim of this project was to screen the same animals for tinnitus-like behavior using both methodological approaches.

Recent research in our laboratory showed that metabotropic glutamate receptors (mGluRs) modulate firing activity of auditory neurons. Our pilot study further suggested that systemically injected Eglumegad, which targets group II mGluRs, can suppress spontaneous neuronal firing that is thought to be related to tinnitus. Therefore, the project also aimed to test whether this drug administered on tinnitus-positive animals that have been identified by two tinnitus screening methods reduced/eliminated tinnitus-like behavior.

Methods

Adult CBA/CaJ mice were first trained to perform a sound classification task in a shuttle box. After the animals reached individual 90% correct performance (about 15 training days), we tested their baseline gap-induced inhibition of the acoustic startle reflex (10 sessions). Then, to induce tinnitus we unilaterally exposed the mice to 116 dB SLP one octave narrowband noise centered at 12.5 kHz for one hour under ketamine/xylazine anesthesia. After that, the mice stayed in the animal facility for three months to allow for tinnitus-related neuroplastic changes to occur. Thereafter, we tested the mice monthly using both tinnitus assessment approaches and also evaluated whether intraperitoneal Eglumegad injection suppressed/eliminated tinnitus-like behavior.

Results

Both tinnitus assessment approaches provided congruent results in some animals: several mice were identified as tinnitus-positive and systemic Eglumegad injection reduced tinnitus-like behavior.

Conclusions

If two conceptually different tinnitus assessment methods demonstrate tinnitus-like behavior in the same animals, this suggests that both techniques might be capable of assessing tinnitus in laboratory animals. Eglumegad should be further investigated as a possible drug to temporarily suppress tinnitus in humans.

ID: 213

Abstract Submissions

Keywords: pupillometry, IADS, affective processing

Evaluation of affective sounds by tinnitus patients

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Tinnitus is to a large extent characterized by the affective reaction to the phantom sound. Not all individuals experiencing ringing of the ears consider it as very disturbing, and there seems to be no direct link between tinnitus-induced distress and the psychoacoustic attributes of the percept, such as matched loudness. Tinnitus-related changes in activity of the limbic system highlight the role of the emotional dimension in tinnitus, but it is not clear whether the observed changes are specific only for the tinnitus percept. Just as hyperacusis can co-occur with tinnitus, it is important to investigate if more generally reactivity to emotion-carrying sounds could explain the experienced tinnitus distress. Individual reactions to sounds might reveal differences between tinnitus and non-tinnitus populations, as well as between tinnitus patients.

We measured affective reactions to sounds from the IADS-2 database in 10 tinnitus patients. Patients subjectively evaluated the valence and arousal of the sounds, and an objective measure of affective processing was obtained by pupillometry. Responses were collected to 60 sounds during two consecutive experimental runs. The sounds were chosen based on the normative valence ratings such that there were 10 negative, 10 neutral, and 10 positive sounds in each run. Subjects also received transcutaneous vagus nerve stimulation (tVNS) during one of the runs (in randomized order). The stimulation was applied to the tragus of the left ear. As there was no significant effect of tVNS stimulation to subjective ratings or pupillometry, the results from the two runs were pooled.

We found that the subjective ratings of the sounds by tinnitus patients differed significantly from the normative ratings. The difference was most pronounced for the positive sounds, where sounds were rated lower on both valence and arousal scales (valence: -1.45 , $t = -5.37$, $p < 0.001$; arousal: -2.16 , $t = -5.04$, $p < 0.001$). For negative and neutral sounds, there were significant differences only for the arousal ratings (negative: -1.19 , $t = -2.57$, $p < 0.05$; neutral: -1.32 , $t = -3.86$, $p < 0.01$).

The pupil responses showed significantly larger responses to negative sounds relative to neutral ($t = -4.43$, $p < 0.01$) and positive sounds ($t = -2.43$, $p < 0.05$). This finding differs from earlier results in normal-hearing subjects, where highly arousing negative and positive sounds elicited similar pupil responses. This discrepancy is likely explained by the lower subjective ratings of the positive sounds.

The current findings suggest that affective processing could be altered in tinnitus patients also on a more general level, and not only in relation to their own tinnitus sound.

ID: 214

Abstract Submissions

Keywords: Tinnitusproject, Pöppel, anechoic cabin, autoimmune, chronic pain

10 Years Tinnitusproject at THI

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The Tinnitusproject was born by chance in spring 2006, when the special anechoic cabin for sound and EMC measurements was shown to visitors at the University of Applied Sciences in Ingolstadt. Leaving the cabin after technical explanations by Prof. Pöppel a visitors feedback astonished: "My tinnitus has gone!". Now, what should we do without experience with such a cabin, without conformant scientists around, without money - but perhaps with the chance to help people with tinnitus very simply only by a stay in the cabin? At that time, we couldn't imagine, that in the past 10 years 1000 pupil/good health and 1000 subjects - even doctors - would come and a lot of would have been helped. After some further positive responses of other visitors in 2008 we started with ENT doctors, to investigate how much we can help such patients - roughly 10% with usual High Tone Tinnitus/30% with local/low tone/HUM could be helped. Thus it was the starting point of a fascinating project at the Faculty of Electrical Engineering and Computer Science at the TH Ingolstadt concerning the most complex electrical circuit man knows: the brain/nervous system. In following tests it was often reported that the Tinnitus in the cabin - without noise - was first perceived louder, but then trailed off. At times, the subjects fall asleep in the quietness of the cabin. Fascinating, only locally perceived Tinnitus - in some cases this has been solved since years: For example, an adolescent that had to deal with temporary noise lasting several minutes and a consecutive headache that would last hours, was cured in a few sessions of 1 hour duration - stable for 7 years now. A student with a local and a global Tinnitus had been treated in a Tinnitus clinic for two months without success. After a series of sessions in the special cabin, the Tinnitus was gone - no fallback in 8 years now. Surprisingly, positive feedback on quite other topics, brought the Tinnitusproject in very different directions. A subject had little success with Tinnitus. However, she reported that after a series of meetings, her fingers and, her knee (osteoarthritis since 15 years) did not hurt anymore - stable for 5 years, was repeated after. Some other subjects reported, that their pollen allergy was behaving unusually calm, another interesting effect - often replied. Best of such autoimmune diseases was one case of Multiple Sclerosis: Since months chairbound, after 6 months weekly visiting the cabin, since 8 years running again. This has led to much simplified cabins at subjects, traditional healers, doctors and in wellness areas. Also chronic pain was often reported positively. Obviously, the special relaxation in the cabin offers influence/chances to improve auditory/sensoric, nervous, immunological, hormone, eupepsia...system. In the future it will be necessary to improve success rates and combination possibilities with therapies and research to understand how this work. Tinnitusproject - a fascinating research to help much people although little powered only by donations.

ID: 215 / Session 9: 1

Abstract Submissions

Keywords: Acoustic trauma; startle reflex; spontaneous activity; inferior colliculus; gap-induced suppression of the acoustic startle reflex.

From the putative mechanism of the residual inhibition of tinnitus to possible tinnitus treatment

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Aims and Objectives

Despite its ubiquity, the pathophysiology of tinnitus is poorly understood, and there is no FDA approved cure or treatment. Tinnitus can be briefly eliminated/reduced after a masking sound stimulus has been terminated, the phenomenon known as "residual inhibition" (RI). About 80% of patients with tinnitus indicate some degree of RI. Although RI was first described more than 100 years ago (Spaulding, 1903) the underlying mechanisms remains unknown.

Recently we demonstrated that sounds can trigger a long lasting suppression of spontaneous firing in auditory neurons after sound cessation. Hyperactivity, or elevated spontaneous firing, in the auditory system has been linked to tinnitus. We hypothesize that suppression of this activity by a sound might be an underlying mechanism of RI and leads to a temporary elimination/reduction of tinnitus in humans.

We also found that metabotropic glutamate receptors (mGluRs) play a key role in sound-induced suppression of spontaneous firing. Therefore, the goal of this research was twofold: (1) to test whether main features of sound-induced suppression of spontaneous firing are similar to basic characteristics of RI and (2) to investigate whether drugs that target mGluRs can suppress/eliminate behavioral signs of tinnitus in animal model.

Methods

Experiments were conducted on 2-6 month old CBA/CaJ mice. For tinnitus induction mice were exposed to a narrow-band noise centered at 12.5 kHz presented at 116 dB SPL unilaterally for one hour under Ketamine/Xylazine anesthesia. Tinnitus was assessed by using gap-induced prepulse inhibition of the acoustic startle reflex. Extracellular recordings were conducted in the inferior colliculus (IC) in awake restrained animals. Pure tones at neurons' characteristic frequency and/or wideband noise stimuli 5 or 30 seconds duration were used for sound stimulation. The group II specific mGluR agonist LY354740 was applied systemically to test whether it suppresses spontaneous activity in the IC neurons and also eliminates behavioral signs of tinnitus in mice.

Results

We found that about 50% of IC neurons showed long-lasting (up to 2 min) suppression of their spontaneous firing following a 30 seconds sound stimulus that typically induces RI in humans. There were several striking similarities between this suppression and RI observed in tinnitus patients. We also found that LY354740 applied systemically reliably suppressed both spontaneous activity in the majority (about 70%) of IC neurons for at least three hours and also significantly reduced behavioral signs of tinnitus in tinnitus-positive mice.

Conclusions

Striking similarities between the RI in humans and sound-induced suppression of the spontaneous firing in the IC in mice strongly suggest that this suppression could be the mechanism underlying the RI. LY354740 should be considered as a potential drug to suppress tinnitus in humans.

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

ID: 216

Abstract Submissions

Keywords: chronic tinnitus, PET, Neuroimaging

Hearing aid impact on chronic tinnitus patients measured by resting state PET-FDG

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One theory of tinnitus generation is that deafferentation resulting from peripheral auditory lesion leads to increased excitability, neural synchronization and increased spontaneous firing rate in neurons of the auditory tract, destabilizing the subcortical and cortical neural maps. The involvement of the cerebral neural network exceeds the limits of the auditory cortex. Neuroimaging research reveals the involvement of the limbic system (insula, amygdala, cingulate gyrus), visual (temporal occipital areas), attention network (prefrontal cortex) and memory (hippocampus) associated with tinnitus generation and chronification.

Hearing aids (HA) amplifies the environmental sounds, reducing the contrast between tinnitus and silence, decreases auditory and cognitive effort, attenuates peripheral damage and induces neural plasticity. Besides, HA promote relief through partial or total masking of tinnitus. *Objective:* We used a prospective self-paired study to compare brain resting state PET, metabolic and functional changes 6 months before and after HA use as treatment for patients with chronic tinnitus and associated sensorineural hearing loss. We also evaluated HA effect on tinnitus perception, annoyance, and hearing handicap reduction.

Method: Nineteen patients (47.8 average age, SD 9.1) with chronic tinnitus (Mean duration was 12.3 years SD 10.1) and hearing loss were included in the study. Data acquisition in the form of resting-FDG-PET, tinnitus loudness, pitch matching and minimal masking levels (MML) measures, was conducted at the beginning and after 6 months of HA use. Tinnitus severity was measured using the tinnitus handicap inventory (THI) questionnaire, tinnitus annoyance with analog visual scale (AVS), and hearing handicap was measured with Hearing Handicap Inventory for Adults (HHIA). Patients were evaluated at the beginning, 1, 3 and 6 months.

Results: The questionnaires and scales used showed a statistically ($p < 0.05$) and clinically (THI reduction > 20 points) significant reduction at the 6-month mark. The MML also showed a statistically significant reduction. The covariate of duration of tinnitus was inversely correlated to the reduction of MML. After 6 months of HA effective use, the neuroimaging data showed increased glycolytic metabolism in the left orbitofrontal cortex area indicating that these regions were more engaged at rest than prior to the intervention. Frontal brain areas are related to attention, salience and executive control network. Results also showed reductions in glycolytic metabolism in the right cerebellum, indicative of reduced neuronal activity in this region. This structure is involved in spectral temporal information identification and storage. Its connections to primary auditory cortex, prefrontal cortex and Amygdala, turns the cerebellum an integral part of auditory processing in humans. Conclusion: HA is an effective resource to tinnitus perception and annoyance reduction, clinically and statistically since de 1st month of use. A less active cerebellum at resting state suggests its involvement in habituation to tinnitus stimulus or induced plasticity due to auditory rehabilitation.

ID: 217

Abstract Submissions

Keywords: Data collection, online survey

The Swedish Tinnitus Outreach Project - an update

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Tinnitus is the phantom perception of sounds. Current models propose that tinnitus derives from a maladaptive response to sensory deprivation, leading to increased central gain and hyperactivity in the auditory pathway. The recent identification that tinnitus may be influenced by genetic factors, in particular tinnitus perceived in two ears (bilateral), in contrast to unilateral tinnitus, raises the possibility to identify molecular pathways involved in tinnitus generation and the maladaptive compensations for missing sensory input.

Data collected for tinnitus patients in clinics are usually too sparse or incomplete for generating optimized case/control study designs. To resolve this limitation, we initiated in spring 2016 the Swedish Tinnitus Outreach Project (STOP), aiming at enrolling participants from the Swedish population with and without tinnitus via national and regional cohorts from the Karolinska Institutet. The goal of STOP is to characterize tinnitus subtypes with careful control of known risk factors and comorbidities, to improve current diagnostic methods, and to develop new objective measures of tinnitus, including blood and genetic biomarkers. The comprehensive efforts in STOP are aimed at elucidating the molecular mechanisms of phantom sound perception.

The first step for participants in the STOP pipeline is completion of an online survey consisting of 9 translated and validated questionnaires (TSCHQ, THI, TFI, FTQ, TCS, HQ, HADS, PSQ-30, WHOQoL-BREF). To facilitate the visualization of multivariate data collected from the questionnaires, we designed radar plots that allow, at a glance, the appreciation of the global burden associated with tinnitus. Here, separate questionnaire scores are normalized and ordered according to different domains (tinnitus severity, fears of tinnitus, hyperacusis, emotional factors, and quality of life). After responding to the survey, participants in STOP are followed up by an in-depth audiological assessment, which consists of otoscopy, tympanometry, pure tone audiometry (.125 - 16 kHz), speech in noise testing, DPOAEs (F2: 1 - 10 kHz), LDL, click ABRs, tinnitus pitch and loudness matching, tinnitus masking levels and residual inhibition. Blood and DNA are available for nearly 80% of the participants.

By October 2017, a total of 10,453 participants had registered and 7,218 consent forms were collected. Collection of questionnaire data (n = 4,015, including 40% non-tinnitus controls, 19% occasional tinnitus, 36% permanent/chronic tinnitus subjects) and audiological measures (n = 427) are currently ongoing, the latter however are for the moment restricted to the Stockholm area. Partnerships and funding are required to achieve the collection of audiological data at a national scale. Here we present the latest findings and interpretations of the collected data. The high participation rate in the STOP cohort together with the extensive accumulated data could provide a basis for prospective studies and deliver insights into the biology of tinnitus.

ID: 218 / Session 7: 4

Abstract Submissions

Keywords: Tinnitus, hyperacusis, adolescents, audiogram, otoacoustic emissions

Improved Sound Level Tolerance Accompanies Remission of Persistent Tinnitus in Adolescents with Clinically Normal Audiometry

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Introduction:

Sanchez et al. [1] found that 27.5% of 170 adolescents in a private school experienced verified tinnitus and reduced sound level tolerance (SLT) during psychoacoustic assessment with no impairment of otoacoustic emissions or clinical audiometry. Risky listening habits were near universal and not more prevalent among those experiencing tinnitus and reduced SLT. However, new cases of tinnitus can resolve over time without explicit treatment in an undetermined percentage of young adults [2].

Objective:

We therefore carried out repeat measurements on 54 adolescents who returned voluntarily for study one year later. In both studies SLT was measured as Loudness Discomfort Level (LDL).

Results:

1) Of the 14 subjects with verified tinnitus in the first study who returned for a second psychoacoustic measurement, 42.9% experienced verified tinnitus on retest while 57.1% did not; 2) SLT measured as LDL was reduced by 17.2 dB in repeating cases ($p < 0.0001$) and normal in resolving cases; 3) Hearing thresholds measured to 16 kHz were <20 dB HL in 98.3% of ears, with only one tinnitus subject showing thresholds >20 dBHL above 11.2 kHz. However, hearing thresholds > 4 kHz were higher in the left ear (8.33 dBHL) than the right ear (3.05 dBHL) of repeating compared to resolving tinnitus subjects ($p = 0.037$; all bilateral tinnitus); 4) Otoacoustic emissions did not differentiate between adolescents with or without verified tinnitus in either study; 5) Among returning adolescents those without tinnitus reported attending fewer parties and raves per week than did those with tinnitus (42.3% versus 62.5% respectively), but this difference was not statistically significant.

Conclusions:

There was a notable remission of persistent tinnitus in this sample (57.1% of cases), confirming previous reports that persisting tinnitus can resolve without explicit treatment in new cases in young adults [2]. Audiometric thresholds and otoacoustic emissions were clinically normal in repeating cases, although thresholds >4 kHz were elevated by ~ 5 dB in the left ear in repeating tinnitus. SLT was decreased in repeating tinnitus and recovered to normal levels in resolving tinnitus, confirming previous reports of a relationship to tinnitus [1]. The time course of SLT and tinnitus could reflect hidden hearing loss followed by synaptic recovery which has been reported in animal models [3].

[1] Sanchez et al. (2016), *Sci Rep*, DOI: 10.1038/srep27109

[2] Roberts (2016), in D. Baguley & M. Fagelson, *Tinnitus*. Plural Press, pp. 13-33;

[3] Song et al. (2016), *Sci Rep* DOI: 10.1038/srep25200.

ID: 219 / Session 2: 5

Abstract Submissions

Keywords: animal model, gamma frequency activity

Changes in gamma frequency activity in the auditory cortex in vitro in an animal model of tinnitus

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In humans, tinnitus has been associated with aberrant cortical network synchronisation, specifically changes in gamma (30-80 Hz) oscillations (Weisz et al 2007, Sedley et al 2012). In animals, such oscillations are critically dependent on the activity of parvalbumin-positive (PV+) inhibitory interneurons. Furthermore, the high frequency firing in these interneurons required to sustain gamma activity depends on Kv3 potassium channels. Such channels are highly expressed in the auditory pathway and their expression is modulated by noise exposure. Thus, Kv3 potassium channels are potential targets for therapeutic interventions to alleviate tinnitus. Here we examine how tinnitus induced by acoustic over exposure (AOE) influences network oscillations in rat auditory cortex, and how the pharmacological modulation of Kv3 channels impacts these oscillations.

Long Evans rats were acoustically over exposed (16 kHz tone, 115 dB SPL, two hours) with the left ear plugged. Evidence of tinnitus was assessed using gap-induced pre-pulse inhibition of the acoustic startle reflex. Animals with reduced inhibition of the acoustic startle at one or more test frequencies were deemed to be 'tinnitus' animals.

In vitro brain slices for electrophysiological recording were prepared from the auditory cortex of tinnitus and control animals (blind to the experimenter), and persistent gamma oscillations were induced by adding kainate (400nM) to the bath.

No difference in the peak frequency of evoked gamma activity was observed in slices from control animals (60.2 ± 3.6 Hz; n=15 slices, 11 animals) or in slices from the cortex ipsilateral to the exposed ear in 'tinnitus' animals (60.1 ± 4.4 Hz; n=10 slices, 8 animals; P=0.99). However, in slices from the cortex contralateral to the exposed ear in 'tinnitus' animals, the peak frequency of gamma oscillations was significantly reduced (44.2 ± 3.5 Hz; n=15 slices, 8 animals) compared with the ipsilateral side (P=0.007). No significant differences were observed between the different groups in the peak amplitude and power of gamma oscillations.

The application of AUT00063 (10 μ M) a positive modulator of Kv3 channels, had no effect on peak oscillatory frequency in slices from either control or tinnitus animals. However, AUT00063 produced a shift in peak oscillatory frequency from the gamma range to the beta/delta frequency range in slices from the cortex contralateral to the exposed ear in 'tinnitus' animals (47.4 ± 4.2 Hz vs. 15.9 ± 5.9 Hz; P=0.0051). In control animals the drug produced a significant reduction in the peak frequency of oscillations, but activity remained within the gamma frequency band (60.7 ± 4.8 Hz vs. 34.7 ± 6.7 Hz; P=0.0114)

ID: 221

Abstract Submissions

Keywords: Vagus nerve stimulation, tone therapy, VNS device, randomised controlled trial

Case studies from a clinical trial of VNS paired tone therapy

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Tinnitus is commonly considered a result of maladaptive neuroplasticity and consequently many tinnitus treatment strategies focus on this concept. One such clinical trial was initiated in 2014 with some subjects continuing to use the treatment, with varying degrees of success.

Animal and human studies suggest that pairing vagus nerve stimulation (VNS) with tones can reverse maladaptive neuroplasticity associated with tinnitus in some cases. ((Engineer et al., 2011; De Ridder, Vanneste, Engineer, & Kilgard, 2014) Vagus-nerve stimulation is known to be a safe and well-tolerated procedure that has been performed in approximately 100,000 patients worldwide for the treatment of severe depression and epilepsy (Grimonprez, Raedt, Baeken, Boon, & Vonck, 2015; Vonck et al., 2014)

A double-blind, randomized, controlled study was undertaken to evaluate the effect of VNS paired tone therapy in as a treatment modality for tinnitus in 4 centers across the U.S. (Tyler, Cacace, Seidman, Stocking, Vanneste, Tarver, 2017).

In this study, all 30 participants were implanted with a VNS device and also used headphones to deliver tones during the therapy. In the active treatment group VNS was delivered simultaneously with tones, whereas in the control group VNS was delivered separated in time from the tones. After the 6 week randomised controlled trial, all recipients continued to use the paired active treatment. Subjects were followed for at least one full year, and had repeated evaluations using both psychoacoustic tests and questionnaires. Results were mixed and will be briefly reviewed.

The main focus of this presentation will be individual case study details and results from the University at Buffalo. The VNS parameters were changed for some subjects after the controlled period in an attempt to maximize the effects of the treatment. Variations on the protocol will be shared. One case study in particular will be included of a subject who showed a positive response to the VNS tinnitus treatment using a modified protocol similar to that used for treatment of depression, without any pairing of tones. This is of particular interest to the investigators in light of known associations between tinnitus and emotional state.

ID: 223

Abstract Submissions

Keywords: Tinnitus, Imaging, MRI, Acoustic neuroma, Retrocochlear lesion

When MRI should be recommended for tinnitus patients?

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The word tinnitus is derived from the Latin word “tinnire”, meaning “to ring” or “a ringing.” Tinnitus is defined as an unwanted auditory perception of internal origin, usually localized, and rarely heard by others. Tinnitus is a common disorder with many possible causes. Most cases of tinnitus are subjective, but occasionally the tinnitus can be heard by an examiner. Initial evaluation of tinnitus should include a thorough history, head and neck examination, and audiometric testing to identify an underlying etiology. There is no doubt to perform audiometric assessment including ABR for all patients with tinnitus, because the subjective complaint usually correlates poorly with actual acoustic properties. Unfortunately, ABR is often useless to detect acoustic neuroma (vestibular schwannoma, VS), especially small one. However, it is still controversial to take MRI or not.

Many facts about VS in patients with sudden sensorineural hearing loss (SNHL) have been known. VS is found in about 1% of patients with sudden SNHL and 10% of patients with VS present the hearing loss of sudden onset. It is relatively well-defined when to take MRI for patients with sudden SNHL: 1) Any patient with asymmetric or sudden SNHL (even after total recovery) should be considered for MRI. 2) The presence of tinnitus in the ipsilateral ear before sudden SNHL is suggestive for the need of MRI.

However, it is not clear to decide when to take MRI for patients with tinnitus. Choi et al. found that patients with unilateral tinnitus & asymmetric HL were most likely to have abnormal findings for VS. So they suggested that clinical judgement should determine the need for further imaging in those patients. Kim et al. reported that tinnitus together with hearing loss was the most common combination of symptoms in patients with VS. Generally, it is recommended for clinicians not to obtain imaging studies of the head and neck in patients with tinnitus, specifically to evaluate the tinnitus, unless they have 1 or more of the following: tinnitus that localizes to 1 ear, pulsatile tinnitus, focal neurological abnormalities, or asymmetric hearing loss.

Author reviewed 12 cases of VS (3 males and 9 females; mean age of 55.4±11.5 years-old). Among 12 cases, two cases presented only tinnitus, two cases tinnitus together with unilateral/asymmetric hearing loss, and three cases tinnitus with sudden SNHL. To find out the need for MRI in cases with tinnitus, this study evaluated characteristics of patients with VS.

ID: 224

Abstract Submissions

Keywords: Tinnitus Retraining Therapy, SLS, STS, SCS

SLS, STS, and SCS : Three Important Dimensions in Tinnitus-Retraining

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As we have moved on during the last years with our efforts to increase the success rate of the Tinnitus-Retraining-Therapy (TRT) we have come up with several significant modifications of the original classical Jastreboffian approach. Inspired by Jastreboffs personal suggestions we introduced variations in the way in which we apply the sound therapy as part of TRT. As is well known from Jastreboffs publications the exposition of tinnitus patients to therapeutic sound is one of the cornerstones of TRT. In order to apply therapeutic sound in the right way for optimal treatment effects not only the category and severeness of tinnitus, but also various degrees of a possible additional hearing loss or of sound intolerance have to be taken into account. External sound sources are used as well as devices placed directly into the external ear canal. One basic and very important feature of the sounds applied during treatment, as was lined out already by Jastreboff himself, is the sound level, so that this has to be taken care of individually for each patient in form of a sound level setting (SLS). It is important for the success of the treatment not to use the same standard sound level in every patient. Instead, it is of great importance to precisely chose the right sound level of the Tinnitus-instrument (Noiser) during treatment in relation to the patients subjectively perceived loudness of the tinnitus and the amount of hearing loss or hyperacusis.

Another parameter not less important for the sound therapy is the type of sound that is chosen for the individual patient during the so called sound type setting (STS). The "pink-noise-paradigm" is still valid for our considerations in our Tinnitus-Center up until today, but several different new types of sound patterns have been proposed for treatment by other providers in the past. Why not use music or faeast repetitive mantras, or tinnitus-specific filtered music, individually shaped sound patterns or the tinnitus itself as a desensitizing treatment signal? The pro's and con's of such options will be discussed on the basis of Jastreboffs neurophysiological model.

The third significant aspect of sound treatment, of course, is the context in which the sound stimulation is taking place. The context during sound therapy also has to be arranged in such a way as to optimize the efficacy of treatment. This is of particular significance for teachers or professional musicians, for instance, since these professionals sometimes have to work in a very loud surrounding. Therefore a separate part of the counselling during TRT has to be devoted to the sound context setting (SCS). All these three important aspects of the sound therapy, sound level setting (SLS), sound type setting (STS) and sound context setting (SCS) are dimensions of TRT which have to be adjusted individually for each patient separately and will be discussed in this paper.

ID: 225 / Session 18: 3

Abstract Submissions

Keywords: Tinnitus, acoustic stimulation, e-Health

Tinnitus suppression in cochlear implant patients using the ReSound Relief™ app

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Background: The use of acoustic stimuli to reduce the prominence of tinnitus has been used for decades. Counseling and tinnitus sound therapy options are not currently widespread for cochlear implant (CI) users. The goal of this study was to determine whether tinnitus therapy sounds created for individuals with acoustic hearing may also benefit CI users.

Method: Sounds from the ReSound Relief App were streamed from an iPod to the CI. 16 sounds were selected from the App to be used for the study. 16 participants were asked to rate the overall acceptability of each of the sounds and to write the description of the sound they perceived. 13 participants completed a 5 minute trial where they rated their pre-trial and post-trial tinnitus and the acceptability of the sound. 10 subjects completed a home-trial and were asked to complete online tinnitus questionnaires and rated the effectiveness of sound therapy.

Results: Individual differences were large. Results from the 5 minute trial showed that sounds perceived as rain, music, and waves were rated the most acceptable. For all of the subjects, the post-trial tinnitus loudness rating was lower than the pre-trial rating, with some subjects experiencing greater difference in their tinnitus loudness than others. At the end of the 2-week home trial, 3 of 10 subjects rated the effectiveness of sound therapy 70% or higher.

Conclusions: The results suggest that the use of tinnitus therapy sounds delivered through a CI can provide relief for some CI users with tinnitus.

ID: 226

Abstract Submissions

Keywords: Tinnitus Retraining Therapy

Tinnitus Retraining Therapy: a Three Year Follow up

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Tinnitus is a widespread phenomenon and roughly 10% of the population in Germany are affected. However, in most cases this "ringing in the ears" is not intrusive and only present as a companion and easily tolerated and not leading to serious disability in the affected individual. For a small fraction of these people, however, the tinnitus is really intrusive and debilitating, and sometimes even devastating up to such a degree that the patient becomes suicidal and does not want to live any more. In order to find new methods of treatment for this serious condition new drugs have been tested, various types of sound-therapy have been introduced during the last years, and a diversity of other approaches exist that promise recovery from this condition.

A manual based cognitive behavioral therapy has been proposed in the past to be the most effective therapy and has been recommended in the guidelines. However, there are only very few therapists offering this therapy especially for the treatment of tinnitus and many patients resent this type of therapy because they do not feel to be psychologically ill or abnormal in any way and therefore do not want to consult a psychotherapist. We therefore continued to offer the classical Jastreboffian Tinnitus-Retraining-Therapy (TRT) in our Tinnitus Center in Frankfurt within a therapeutic setting of a specialized ENT- medical doctors team including co-therapists like psychotherapists, physical therapists, music-therapists, hearing therapists, etc.. Some new aspects of the treatment procedures, especially concerning the context in which the technical devices are provided, have been developed in our center. Three basic components are indispensable in TRT. The first component is the sound treatment, which in less severe cases may consist merely in an enhancement and enrichment of environmental sounds. In more severe cases individually designed technical tinnitus-instruments are provided for the patients. The second component is a special directive counselling aimed to inform the patient about the anatomy and physiology of the inner ear and central hearing system and convey to him the information scientists have found out about the mechanisms of tinnitus development. Using the information of how tinnitus comes about and can develop in the human hearing system one can derive in turn ways to reduce tinnitus again. The third component of TRT is the training itself. During TRT like in sport or other skills nobody else but the patient himself can do the training and do the work in order to change synaptic connections within the central hearing system. This is the way in which the tinnitus signal itself may be reduced and weakend and habituation can be initiated. The results before and after three years of treatment with TRT in a group of 237 patients will be presented.

ID: 227

Abstract Submissions

Keywords: the German Tinnitus Guidelines

A Truly Disruptive Innovation in Tinnitus: The German Tinnitus-Guidelines

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In cases of clinically relevant Tinnitus various methods of treatment are applied by ENT-specialists as well as other providers in Germany, in Europe and in countries overseas and further abroad. The methods used depend on the experience of the treatment provider and the peculiarities of the individual Tinnitus-patient. In order to get a structure into this diversity and to help patients as well as providers to find an orientation and a support for their decision making process, which method to choose and which way to follow, in many countries guidelines have been issued. Also in Germany new guidelines have been issued for the treatment of the so called "chronic tinnitus", strictly categorizing methods of treatment according to the so called "evidence based principles". Using these criteria major national and international publications in journals and monographs had been subjected to a critical evaluation. Only publications that formally fulfilled the methodological criteria of being "evidence based" were included in this survey and were evaluated. In this way everyday clinical experience and treatment results that had been published as clinical observational studies only, were completely excluded from evaluation and not taken into account. Especially the famous and effective "Tinnitus-retraining-Therapy" of Jastreboff got completely excluded from the list of recommended treatment methods in this way in spite of the numerous clinical studies demonstrating the success and effectiveness of TRT. This led to the bizarre situation, that even relieve-strategies that intuitively had been taken up by many patients to reduce the severeness and intrusiveness of their tinnitus, that everybody knows are helpful, now were excluded from any recommendation. Moreover, as a consequence based on these guidelines insurance companies started to refuse compensation for sound generators or hearing aids which had been provided to reduce tinnitus or hyperacusis. Furthermore, strict regulations were given out in these guidelines as to what kind of treatment apart from TRT could be partially or fully recommended or not recommended at all. In this way these guidelines now tend to completely regulate and dominate the strategies of treatment in the various tinnitus treatment centers in Germany on an outpatient basis and in hospitals as well. A specific German way of treatment is to hospitalize tinnitus patients in specialized tinnitus clinics for a period of four or more weeks in order to enable an interdisciplinary approach. Here as well the new German guidelines for chronic tinnitus have caused a shift from the effective ENT-provided Tinnitus-Retraining-Therapy to more psychotherapeutic treatment strategies like cognitive behavioral therapy, for instance, which unfortunately have to be finished off as soon as the patients stay in the hospital ends. A new therapy then has to be initiated to be continued in the patient's home town. The underlying reasons for the development of this truly disruptive innovation in tinnitus - i.e. the German tinnitus guidelines - will be discussed.

ID: 228

Abstract Submissions

Keywords: Tinnitus Misophonia, central auditory system, Misophonia-Retraining-Therapy

Misophonia and Tinnitus: Similar Underlying Mechanisms Lead to Similar Treatment Strategies

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Since Pawel Jastreboff coined the term "misophonia" to be the diagnosis of a special type of sound intolerance in 2001 a growing number of scientific publications have dealt with this condition. It consists in an abnormally intense aversive emotional and physical reaction to particular patterns of sounds. Patients suffering from this disorder often are unable to take part in a family breakfast, for instance, because of the chewing sounds of close family members. Sometimes even a mere breathing sound of a close friend or family member may cause feelings of severe discomfort and aggression. As a consequence the psycho-social situation of patients suffering from misophonia eventually becomes very tense. The patient is getting caught up in a complex mutual reaction pattern between himself and his own reactions and the reaction of other closely related members of society (family, school, workplace etc.). The severeness of this condition can range from being simply unpleasant to extremely disabling. Since Jastreboff's discovery in 2001 more and more patients with this disorder have visited us in our Tinnitus-and Misophonia Center in Frankfurt. Almost all of these patients had consulted other ENT-specialists before coming to us. In most of these cases the ENT-specialists had been unaware of the true nature of this dysfunction and had therefore referred these patients to be treated by psychotherapists. Psychotherapy alone, however, was generally not effective at all in order to reduce the dysfunction. Realizing, however, that the underlying mechanisms causing "misophonia" can be explained on the basis of the neurophysiological model of Jastreboff, a treatment of the patients central auditory system by an ENT-specialist using the Misophonia-Retraining-Therapy on the basis of this model should always be mandatory and should not be substituted by other treatments of other providers or even be omitted completely. In a few cases only, where these patients suffer not only from misophonia but also from certain types of psychological disorders, a psychotherapist may be helpful or even necessary to support the ENT-misophonia-desensitization treatment. Since the underlying mechanisms leading to misophonia are in part similar or even identical to the neuronal mechanisms causing clinically relevant tinnitus the effective therapy is similar as well. Using the method of Jastreboff we have so far treated 27 patients suffering from misophonia. In all of these cases sound therapy was applied in addition to a misophonia specific directive counselling. The results and treatment outcomes in our patients were promising and will be discussed in this paper.

ID: 229 / Session 16: 1

Abstract Submissions

Keywords: hearing loss

Accumulation of rare and common variants in genes included in multiple neural pathways in a family with tinnitus

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Introduction

Familial cases with tinnitus are a rare condition. We describe a family with 6 patients with high frequency sensorineural hearing loss (HF-SNHL) involving 4-16 kHz and tinnitus. We have conducted exome sequencing in a Swedish family and analysed single nucleotide variants (SNV) and indel variants segregating the phenotype focusing in genes differentially expressed in neuropil and cochlea.

Material and methods

We sequenced 6 individuals (4 of them had tinnitus and HF-SNHL, one subject had tinnitus without SNHL and one was a subject without tinnitus or SNHL). Variant calling was made through GATK+VarScan2 pipeline. We generated merged files segregating tinnitus phenotype and all familial cases to include all common and rare variants contributing to tinnitus in tinnitus cases. We performed SNV and indel analyses. Pathogenicity of the variants was estimated using in-house pipeline including multiple bioinformatics tools. By using differentially expressed genes datasets from the mouse cochlea and human neuropil, we extracted pathways and genes using KGGSeq SharedPathways function and PPI function looking for shared affected pathways in cases in contrast to controls. We chose candidate pathways with included genes with accumulation of rare variants with significant p-values. Rare variants in candidate genes were validated by Sanger sequencing in the family.

Results

The top pathways including accumulation of rare and common variants were "Neuronal system" general pathway ($p < 10E-20$), "Ageing brain" pathway ($p = 1.11E-16$), "Neuroactive ligand receptor interaction" pathway ($p < 10E-20$), "Calcium signalling" pathway ($p < 10E-20$) and "Transmission across chemical synapses" pathway ($p < 10E-20$). Most relevant shared pathways were highly related to neuronal signalling and ageing brain, as expected after choose differentially expressed genes from neuropil. Next, we performed an enrichment analysis of rare variants including cochlear differentially expressed genes in the basal turn. We found that "cAMP-mediated signalling" and "Axonal guidance signalling" were the most significant shared pathways ($p = 3.22E-13$ and $p = 1.27E-12$, respectively) correlating with neuronal signalling.

Conclusions

Common and rare SNV found in differentially expressed genes at the base of the cochlea and neuropil may form a molecular interaction network able to explain the cause of hereditary tinnitus associated with HF-SNHL.

Acknowledgements

COST Action BM1306 TINNET

ID: 230 / Session 17: 4

Abstract Submissions

Keywords: Meniere's disease

Psychoacoustic characterization of tinnitus and perceived discomfort in patients with Meniere's disease

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Introduction: Meniere's disease (MD) is a chronic disorder of the inner ear characterized by vertigo attacks with aural fullness, tinnitus and sensorineural hearing loss. Tinnitus is considered the most annoying symptom, but it is seldom investigated. Although there is no evidence that tinnitus is induced by anxiety, some studies suggest a possible association between these symptoms. Our objective is to perform a psychoacoustic characterization of tinnitus in MD, and to determine if the tinnitus perception is related to anxiety or to the cochlear damage itself, to define an extreme phenotype for tinnitus .

Methods: A cross-sectional study was designed, including 75 patients diagnosed with defined MD who reported tinnitus. A detailed anamnesis was carried out, including clinical variables (age, gender, age of onset, duration of the disease, uni or bilateral involvement, hearing thresholds, fluctuation and location of the tinnitus) and psychoacoustic variables (type of sound, tinnitus loudness matching, minimum masking level, and residual inhibition). Perceived disability was assessed by a visual analogue scale (VAS) and the Tinnitus Handicap Inventory (THI). Anxiety and depression symptoms were evaluated by the Hospital-Anxiety Depression Scale (HADS).

Results: We found a statistically significant correlation between the scores obtained in VAS and THI ($r = 0.61$; $p = 0.001$). Both scales showed a moderate correlation with the total HADS score (VAS-HADS, $r = 0.44$, $p = 0.006$; THI-HADS, $r = 0.55$, $p = 0.001$). No statistically significant association was found between these scores and the intensity of tinnitus, the age of patients or the duration of the disease.

Conclusions: Tinnitus discomfort is associated with higher scores in THI and HADS in MD and high risk of anxiety or depression. Clinical or psychoacoustic variables are not associated with worse tinnitus scores, and additional genetic or environmental factors likely contribute to tinnitus persistence in MD.

Acknowledgements

COST Action BM1306 TINNET

ID: 231 / Session 10: 2

Abstract Submissions

Keywords: Auditory evoked potentials, Tinnitus

The Role of Auditory Evoked Potentials in the Study of Tinnitus. About a Case.

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In clinical practice, the study of tinnitus has as main goals not only the localization, quantification and classification of the origin of the disorder but the etiology study in order to establish the most adequate treatment for each case.

Here, we inform the clinical case of a patient who came to audiology appointment to confirm the two years evolution of a left unilateral tinnitus.

The patient's history included noise exposition, hearing loss, sound hypersensitivity, and sporadic dizziness accompanied by vegetative symptoms. For that period, the patient underwent ATM treatment as tinnitus treatment, as well.

The initial diagnostic was tinnitus secondary to symmetric bilateral endocochlear hypoacusis due to Acoustic Trauma. However, after the inconsistency of the results obtained in the Psychoacoustic Tests, we suspect other disorders. For that reason, Auditory Evoked Potentials were carried out. As results, alterations in latency, interpic intervals and interaural asymmetry were obtained. Therefore, imaging study by MRI was justified. The results of this study allow establish the definitive diagnosis left unilateral tinnitus of severe degree secondary to intraaxial injury (glioma) by compression of the acoustic path at the level of the Protuberance (Nucleus Olivar Superior) and Mesencephalon (Lower Colliculus). Therefore, the performance of Auditory Evoked Potentials was essential to detect the lesion and perform the conclusive diagnostic tests for the differential diagnosis.

ID: 232 / Session 8: 2
Abstract Submissions
Keywords: acute tinnitus

Putative factors for chronic manifestation of tinnitus

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Aim: Acute tinnitus is a clinical common, but in research so far neglected symptom. There is only limited evidence which factors contribute to chronic manifestation of tinnitus. Aim of the present longitudinal study was to follow up the development of acute tinnitus and relevant factors over six months.

Methods: Between 2013 and 2016 patients from two centers in Germany with acute tinnitus were included in our study. They filled in questionnaires and returned for a follow-up visit after three months. After six months only questionnaires were send to the patients. Factors of interest were hearing function, tinnitus characteristics, pre-condition disorders, therapeutic interventions and psychological factors.

Results: 49 patients with tinnitus onset between 1 and 28 days were included in the analysis. Nine patients lost their tinnitus. Only hyperacusis and ear pressure was associated with chronic manifestation of tinnitus. In patients with chronic tinnitus, tinnitus distress decreased and hearing function improved over the six months. Tinnitus characteristics such as loudness, awareness, laterality, type, pitch, etc. remained relatively stable.

Discussion: Due to the preliminary and not representative character of this study the high number of patients with chronic manifestation might be biased. Tinnitus distress seems to ameliorate over the first months after tinnitus onset. Investigation of psychological factors related to hyperacusis might be helpful for identification of risk factors for chronic manifestation of tinnitus.

ID: 233

Abstract Submissions

Keywords: tinnitus treatment

A Novel Treatment Protocol for the Management of Tinnitus through Multimodality Brain Stimulation

PRAJAKTA PATIL

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AIM:

To develop a novel treatment protocol for the management of tinnitus through multimodality brain stimulation.

METHODOLOGY:

Present study included 33 adults with unilateral (31 subjects) and bilateral (2 subjects) chronic tinnitus with and/or without hearing loss independent of their etiology.

The Treatment protocol included 5 consecutive sessions with follow-up of 6 months.

Each session was divided into 3 parts:

- Pre-treatment: a) Informed consent b) Pitch and loudness matching
- Treatment: Bimanual paper pen task with tinnitus masking for 30 minutes.
- Post-treatment: a) Pitch and loudness matching b) Directive counselling and obtaining feedback.

Paper- pen task is to be performed bimanually that included carrying out two different writing activities of different context. The level of difficulty of the activities was increased in successive sessions. Narrow band noise of a frequency same as that of tinnitus was presented at 10 dB SL of tinnitus for 30 minutes simultaneously in the ear with tinnitus.

RESULT:

The perception of tinnitus was no longer present in 4 subjects while in remaining subjects it reduced to an intensity that its perception no longer troubled them without causing residual facilitation. In all subjects, the intensity of tinnitus decreased by an extent of 45 dB at an average. However, in few subjects, intensity of tinnitus also decreased by more than 45 dB. The approach resulted in statistically significant reductions in Tinnitus Functional Index and Tinnitus Handicap Inventory scores. The results correlate with pre and post treatment score of Tinnitus Handicap Inventory that dropped from 90% to 0%.

DISCUSSION:

Brain mapping(qEEG) Studies report that there is multiple parallel overlapping of subnetworks in the non-auditory areas of the brain which exhibits abnormal, constant and spontaneous neural activity involved in the perception of tinnitus with each subnetwork and area reflecting specific aspect of tinnitus percept.

The paper pen task and directive counselling are designed and delivered respectively in a way that is assumed to induce normal, rhythmically constant and premeditated neural activity and mask the abnormal, constant and spontaneous neural activity in the above mentioned subnetworks and the specific non auditory area. Counseling was focused on breaking the vicious cycle causing and maintaining the presence of tinnitus.

Diverting auditory attention alone is insufficient to reduce the perception of tinnitus. Conscious awareness of tinnitus can be suppressed when individuals engage in cognitively demanding tasks of non-auditory nature as the paper pen task used in the present study. To carry out this task selective, divided, sustained, simultaneous and split attention act cumulatively. Bimanual paper pen task represents a top down activity which underlies brain's ability to selectively attend to the bimanual written activity as a relevant stimulus and to ignore tinnitus that is the irrelevant stimuli in the present study.

CONCLUSION:

The study suggests that this novel treatment approach is cost effective, time saving and efficient to vanish the tinnitus or to reduce the intensity of tinnitus to a negligible level and thereby eliminating the negative reactions towards tinnitus.

ID: 234

Abstract Submissions

Keywords: tinnitus, hearing loss, hyperacusis

Considering psychoacoustic parameters contribution is sufficient in predicting gain preference

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Neurofunctional tinnitus model proposes that tinnitus is developed and maintained through conscious attended awareness perception of phantom sound through evaluative conditional (EC) learning during clinical distress stage (I. GhodratiToostani et al., 2016). The intermittent contingency of hearing difficulty with conscious attended awareness perception of tinnitus may exacerbate negative cognitive, emotional value of tinnitus sound. Accordingly, treatment of hearing loss with Hearing Aid (HA) can reduce this negative valence because of the decrease in frequency of tinnitus conscious attended awareness perception and clinical distress reactions.

Tinnitus is usually comorbid with hyperacusis which is defined as an unusual tolerance to ordinary environmental sounds (Baguley, 2003). Both tinnitus and hyperacusis have been hypothesized as enhanced response-gain in subcortical brain regions to compensate abnormal sensory input. HA can reduce the central auditory gain by magnifying the activity of the auditory nerve (Moffat et al., 2009) that effectively can result in tinnitus suppression (Jalilvand, Pourbakht, & Haghani, 2015).

Current HA prescription algorithms dismiss tinnitus and hyperacusis patients' requirement to support comfort.

On the other hand, Gain Preference (GP) can facilitate comfort as one of the major hearing aid fitting factors, especially in first time hearing aid users. Additionally, comfort motivates patients to enhance the duration of hearing aid daily use that results in reducing tinnitus conscious attended awareness perception experience and weakens the negative cognitive-emotional value.

All taken together, hearing aid can be administered as a tinnitus suppressor through amplification of environmental sound in hearing impairment bandwidth.

In this paper, we investigated GP magnitude in 626 sound-blast veteran patients that received monaural hearing aid, and these data were assessed in Tehran Veteran Center. We aimed to reach to the correction process in the NAL-NL1 prescription for hearing loss compensation.

Our finding exhibited that although most of our patients have mild to moderate hearing loss (68%), GP (Mean=4 dB, SD= 2 DB) is needed to provide comfort.

The Predictive analytics (K-nearest neighboring Model) results, strongly indicated that hearing loss severity and audiology related factors (Linear Correlation= 0.453, Absolute Error= 1.594 DB) are the most correlated factor to GP. However, the psychoacoustic factors such as Tinnitus type, Loudness, Pitch, Minimal masking level can predict the GP (Linear Correlation= 0.842, Mean Absolute Error= 0.634 DB) magnitude precisely. These findings suggest that acclimatization in first time HA users and hyperacusis are highly correlated in recruited tinnitus population. It hypothesizes that considering loudness discomfort level assessment in_HAs prescription might improve comfort by applying GP in HAs fitting process.

Further evidence-based investigations need to demonstrate the role of loudness discomfort level in tinnitus, hearing loss, and hyperacusis populations.

ID: 235 / Session 1: 3

Abstract Submissions

Keywords: Tinnitus, Magnetic stimulation

The application of magnetic stimulation of the ear in tinnitus treatment

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Subjective tinnitus is a term given to describe an auditory phantom sound perception in the absence of corresponding external stimulation. Tinnitus is a highly heterogeneous symptom, with many factors accounting for its generation. One of the most common conditions associated with tinnitus is sensorineural hearing loss (The place and mechanism of tinnitus generation still remain to be fully explained. One concept is the peripheral (vs central) model of tinnitus, which suggests that tinnitus arises as a consequence of deafferentation (8,9). Decreased input in the auditory nerve results in the downregulation of inhibitory cortical processes, leading to hyperexcitability in the central auditory structures. Based on this model, forms of peripheral stimulations (electric or magnetic) via external ear canal may be a form of treatment. The rationale for peripheral stimulation is to increase the reduced peripheral input due to sensorineural hearing loss.

The aim of the study was to assess the efficacy of ear magnetic stimulation in tinnitus treatment. Material and methods: The material of the study was a group of 10 tinnitus patients – 12 tinnitus ears (8 patients with unilateral, and 2 - with bilateral tinnitus, 5 females and 5 males, aged 30-74 years, average 62 years). In 10 ears tinnitus was permanent, in 2 was temporary. 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.

The tinnitus treatment was conducted with the use of a prototype device. The stimulating magnetic coil was inserted in the external ear canal. Stimulus of 20Hz and 200mT was used. Ten 5-minute stimulations performed every workday were entire treatment. Before, directly after and 3 months later, tinnitus character (permanent vs temporary), tinnitus loudness (in visual analogue scale) and hearing (in pure tone audiometry) were assessed.

Results. Directly after the treatment in 9 ears (75%) tinnitus loudness was reduced by 50-85%. In one ear (8.4%) tinnitus ceased to be audible, in 4 ears (33.3%) –tinnitus appeared temporarily. In 2 ears (16.6%) tinnitus remained unchanged. No tinnitus deterioration was observed. Hearing assessment conducted before and after treatment demonstrated unchanged hearing thresholds.

In follow up period the obtained therapeutic effect remained stable.

Conclusions. The preliminary results demonstrate a good therapeutic effect of ear magnetic stimulation in tinnitus treatment.

ID: 236

Abstract Submissions

Keywords: Tinnitus, sleep, insomnia, CBT

The contribution of Tinnitus negative valence in sleep-threat development

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Tinnitus is conscious (attended) awareness perception of unsourced sound. Neurofunctional tinnitus model hypothesized that negative reaction related to tinnitus emerge during tinnitus clinical distress stage through cognitive-emotional appraisal and evaluative conditioning learning processes (Ghodratitoostani et al. 2016).

Tinnitus patients frequently experience tinnitus perception and failure in falling asleep simultaneously which triggers a negative cognitive-emotional appraisal in pre-sleep time. In this period, tinnitus sound is appraised as a sleep threat and results in comorbid insomnia that impairs the process of getting to sleep. In tinnitus patients without insomnia complain, the cognitive-emotional appraisal (negative valence) of tinnitus is insufficient to be recognized as the sleep-related threat.

The cognitive-emotional appraisal plays a crucial role in governing attention allocation and developing annoyance within tinnitus clinical distress. Allocating attention to perceive tinnitus more frequent and label it as a new threat leads to experiencing more distress and arousal.

Through evaluative conditioning (EC) learning mechanism, the contingency of conscious (attended) awareness perception of both tinnitus and an emotionally negative or positive stimulus changes the tinnitus valence. This change in the valence is the retained appraisal response to the tinnitus. Therefore, the Intermittent occurrences of evaluative learning reinforce the tinnitus-related sleep-threat valence and gradually make the patients' feeling negative toward perceiving tinnitus in pre-sleep time. Accordingly, previously neutral stimulus or thoughts consciously accompanied with tinnitus sound can be considered as sleep preventing (like the clock to see how long it is taking to fall sleep) which makes a negative valence to trigger stronger distress and arousal. This accumulative procedure as well as being resistant to extinction indicates the role of evaluative conditional learning not classical conditioning in tinnitus distress development.

As an intervention for tinnitus patients with insomnia, cognitive behavioral therapy (CBT) is suggested. CBT techniques can help to modify the negative cognitive-emotional value of both tinnitus and insomnia. In CBT protocol, the patient needs to be aware of the defective loop of tinnitus perception which leads to sleep threat followed by more distress and arousal for the patients. All these processes of reappraisal and evaluation need to occur through conscious (attended) awareness perception of tinnitus and insomnia contingency. In the treatment plan or therapeutic protocols, we need to design a task, practice or application for the patients in which conscious attended awareness perception of both thoughts related to tinnitus and insomnia is involved and modified in connection with together.

RECOMMENDATIONS FROM THE COMIT'ID STUDY: INTERNATIONAL CONSENSUS ON CORE OUTCOME DOMAINS FOR EARLY-PHASE CLINICAL TRIALS OF SOUND-, PSYCHOLOGY-, AND PHARMACOLOGY-BASED INTERVENTIONS TO MANAGE CHRONIC SUBJECTIVE TINNITUS IN ADULTS

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Background: On Wednesday, we held an interactive consensus workshop to listen to your views on the recommendations arising from the COMIT'ID study ('Core Outcome Measures in Tinnitus: International Delphi'). The main purpose of COMIT is to develop Core Outcome Domain Sets for the three different intervention strategies (sound, psychological, and pharmacological) for adults with chronic subjective tinnitus that should be measured and reported in every clinical trial of these interventions (even if they are not one of the primary outcomes).

Methods: The COMIT'ID study used a mixed methods approach for achieving consensus, designed with input from healthcare users, clinical experts and a trialist. Healthcare users, healthcare practitioners, clinical researchers, commercial representatives and funders all participated in online Delphi surveys (over 650 participants, from over 30 countries) and face-to-face meetings (over 55 participants). For transparency, our methods have been published ahead of the analysis (Fackrell et al., 2017).

Results: Here are the other core assessments that our stakeholders have recommended to investigators, and that are discussed on Wednesday. These are our **minimal** reporting standards which will enable findings to be compared across studies. Investigators will always be free to add other assessments to their clinical trial design, if they wish.

Sound-based Psychology-based Drug-based treatments treatments treatments

tinnitus tinnitus intrusiveness tinnitus intrusiveness intrusiveness

ability to ignore tinnitus acceptance tinnitus loudness

Concentration mood (including feelings of anxiety and depression)

quality of sleep negative thoughts and believes

sense of control sense of control

Discussion: The COMIT'ID study seeks to improve future tinnitus research by creating an evidence-based consensus about minimum reporting standards for outcomes in clinical trials of a tinnitus intervention. Endorsement by reputable and influential organisations such as TRI and TINNET, and wide dissemination will be crucial for promoting uptake across the community.

Funding: We acknowledge support from NIHR Nottingham Hearing Biomedical Research Unit, NIHR Nottingham Biomedical Research Centre, British Tinnitus Association, Action on Hearing Loss, and European Cooperation in Science and Technology (COST) Action (BM1306).

Reference: Fackrell K, Smith H, Colley V, Thacker B, Horobin A, Haider HF, Londero A, Mazurek B, Hall DA (2017) Core Outcome Domains for early phase clinical trials of sound, psychology-, and pharmacology-based interventions to manage chronic subjective tinnitus in adults: the COMIT'ID study protocol for using a Delphi process and face-to-face meetings to establish consensus. *Trials* 18(1): 388.

ID: 238 / Session 1: 5

Abstract Submissions

Keywords: Tinnitus, HD-tDCS, visual stimulation, Tinnitus loudness

The effect of positive emotion induction and HD- tDCS on tinnitus loudness scale

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Neurofunctional tinnitus model (I.G. Toostani et al., 2016) proposed conscious evaluation of tinnitus valence (cognitive-emotional value) performs in prefrontal cortex which alters through both evaluative conditional learning and appraisal.

Moreover, Probst et al. (2016) reported that emotional states could mediate between tinnitus loudness and bothersome.

Accordingly, we hypothesized that adequate positive emotional induction could modulate tinnitus loudness perception and bothersome.

To investigate the hypothesis concerning tinnitus loudness perception, we conducted a randomized cross-over study designed in three sessions.

Study Design:

Intervention (a): visual stimulation (through presenting a set of validated high positively valenced pictures). Intervention (b): Visual stimulation with high definition tDCS (HD- tDCS), and Intervention (c): Visual stimulation with Sham.

HD-tDCS Anode-center was applied in the left hemisphere on dorsolateral prefrontal Cortex (Anode_F3, and, Cathodes_ F1, F5, CP3 and PO3) for 20minutes in 2mA. To do so, we expect to reinforce the positive emotional induction process in emotional evaluation network.

Method and Material:

Thirty-two patients were instructed to sit on a fixed chair with 85 cm distance from the 40-inch installed LCD. During this study (the chairs attitude were calibrated according to the height of each patient to make sure that the nasion is in the same line from the center of LCD), during each session, we frequently asked them to scale their tinnitus loudness by means of pressing the keys from F1 to F10 on the keyboard. Their responses were recorded via Superlab software.

Each session contained two blocks of neutral pictures presentation, pre and post interventions.

Results:

Generalized linear mixed model employed as statistical approach to analyze the acquired dataset. A meaningful difference between visual stimulation with HD-tDCS and others (One-Level, $P < 0.0001$) was shown. Furthermore, gradual decrement in tinnitus loudness scaling over the time (from the beginning of stimulation) was indicated.

Discussion:

The results are in line with our hypothesis that positive emotional induction can reduce the loudness perception in tinnitus patients. Further investigation is needed to find out its effect on bothersome and the ability to ignore tinnitus.

ID: 239 / Session 10: 3

Abstract Submissions

Keywords: hyperacusis

The putative involvement of the middle ear in hyperacusis and tinnitus

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Abstract:

We report the case of an acoustic shock injury (ASI), which did not result in a significant hearing loss, but was followed by manifold chronic symptoms both within (tinnitus, otalgia, tingling in the ear, tension in the ear, and red tympanum) and outside the ears (blocked nose, pain in the neck/temporal region). The pathophysiological mechanisms underlying these symptoms remain unknown, even though some authors have hypothesized a dysfunction in the tensor tympani muscle (TTM). The patient described here was able to precisely report his symptoms, their temporal evolution, and take pictures of his eardrums over time during symptom severity fluctuations. The psychoacoustic characteristics of his tinnitus and the functional integrity of the middle ears were also investigated. We suggest that these symptoms may result from a loop involving injury to middle ear muscles, peripheral inflammatory processes, activation and sensitization of the trigeminal nerve, the autonomic nervous system, and central feedbacks. The pathophysiology of this ASI is reminiscent of that observed in post-traumatic trigeminal-autonomic cephalalgia. This framework opens new and promising perspectives on the understanding and medical management of ASI. In addition, we report the case of a subject who is able to voluntarily contract the tensor tympani bilaterally. The experiments carried out in this subject, with and without tensor tympani contraction, was aimed at exploring different means to objectify the tensor tympani contraction, namely changes in compliance, acoustic recordings in the ear canal and electromyography.

ID: 240

Abstract Submissions

Keywords: Tinnitus, assessment instruments, questionnaire, Tinnitus and Hearing Survey

Tinnitus and Hearing Survey: A Polish study of Validity and Reliability

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This study investigates the psychometric properties of the Polish version of the Tinnitus and Hearing Survey THS (THS-POL), which is a tool for evaluating what proportion of patients' tinnitus complaint is due to hearing problems and what specifically to the tinnitus. The THS-POL was created using the translation-back translation method. Study participants completed THS-POL twice over a period of three days. The test-retest analysis shows excellent strength of correlations (THS-POL subscale A $r=0.89$, subscale B $r=0.9$). Reliability measured using Cronbach's alpha was respectively for subscales A and B in the first administration $\alpha=0.86$ and 0.95 and in the second administration $\alpha=0.91$ and 0.94 . CFA analysis confirmed good two factors structure of THS. Convergent validity evaluated using the Pearson's product-moments correlation between the subscale A (Tinnitus and Hearing) and Tinnitus Handicap Inventory (THI) shows good correlations. Concluding, the THS-POL is a valid and reliable screening tool to assist in deciding about the optimal management approach.

ID: 241

Abstract Submissions

Keywords: Tinnitus assessment, questionnaires, Visual Analogue Scales, VAS

Visual Analogue Scales as a tool for assessment of the tinnitus: Psychometric evaluation in a clinical population

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Objective: to evaluate psychometric properties of VAS scales for measuring subjectively perceived tinnitus loudness, annoyance, distress and possibility of coping with this condition.

Method: criterion and construct validity, reproducibility (agreement and reliability), floor and ceiling effects of VAS scales were measured. To assess criterion and construct validity of VAS scales THI, TFI, BDI and THS questionnaires were used. Cutoff points for VAS scales were determined.

Study sample: 100 adult patients.

Results: correlations among VAS-L and TFI amounted: VAS-L: $\rho=0.73$, VAS-A: $\rho=0.81$, VAS-D: $\rho=0.77$ and VAS-C: $\rho=0.52$. Within the identified agreement limits of VAS-L amounted 95% scores, of VAS-A: 93%, of VAS-D: 96% and VAS-C: 94%. Results of measuring ICC amounted for VAS-L: ICC= 0.76, for VAS-A: ICC=0.90, for VAS-D: ICC=0.80 and for VAS-C: ICC=0.67. Determined cutoff points of VASs were set: VAS-L: 59 points, for VAS-A: 56 points, for VAS-D: 66 points and for VAS-C: 45 points. Floor and ceiling effect was not present.

Conclusions: VAS scales are valid and reliable brief screening tool for obtaining quick information about tinnitus during the first intake with a patient. Determined cutoff points of VASs are the criterion of tinnitus severity helping in taking decision whether further specific intervention is needed.

ID: 243 / Session 8: 4

Abstract Submissions

Keywords: self-help platform, Tinnitus patients

Patient Empowerment through Summarization of Discussion Threads on Treatments in a Patient Self-Help Forum

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INTRODUCTION: Self-help internet fora allow patients to share experiences on their disease. However, new forum users may have difficulties in acquiring a fast overview of the discussed contents. We propose TinnitusTreatmentMonitor, a proof-of-concept framework that gives an overview of discussions on tinnitus treatments.

MATERIALS : We used data from 9 TinnitusTalk subfora, collected in July 2017. They sum up to 227,374 postings.

METHODS: TinnitusTreatmentMonitor contains components for data collection, identification of sentences that mention treatments, sentence labeling, aggregation and scoring. An initial seed of treatment names was acquired from the titles of postings. A small set of sentences was sampled from the postings, labeled manually for the targets "sentiment" and "personal experience", and used also to extract further treatment names. A multi-target classifier was trained and tested on this sample and then used to assign pairs of labels to the remaining sentences. After label assignment, the values of the target "personal experience" were used as weights for the sentiment values. The mentions were linked to the treatments they referred to and aggregated at month or year level. The front-end of TinnitusTreatmentMonitor is responsible for the visualization of these data.

RESULTS: We run TinnitusTreatmentMonitor on TinnitusTalk. We found 41,193 mentions of treatment names. Only 9 of the 48 treatments had opinion scores with a positive average. On the testing subsample of our manually annotated sample, our multi-target classifier achieved an accuracy of 60% for the polarity target, and 68% for the personal experience target.

DISCUSSION: TinnitusTreatmentMonitor aims at giving a comprehensive treatment overview over time. The back-end contributes to this goal by identifying the postings mentioning treatment and classifying them. The front-end visualization provides two interactive "views" over the extracted information. The "summary view" gives an overview of all treatments. Using the leftmost column of the layout, users can figure out which names/synonyms were used for a treatment. Using the middle column, they can see whether discussions on a treatment were vivid or stalled. The rightmost column shows whether the treatment was perceived positively or negatively. The "detailed view" provides three graphs with plots of the treatment mentions over time, covering different perspectives. By juxtaposing the area under each color in the graphs, it can be seen whether the discussion on the specific treatment was mostly neutral or mostly sentimental. Hence, a first impression on the opinion of other patients on the treatment over time can be acquired without reading the postings.

The next steps are to test this environment with volunteers, and to partially automate the treatment identification process.

ACKNOWLEDGEMENTS: Partly, the work done by U. Niemann and M. Spiliopoulou was within the German Research Foundation project OSCAR "Opinion Stream Classification with Ensembles and Active Learners": U. Niemann is partially funded by OSCAR, whereas M. Spiliopoulou is project investigator.

NOTE: The text of this abstract has appeared, MOSTLY AS IS, in the publication of the authors under the same title in the International Conference on Biomedical and Health Informatics (ICBHI 2017).

ID: 244

Abstract Submissions

Keywords: biomodulation

Can a steady state coherent biomodulator relief tinnitus and be safe? A summary of the clinical study program performed.

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TITLE: Can a steady state coherent biomodulator relief tinnitus and be safe? A summary of the clinical study program performed.

OBJECTIVES: The objectives were to evaluate the performance and safety of an innovative passive light photon driven microscopic biomodulator patch creating coherency as an alternative medical device for tinnitus relief.

MATERIALS and METHODS: Three independent clinical studies have been performed during the year 2012 to 2017. The first was a limited interventional investigation with 10 patients, the second was a larger interventional study with 48 patients and the third a randomized, placebo-controlled, double-blind, parallel groups dual-centre study with total 82 patients. Patch performance evaluated with questionnaires related to tinnitus and quality-of-life and safety were assessed during and after the end of treatment. In all studies the treatment time was 3 weeks and the patches were placed behind one year.

RESULTS: The first study indicated a relief with half of the patients at the end of the treatment. Still two years after the study one third reported tinnitus relief. However, the number of patients were low. The second study showed a responder relief in 58 % directly after end of treatment and 60 % one month after. The third study showed that the biomodulator patch had statistical significant ($p < 0.05$) three times more responders than placebo one month after end of treatment, measured as a decrease from baseline in at least 2 points in tinnitus annoyance visual analogue scale as a minimal clinical significant difference. Tinnitus handicap inventory improved by mean -16 points significantly ($p < 0.05$) for the active responder group, but with no statistically significant changes for the placebo group or between the groups. Well-being questionnaire also improved for the active responder group, but not statistically significant. The biomodulator patch was safe and well-tolerated in all three studies.

CONCLUSION: In a cost-risk-patient effort and time-benefit rationale according to this clinical study program with three different studies it can be reasonable to recommend the biomodulator patch for treatment of tinnitus. Further studies of how this biomodulator more specific act on the hearing system, how long this may sustain and if there can be subgroups of patients or variations in the treatment time, number of patches, and frequency for more efficiency needs to be considered.

KEYWORDS: Tinnitus, treatment, medical device, patch, coherency, biomodulation

ID: 245 / Session 5: 3

Abstract Submissions

Keywords: tinnitus, spinal decompression, neck conditions, craniocervical dysfunction

Spinal Decompression: Its Effect on subjective intensity in Tinnitus Patients with Craniocervical Dysfunction and other neck conditions - the grow concept spinal decompression chair

Thomas Zudrell

Academy for Holistic Healing Arts International AHHA, Germany

It seems possible for neck conditions to be a cause of tinnitus. Strain of neck muscles, sprain of neck ligaments, whiplash injuries, along with degenerative cervical spine changes can make patients more susceptible, aggravate, and may actually cause tinnitus. Several case studies suggest a connection between Craniocervical Dysfunction and the subjective intensity in Tinnitus Patients that improve following Spinal Decompression. The grow concept Spinal Decompression Chair allows a Patient controlled Spinal Decompression that leads to noticeable changes in the subjective intensity of symptoms after 15 to 20 minutes Spinal Decompression in a reclined body position without stressing the spinal ligaments. Different parts of the Spine can be decompressed individually including the cervical spine and the possibility of repeated Decompression sessions over an extended period of time may assist other forms of tinnitus therapy and suggest that more case studies are indicated and Spinal Decompression should be an integral part of any tinnitus therapy.

ID: 246

Abstract Submissions

Keywords: tinnitus, longitudinal data, data base

Tinnitus profiling to guide personalised therapeutic decisions - diagnosis improved with large-scale, longitudinal data

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Current treatments for chronic, subjective tinnitus have different rates of success, and no treatment is able to consistently and effectively suppress the phantom perception and/or the accompanying distress. The reasons why certain patients react to some treatments but not to others is not fully understood, but one possible explanation relies on the fact that tinnitus is a heterogeneous disorder both in terms of aetiology and manifestation. Differences in gender, age, onset of tinnitus, primary causes, laterality, personality profiles and comorbidities are just a few of the potential predictors of treatment success, but little is known about how those predictors influence treatment outcomes *de facto*.

For this PhD project we aim to use at least three sources of “big-data”, namely: 1. the Tinnitus Hub Survey (THS), 2. the database of tinnitus patients from the Tinnitus Centre Regensburg, and 3. the database of the European School of Interdisciplinary Tinnitus (ESIT) Research.

In this poster, we present preliminary results obtained from the THS as an example of the type of studies to be conducted in the next two and half years during this PhD project. The THS is part of the Tinnitus Hub, a support website that conducts crowdsensing activities. Participants of the THS filled in a survey containing a wide range of topics related to their tinnitus, some relevant demographics are displayed. Two main goals of this PhD project and means to achieve them are presented, respectively a) to deliver intuitive and clinically relevant insights with the potential to bridge the gap between patients, care takers and researchers in the tinnitus field, and b) to identify predictors of treatment success in order to promote individualised, optimal care to tinnitus patients.

ID: 247

Abstract Submissions

Keywords: Tinnitus, ANOVA, tinnitus type, tinnitus distress

On the “Tinnitus Gestalt”: How the Characteristics of the Tinnitus Phantom Sound Influence the Perceived Tinnitus Distress

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Objectives: Tinnitus is the perception of a sound when no corresponding external sound is present. The severity of tinnitus varies but can be debilitating for many patients. In the present study we raised the question why some patients suffer a lot from their tinnitus, while others report only little tinnitus-associated distress.

Participants: We present results of analyses based on data from 1334 patients registered in the *Tinnitus* Research Initiative Patient Database.

Aim: We tested the impact of various tinnitus characteristics, namely tinnitus type, loudness, and pitch on the tinnitus distress assessed by two tinnitus questionnaires: the Tinnitus Handicap Inventory (THI) and the Tinnitus Questionnaire (TQ). We also made an attempt to detect significant covariates for tinnitus characteristics (e.g. age, gender, tinnitus duration, onset, depression).

Methods: We performed standard statistical analyses based of linear model and ANOVA type. The necessary assumptions for the application of these methods, such as normality and homoscedasticity, were verified.

Results: We detected a dependence of tinnitus characteristics (tinnitus type, loudness) on the tinnitus distress. Patients with noise-like tinnitus seem to report higher tinnitus distress. Tinnitus pitch does not seem to have a significant influence on results obtained by patients in the tinnitus questionnaires. Among the models tested, those that include tinnitus type, loudness and depression seem to be the best fits for our data.

ID: 248

Abstract Submissions

Keywords: genetics, risk factors

Environmental and Genetic Risk factors for tinnitus

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Background: For many years, it has been believed that tinnitus is a consequence of environmental factors only. Several studies have failed to show the genetic influence on tinnitus, therefore contributing to the notion that genetics do not have a significant role in the generation of tinnitus. However, our lab has recently shown that different forms of tinnitus (unilateral, bilateral, gender grouped) can show significant heritability and have a predominant genetic influence over environmental factors. These findings are of major scientific and clinical relevance, since they set a milestone in tinnitus research. As a consequence, this project aims at better understanding the genetic mechanisms underlying tinnitus, and how their combination with environmental factors would increase the risk of developing tinnitus.

Aims and Methods:

Aim 1 – Systematic review of environmental risk factors for tinnitus and identification of novel risk factors using large Swedish cohorts.

Aim 2 – Identification of loci involved in bilateral tinnitus using Genome Wide Association Study using the Swedish Twin Registry. GWAS is based on linkage disequilibrium and relies on association of common variants with a genetic trait.

Aim 3 – Identification of rare variants of bilateral tinnitus by performing Whole Exome Sequencing (WES) using the Swedish tinnitus Outreach Project (STOP) cohort. WES is a genetic method with very high resolution on all coding sequences.

Expected insights:

We have set 3 major aims that will enlighten future research in the field. With achieving these goals, we are expected to render new predictors of tinnitus development that can be used to stratify disease risk and elaborate preventive medical recommendations for high-risk subgroups of tinnitus patients. Furthermore, accomplishing these aims will help define molecular drivers and biological pathways relevant for the development of tinnitus that will be used to identify and validate new therapeutic targets.

Significance:

With the exception of cognitive behavioural therapy, there are no effective treatments for tinnitus, and drug discovery in the field is reaching an impasse. Human genetics has proven to increase the likelihood of successful trials and our project has great odds of yielding promising data that will provide a new basis of drug discovery and provide benefits to tinnitus patients.

ACKNOWLEDGEMENTS: We acknowledge The Swedish Twin Registry for access to data. The Swedish Twin Registry is managed by Karolinska Institutet and receives funding through the Swedish Research Council under the grant no 2017-00641

FINANCIAL SUPPORT: This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement number 722064.

ID: 249

Abstract Submissions

Keywords: TMS, Tinnitus

Activate & Fire: Pairing auditory stimulation with repetitive transcranial magnetic stimulation for the treatment of tinnitus

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Tinnitus is the perception of a sound without an external source. Several different treatment approaches exist, but due to the heterogeneity in phenotype and etiology, the achieved effects are very variable. Acoustic stimulation with amplitude-modulation tones, broad-band noise or filtered noise was shown to be a promising tool to suppress tinnitus temporarily and concomitantly tinnitus-dependent brain activity. Repetitive transcranial magnetic stimulation (rTMS) represents another promising treatment method for tinnitus. However, results of studies are still rather small and show high variability. Exact stimulation positions or brain state before or during stimulation are putative applications for the augmentation of its effectiveness. This PhD-project tends to conduct three topically linked experiments. First of all, the effects and the characteristics of noise and amplitude-modulated sounds on subjective tinnitus suppression and corresponding brain activity as measured by electroencephalography will be investigated. In a next step, systematical testing of several rTMS protocols and different stimulation sites/positions should shed light on the optimal rTMS parameters for tinnitus inhibition. Building up on this, a final experiment aims to combine these two techniques by acoustically stimulate subjects before or during rTMS is applied, to modulate the intrinsic brain activity and increase the effects of a magnetic stimulation.

ID: 250

Abstract Submissions

Keywords: patient assessment, standardization

Harmonizing scientific and clinical perspectives on tinnitus subtypes and measures: synthesizing evidence and expert opinion

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Background: Tinnitus is a rather heterogeneous condition and finding a meaningful way to subtype it is a longstanding problem in tinnitus research. Many frameworks have been proposed over the years [1-4], but consensus has not been reached among the scientific community. One of the issues is that many variables contribute to tinnitus heterogeneity and the relationships between them are not well-characterised [5]. The aim of this project is to examine the underlying structure between these variables and to develop an evidence-based framework for tinnitus subtyping with recommendations for minimum standards for data collection.

Objectives: The main objectives of this project are to:

(1) Develop a protocol for standardized patient assessment for ESIT projects in collaboration with all ESRs and supervisors across ESIT.

(2) Review literature of previously proposed frameworks and methods used to identify variables for tinnitus subtyping and systematically identify the potential confounds that hinder tinnitus subtyping.

(3) Systematically identify the etiologic factors for tinnitus by conducting a systematic literature review in collaboration with ESRs and supervisors of ESIT projects 3 and 4.

(4) Define meaningful tinnitus subtype constructs by designing and conducting an observational study to gather and analyse data from the tinnitus population.

(5) Develop a position statement proposing a global framework for tinnitus assessment and subtyping.

Conclusions: Due to the high heterogeneity of the tinnitus population, defining distinct subtypes is needed both in tinnitus research and clinical management. Although there are many proposed ways to subtype tinnitus, consensus has not been reached. The focus of this project will be the development of an evidence-based subtyping framework for adults with tinnitus.

Funding: This project is funded through the Marie Skłodowska-Curie Innovative Training Network scheme: European School for Interdisciplinary Tinnitus Research (ESIT, H2020-MSCA-ITN-2016, grant agreement number 722064)

References: [1]. Douek, E., 1981. Classification of tinnitus. In Tinnitus Ciba Foundation Symposium, vol. 85, pp. 4-15. [2]. Nodar, R.H., 1996. Tinnitus reclassified: new oil in an old lamp. *Otolaryngology--Head and Neck Surgery*, 114(4), pp.582-585. [3]. Levine, R.A. and Oron, Y., 2015. Tinnitus. *Handbook of clinical neurology*, 129, pp.409-431. [4]. Cianfrone, G., Mazzei, F., Salviati, M., Turchetta, R., Orlando, M.P., Testugini, V., Carchiolo, L., Cianfrone, F. and Altissimi, G., 2015. Tinnitus Holistic Simplified Classification (THoSC) A new assessment for subjective tinnitus, with diagnostic and therapeutic implications. *Annals of Otology, Rhinology & Laryngology*, 124(7), pp.550-560. [5]. Hoekstra, C.E., Wesdorp, F.M. and van Zanten, G.A., 2014. Socio-demographic, health, and tinnitus related variables affecting tinnitus severity. *Ear and hearing*, 35(5), pp.544-554.

ID: 251

Abstract Submissions

Keywords: tinnitus, pitch matching, residual inhibition, EEG

Tinnitus pitch matching by amplitude modulated sounds

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Tinnitus is the perception of sound in the absence of an auditory stimulus and it's experienced by 15% of the population. There is enough evidence to support the idea that tinnitus is related to unfavorable cortical plastic changes. After hearing loss, e.g., an augmented synchronous neural activity may contribute to the generation and maintenance of subjective tinnitus. Since cortical organization can be modified by training, restoring hearing by hearing aids may ameliorate tinnitus as a result.

Hearing aids and many other tinnitus therapies are being developed targeting the patient's tinnitus frequency. This frequency is traditionally estimated by a pitch matching procedure, in which the patient has to report how similar is the perceived tinnitus frequency and different pure tones. However, this strategy is often criticized as unreliable since it is based on a subjective patient self-report.

The residual inhibition functions relate the tinnitus suppression to the center frequency of masking sounds, and they usually cover the hearing loss spectrum. Therefore, they might be a useful psychoacoustic measure towards the tinnitus pitch estimation.

We propose a method to obtain the residual inhibition functions by using amplitude modulated (AM) sounds at different frequencies, covering the patients' audiogram. The tinnitus loudness suppression will be also investigated by means of EEG to test if it is reflected by neural oscillations, thereby obtaining a possible objective technique for pitch matching.

ID: 252

Abstract Submissions

Keywords: electric stimulation, suppressing tinnitus

Developing new strategies of cochlear electric stimulation to suppress tinnitus

Vinay Parameshwarappa

Aix Marseille University, France;

Our project is aimed at suppressing the tinnitus related activity using extra-cochlear electric stimulation in guinea pigs. Tinnitus will be produced by noise trauma (115 dB SPL, 8kHz tone, during 4 h). As preliminary experiments, we will develop an experimental preparation where we can record neural activity in the auditory cortex of awake animals before and at different times after the noise trauma. Briefly, high-impedance microelectrodes are implanted chronically in the right auditory cortex of the guinea pig. Multi-unit activity and local field potentials will be recorded during silence (spontaneous activity) and after acoustic stimulus presentation. to record cortical activity. Data analysis on spontaneous LFPs before and after noise trauma is performed using various signal processing algorithms in MATLAB.

ID: 253

Abstract Submissions

Keywords: Tinnitus, Smart Sensors, Mobile Sensing

Smart Mobile Sensing to Support Tinnitus Patients

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Tinnitus is a common disorder, which is associated with the perception of a ringing sound or noise in the ears. The causative factors of tinnitus are unknown, however, it usually is intertwined with an underlying condition in the ear. In addition to general health complications, tinnitus might be also responsible for provoking other psychological disorders (e.g., stress, anxiety, depression, or obsessive-compulsive disorder) and may affect the common as well as social lifestyles. Furthermore, tinnitus has also been described to may have a direct proportionality with migraine and vertigo. In this context, a plethora of scientific literature has reported an alleviation in the tinnitus condition, which can be related to the surrounding atmospheric and environmental conditions of the patient. Among others, factors like a decrease in the atmospheric pressure, a weather change (specially rainy and cold weather), intensity of light, the current sound environment, or (sudden) change in altitude are some of the most pertinent. The orientation, movement speed, and direction of movement of the patient are some of the less common, yet still significant set of factors that may also induce a spike in tinnitus. Interestingly, the extraordinary advancements in the smart sensing technologies and wide availability of smart sensors allow for a monitoring of the aforementioned factors. Today, most of the smart devices, ranging from notebooks, smart phones, tablets, and even wrist watches are equipped with smart sensors. Specially, many mainstream smart phones are equipped with sensors, which enable sensing motion (using accelerometers, gravity sensors, gyroscopes, and rotational vectors), environment (using barometer, thermometer, and photometer), and position (using orientation sensors, and magnetometers). These mobile or smart phone sensors, in turn, can be then used to monitor the aforementioned factors (most, if not all) that induce or provoke tinnitus and, hence, enabling smart mobile sensing. Moreover, the raw data gathered with these sensors can be processed to identify (drastic) changes in the circumstances (motion, environment, and position) of a tinnitus patient. In this context, if a sudden change in the circumstance of the patient is detected, the patient is prompted to respond and report the current severity of the tinnitus (impromptu feedback). Following this, we believe that feedback is beneficial for patients, healthcare professionals, or clinicians specialising in tinnitus. From the perspective of clinicians, this information may be used to specify a patient profile. The latter can be used by these professionals to potentially mitigate tinnitus or control its symptoms by the provision of instant therapy solutions, for example, acoustic therapy (calming sounds, music therapy, listening pink or brown noise), intake of supplements, or personalised sound frequency treatments. In addition to this, from the perspective of the patient, this profile may keep the patient aware of specific triggers and what may cause their tinnitus symptoms. Furthermore, these profiles, as well as the sensed data, can be used by data analysts and may support them in incentive management by improving existing incentives and creating new incentives from the point of view of both patient and clinicians. In conclusion, we believe that a sophisticated smart mobile sensing app to monitor patient surroundings and profiling patients for personalised therapy may foster the controlling and mitigating of tinnitus symptoms, as well as promote community or participatory sensing.

ID: 254

Abstract Submissions

Keywords: Tinnitus, Mobile Crowdsensing, Incentive Management, Data Analysis, Machine Learning

Incentive Management in the Context of Tinnitus Patient Treatments by the Use of Mobile Crowdsensing Technologies

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Incentive Management (IM) pursues the idea of offering benefits or rewards to participants involved in an endeavor that requires the achievement of specific goals or the completion of certain activities. Today, IM is increasingly used in various industries and research fields. In principle, IM techniques focus on the concrete actions and methods to increase the motivation of the participants, either by offering rewards or recognition. To give some examples, commercial applications like Badoo, Duolingo, or Facebook use IM techniques to keep their users motivated. One particular IM technique that is also used vividly is Gamification. The latter enhances the user experience of applications through the application of game features (e.g., score, rewards, etc.). Moreover, IM techniques are supported by economic theories and mathematical models like the Game Theory, which illustrates the strategic behavior of the participants involved in any particular setting and further studies the decision making of these participants. However, these models are useful to design and run the strategically balanced system, in which the total resource at any given point is a fixed constant. When dealing with medical data, in turn, an added challenge emerges with respect to privacy aspects as the data contains sensitive and personal information. In this context, Mobile Crowdsensing (MCS) is a technique that is increasingly used for gathering medical data in everyday life, building on the notion of 'bring your own device' and the capabilities of contemporary smart mobile devices. Furthermore, MCS eases the capturing of environmental data of patients through the inherited sensors of their smart mobile devices. Then, by using these information, statistical analysis or data science methods can be carried out to better understand the utility of the system and indicators may be revealed to provide incentives and/or improve the features of the application. In addition, data analysis may help to re-tune the performance of the system by resource optimizations. Moreover, the application of machine learning techniques are the next step towards predictions. To conclude, the design of useful MCS applications should consider IM techniques. Thereby, two entities should be distinguished: the platform (the application) and the users. To be more specific, it should be focused on the computational efficiency, individual rationality (the user gets a non-negative utility), profitability (the platform gets a non-negative utility) and truthfulness (incentive compatible). In our work, we therefore base our considerations on three major pillars to integrate IM into MCS applications that focus on the medical domain in general : a) Theoretical Models (Game Theory), b) Performance Metrics (Architecture and Algorithms), and c) Experiments (Data Analysis). On the other, we particularly focus our work on the application of MCS in the context of tinnitus and the way how tinnitus patients can be motivated to share data that can be evaluated to work on new treatment methods.

ID: 255

Abstract Submissions

Keywords: tinnitus in kids, online evaluation

An evaluation of paediatric tinnitus services in the UK

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Background/objective: Children who have distressing tinnitus are known to experience significant physical, emotional and behavioural problems in addition to hindered educational performance. There is mixed evidence around the prevalence of tinnitus in children. However, some studies suggest that the experience is common and there is data to suggest that paediatric cases are on the increase. Compared to well-established adult services across the UK, fewer child-specific tinnitus services currently exist.

Methods: An online service evaluation questionnaire, including eight specific items on paediatric tinnitus, was distributed to UK national health tinnitus services via email and social media. Ninety-one questionnaire responses were obtained between July and September 2017.

Results: Interim results found 49 (54%) of 91 UK tinnitus services to provide a paediatric service. Within these services, audiologists were most commonly responsible for the treatment of children (65%), followed by Hearing Therapists (37%) and ENT specialists (35%). Thirty-seven percent of paediatric services did not report use of measurement tools to assess tinnitus in children. Others reported using visual analogue scales (33%) and/or selfdevised questionnaire measures (25%). Five services reported using tinnitus questionnaires developed for use with adults (Tinnitus Handicap Inventory or the Tinnitus Functional Index) to assess children, particularly for older age groups. Commonly used management approaches were 'explanation, advice and information giving' (92%), non-wearable sound enrichment (78%), and hearing aids (76%). Less commonly used approaches were Narrative Therapy (12%), Cognitive Behavioural Therapy (20%), or Mindfulness techniques (25%).

Discussion: The provision of child-specific tinnitus services is aligned with the 2015 British Society of Audiology Practice 'Tinnitus in Children. Practice Guidance' which calls for a childcentred approach to tinnitus management. Although adult strategies are acknowledged to have some relevance to children, guidelines stress that assessment and management techniques must be adapted specifically for use with children, and cases should be managed by healthcare professionals who are experienced with paediatric caseloads. Guidelines also highlight that it is important for psychological therapies such as Narrative Therapy and Cognitive Behavioural Therapy to be provided by staff with relevant training in these therapeutic techniques.

Conclusions: Paediatric tinnitus services are active across the UK. The limited and inconsistent use of measurement tools, in addition to the employment of adult-specific questionnaire measures, suggests a need for a child-specific measure of tinnitus in children. As services develop, it will be important to ensure that where needed, children have access to psychological therapies as well as other management options, either via the tinnitus service itself or via referral to mental health services or other appropriate local services.

ID: 256

Abstract Submissions

Keywords: Tinnitus assessment, Avoidance behavior, clinical assessment, outcomes

DEVELOPMENT OF A NOVEL MEASURE TO ASSESS AVOIDANCE BEHAVIOUR IN TINNITUS PATIENTS

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Background: Based on earlier results, and the potential benefits of a fear-avoidance approach in treating chronic tinnitus suffering, avoidance behaviour is thought to play a key role in the suffering of patients with chronic tinnitus. Currently, a measure designed to inventorize, assess, and measure changed over time in tinnitus-related avoidance behaviour over time does not exist. Here we introduce a new measure for this purpose.

Aims: A new self-report measure to assess self-reported avoidance behaviours in patients with chronic and bothersome tinnitus, The Inventory of Tinnitus Avoidance Behaviours (ITAB), is developed and psychometrically tested.

Methods: In phase-I, 2 expert judges reviewed existing measures and evaluated avoidance items. New items based on clinical experience were scripted and added, leading to a first draft-version ITAB 1. In phase-II, an online survey with 17 clinicians (from 7 different disciplines) was carried out in order to assess face- and construct validity. Subsequently, 6 clinical expert judges evaluated the ITAB 1 items during an expert panel session to achieve consensus (>60%) on consistency, intelligibility, relevance, wording, domain (covert-, versus overt avoidance or escape) and in-/exclusion of items. In phase-III, expert opinions by tinnitus patients (n=12, with mild-severe tinnitus-severity; referred to the study by clinical experts) were gathered via individual semi-structured interviews. Patients were asked to evaluate the ITAB 1 using the same variables as in the previous phase. The instructions and scoring were clear according to the patients, and no major adjustments were proposed. In phase-IV the final draft of the ITAB will be administered to a large sample of patients in order to evaluate its psychometric properties.

Expected outcome: ITAB is expected to be a valid and reliable instrument to inventorize and assess tinnitus-related avoidance behaviors designed for both clinical and research purposes.

Funding acknowledgements: This study is financially supported by University Fund Limburg/SWOL and NWO Veni grant number 016.165.105. Johan W.S. Vlaeyen is supported by the Asthenes long-term structural funding—Methusalem grant by the Flemish Government, Belgium.

ID: 257

Abstract Submissions

Keywords: Neurofeedback

Developing Individual tomographic Neurofeedback Protocols for Tinnitus Treatment

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Background: Despite rising prevalence of the phenomenon of subjective tinnitus, there is still a lack of effective treatment methods. EEG-based Neurofeedback, as a special form of biofeedback, has shown promising results [2-6]. Nevertheless, regarding changes at individual level, not all participants did profit equally from the training. Whether there are predicting factors in participants that would indicate success in neurofeedback training for improving tinnitus symptoms has to be examined in this project [1]. In addition, these factors are to be used as a basis for preselection, in order to ensure better treatment success by means of individual protocols.

Objectives: The main objectives of this project are to:

(i) Develop a general guideline for neurofeedback tinnitus studies, to produce more comparable and consistent results in future studies.

(ii) Review literature of previous proposed frameworks and methods, used to identify predictors (e.g. age, questionnaires, base line EEG, ...) for better treatment effects, in order to systematically recognize the potential confounds too.

(iii) Draw attention to the discussion of defining success and failure in neurofeedback, as they seem not clearly established.

(iv) Designing and conducting a clinical study to gather and analyze data from tinnitus patient treated with personalized neurofeedback protocols.

Conclusions: Although there are proposed ways to define predictors for neurofeedback responders, consensus has not been reached due to the high heterogeneity of the tinnitus population. The focus of this project will be the development individual tomographic neurofeedback protocols to address the problem of diversity within the tinnitus population.

Funding: This project is funded through the Marie Skłodowska-Curie Innovative Training Network scheme: European School for Interdisciplinary Tinnitus Research (ESIT, H2020-MSCA-ITN-2016, grant agreement number 722046)

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ID: 258 / Session 14: 5

Abstract Submissions

Keywords: support, patient empowerment

Tinnitus Hub: Support and Crowdsensing in the digital domain

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Tinnitus Hub: Support and Crowdsensing in the digital domain

ID: 259 / Session 4: 5

Abstract Submissions

Keywords: animal models, pharmacological treatment, lidocaine, chronic pain

New ways forward in Tinnitus Research?

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Despite exciting new theories being developed about the causes of tinnitus in the brain, the field is stagnating in terms of therapies. What could be done to come up with new treatments that give patients new hope for escape from a state that they sense as inescapable?

One way, though not the most direct way, would be to develop new animal models. Rodents have been the model of choice for decades and, while some progress has been made, rodent brains lack one essential ingredient that primate (and human) brains possess: a prefrontal cortex, as part of a central executive system, which we believe is capable of suppressing internally generated noise, such as tinnitus. One of the goals in my lab has, therefore, been to establish a primate model of tinnitus, which builds on our human work in a reverse-translational way.

The second approach we have been pursuing more recently is to build on the single pharmacological method that has been proven successful in suppressing tinnitus in 75-80% of cases: intravenous injection of lidocaine (Goodey, 1981). Despite its high effectiveness and relative safety, it has never been developed into routine treatment. One reason is obviously the short duration of its effect on tinnitus, and one of our goals is to extend this duration. Recent studies of chronic pain are encouraging in that respect (Challapalli et al., 2017; Daykin, 2017).

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ID: 260

Abstract Submissions

Keywords: epidemiology

A coherent European Epidemiological survey of Tinnitus

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Introduction: Epidemiological prevalence studies on tinnitus show widespread variability globally and very limited prevalence data are available for multiple countries. Lack of standardized assessment tools is the main cause for this variability and makes inter-country comparisons difficult. Moreover, studies to investigate the etiology of tinnitus are mostly cross-sectional. Due to the lack of analytical studies, understanding the etiology of tinnitus and associated risk factors becomes problematic.

Research objectives: This PhD project has two main objectives. The first one is to identify the Pan European burden of tinnitus. The second objective is to quantify the association between relevant risk factors and tinnitus, with particular emphasis on avoidable lifestyles and other environmental factors.

Research Projects: To assess the burden of tinnitus, data from a representative survey conducted in 12 strategically selected European countries (the European Tinnitus Survey, ETS), using a standardized tinnitus assessment tool (i.e., a set of four tinnitus and hearing loss related questions translated into 12 European languages), will be used. I am currently working on a paper documenting the translation process of the ETS questionnaire, and will analyze the final data obtained from the fieldwork. In order to assess the etiology of tinnitus, we are conducting a comprehensive systematic review in collaboration with other ESIT partners. I will use meta-analytic approaches to estimate the association between relevant environmental and lifestyle related risk factors and tinnitus. More importantly, I will analyze data from the longitudinal and case-control studies conducted in Sweden and Italy, respectively.

Public Health Impact: ETS data are important to estimate the disease burden and compare geographic, ethnic and cultural variability of tinnitus across different countries. Knowledge of risk factors are essential to prevent the condition and could potentially reduce the disease burden. Moreover, this will contribute in reducing the gap of knowledge regarding tinnitus etiology.

ID: 261

Abstract Submissions

Keywords: Tinnitus Matching methods, Pitch Match

Head-to-head comparison of concurrent tinnitus matching methods with a focus on reliability and duration: towards optimized mobile methods in research and intervention

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Tinnitus matching still is a challenging endeavor given the heterogeneity of tinnitus percepts and the reliance on subjective ratings. This unsatisfying situation and a lack of consensus among researchers limits the reliability and validity of pitch matchings of tinnitus. Tinnitus pitch matchings are key for interventions like acoustic stimulation or neuromodulation. Furthermore, reliable mobile matching methods are needed to study tinnitus variability in real life.

The present study aimed at comparing the three most common and current tinnitus pitch matching methods with a focus on reliability and duration. Beyond that, ease of use and matching accuracy was assessed by subjective ratings. Main outcome variables were the resulting tinnitus frequency and its reliability over five sessions.

The methods of adjustment's (MOA), forced-choice double staircase (FCDS) and pitch likeness (LM) were chosen for the comparison given their concurrent ubiquitous use.

All three methods were tested five times consequently with short breaks in between. 59 healthy subjects with subjective, tonal tinnitus were recruited for this single session study and randomly assigned to three groups (i.e. FCDS, LM, and MOA) matched for age, sex, hearing loss, and musicality.

Results point at a good (FCDS = .88, LM = .83) and excellent (MOA = .91) mean reliability of the matching methods. In the last of the 5 matching sessions, participants needed 131 seconds (SD = 81) to match their tinnitus with MOA, 161 (SD = 78) with FCDS, and 233 (SD = 72) with LM. Ease of use (scale: 1 (not at all) to 10 (very easy)) was rated highest for MOA (mean = 9.2, SD = 0.9) followed by LM (mean = 8.9, SD = 1.1) and FCDS (mean = 7.8, SD = 2.1). Finally, mean subjective accuracy (scale: 1 (not matching) to 10 (perfect match)) was 8.7 (SD = 1.03) for MOA, 8.63 (SD = 1.11) for LM, and 7.9 (SD = 1.37) for FCDS. Notably, no significant differences were found between the methods except for duration (MOA < LM, $p < .05$)

The evaluation and comparison of three established concurrent tinnitus matching methods produced an overall good reliability, ease of use, and subjective accuracy as well as acceptable durations (< 5 minutes) for all methods. Generally, MOA slightly outperformed the other methods while duration and ease of use should be cautiously interpreted given inherent differences in the procedures. While, in general, reliability, duration, ease of use and subjective accuracy may be continuously improved, validity is still limited given both the possibly fluctuating nature of the phantom percept as well as the ability of tinnitus sufferers to match in- and external sounds. Therefore, a proper familiarization to the methods as well as fundamental training in pitch discrimination is advisable.

Future mobile implementations of tinnitus matchings could profit from the insights of this study in that MOA may be most suitable for fast matching while between-method reliability of this user-driven approach could be improved by combining it with the algorithm-driven approaches of LM or FCDS.

ID: 262

Abstract Submissions

Keywords: salicylate-induced Tinnitus, noise-induced Tinnitus, animal models

Comparison of salicylate-induced and noise-induced tinnitus rat models

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Tinnitus, the perception of a “phantom” sound in the absence of external stimulation, is a common consequence of damage to the auditory periphery. It affects around 15% of the population and may induce intolerable discomfort. Whereas some drug candidates are in the process of being developed, nowadays no effective treatment exists to cure tinnitus. Because it remains very difficult to detect tinnitus objectively in animal models, carry out new quantitative methods become the key step to develop new compounds involved in tinnitus treatment.

Aim: The objective of this study is to compare the salicylate-induced and the noise-induced tinnitus rat models using three robust and validated experimental *in vivo* techniques: behavioral tests, auditory cortex electrophysiology and brain *in vivo* imaging.

Material and methods: For salicylate-induced tinnitus model, salicylate is administered by intraperitoneal injection at 300mg/kg/day. For acoustic trauma-induced tinnitus model, animals are exposed to a unilateral acoustic trauma of 116 to 118dB SPL of two octaves (8-24KHz) band noise centered at 16 kHz during 1h. Two hours after salicylate administration or 30 days after acoustic trauma the presence of tinnitus is determined using gap prepulse inhibition test, unicellular electrophysiology of primary auditory cortex and *in vivo* manganese enhanced MRI.

Conclusion: The combination of behavioral test, electrophysiology recording and *in vivo* imaging allows to measure putative signs of tinnitus in both rat models. Similar results were observed in electrophysiology and MEMRI imaging read-outs for salicylate and noise induced tinnitus model. However, using gap prepulse inhibition test, we observed that salicylate induced tinnitus at the broadband noise (bbn) whereas the acoustic trauma induced tinnitus at 12, 16 and 24 kHz but not at the bbn. Taken together, these data open the door for screening and characterization of new drug efficacy on tinnitus disorder.

ID: 263

Abstract Submissions

Keywords: oscillation

Translational perspectives in tinnitus research: Investigating influence of top-down processes on tinnitus through alterations of oscillatory activity

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The role of top-down processes such as formation of predictions and selective attention in mediating tinnitus symptoms as well as "chronification" of this condition is not yet fully understood. A better insight into these processes could yield possibilities to improve treatment in a scientifically-informed manner.

A link between altered top-down processes in tinnitus and changes in the neural oscillatory activity is unknown. Abnormal oscillatory processes in tinnitus have been mainly established in previous resting-state measurements, providing evidence for changes such as an increased delta-to-alpha power ratio, increased gamma and altered activity in the range of slow frequencies. However, the task-free nature of resting-state measurements make strong conclusions with regards to the functional (e.g. perceptual, emotional) relevance of these changes impossible.

In the present research project, we aim to advance our understanding on how altered oscillatory processes in tinnitus may indeed reflect altered top-down processes. For this purpose, we will apply a paradigm recently developed in our group and magnetoencephalography (MEG) measurements. This study allowed us to establish for the first time in healthy individuals that auditory predictions can be sharply tuned down to the tonotopic level. Currently, we are following up this study by investigating differential oscillatory contributions to this effect. In the next step, we will also investigate whether selective auditory attention lever the same top-down processes as passively formed predictions and will test how these processes are altered in individuals with tinnitus.

Going beyond this basic scientific investigation, our project will also provide an urgently needed translational perspective: In the latter phase of the project, we will take part in development of the clinical trial with a use of transcranial electric stimulation (tES) which will be tailored to normalise altered brain waves relevant to tinnitus perception. We will scrutinize the online influence of electric stimulation on neural activity in tinnitus patients while undergoing the aforementioned paradigm in the MEG prior to actual treatment. This will provide important insights into what extent typical tES strategies affect neural processing *at all* and whether and how top-down processes are in particular affected. Our work could provide an important fundament for predicting individual treatment outcomes and / or optimizing individual treatment parameters.

ID: 264

Abstract Submissions

Keywords: electric stimulation

Optimal parameters for non-invasive extracochlear electrical stimulation for subjective tinnitus

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Tinnitus is one of the otological conditions that has allured the scientists since last few decades to find an optimal treatment for this condition. At the beginning transtympanic electrical stimulations (ES) were used, nowadays non-invasive techniques are in use. Despite intensive research conducted in the past, optimal parameters of the stimulus in the ear electrical stimulation remain to be established.

Aims- The aim of the study is to compare different stimulation conditions and explain further the mechanism in which ES influences tinnitus and the auditory system.

Methods- The study will comprise 90 adult patients suffering from subjective tinnitus, divided equally into two groups: experimental (treated with ear ES), and a placebo group (sham ES).

Before the beginning of the therapy, patients will undergo ENT examination and hearing tests. ES will be performed with the use of a prototype device. The active, stimulating probe will be immersed inside external ear canal, filled with 0.9 % saline solution. The passive electrode will be placed on the forehead after skin abrasion. The two electrodes will be placed to obtain the transmission of the current throughout the hypothetical plane (longitudinal axis) of cochlea. Alternating current will be delivered via the active electrode to the effected ear. 10 E.S. session will be conducted every working day will be entire treatment.

Different stimulation conditions will be explored. A wide band stimulus will be used. The exact stimulating frequency spectrum will be adapted according to e.g. the sound evoking residual inhibition, the spectrum of the impaired hearing or a whole human hearing spectrum will be stimulated. Furthermore, different ES duration will be analyzed (5 min. vs 10 min).

In order to further explain the mechanism how ear ES influence the auditory system (thus tinnitus) additional audiometric measurements (otoacoustic emission, auditory brainstem responses) and electroencephalography will be performed.

Expected Result- Based on the comparison of the different stimulating conditions it is expected to conclude about the optimal parameters for ear ES in tinnitus treatment. Furthermore, performing complex audiometric tests together with electroencephalography registration, it is expected to get closer to the explanation of the mechanism in which the ear ES influences tinnitus and the auditory system

Conclusion- Based on this study results' analysis, we expect to be able to give some recommendations about the parameters for ear electrical stimulation as well as recommend these findings for clinical management of this symptom.

ID: 265

Abstract Submissions

Keywords: tinnitus

Alienation, burden and Tinnitus: Unspecified group effect of specialized cognitive behavioral therapy for tinnitus

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Background: tinnitus, commonly described as a ringing in the ear, is estimated to affect over 70 million people in Europe alone. While tinnitus is a harmless experience for most, a small portion of the population suffers from chronic distressing tinnitus with debilitating results. It is not uncommon among the more severely affected tinnitus patients to experience suicidal ideation. In similar chronic psychosomatic disabilities, health-related absenteeism, social isolation or early retirement, are considered to foster perceptions of alienation and burdensomeness which give rise to suicidal ideation (Joiner, & Silva, 2012). While no pharmacological or surgical cure for tinnitus currently exists, cognitive behavioral treatment for tinnitus (CBT4T), a multidisciplinary stepped care approach, has been proven to be an effective treatment in reducing tinnitus related disability (Cima et al., 2012). This intervention is mostly conducted in groups and it is hypothesized that the unspecified group effect reduces perceptions of alienation and burdensomeness in chronic tinnitus patients, and might therefore decrease suicidal ideation.

Method: we propose to examine the effects of group treatment (component "C"), compared to individual treatment (component "B"), and no-treatment (component "A"), within a sequential replicated single-case experimental design (SCED), employing a multiple-baseline ABC-scheme. This study design allows for participants to act as their own control while also making it possible to exclude external factors as an explanation for observed changes in the dependent variables. Importantly for strengthening the internal validity of the study, start dates of the intervention components will be randomly determined. Repeated observations of the tinnitus related variables (e.g. severity, alienation, burdensomeness, stigma, suicidal ideation) will be collected applying ecological momentary assessment methods. Data will be analyzed using randomization tests, visual analytical methods, and effect sizes will be calculated.

Results and discussion: the repeated assessment of perceived severity, alienation, burdensomeness, stigma, suicidal ideation and other tinnitus-relevant variables, will provide a large ecologically valid data-set. This way, the timing and extent of the intervention effects that occur will be revealed. Results from this study could inform decisions regarding the method of delivering (group vs individual) CBT based interventions, likely to be more effective for specific tinnitus patient-groups.

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ID: 266 / Session 3: 5

Abstract Submissions

Keywords: Guidelines for Diagnostics

Multidisciplinary European Guideline for Tinnitus: Diagnostics, Assessment and Treatment

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Multidisciplinary European Guideline for Tinnitus: Diagnostics, Assessment and Treatment

ID: 268

Abstract Submissions

Keywords: Meniere's disease

Genetic Contribution to Chronic Tinnitus in Patients with Meniere's Disease Tinnitus Extreme Phenotype

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Meniere Disease (MD) is an inner ear disorder that is characterised by episodes of vertigo, sensorineural hearing loss, tinnitus and aural fullness. Vertigo is considered to be the initial symptom whereas tinnitus is described as the most troublesome symptom by most of the MD patients. MD can affect one or both ears (bilateral MD), as well as sporadic or familial. Meniere Disease Consortium has defined five clinical subgroups of patients under unilateral and bilateral MD. Due to this clinical heterogeneity, it is difficult to investigate the molecular bases in these patients. One popular approach could be to select only those individuals who have a severe set of clinical symptoms known as Extreme Phenotype (EP).

We have defined Tinnitus Extreme Phenotype (TEP) in patients who show an early onset (before 30 years old) and have a fast progression of hearing loss and vertigo with persistent and disabling tinnitus (<10 years). TEP may show an enrichment of rare genetic variants that usually occur at low frequency in population but it may play an important role in these patients. The basic objective of this project is the Identification of novel and ultra-rare mutations in MD patients.

The study will be carried out by performing a detailed clinical phenotyping of the patients to select individuals with MD - Tinnitus Extreme Phenotype (MD-TEP). We will conduct target sequencing and whole exome sequencing (WES) to search for rare variants. These results will generate VCF files consisting of 50.000 variants per file. Files will be processed by quality controls, annotated and filtered by using a cluster node. In order to find out rare variants and to cluster it various techniques of machine learning, data mining and statistical analysis will be considered. Analysis of these variants will be performed in MD patients with or without tinnitus to identify driver genes in tinnitus generation. The expected outcome of this research would be the identification of relevant genes associated with the tinnitus phenotype in MD. Finally, both results will be merged to generate molecular network and signalling pathways involved in tinnitus.

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ID: 269

Abstract Submissions

Keywords: cochlear implants

Improving Cochlear Implantation as a Treatment for Incapacitating Tinnitus in Single Sided Deafness

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Background: Tinnitus can be described as a symptom that can occur due to multiple factors. Hearing loss is one of the major reasons for tinnitus development. Since the problem of tinnitus is of heterogeneous in nature, treatments comprise multiple approaches. Cochlear implantation represents a successful electrical stimulation reduces the tinnitus burden of the affected patients especially in the situation of single sided deafness [1]. Still there are issues remain in recommending cochlear implants (CI) for tinnitus patients due to lack of evidence, cost, risk, strong parameters for outcome measurements, patient selection criteria [2-5] and preference. This project aims to address those issues and to improve CI as a viable treatment option for patients with incapacitating tinnitus. Further, improvements in the cochlear implant device might lead to a fully implantable medical device with better acceptance [6].

Objectives:

1. Literature review of the previously published research in cochlear implantation for single sided deafness to classify the indicators used and analyze their positive and negative outcomes.
2. Identify the impact on the clinical community to consider cochlear implantation as a promising treatment for tinnitus patients with single sided deafness.
3. Further research on developing a fully implantable CI system.

Conclusions:

Cochlear implantation is one of the most promising treatment options for tinnitus patients with underlying some form of a hearing loss. Due to the heterogeneity of the causes for the tinnitus, it is important to identify clearly, which subgroup of patients will benefit through cochlear implantation. Because of the remaining hearing on the contralateral ear, the stigma of a visible auditory prosthesis is unacceptable for a certain subgroup of patients. The development of a fully implantable CI system might extend the number of candidates with that specific indication.

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Abstract Submissions

Keywords: Delphi, MRI, Imaging

Consensus on MRI studies in tinnitus: a TINNET Delphi Study

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Aim: To identify clinical and technical items that are critically important to report when publishing research on tinnitus using Magnetic Resonance Imaging (MRI).

Methods: A Delphi study was conducted in a three-step procedure, with pre-defined criteria for consensus. (1) Fifty-one tinnitus researchers completed an online questionnaire to identify which items should be included in a scientific report on an MRI tinnitus study. (2) A second survey was sent out soon after that and completed by 42 scientists. This second survey enclosed feedback on the first-round outcome according to Delphi techniques. (3) After these two rounds, items that did not reach consensus were discussed in an expert meeting including 10 participants.

Results: After round 2, consensus was reached for 19 items. The expert meeting added 4 more items to the list.

Conclusion: The three-step Delphi survey allowed us to identify items that are critically important to describe when reporting MRI tinnitus studies, thus providing a basis for improved comparability of future MRI tinnitus studies.

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Abstract Submissions

Keywords: hemorheological investigation, hamostatic investigation

The role of hemorheological and haemostatic changes during Tinnitus of central origin

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Introduction: Ear tinnitus is a disorder of peripheral or central origin which is characterized by the perception of noise in the auditory analyser in the absence of any objective or physical source of sound. Tinnitus originating from the peripheral part of the auditory analyser mainly manifests in the pathology of middle ear. Thanks to the advances of otosurgery, we can now reduce the intensity of tinnitus in these patients if not sometimes fully eradicate it. According to common decree, tinnitus of central origin is the result of disbalance between excitation and inhibition processes, more precisely, hyperexcitation and over-inhibition of certain parts of the auditory analyser. However, to date, it is still unclear as to why there are patients who develop tinnitus and patients who don't, regardless of the degree of hearing loss. Tinnitus in the absence of auditory analyser pathology holds great interest, specifically the neurogenic causes and neuronal mechanisms that are worth being further investigated into.

Methods and Materials: A group of 58 adults, who only complained of tinnitus - was investigated. A thorough complex audiological investigation which included otomicroscopy, tuning fork testing, pure tone audiometry, impedance audiometry (tympanometry, acoustic reflex testing) was conducted.

Results: Otomicroscopic, tuning fork and pure tone audiometric test results were within normal range. Tympanometry results showed A type wave for all participants, whereas during the contralateral stimulation of acoustic reflexes of both ears, some changes were recorded. These changes were observed in the configuration and amplitude aspects of the test. After a thorough clinico-audiological investigation, a decrease of contralateral acoustic reflex threshold was determined in all of the participants. Taking into consideration the contralateral acoustic reflex pathway, we can presume based on these data, that vascular or metabolic dysfunction in the brainstem may lead to the central genesis of tinnitus. This presumption leads us to conduct hemorheological and haemostatic investigations which in turn shed light on substantial changes.

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Abstract Submissions

Keywords: Data Visualization

HOLOVIEW: Exploring Patient Data in Mixed Reality

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Over the last years, data from tinnitus patient has been collected in the project TrackYourTinnitus. This data set is high-dimensional and therefore challenging for visual data analytics task. We visualize three dimensions of the tinnitus record using a mixed- reality approach, which projects the data as a hologram into the real world. The developed prototype tackles three problems of visual analytics. First, the detection of correlation between dimensions is simplified by highlighting the relations between the diagram access

and visually displaying the correlation coefficient. Second, an outlier detection method reveals unusual data points and, third, a clustering approach allows the recognition of related data points. The performance of the prototype can be controlled by subsampling the dataset in order to receive different types of resolutions.

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Abstract Submissions

Keywords: data analysis, precise medicine, individualized treatment

Bayesian Inference for Treatment Outcomes in Tinnitus

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Introduction

The Tinnitus Hub (<https://www.tinnitushub.com/>) is a social enterprise dedicated to help individuals with tinnitus. It does so by providing tools and services that promotes awareness and knowledge about the disorder. The Tinnitus Hub Survey (THS) is a digital platform in which a large number of tinnitus bearers are invited to answer to questions about their tinnitus. Crowdsensing techniques have shown to be a powerful resource in a wide range of fields; in the context of tinnitus it could lead to novel insights about coping strategies adopted by those affected by the disorder. More specifically, the large data from the THS could be modelled with Bayesian Inference in order to make predictions of optimal treatments for patients based on their medical history. In other words, the combination of crowdsensing technology and Bayesian Inference to be applied in this project could be a venue to deliver personalized treatment to tinnitus patients.

Objective

To investigate whether the outcome of a given treatment (i.e., success, no effect, or failure) can be used as a prior to predict the successfulness of other tinnitus treatments.

Methods

Participants of the study received through a mobile app a survey with anamnestic questions, including previous treatments. Treatments that were successful in reducing tinnitus distress will then be used as priors in Bayesian model in order to predict other treatments likely to be beneficial to patients.