

ANNUAL TINNITUS RESEARCH REVIEW 2016

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British Tinnitus
Association

Editors

David Baguley & Nic Wray

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DR DAVID BAGULEY

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David Baguley worked for many years as Head of Service: Audiology / Hearing Implants at Cambridge University Hospitals, and is moving to a new post as Professor of Hearing Sciences at Nottingham University and Deputy Director of the Nottingham Biomedical Research Unit in Hearing in Autumn 2016. He has over 150 peer-review publications, and a PhD on the subject of tinnitus from the University of Cambridge [2005]. He has co-authored several books, including a popular self help book: *Living with tinnitus and hyperacusis* [McKenna, Baguley and McFerran, 2010, Sheldon Press]. He has recently edited the book *Tinnitus: Clinical and Research Perspectives* with Prof Marc Fagelson [Plural, 2016]. In 2006 David received an International Award in Hearing from the American Academy of Audiology, and has twice been awarded the Shapiro Prize from the British Tinnitus Association for tinnitus research [2005, 2008]. David is the current President of the British Tinnitus Association.

INTRODUCTION

Dr David Baguley

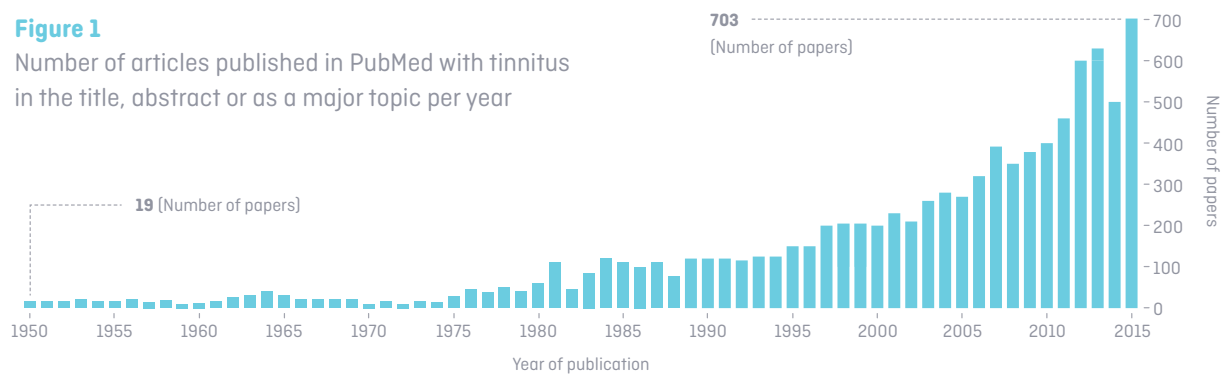
If the understanding and treatment of tinnitus is to improve, a vibrant and innovative field of research is needed, exploring new insights into mechanisms of tinnitus, associated impact, and interventions that both reduce tinnitus perception and the associated distress. Over the years the British Tinnitus Association (BTA) has monitored tinnitus research with substantial interest, often noting shortcomings in the breadth, depth, quality, and relevance of the studies undertaken. In 2003, the BTA Professional Advisers' Committee formulated a vision of tinnitus research in the *International Journal of Audiology* [1], imploring research colleagues to undertake well designed collaborative, multidisciplinary and translational tinnitus research, and since that time have been involved in funding many such projects.

Over time the number of tinnitus research projects published in scientific journals has risen year by year ([Figure 1](#)). This gives rise to a new problem, that of busy clinicians and researchers keeping up with a field where about 50 tinnitus research papers are published each month, and separating the wheat from the chaff.

In this present publication, the first of a planned yearly series, the BTA have commissioned experts in tinnitus to review relevant research published in 2015, with the aim of summarising the highest quality and most relevant papers, giving both professional and lay readers an overview of the themes and developments in the field. The hope is that this will encourage and inform those clinicians dealing with people with troublesome tinnitus, and inspire further research to be undertaken, building upon the new knowledge described herein. Each writer has taken a specific theme in research to review, and whilst there is some overlap, the intention was to have an in depth consideration of the new knowledge regarding tinnitus, and where that takes us in understanding and developing new and effective treatments. Dr Magda Sereda, the BTA Head of Research, opens play with an overview of the research presently funded by the BTA, indicating both the wide scope of these projects, and also the substantial commitment of the BTA in funding research. Dr Roland Schaette is based at the Ear Institute in London, and has reviewed publications considering the mechanisms of tinnitus, indicating that significant progress is being made in this area. Research into the impact of tinnitus is surveyed by Dr Elizabeth Marks, a gifted Clinical Psychologist

Figure 1

Number of articles published in PubMed with tinnitus in the title, abstract or as a major topic per year



who works at the Royal National Throat Nose and Ear Hospital in London, with Dr Laurence McKenna. Tinnitus impacts people in varied and sometimes subtle ways, and Dr Marks navigates the research in this field with an eye to clinical implications.

The questions of “How can people with tinnitus best help themselves?” and “Are any of the new technologies being introduced for tinnitus of proven benefit and minimal harm?” are addressed by Dr Derek Hoare of the NIHR Biomedical Research Unit at the University of Nottingham. Whilst all in the field earnestly desire a breakthrough, patients and professionals alike, we must balance this enthusiasm with a diligent and careful evaluation of benefit, and of possible harm, so that new approaches can be safely and effectively applied. Reading this article by Dr Hoare will draw the reader into a deeper understanding of this area.

In the last few years the increased interest into drug treatment of tinnitus has been very welcome. Writing from his perspective as both a busy Ear Nose and Throat Consultant and tinnitus researcher, Mr Don McFerran (Colchester University Hospitals) reviews the research literature regarding the pharmacological treatment of tinnitus, noting some developments that need further investigation.

Another area of increased interest is that of tinnitus in childhood. Research in this area has gone from a smattering of research papers scattered in various scientific journals to a major theme in the field, and those of us who know a child with tinnitus, or treat them in our clinics, will be delighted with this development. Dr Veronica Kennedy has a long-standing interest in this area, and the recent British Society of Audiology guidelines for tinnitus treatment in children [2], with which she was highly involved, have been applauded internationally. Dr Kennedy reviews the research literature, which holds many ideas of interest.

In any overview of research literature there is a danger of self-congratulation: “look at

what everyone has achieved!” It is important that we avoid this in tinnitus, as the present lack of clinically (and cost) effective treatments is satisfactory to no one. David Stockdale, Chief Executive of the BTA, writes about “what the tinnitus community wants from research”, and his timely and wise insights should be a deep encouragement to professionals and patients alike.

Finally, two personal perspectives are interspersed within this review. Lucy Handscomb is a Hearing Therapist, working at the Ear Institute in London, and who is undertaking a PhD on the topic of tinnitus at the University of Nottingham. This model of experienced audiology clinicians turning towards research holds great potential. Dr Mike Mulheran is an experienced auditory researcher at the University of Leicester, and his group have long held tinnitus as an area of interest and research activity. These interviews glean useful insights into the research community, and the personal commitment shown by many tinnitus researchers.

It is my hope that many will be inspired and excited by reading this expert and reflective summary of recent tinnitus research. There is a clear need for more research, and research of better quality, but on that journey it is important to pause and reflect on what is been undertaken and achieved, and where our trajectory may take us. I'd like to thank the BTA for funding and producing this publication for the whole tinnitus community, and Nic Wray my co-editor for her diligent hard work and friendly partnership. Thank you also to all the authors, to the tinnitus research community, and to the many individuals who generously support tinnitus research.

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DR MAGDALENA SEREDA
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Dr Sereda joined the NIHR Nottingham Hearing BRU in February 2012 as a Research Fellow. Her research focuses on assessing the efficacy of hearing aid provision for people with tinnitus and addressing current lack of research evidence on the specific benefits of hearing aids for tinnitus and standard treatment pathways. Magdalena was appointed to the post of Senior Research Fellow - British Tinnitus Association Head of Research in July 2015.

Magdalena graduated from Warsaw University in Biology and obtained a PhD in Neuropsychology from the Institute of Experimental Biology in Warsaw, Poland. She then accepted a Guest Researcher position at Humboldt University in Berlin. In 2007 she moved to Nottingham to work as a Career Development Fellow at the Medical Research Council Institute of Hearing Research (MRC IHR).

THE BRITISH TINNITUS ASSOCIATION RESEARCH PROGRAMME

Dr Magdalena Sereda

The British Tinnitus Association (BTA) Research Strategy concentrates on the areas of tinnitus research that are overlooked or not a priority for other organisations but which have been identified as important for people with tinnitus. Patients and clinicians identified the current priorities during the James Lind Alliance (JLA) Tinnitus Priority Setting Partnership exercise [1][2]. This article provides an overview of current BTA funded research and possible future research directions.

The four areas around which BTA supported research concentrates are:

- 1 **Mechanisms of tinnitus/identifying potential therapeutic targets**
- 2 **Existing and novel practice/treatment**
- 3 **Prevention**
- 4 **Population/demographic/epidemiology/economic studies.**

Figure 1

Magda Sereda at work at the Nottingham Hearing BRU



Mechanisms of tinnitus/identifying potential therapeutic targets

Currently there is no effective pharmaceutical treatment for tinnitus. Researchers at the University of Leicester are looking at molecular mechanisms of tinnitus to identify new therapeutic target for pharmacological therapy. Dr Martine Hamann is investigating the role of microRNAs (recently discovered small molecules present in animal and human cells) in tinnitus. Micro RNAs are involved in many biological processes and recent studies suggest that they contribute to hearing loss. Dr Hamann's plan is to firstly confirm the role of microRNAs in tinnitus in animal model and then test the possibility of alleviation of tinnitus through pharmacological treatment, targeting the level of those molecules.

Existing and novel practice/treatment

Research studies funded within this theme span a wide range of approaches to the management of tinnitus, from testing or improving options currently available within the NHS, to novel treatments and therapies. Other projects look at the current clinical practice and potential areas for improvement as well as develop tools for assessing efficacy of different management options in clinical trials.

In July 2015, the BTA funded a four-year Head of Research post for Dr Magdalena Sereda at NIHR Nottingham Hearing Biomedical Research Unit (BRU). Dr Sereda's research programme will focus on National Health Service (NHS) contracted sound therapy options ie hearing aids and combination hearing aids for tinnitus. The programme comprises studies to:

- 1 Identify current clinical practice regarding sound therapy for tinnitus (Delphi reviews, surveys, focus groups)
- 2 Define the current state of knowledge and quality of the research evidence behind treatment options with the aim to identify gaps in current knowledge and topics where evidence needs to be provided (scoping and systematic reviews)
- 3 Address those gaps by designing and conducting high quality clinical trials, including Randomised Controlled Trials (RCTs)
- 4 Disseminate results to inform and influence clinical practice and guidelines, and to engage the general public.

The projects within the programme include designing a UK-wide clinical trial looking at the effectiveness of hearing aids for people with tinnitus and hearing loss and exploring current UK clinical practice around provision of combination hearing aids (amplification and sound generation within one device) with the goal of developing professional guidelines around candidacy and fitting of combination aids. The programme was designed around JLA priority questions including those asking about the most effective digital hearing aid to manage tinnitus as well as alternatives to usual care.

In a BTA-funded PhD project, Lucy Handscomb at the University of Nottingham is assessing a new cognitive model of tinnitus distress and its applications to patient management. Patient reported outcome measures were used to assess such elements as tinnitus distress, anxiety, coping, insomnia, depression, and general wellbeing and fit to the model will be tested. The ultimate goal of the project is to evaluate the interplay between current practice, patient priorities and components of the model to improve patient care.

Psychological therapies might be a successful management option for those people suffering from tinnitus. A question related to psychological therapies in tinnitus management was one of the JLA priority questions. Among psychological approaches, therapist led Cognitive Behavioural Therapy (CBT) has good evidence of effectiveness in managing tinnitus distress. However, other psychological approaches are not as well evaluated. Dr Laurence McKenna and Dr Liz Marks from University College London Hospitals (UCLH) assessed the effectiveness of Mindfulness Behavioural Cognitive Therapy (MBCT) in managing tinnitus. MBCT involves teaching meditation techniques - usually in a group format - over a course of eight weeks, paying careful attention to one's physical, emotional and cognitive experiences. MBCT has been successfully applied to managing depression and chronic pain, but there is no evidence for its effectiveness for tinnitus. The use of MBCT in the treatment of tinnitus may offer a new approach benefiting both patients and clinicians. The study is now complete and the findings are being assessed and analysed.

About 70% of people with tinnitus complain of sleep disturbance [3] [4], and poor sleep might contribute to tinnitus distress. Currently there is little research addressing this common problem in people with tinnitus and investigating possible sleep management options. There is a strong evidence base that CBT

**Figure 2**

Man undergoing Eye Movement Desensitization and Reprocessing therapy

for insomnia (CBTi) is an effective treatment for sleep disturbance both as a primary problem and when co-morbid with other health problems. Dr Laurence McKenna is now looking at the benefits of CBTi in people with tinnitus and comparing it to standard audiological rehabilitation management of tinnitus related insomnia (sleep hygiene).

Dr Sally Erskine from Norfolk and Norwich Teaching Hospitals NHS Foundation Trust is exploring the application of Eye Movement Desensitisation and Reprocessing (EMDR) to treat tinnitus (Figure 2). Eye movement therapies have previously been used for treating phantom sensations, such as phantom limb pain - the sensation of pain in an amputated limb [5] [6]. Tinnitus may be considered a phantom auditory sensation so EMDR is a plausible treatment to test. The study will provide information on the feasibility, acceptability and outcomes of EMDR in patients with tinnitus that will inform the development of a larger study looking at effectiveness of this approach.

In response to one of the JLA priority questions, the BTA commissioned The Ear Foundation to investigate experiences of people with different degrees of hearing loss and tinnitus including those with severe/profound hearing loss. An online questionnaire and interviews explored peoples' experiences with tinnitus, its impact and management. A large group of 1432 adults responded to the survey, included 286 with severe/profound hearing losses. A number of recommendations for clinical practice have been formulated based on the results of the study [7] and a full report can be accessed at www.tinnitus.org.uk/tef.

Dr Helen Pryce from Aston University is conducting a project on shared decision making ie involving patients in the decisions about their treatment when there is more than one option possible in tinnitus care. Shared decision making is a principle of healthcare provision highlighted by the NHS mandate; it also facilitates better outcomes and satisfaction with care. The project aims to develop 'Option Grids', which are one-page evidence-based summaries of available options, including trade-offs and frequently asked questions. The next step would be to trial the grid in a larger scale randomised controlled trial.

Last year saw the development of Practice Guidance by the British Society of Audiology (BSA) on tinnitus in children and teenagers [8]. There is limited research on tinnitus in children, concentrating mostly around prevalence and co-morbidity, with very little information on management. Two projects funded by the BTA will concentrate on different aspects of tinnitus in children. Dr Derek Hoare from NIHR Nottingham Hearing BRU will be developing a clinical questionnaire to measure tinnitus in children. During the three-year project, he will gather perspectives from children with tinnitus, their parents and clinicians, as well as from existing information, to create a questionnaire to measure problems experienced by children. Dr Sam Lear from Sheffield Children's Hospital is exploring the relationship between tinnitus, hyperacusis and anxiety in children.

Appropriate outcome measures are of major importance in conducting clinical trials. However, there is a considerable variability in outcome measures (usually questionnaires) used in tinnitus research. Two studies funded by the BTA look at the problem of outcome measures from two different perspectives.

In 2014, the European Cooperation in Science and Technology programme (COST) funded the European tinnitus research network TINNET, with a working group looking at development of standards for outcome measurements in clinical trials. Within that working group, a pan-European initiative called Core Outcome Measures in Tinnitus (COMiT) emerged with an aim to develop a 'core outcome set' to be used in tinnitus trials worldwide. This initiative is led by NIHR Nottingham Hearing BRU and Dr Adele Horobin is contributing by looking to incorporate the patient's voice in agreeing which aspects of tinnitus are important to measure. This BTA funded project will use an established method of gaining agreement between different people to achieve the first stage in identifying and agreeing on a core outcome set for tinnitus.

Dr James Jackson from Leeds Trinity University is exploring the potential to use the Cortisol Awakening Response (CAR) as a biomarker of distress in people with tinnitus. Cortisol is a stress hormone that regulates the release of sugars into the blood. CAR is a well described and consistent phenomenon and any deviations from the usual profile might indicate that the body is under stress. Dr Jackson is investigating if tinnitus distress is associated with an impaired stress response and if it can be used as an objective outcome measure of treatment effectiveness alongside questionnaires.

“The long-term goal is to develop an intervention that will improve young adults’ attitudes and behaviours, and ultimately reduce the incidence of tinnitus and/or hearing problems.”

Prevention

In line with the new tinnitus prevention campaign Plug'em [9] aimed at raising awareness in younger people of the need to wear earplugs at clubs, gigs & festivals, the BTA is supporting Dr Abby McCormack from the NIHR Nottingham Hearing BRU to explore young people's attitudes to loud music. A series of focus groups will investigate young adults attitudes, beliefs and behaviours concerned with tinnitus, hearing problems and leisure noise. The long-term goal is to develop an intervention that will improve young adults' attitudes and behaviours, and ultimately reduce the incidence of tinnitus and/or hearing problems in this population.

Population/demographic/epidemiology /economic studies

A questionnaire study by Dr James Jackson from Leeds Trinity University is investigating the association between personality and individual differences on tinnitus distress. Whilst most people habituate to their tinnitus over time, many do not. Understanding the relationship between personality and tinnitus distress might contribute to understanding why some treatments and strategies work for some people, but not others.

The BTA commissioned Matrix Consulting to undertake a project to quantify the cost of current tinnitus therapies available within the NHS. The findings have been appraised by Dr Derek Hoare and Mr Don McFerran. The study provides a benchmark for the cost-effectiveness evaluation of new tinnitus therapies, and is being reviewed for publication at the time of writing.

Recent years have seen an increase in tinnitus research in the UK with the BTA funding a variety of projects across range of topics. As a result of that research activity, we are looking forward to the increased representation of UK tinnitus research published in scientific journals.

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Dr Roland Schaette leads the tinnitus research program at the UCL Ear Institute, with the goal of understanding how tinnitus is triggered, how it manifests itself in the brain, and how pathological nerve cell activity could be re-normalised in order to turn off the phantom sound. Dr Schaette started his research on tinnitus during his PhD at Humboldt University Berlin (2003-2007). In 2008, he moved to London to take on the position of BTA Senior Research Associate at the UCL Ear Institute. In 2013, he became lecturer for tinnitus research at the UCL Ear Institute.

In his research, Dr Schaette combines measurements in humans, animal studies and computer models. Recent projects have also included investigations in the mechanisms of hyperacusis. He is a member of the Association for Research in Otolaryngology, the American Physiological Society, and the Society for Neuroscience.

MECHANISMS OF TINNITUS

Dr Roland Schaette

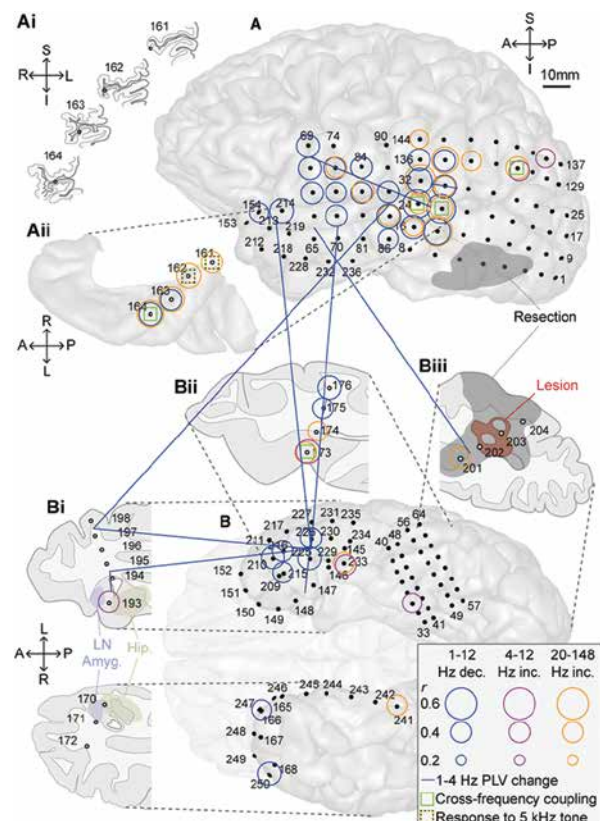
In the past decade, a number of studies have investigated neural correlates of tinnitus in human subjects using Magnetoencephalography (MEG) and Electroencephalography (EEG) recordings. A consistent finding across these studies was an increase in activity in the delta frequency band, whereas results for other frequency bands were more variable [1] [2] [3] [4]. A new study [5] using intracranial recordings in a human patient who had an electrode array implanted as part of his epilepsy treatments has now provided additional, highly detailed insight into these tinnitus-related changes in brain activity (Figure 1).

Figure 1

Oscillatory power and phase coherence changes with tinnitus suppression [5]. © 2015 The Authors.

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The tinnitus was modulated in the patient by presenting stimuli that induced residual inhibition. Tinnitus suppression correlated with decreased delta and theta power in all auditory cortex regions except the primary auditory cortex, and similar tinnitus-correlated changes were seen in large parts of the temporal, parietal, sensorimotor, and limbic cortex. Surprisingly, suppression of tinnitus was also correlated with increases in gamma power, showing exactly the opposite of the anticipated effect. Similarly, alpha power was found to be reduced during suppression, whereas the prevailing theory would have predicted an increase. These findings thus corroborate a role for low-frequency oscillatory activity in the generation of tinnitus, and illustrate a need for more research to understand the changes in other frequency bands.

Potential difficulties in the interpretation of human neuroimaging results are underlined by recent reports [6] that putative “tinnitus networks” in neuronal resting state activity could not be found when tinnitus and control subjects were carefully matched, and that there might be no relation between EEG findings and psychometric or psychoacoustic properties of tinnitus [7]. Thus a certain degree of caution might be warranted, especially when the goal is to measure changes in tinnitus-related neural activity in single subjects to evaluate treatment effects, as has been attempted in recent treatment studies [8] [9].

Animal studies have identified a range of potential mechanisms that could lead to the emergence of neural correlates of tinnitus, but direct comparisons to human data have been difficult. Human studies cannot use invasive methods and thus they yield less detailed results. Part of this problem has been overcome by a recent study [10] that used magnetic resonance spectroscopy to non-invasively quantify the levels of the neurotransmitter GABA in the auditory cortices of tinnitus patients and control subjects. The presence of tinnitus was associated with a significant decrease in GABA levels in the right auditory cortex, suggesting that a reduction in inhibition might be responsible for the emergence of tinnitus, as also reported in animal studies [11].

In the past years, many animal studies on tinnitus have combined behavioural testing for signs of tinnitus with electrophysiological recordings from the brain in order to investigate the neural manifestations of the phantom sounds. Using this approach, two recent studies have

provided new evidence for increased spontaneous firing rates in the auditory brainstem and midbrain as neural correlates of tinnitus. In the dorsal cochlear nucleus (DCN), such neural hyperactivity was only observed in those animals that developed behavioural signs of tinnitus after noise exposure [12]. Apart from increases in spontaneous firing rates, neural synchrony and bursting also correlated with tinnitus [13]. In the inferior colliculus, hyperactivity was firstly observed in animals with behavioural evidence for tinnitus, and secondly decreased with furosemide injections that also reduced behavioural signs for tinnitus [14]. However, another study [15] has reported increased spontaneous firing rates in the inferior colliculus of animals with and without behavioural evidence for tinnitus following noise trauma, thus indicating that hyperactivity could also be a simple consequence of hearing loss. To finally resolve these issues, further progress in behavioural testing procedures for tinnitus in animals might be required. All three studies mentioned above used methods based on gap pre-pulse inhibition of acoustic startle, and recent results from applying this test to humans with tinnitus [16] indicate that the interpretation of the results of this test might not be as straightforward as initially believed.

A few years ago, a new approach [17] for using a combination of auditory and vagus nerve stimulation to trigger targeted plasticity in order to abolish tinnitus-related neuronal activity patterns in the brain created a stir. Since then, the proof-of-concept study in an animal model has been followed up by two small-scale studies [18] [19] in humans indicating that the approach can lead to a clinically meaningful reduction of tinnitus. However, since implantation of an electrode is required to deliver the vagus nerve stimulation, it might always remain a last-resort approach for extreme cases where other strategies have failed. Nevertheless, the concept of altering pathological brain activity through specifically targeted plasticity has a lot of appeal, as it promises to eradicate the basis for the tinnitus itself, instead of changing the patient’s reaction to it. It is therefore quite promising to see that another, less invasive approach, has been developed in the lab of Susan Shore, based on a combination of somatosensory and auditory stimulation [20] (Figure 2). The auditory system also receives somatosensory information, for example through a projection from the trigeminal nuclei to the dorsal cochlear nucleus, and the strength of these projections can be altered through

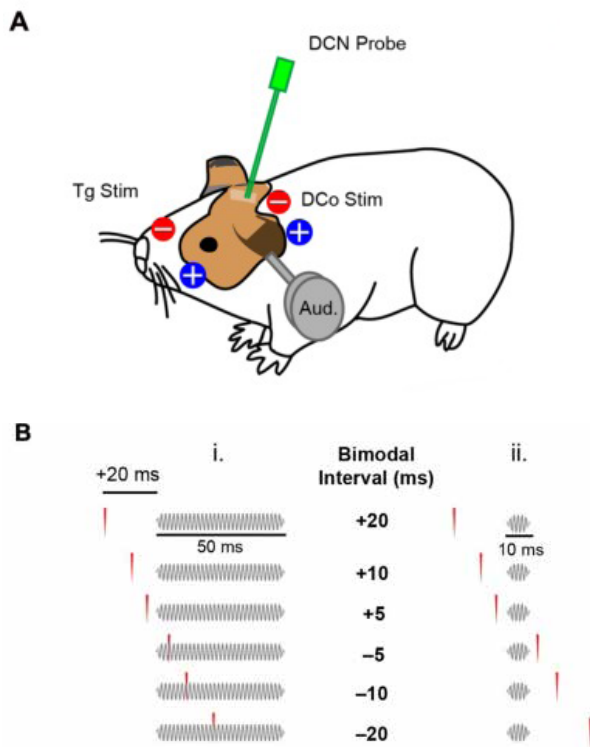


Figure 2

Transcutaneous electrical stimulation and bimodal pairing protocol [20] © 2015 Wu, Martel and Shore. Used under the terms of the CC BY 4.0 license (<http://creativecommons.org/licenses/by/4.0/>).

plasticity in an activity-dependent fashion. For tinnitus, the seminal finding [21] was that the strength of these projections to the DCN was altered in neurons showing increased spontaneous firing rates after noise trauma, suggesting a relation to tinnitus. Specific details of the plasticity mechanisms were further investigated in a follow-up study [22], which revealed that the strength of the connections could be up- or down-regulated when auditory and somatosensory stimulation were applied in a specific temporal order on a time scale of tens of milliseconds. Moreover, behavioural experiments strengthened the link to tinnitus [22] [23], revealing that the plasticity mechanisms were specifically altered in animals with tinnitus [22] [24]. Moreover, further experiments showed that similar effects could also be observed in the auditory cortex [25]. All these experiments were carried out *in vivo*, thus demonstrating the potential for using this approach to influence tinnitus.

At the Midwinter meeting of the Association for Research in Otolaryngology in February 2016, the latest results were presented by Susan Shore and her team demonstrating that behavioural and neural signs of tinnitus in animals could be reduced with this treatment, and it was hinted that pilot studies in humans are currently under way.

While a good case can be made for hearing loss as a trigger for tinnitus (reviewed for example by Roland Schaette [26]), the degree of hearing loss in tinnitus patients is nevertheless very variable [27]. It has been difficult to establish a close relation between psychoacoustic properties of tinnitus and features of the audiogram [28] [29] [30]. A recent animal study [31] has provided some interesting food for thought related to this problem: Kiefer and colleagues investigated the effects of different severities of noise trauma in a gerbil model. They found that - surprisingly - the less severe exposure that only caused temporary, but not permanent, hearing threshold shift, had a higher likelihood of causing tinnitus in the animals. These results illustrate that the relationship between cochlear damage and tinnitus might be quite heterogeneous and variable, with some damage configurations being more likely to induce tinnitus than others. The simple notion that more hearing loss will create tinnitus more often and lead to more severe symptoms thus might not be true, at least not in gerbils.

It is often suspected that tinnitus and hyperacusis might be caused by similar processes, with speculations revolving around increased neuronal gain in the central auditory system [32]. Around 40% of tinnitus patients also report sound sensitivity problems [33], and about 85% of hyperacusis patients also perceive tinnitus [34] [35]. However, our understanding of the mechanisms of hyperacusis is still in its infancy. This is especially true for 'pain hyperacusis', the feeling of intense pain in the ear that is elicited through sound at relatively moderate intensities, which is reported by a substantial fraction of patients with sound sensitivity. Recent results from two different research groups have now provided a first insight into the potential physiological basis for such a sensation of pain from sound. The first study [36] has provided direct evidence for type II auditory nerve fibres as damage sensors in the ear. Type II fibres are the thin, unmyelinated fibres that contact

40%

Around 40% of tinnitus patients report sound sensitivity problems.

the outer hair cells (OHCs) and make up about 5% of all auditory nerve fibres (ANFs), and their function had remained largely obscure up to now. In a technical tour de force, Liu *et al* managed to record from type II ANFs in excised cochleas, and demonstrated that the fibres were selectively activated when OHCs were mechanically damaged. In the second study [37], it was demonstrated that sound presentation at damaging levels (120 dB SPL) leads to an activation of neurons in the cochlear nucleus via projections from type II ANFs *in vivo*. Taken together, these studies provide strong evidence that type II ANFs act as a damage sensor for the auditory periphery, and that their signal activates specific populations of neurons in the central auditory system. These results demonstrate for the first time that there is a specific pathway in the auditory system that reports peripheral damage, which thus constitutes a prime candidate for the mechanism that leads to a perception of sound-induced pain. However, it has so far remained unclear which pathological changes might lead to the pathway getting activated at relatively moderate sound levels, as experienced by patients with pain hyperacusis.

85%

Around 85% of hyperacusis patients also perceive tinnitus.

Increases in neural response gain as a potential mechanism for tinnitus have been investigated in a computer modelling study [38]. The results showed that some features of hyperacusis can be explained by an increase in non-linear gain in the central auditory system, but the model also indicated that a single gain mechanism might not be sufficient to explain both tinnitus and hyperacusis. Moreover, when the average level of hearing loss is compared in tinnitus [27] and hyperacusis patients [34] [35], the degree of hearing loss turns out to be substantially higher in the tinnitus group. Together with the indications of a specific auditory pain pathway that might be involved in pain hyperacusis, it therefore appears that each condition might have its own core mechanism. However, the presence of hyperacusis could facilitate detecting tinnitus, due to increased attention and vigilance to sound. This could explain why hyperacusis often precedes tinnitus, so much so that it had been proposed that hyperacusis might be a pre-tinnitus state, and why almost everyone with hyperacusis also perceives tinnitus, whereas the majority of tinnitus patients do not experience hyperacusis.

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THE IMPACT OF TINNITUS

Dr Elizabeth Marks

Around 600,000 people in the UK have tinnitus that has a severe impact on their day-to-day life [1]. This impact can be on one or more of attention and memory, sleep, mood, and can lead to depression, anxiety, stress and insomnia. It can also have a negative effect on personal relationships and employment. As tinnitus is an invisible condition, the impact that it can have is often underestimated, and research in this area is key to improving quality of life in people with tinnitus.

Introduction

A database search conducted in Scopus and PubMed using the search term 'tinnitus' within the title, abstract and key word, for items published in 2015 retrieved 979 articles from Scopus and 688 from PubMed. However, after closer inspection and evaluation, a total of 39 articles were found to refer to the topic of the impact of tinnitus and have been included in this review.

Impact associated with attention and memory

Amaral & Langers [2] used an experimental functional Magnetic Resonance Imaging (fMRI) paradigm to assess the impact of tinnitus on attention and other executive functions (the selection of relevant and inhibition of irrelevant visual and auditory information). Distracting stimuli were presented to participants with tinnitus (n=13) and healthy controls (n=21). Tasks included a 1-back task (attending to a stream of stimuli (auditory or visual), and comparing consecutive stimuli for equivalence) and an interference task (requiring selection of relevant/inhibition of irrelevant stimuli). Despite involving a task requiring focus and sustained attention, there was no evidence of impaired behavioural outcomes in the tinnitus group. However, performance did decrease with increasing tinnitus severity on the Tinnitus Handicap Inventory (THI) [3]. fMRI found that the tinnitus group showed significantly different neural signals in brain regions usually attributed to attentional control, consistent with previous studies suggesting involvement of brain networks for attention in tinnitus.

Cognitive performance in tinnitus with normal hearing was explored by Waechter & Brännström [4]. A visual Stroop paradigm [5] with 40 participants (20 with

tinnitus and normal hearing, 20 healthy controls) was used, along with audiometric evaluation, Tinnitus Questionnaire (TQ) [6], Hospital Anxiety and Depression Scale (HADS) (Swedish version) [7] and a tinnitus-characteristics interview. On the visual Stroop there were no significant differences in cognitive performance. The study did not include a group of tinnitus patients with hearing loss however, so cannot offer comparisons in terms of the effect of hearing loss on this task. Generalisability is also limited as the Stroop is brief and limited to assessing visual attention.

In a review of the behavioural literature on cognitive performance in tinnitus, Mohamad, Hoare and Hall [8] concluded that limited empirical support exists for tinnitus interfering with executive attention. However, in summary, evidence of impairments in working memory and selective attention is equivocal.

Impact on functioning, Quality of Life (QoL) and daily performance

To see if tinnitus distress is associated with type of tinnitus sensation, Moring *et al* studied 370 participants using an online survey [9]. Tinnitus distress was measured using the THI and TRQ (Tinnitus Reaction Questionnaire) [10], and participants were asked to

briefly describe the character of their tinnitus. Descriptions of tinnitus were analysed with inductive coding, resulting in six descriptors. Results found that type of tinnitus was not associated with levels of distress, but functional distress (sleep, concentration, irritability, work, enjoyment) was significantly higher in multiple tinnitus sensations than simple tinnitus. Multiple tinnitus sensation patients also engaged in more behavioural avoidance. The researchers highlight the importance of categorising types of tinnitus sensation when assessing functional and emotional impact. The study is limited by reliance on self-generated descriptions and a lack of objective diagnostic criteria. There is also the probability of self-selection bias occurring due to recruitment of active members of a tinnitus association.

Cantley *et al* used a retrospective analysis to assess the contribution of audiological factors to risk of acute injury in 8818 maintenance workers from six aluminium manufacturing plants [11]. They found that tinnitus in conjunction with high-frequency hearing loss could be a predictor of injury risk in this environment. There was less evidence for associations between low frequency loss and minor injury risk, and asymmetrical hearing loss did not elevate risk here. The authors argue that tinnitus and high frequency hearing loss can impact on



Figure 1

Emergency ambulance in Brazil. © Ministry of Health, Brazil. Used under the terms of the CC BY 3.0 BR license (<https://creativecommons.org/licenses/by/3.0/br/deed.en>)



Figure 2

Insomnia was reported by 76% of chronic tinnitus patients [18]

communication and hearing, indicating a need for support in such environments. The study is limited by a lack of information about tinnitus severity, use of hearing protection and unrecognised job or plant factors influencing injury risk.

The impact of auditory (and non-auditory) symptoms in 36 ambulance workers in Brazil was reported on by Oliveria *et al* [12] (Figure 1). Via a questionnaire study, tinnitus, sound sensitivity and ear-fullness were found to be the most frequent auditory symptoms. Self-perception of drivers and nursing technicians was associated with hearing loss and tinnitus severity, and the authors therefore concluded that tinnitus could effect work-related performance in ambulance workers.

The effect of tinnitus severity on Quality of Life (QoL) and its association with physical activity was examined by Carpenter-Thompson, McAuley and Husain [13]. An online questionnaire study with 1030 adults (60% completed) assessed tinnitus severity with the TFI (Tinnitus Functional Index) [14] and QoL with the SF-36, a measure of satisfaction with life [15], and additional questions about exercise. Increased activity was associated with significantly greater QoL and reduced tinnitus severity. Tinnitus severity and activity together accounted for variation in the QoL, with physical activity accounting for 0.8% variation in tinnitus severity. They suggest activity in tinnitus plays an important role in QoL, but unfortunately the correlational design means direction of effect cannot be ascertained.

Adoga *et al* explored the impact of tinnitus reported by 49 patients of an otorhinolaryngology department in Nigeria [16]. Scores on the HADS showed depressive symptoms present in 29% of female and 22% of male patients and anxiety symptoms present in 37% of female and 33% of male patients. QoL was reduced in all areas except pain in 69% of the sample. Correlations showed greater tinnitus distress in younger sufferers. The conclusion that tinnitus impacts upon psychological health and health related QoL, is limited by the cross-sectional design and a small sample size limiting generalisability.

An intervention for tinnitus which provided customised sound stimulation during sleep was looked at by Drexler *et al* [17] to see if it could change the impact of tinnitus. The treatment was given to 12 patients and tinnitus intensity and distress were assessed via THI, TRQ and a Visual Analogue Scale (VAS) and QoL. Reductions in tinnitus intensity were associated with

improved QoL, suggesting that tinnitus severity has an impact on QoL.

Impact on sleep

The prevalence and associations between tinnitus, distress and sleep disturbance were explored by Schecklmann *et al* [18] (Figure 2). They used a retrospective analysis of 182 chronic tinnitus patients who completed the TQ and Regensburg Insomnia Scale (RIS) [19]. Insomnia was reported by 76% of patients, and there was a moderate correlation between TQ distress and sleep disturbance ($r=0.558$). The authors discuss that chronic tinnitus and primary insomnia are closely related and could share similar underlying mechanisms affecting sleep quality.

Impact associated with psychological distress

A population-based cohort study of individuals over 50 years in New South Wales was used by Mitchell *et al* to look for associations between self-harm injuries and different physical illnesses [20]. Tinnitus was one of a number of illnesses associated with an increased likelihood of self-harm (as were pain, malignancies and diabetes). This was true even after controlling for mental health conditions, number of comorbidities and substance misuse. This suggests that tinnitus could be a risk factor for self-harm in older people, so targeted screening may be warranted.

A study which explored the association between hearing threshold and mental health was conducted by Wallhäusser-Franke *et al* [21]. Twenty-eight patients with acute tinnitus of less than four weeks duration completed an audiogram and questionnaires of tinnitus distress (short form TQ), tinnitus loudness, sound sensitivity on numeric rating scales. Mental health, personality and somatic severity were measured using the depression, anxiety, somatic and resilience scales of the Patient Health Questionnaire (PHQ) [22]. Measures were repeated at six weeks, three and six months. Tinnitus loudness and distress remained stable but sensitivity to sound decreased over time. Resilience did not predict tinnitus severity at six months. However, depression and hearing loss was associated with later tinnitus loudness, and depression and age was associated with sound sensitivity. The authors conclude that tinnitus severity is stable during the six months after onset. They suggest that psychological distress and hearing impairment are associated with later tinnitus severity. As such, early treatment should probably include hearing aids and screening for depression to identify psychiatric need.

The UK Biobank database has responses to questionnaires from 171,728 UK adults aged 40-69 year. McCormack *et al* used the UK Biobank to look at associations between tinnitus, depression and anxiety - if neuroticism is controlled for - to assess whether neuroticism fully explains such associations [23]. Measures used included questionnaires of symptoms of anxiety and depression, self-reported tinnitus presence and severity, self-reported hearing problems, neuroticism based on the Eysenk Personality Inventory [24], and QoL. General linear modelling was used to assess for strength of associations between these factors. Results showed that people with severe tinnitus were at a greater risk of depression (OR=1.27) and to a lesser extent, of anxiety (OR=1.11) than those without tinnitus, after statistically controlling for neuroticism. The cross-sectional design limits conclusions about the direction of causation, although the finding of these associations in a large sample size support the call for further research into potential mechanisms of depression / anxiety and tinnitus severity. It may suggest that early psychiatric screening and treatment could reduce the risk of later distress.

A summary of previous findings on emotional stress and impact on the auditory system and hence tinnitus was offered by Mazurek *et al* [25]. They offer some clinical examples to illustrate how HPA-axis dysregulation is associated with tinnitus (as in other stress-related illness). Overall the authors discuss that the main issue in the literature is the difficulty in finding direct causal links between stress and tinnitus, and that translational research is required to indirectly measure tinnitus-induced psychological distress in animals.

Gül *et al* explored anxiety sensitivity and psychiatric symptoms in 50 chronic tinnitus patients, compared to 50 healthy controls [26]. Based on self-report questionnaires (Anxiety Sensitivity Index-3 [27], State-Trait Anxiety Inventory [28] and SCL-90-R [29]) they found that the tinnitus group had statistically higher scores on anxiety sensitivity, trait anxiety and on the SCL-90-R. The study suggests that anxiety sensitivity may affect the degree to which tinnitus impacts on a patient, and that chronic tinnitus is associated with psychiatric disorders. Again, the cross-sectional study cannot clearly define the direction of causality.

A review of the literature on tinnitus and anxiety disorders conducted by Pattyn *et al* found a 45%

lifetime prevalence of anxiety disorders reported by tinnitus populations [30]. They also found an overlap in associated brain areas involved in attention, distress and memory, probably related to disturbed HPA-Axis function. Again, they highlight the fact that evidence of comorbidity is not evidence for direction of dysfunction. However comorbidity and overlap in neural correlates of anxiety and tinnitus, suggests that treatment of anxiety could lead to improved (subjective) tinnitus.

Correlations between psychoacoustic and subjective outcome measurements in tinnitus over time were assessed by Rabau *et al* [31]. Thirty-five chronic tinnitus sufferers completed minimal masking level and loudness matching and subjective measures (Tinnitus Impairment Questionnaire [32], TQ and numeric ratings of loudness and annoyance) and again 90 days later, after treatment. Effect sizes were calculated. There were no significant correlations between psychoacoustic and subjective measurements. Subjective measurements were more responsive to change in tinnitus complaint. Thus subjective outcomes should be primary outcomes in clinical settings, as they capture the impact of tinnitus, regardless of audiometric measurements.

Sisler *et al* report on a single case-study of an individual with severe tinnitus in the context of multiple and severe psychiatric comorbidities [33]. Tinnitus was treated with high-dose corticosteroids, at a time when the patient's antipsychotic medication had been recently adjusted. Following corticosteroid treatment the patient attempted suicide, and on recovery cited tinnitus and abdominal pain as contributory factors to the attempt. The original psychiatric medication was reinstated and no further suicidal ideation was reported. The authors discuss the possible severe impact of tinnitus, but the equal importance of concurrent contributory factors including severe and enduring psychiatric illness, changes in medication and glucocorticoid treatment. Previous reports describe glucocorticoid association with increased risk of suicide attempts [34]. This clearly requires careful consideration when treating tinnitus.

Other issues that affect the impact of tinnitus: Seasonal Affective Disorder (SAD).

The point prevalence in 100 chronic tinnitus patients of SAD, anxiety, depression and insomnia was investigated by Kim [35]. 20% of patients met criteria for SAD (suspect and subsyndromal). SAD was significantly

correlated with tinnitus distress on the THI. Levels of anxiety and depression were greater in the SAD group compared to a healthy control group. The author suggests that SAD should be considered when working with tinnitus patients.

Acceptance and negative cognitions

Studies have suggested that the level of tinnitus acceptance may affect the impact it has. Riedl *et al* therefore investigated QoL and distress in chronic tinnitus patients with different levels of acceptance [36]. Based on the Tinnitus Acceptance Questionnaire (German version) [37] participants were placed into two groups of tinnitus acceptance ('low – moderate' and 'moderate – high') and compared. The higher acceptance group reported significantly higher QoL and lower psychological distress. Thus acceptance of tinnitus appears to affect impact on distress and functioning.

Hesser, Bånkestad and Andersson extended this further, by assessing the contribution of acceptance to severity of tinnitus beyond its effect on anxiety and depression [38]. Using a cross-sectional design, 362 participants with tinnitus in an ENT hospital completed questionnaire measures of tinnitus acceptance, severity, anxiety and depression, tinnitus and personal characteristics and audiological problems. Correlational analyses again found tinnitus acceptance to be inversely correlated with anxiety, depression and tinnitus severity. After controlling for patient characteristics, multivariate regression demonstrated that acceptance alone accounted for more variance in tinnitus severity than anxiety and depression combined. Acceptance also mediated the association between self-rated loudness and severity, after controlling for depression and anxiety. This demonstrates the importance of understanding acceptance of tinnitus in order to understand its impact.

On a similar theme Moring *et al* investigated the relationship between negative tinnitus-related thoughts, acceptance, anxiety sensitivity and emotional distress [39]. 267 participants completed an online survey that included the THI, the Acceptance and Action Questionnaire [40] and the Anxiety Sensitivity Index–3. Hierarchical regression found full mediation by acceptance of the relationship between tinnitus-related cognitions and anxiety sensitivity, again demonstrating that tinnitus impact is dependent on acceptance, tinnitus sensation, duration and intensity. This could warrant further development of acceptance based approaches.

Factor analysis was used on cross-sectional data of 373 chronic tinnitus patients who completed the Tinnitus Cognitions Scale (TCS) [41], a 22-item self-report questionnaire assessing dysfunctional cognitions. Two factors emerged, tinnitus-related catastrophic thinking and avoidance. Conrad *et al* found that these were strongly associated with tinnitus distress, depression, anxiety and acceptance [42]. Specifically, more catastrophic thinking and avoidance cognitions were found in patients with more distressing tinnitus. The TCS partially mediated relationships between tinnitus distress and depression. Thus the impact of tinnitus (distress and depression) in part depends upon catastrophic and avoidant cognitions.

Differences in tinnitus experience and impact

A group of patients who had enrolled onto clinical trials were to report on what makes tinnitus worse and what makes tinnitus better, with a number of options to select. Variation amongst the 258 patients was huge, but overall tinnitus was improved by noise (31%) and relaxation (15%) and worsened by quiet (48%) and noisy environments (32%), stress (36%) and lack of sleep (27%) [43]. Coffee/tea (6%) and certain foods (4%) were said to worsen tinnitus. If tinnitus is not worse in quiet then it is not usually not reduced by noise. For those whose tinnitus is not worse in noise, it is not usually reduced in quiet.

Impact associated with hearing loss

The presence of audiological difficulties in a sample of 141 patients with diabetes in India was investigated by Fernandes *et al* using interview and questionnaires [44]. They adapted the Hearing Handicap Inventory for Adults [45] and found that 36.9% reported a self-perceived hearing handicap, and tinnitus was found to contribute to a higher hearing handicap score, suggesting that tinnitus can impact upon perceived hearing ability.

Joo, Han and Park conducted a large cross-sectional study in South Korea looking at the relationship between hearing loss and tinnitus and Health Related Quality of Life (HRQoL) [46] (Figure 3). The Korea National Health and Nutrition Examination Survey [47] was completed by 11,266 adults and they were divided into four groups: normal hearing without tinnitus; normal hearing with tinnitus; hearing loss without tinnitus and hearing loss with tinnitus. Overall, tinnitus was found to impact on HRQoL. Hearing loss and tinnitus patients reported the greatest impact, followed by tinnitus and normal hearing patients and hearing loss without tinnitus.

In São Paulo, Brazil, Oiticica and Bittar conducted a cross-sectional study of 1960 individuals to determine prevalence and characteristics [48]. They found a 22% prevalence with most of these reporting annoyance (64%). This was higher in women (74%) than men (50%). Interference with daily activities was reported in 18% of people reporting annoyance.

A two part study funded by the British Tinnitus Association explored how tinnitus associated with hearing loss may affect the impact of tinnitus [49]. A questionnaire was completed by 1288 participants reporting hearing loss and tinnitus. A sub sample of 8 profoundly deaf adults were then interviewed. Over 50% of the main group reported how tinnitus had an impact on stress, relating to others, concentration, attention and sleep. The impact of tinnitus was significantly greater in the severe/profound (compared to the mild/moderate) hearing loss group. More people with severe/profound hearing loss (44%) describe it as a severe problem than those with mild/moderate hearing loss (27%). Overall, the impact was particularly large in communication and relationships.

Tinnitus in 212 cochlear implant patients and changes following implantation was looked at by Klooststra *et al* [50]. Reduced tinnitus after implantation and reduced scores on the THI and THQ from pre- to post-operation was reported by 56%. A small proportion (8%) reported

some post-operative deterioration in tinnitus. 20% reported tinnitus starting after implantation, although their self-reported handicap was mild.

Impact and lateralisation

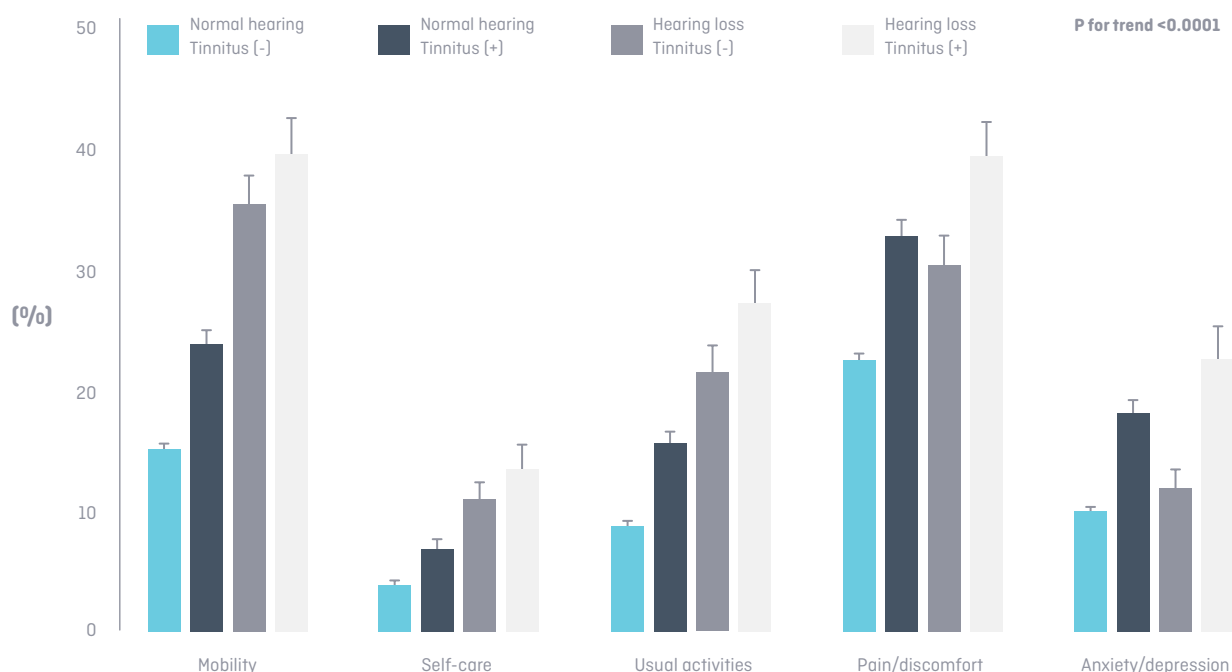
Yang *et al* [51] looked at the clinical characteristics of 105 patients with unilateral and 102 patients with bilateral tinnitus. They found that the mean age was significantly higher in the bilateral group, with equal gender distribution and tinnitus duration. The bilateral group reported higher scores on the THI and Beck Depression Inventory (BDI) [52]. Hyperacusis, ear fullness, vertigo and audiology tests showed no significant differences. Thus the psychological impact of tinnitus may be associated with bilateral versus unilateral tinnitus.

Impact and balance

The impact of tinnitus on postural control in 66 participants with tinnitus was explored by Martines *et al* [53]. Patients undertook a 'Romberg test' [54], 'static balance' and 'posture analysis'. They found that, compared to standardised scores, tinnitus

Figure 3

Prevalence of health-related quality of life according to four categories based on hearing status and presence of tinnitus [46]. © Joo *et al*. Used under the terms of the CC BY 4.0 license (<http://creativecommons.org/licenses/by/4.0/>).



patients showed poor postural control, with significant differences between open and closed eye conditions. The authors conclude that tinnitus could have an impact on balance, but this small pilot study requires replication and development.

Impact and headache

Significant relationships between headache and tinnitus laterality, and interrelationships between fluctuations in severity of tinnitus and headache symptoms have been reported by Langguth *et al* [55] following a study looking at the occurrence of headache and tinnitus in 193 patients attending a tertiary referral centre. Overall, the authors conclude that headache and tinnitus symptoms interact over time, and that there may be a common underlying mechanism, although the direction of cause is unclear.

Positive Experiences

Fifteen studies that explored positive experiences associated with acquired hearing loss, Ménière's disease and tinnitus were reviewed by Mancaiah *et al* [56]. They note a range of positive experiences were reported, but it is only in Ménière's disease that these predicted the impact of the condition. The authors suggest that we need more long-term assessment of how positive experiences and attitudes occur in people with tinnitus.

Sara Wheeler and Andrew Hopwood are cousins, one profoundly Deaf and the other hearing. In their paper, they reflect on their shared experience of tinnitus through a conversation that began on Facebook [57]. They share their experiences of tinnitus (the variety of sounds and how it changes), the association with other symptoms like balance problems and sensations like 'shock waves', and how listening to music can help if you have sufficient hearing.

Summary

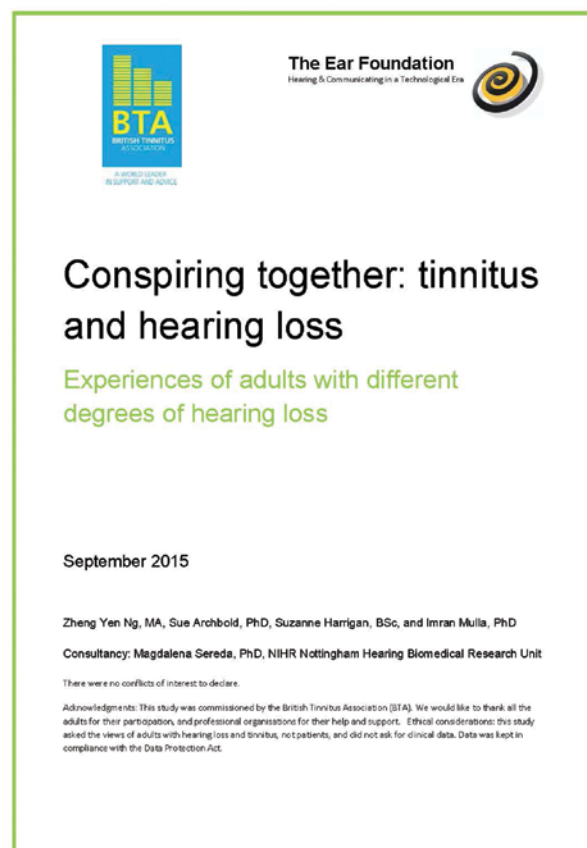
Overall research in 2015 has furthered our understanding of the potential impact of tinnitus. There is increasing evidence that tinnitus can have an impact on attention and control, although findings clearly depend upon the paradigm and modality used experimentally. Evidence continues to support the finding that tinnitus is associated with heightened levels of anxiety and depression, insomnia, reduced quality of life, daily functioning and even risk of injury. The main limitation of research is the fact that most studies are cross-sectional, so it is difficult to draw conclusions about

how tinnitus itself causes certain impact. Clearly, more longitudinal research is required. It is also worth considering how and why tinnitus impact may reduce after successful intervention.

It is of interest to discover when, why and how tinnitus has a positive impact, as this offers a new way of thinking about tinnitus, and potential new routes to resilience and positive outcomes. Increasingly, research suggests that the impact of tinnitus on an individual is dependent upon cognitive factors – how patients think about tinnitus – and whether it is 'accepted'. This could offer further insight into potential mechanisms that mediate and moderate the outcome of tinnitus. We should also consider the implications of tinnitus characteristics on impact, as well as the effect of comorbidities, such as headache, balance and, particularly hearing loss on the degree of impact tinnitus can have. As Ng *et al* [49] put it; tinnitus and hearing loss 'conspire together'.

Figure 4

Conspiring together: tinnitus and hearing loss [49]



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LUCY HANDSCOMB

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Lucy Handscomb trained as a hearing therapist in the 1990s. She worked in a number of NHS clinics across the UK offering one-to-one counselling and support to adults with acquired hearing loss and their communication partners. Over time she developed a special interest in tinnitus, and for 10 years ran the tinnitus therapy clinic at St Mary's Hospital, London. Alongside her clinical career she developed a teaching role and has worked as a lecturer on hearing therapy and audiology courses in Bristol and London and has run several short courses on tinnitus. She is currently a lecturer at the UCL Ear Institute, teaching undergraduate and graduate students.

Lucy began undertaking tinnitus research in 2006 and is now studying for a PhD at the University of Nottingham, investigating tinnitus distress. She is a former chair of the BTA's Professional Advisers' Committee and is now a Trustee of the BTA.

FROM CLINICIAN TO RESEARCHER: Lucy Handscomb talks to Nic Wray

What first made you interested in tinnitus?

To be honest, it was a person - Sandy Grimes, who is still working as a tinnitus therapist. My very first job as a hearing therapist, just after I'd qualified, was in Doncaster, at Doncaster Royal Infirmary, and I turned up there not knowing very much about anything at all. I ended up getting to know Sandy, who was one of the audiologists there, and she'd fairly recently set up a tinnitus clinic in Doncaster, where there hadn't really been one before, and she was starting to see clinical patients. Quite soon after I started, I think, she went on the European Tinnitus Course, and came back from that absolutely enthusing about it: "There are all these things we could do for our people with tinnitus, and you've got to help me!"

So it was through that, really: I think her enthusiasm sort of infected me, and having not really set out to be interested in tinnitus when I qualified as a hearing therapist, through her, I started to find out more about it and started to see more tinnitus patients.

Excellent, I know Sandy is still very passionate about tinnitus and helping tinnitus patients, and she frequently teaches on our Tinnitus Adviser Training courses as well, so you're not the only one.

I can well believe that!

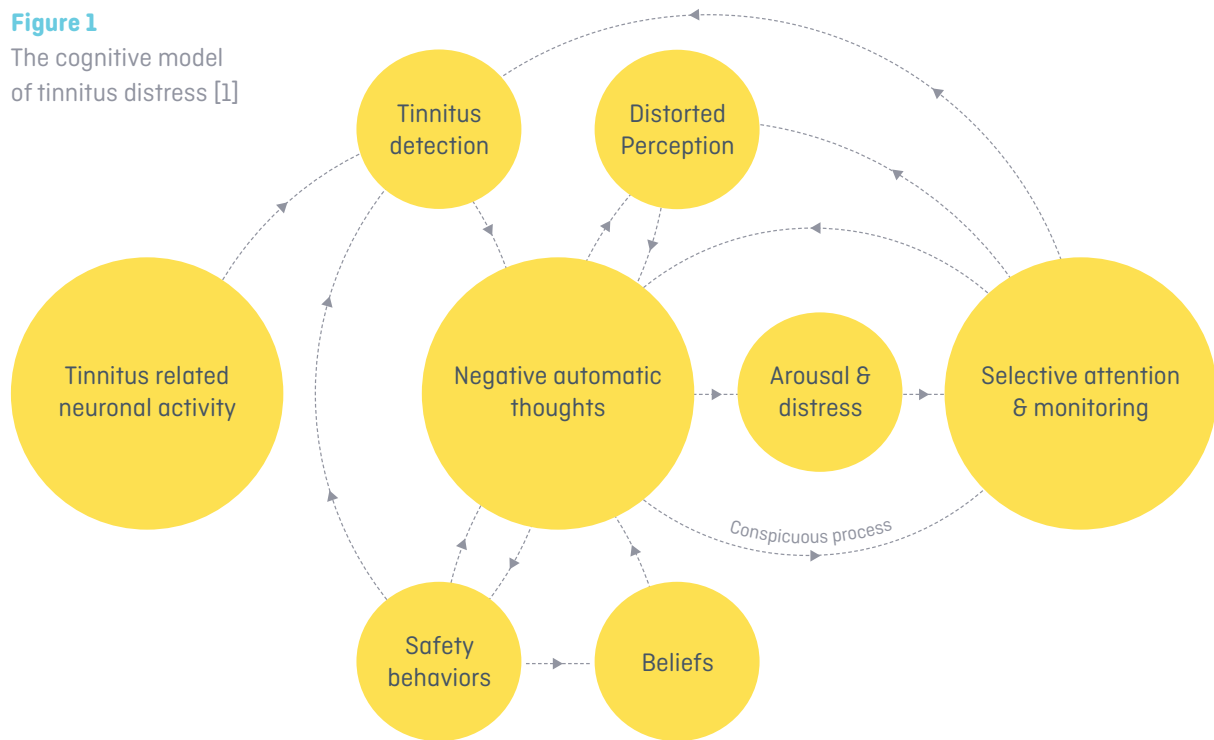
Moving forward to the present day, could you tell us a little bit about the research that you're involved in at the moment?

I'm doing my PhD in tinnitus: I'm doing it part-time, so it's a fairly long process. I've got probably about a year and a half still to go. I'm testing a cognitive model of tinnitus distress, which was a model developed by Laurence McKenna [1], who is a clinical psychologist who specialises in tinnitus work.

The cognitive model is basically a way of explaining why tinnitus is so much more of a problem for some people than others. I've always been very interested in that sort of thing you see in tinnitus patients - the range of responses you get, from "This is absolutely the worst thing that's ever happened to me," to "It

Figure 1

The cognitive model of tinnitus distress [1]



doesn't really bother me, if I think about it, I might hear it, but otherwise, it doesn't really affect my life". We know that there's some relationship between how loud people's tinnitus is and how much it bothers them, but it's a very imperfect relationship, and it's certainly not all about loudness.

So, for a long time, people have thought that there is some kind of connection between how much people are bothered by tinnitus and how much they think about it, what their mood is like, how much attention they pay to it. So the cognitive model is a way of conceptualising that. It's based on other psychological models of distress, so people who work in the world of chronic pain, for example, think in a similar way: people might react to chronic pain differently, depending on their negative thoughts, their emotions and how much attention they pay to the pain, and the sort of behaviour they use.

There have been various models of tinnitus proposed in the past. The very positive thing about this model is that it's actually made up of a series of testable hypotheses (Figure 1).

The cognitive model makes various predictions: it says people who are, for example, having negative thoughts about their tinnitus are more likely to feel emotional distress; people who are having negative thoughts about their tinnitus are more likely to pay more attention to it; and people who are having negative thoughts about tinnitus are more likely to engage in avoidance behaviour which, in turn, is likely to enhance their negative experience of it.

So that's really what I'm looking at, and what I've done so far is conduct a big questionnaire study. I've got a questionnaire which enquires about each separate aspect of the model, and I put them all together in

a survey, so there's one about thoughts about their tinnitus, there's one about emotional distress, there's one about the attention and monitoring their tinnitus, and so on. The survey was available online and by post, and lots and lots of people with different degrees of tinnitus filled it in.

From the survey, I've been able to look at how people who rate their tinnitus as a problem or not a problem, or a very big problem or a bit of a problem compare in terms of how they score on those questionnaires. I've also looked at the relationships between them, for example, whether there are connections between negative thinking and emotional distress and attention to tinnitus.

The next part of my research, which I'm just starting on now, is looking at how people who have tinnitus think about the cognitive model, so they've actually had a look at this diagram and had it explained to them. I want to know does it make sense to somebody with tinnitus, and does it tie in with their experience.

That will be interesting, because even if the clinicians believe that it's a valid hypothesis, it's what people feel about their own situation, isn't it?

Exactly, yes, and the two things aren't necessarily the same! We have statistical evidence that most of those predictions within the model are accurate – we know that now, so that's really good – but it doesn't necessarily mean that it's a helpful thing for somebody with tinnitus to look at. But it might be: that's what I'm trying to find out.

Obviously, this research has been influenced by your clinical experience. How did you find moving to a research role after a predominantly clinical career?

I think it's really helpful to have had that clinical experience behind me as it's always in my mind what – and who – I'm doing this for. For example, as students, we all have to go through the process of going through an Impact Statement, where we're supposed to describe the potential impacts of our research on people, and some people really struggle with that, because it's quite theoretical, but for me, it's an absolute no-brainer: it's quite easy for me to do that. And I think that's partly because I've sat in front of lots of people with tinnitus and heard about their experiences, so that makes me quite motivated, I suppose, to try and find out more about it, for their benefit.

Other things have been more difficult, because I'm not from a research background, so I've had to learn the language a little bit in terms of writing papers and how to engage with journals and those kinds of things which weren't really part of my life much before.

Is there any advice you'd give to others considering a similar sort of move or shift in emphasis?

I'd say, if you're able to do both and if that works for you, keep up some kind of clinical work alongside the research that you're doing. I haven't been able to do that, for various reasons, but I think that would be an ideal situation, really, where you're actually still seeing patients, and you're doing the research alongside that, because the two things really complement each other both ways round. So, as I say, having the experience with patients helps with your motivation, but while you're doing the research, you are learning lots of useful stuff, and that's stuff that you could pass on to patients, as well.

If you're not able to do both, I think at least try and keep in touch with your clinical side in some way, whether that's by attending meetings or talking with with your clinical colleagues and that type of thing, so you don't lose touch with that world.

Moving away from your own research, what's your favourite bit of tinnitus research that's been done by others?

One of the things I've always been really impressed by is the internet research that they've been doing in Sweden. Gerhard Andersson has been responsible for a lot of that, and Viktor Kaldö, who works with him. I really like that research, partly because it's always very well-conducted, you can trust them to do a well-designed study, but also because the benefits are very clear. The possible application of that, being able to deliver really good quality internet-based Cognitive Behavioural Therapy for people with tinnitus is huge. It means that you no longer have to have people turning up at clinics, they can be anywhere and be able to access this kind of help.

Is that the aspect of research that gives you the most hope for future treatments for tinnitus, do you think?

Yes, it's partly that, because at the moment the most benefit is coming from the psychology-based treatments. That might change, but it's still true to say at the moment that that's the best hope that people with tinnitus have. The kind of research that makes

“The world of tinnitus research is quite small, and you could say it should be bigger, and with more people involved we’d be able to make more progress, but at the same time, the fact that it’s quite small means there is this sort of sense of community.”

those treatments much more accessible to more people gives me some hope. Unfortunately, I had quite a few comments on my survey that I sent out to people from members of the public with tinnitus: quite a few people wrote at the end, “I haven’t had any help,” “There’s no tinnitus service where I live,” “I can’t access help in this area,” so anything that makes help more accessible I think is really good.

I think the other thing that gives me some hope are the recent mindfulness studies that are going on. They seem to be showing a positive effect, especially the large BTA-funded study that’s just, I think, in the process of being written up. I think that’s really helpful, because it gives us a slightly different approach from what we’ve had before, that seems to be successful for a lot of people, in the long term. It’s not just a short-term coping solution, but something that seems to make a difference to people on an on-going basis.

What are you especially enjoying about your research?

I think what’s been a really good experience for me doing the PhD is just the amount of conversations I’ve had with other people who are interested in tinnitus and that’s seemed like a little bit of a luxury. I remember when I first started my PhD I sat down in the supervision meeting and had an hour and a half-long conversation all about tinnitus and different ways of measuring it. I thought, “That’s amazing, I’ve never done this before,” because normally you just catch people in the coffee break at a conference and you chat for five minutes and then it’s time to go back

in. It’s something that I’ve found helpful while I’ve been doing research - the conversations that go with it as well as just the reading and the studying parts.

It seems to me that as somebody watching research and going to the conferences as an observer, there is such willingness within the tinnitus research community to actually share knowledge and information in that kind of way and have those conversations.

Yes, I think that’s the good thing about it. It’s a fairly small community still. The world of tinnitus research is quite small, and you could say it should be bigger, and with more people involved we’d be able to make more progress, but at the same time, the fact that it’s quite small means there is this sort of sense of community. Lots of people know each other, and if you go to one of these conferences, you’ll know somebody who knows someone else, and they introduce each other, so there’s lots of opportunity to share ideas and discuss things.

And I think that’s a cue to say thank you Lucy, for taking time to share your ideas and have this conversation!

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Derek Hoare is Senior Research Fellow in tinnitus at the NIHR. Derek trained in neuroscience at the University of Manchester and has particular expertise in trials, health service evaluation, psychological and self-management of tinnitus. He is a member of the British Tinnitus Association Professional Advisers' Committee, and vice chair of the British Society of Audiology tinnitus and hyperacusis special interest group.

Conflict of Interest: Derek Hoare was an investigator on a trial of acoustic Coordinated Reset (CR®) Neuromodulation part funded by The Tinnitus Clinic.

NEW TECHNOLOGIES AND SELF-HELP

Dr Derek Hoare

Proposed approaches to managing tinnitus include cognitive behaviour therapy, hearing aids and cochlear implantation, sound generator, electrical, or pharmacological interventions. Whilst some approaches are commonly used in clinical practice, most can still be considered as emerging or experimental. For some practices, such as transcranial magnetic stimulation, dietary supplements, and drug treatments, there are clear recommendations against routine use [1].

A scan of tinnitus research reports published in 2015 tells us that the vast majority of recent work explored tinnitus physiology and the associations between tinnitus and health, wellbeing, or lifestyle factors. Only a handful of reports recounted development or trials of treatment or management interventions.

Figure 1

Acoustic Coordinated Reset (CR®)
neuromodulation device [12]



These included some small scale studies of technologies that have been around for some time such as repetitive transcranial magnetic stimulation (rTMS), cochlear implantation, and transcranial direct current stimulation (tDCS) [2] [3] [4]. However, some newer technologies such as vagus nerve stimulation (VNS) using an implanted electrode, a non-invasive transcutaneous version of VNS (tVNS), direct electrical brain stimulation, sound-based, cognitive and psychological interventions have also been investigated, and will be described below.

Technology

Technological innovations aim to suppress or alter tinnitus-related brain activity, or to reduce percept of the tinnitus sound. De Ridder *et al* reports the case of a single patient with refractory tinnitus who received a VNS implant and had a clinically significant reduction in tinnitus severity after treatment for four weeks [5]. Building on this, MicroTransponder Inc. have a pilot study ongoing (NCT01962558) involving 30 participants who received either VNS paired with sound stimulation (predicted to affect tinnitus), or VNS with random sounds (predicted to be ineffective for tinnitus). The results of this study will be informative to further randomised controlled trials. The non-invasive version of this treatment was investigated in one study [6]. Hyvärinen *et al* found that tVNS changed brain wave patterns, and that these changes corresponded to the participants self-rating of tinnitus distress. The picture is quite complicated however and needs further investigation. Li *et al* are now conducting a randomised, single-blind, controlled clinical study with 120 participants (ChiCTR-TRC-14004940) comparing tVNS alone to tVNS with sound stimulation, and to other treatment [7]. This study will provide good quality evidence for how effective this treatment approach is.

Another case study reports the effects of an auditory cortex implant in a single tinnitus patient [8]. The patient had suffered from severe unilateral right-sided tinnitus for over a year, and experienced only a partial suppression of tinnitus after implantation. De Ridder *et al* also report the results of a study on two patients who underwent implantation of electrodes in the dorsal anterior cingulate cortex [9], a region of the brain associated with attention and emotion. One patient reported dramatic improvement in tinnitus after one week. However, the second patient did not report any change as a result of the implant which was trialled at various stimulation settings. Given these single cases it is not possible to speculate on general effectiveness of brain implanted electrodes.

A small number of studies conducted in 2015 looked at sound-based interventions. Sereda *et al* conducted

a Delphi review to examine practical aspects of designing a clinical trial to test whether or not hearing aids should routinely be offered to people who have tinnitus but only mild-to moderate hearing loss [10]. Clinical practices vary significantly on this issue and so a clinical trial that can inform evidence-based practice is of real importance. Henry *et al* examined the effects on tinnitus of a combination device (hearing aid with sound generator features) to that of standard hearing aids in a randomised trial [11]. Both groups in the trial showed similar improvement in tinnitus handicap after six months. This study only included 30 patients so the results are not conclusive and statistically powered trials of combination devices are indicated. Two further studies using combination devices are registered. One completed study compared white noise to non-traditional sounds such as pink noise, red noise, nature sounds, or modulated sounds (ISRCTN27770434). The other, ongoing, is a randomised controlled trial comparing the effectiveness of combination devices and hearing aids for tinnitus (ISRCTN15178771).

Another sound technology is acoustic Coordinated Reset (CR®) neuromodulation (Figure 1). This therapy involves patterned sound stimulation and explicitly targets abnormal (synchronous) brain cell activity in people with pure (single) tone tinnitus. Two reports in 2015 relate to this therapy. Williams *et al* performed a retrospective review of the records of 66 patients [12] noting a 19% improvement in tinnitus handicap after five months. Hauptmann *et al* performed a prospective clinical study with 200 patients [13] also reporting improvements in tinnitus handicap after 12 months. Neither study was controlled however, so the mechanism of any benefit was not determined. Careful randomised controlled trials are needed in the future to determine if and how specifically the treatment is effective [14].

Music therapy also featured in two studies. In a parallel group study, involving 290 patients, Argstatter *et al* compared a structured eight-session programme of music therapy to counselling [15]. They found that twice as many patients reported a clinically significant improvement in the music therapy group. A neurophysiological mechanism of this improvement after music therapy is proposed by Krick *et al* [16], who found grey matter changes in regions of the brain including hearing centres in patients with acute tinnitus who underwent the therapy. This approach does not appear to have been trialled outside of Germany and is important to replicate.

Psychological interventions and self-help

The aim of psychological or self-help interventions are to reduce the negative emotional reaction people

have to their having and hearing tinnitus. Recent research in this area has examined cognitive training, mindfulness-based stress reduction, internet-delivered cognitive behaviour therapy, and internet-delivered self-management interventions.

Krings *et al* reports a small double-blind randomised clinical trial asking whether D-cycloserine, a drug proposed to enhance changes in nerve cell activity, increased the benefit of a five-week course of computer-based cognitive training for tinnitus [17]. Whilst the ‘drug’ group self-reported an improvement in cognitive difficulties, both groups showed a similar small improvement in tinnitus that would not be considered clinically significant.

Roland *et al* evaluated an eight-week mindfulness-based tinnitus stress reduction intervention delivered face-to-face in an open-label pilot study involving 13 people with tinnitus [18]. At four-week follow-up, there was a clinically significant improvement in self-reported tinnitus severity and depression. Another pilot study with 12 months follow-up by Gans *et al* reported sustained improvements in tinnitus severity [19]. One related study is registered as completed. McKenna and colleagues conducted a randomised trial comparing mindfulness and relaxation therapy (NCT02059447). This will be the first robust study to provide an estimate of the effectiveness of mindfulness for tinnitus so its publication is of real interest to those in the field.

The internet provides an alternative route to deliver psychological interventions. In a systematic review, Andersson pooled data from multiple studies, largely conducted in Sweden and Germany, where clinician-guided internet-delivered cognitive behaviour therapy (CBT) for tinnitus was compared to no-treatment controls or face-to-face therapy [20]. Reporting small to medium effect sizes, he concluded that internet-delivered CBT holds promise but that larger studies are required. He also identified a need for studies on how to integrate internet-delivered therapy into routine clinical services. Following on from this recommendation, Beukes and colleagues are planning a powered randomised trial to compare an 8-week internet-delivered cognitive behaviour therapy intervention to usual face-to-face clinical care (NCT02665975). This will be the first such study in the UK, where tinnitus management is largely in the hands of audiologists. The results of this trial will be interesting both clinically and culturally.

Unguided online self-help interventions have been available for some time. The Tinnitus E-Programme

(Figure 2) was developed by a UK-based therapist, Debbie Featherstone, and made freely available online in 2009 [21]. Greenwell *et al* describe the main components of the programme as education about tinnitus, education about the role of psychological mechanisms in tinnitus, relaxation and attentional-focus exercises [22]. A qualitative evaluation of the programme to explore the acceptability, usability, and potential psychosocial outcomes is currently in progress.

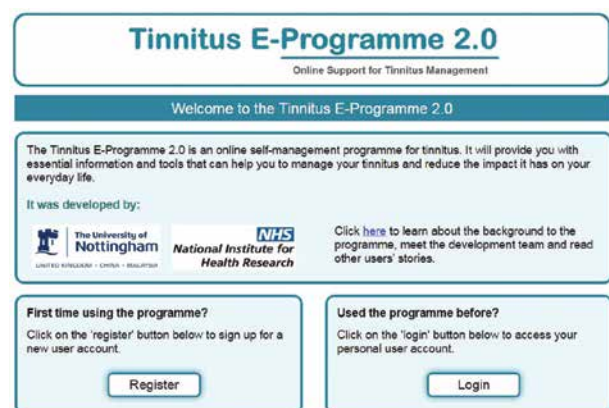


Figure 2

Screenshot of the Tinnitus eProgramme [20]

Conclusions

The volume of tinnitus research and the rate of scientific publication on the subject are rising all the time. At the time of writing however, there were just 31 open tinnitus studies registered on clinicaltrials.gov, the main international register of clinical studies. These included studies on transcranial magnetic stimulation, transcranial random noise stimulation, deep brain stimulation, transcranial direct current stimulation, tinted light, sound therapy, psychoeducation and internet-based CBT. However, there is no critical mass in any one area, with just one or maybe two studies at any time examining a particular intervention. Reliable estimates of effect are best determined by pooling data from independent replicated studies. For tinnitus and many of the interventions researchers appear interested in working with, this possibility is some way off. This is equally the case for common interventions such as hearing aids and combination devices where there have to date been few clinical trials. Preparatory work is important to optimise interventions and design feasible clinical trials. Ultimately however, sights have to be set at those trials happening, being replicated, and their findings translating into patient benefit.

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Conflicts of interest: I have undertaken work for (and been paid by) the following drug companies who were/are trialling drugs for tinnitus or conditions that incorporate tinnitus as one of the constituent symptoms: GSK, Autifony, Otonomy. I have received fees for lecturing about the treatment - including drug treatment of tinnitus.

PHARMACOLOGICAL TREATMENTS FOR TINNITUS: AN UPDATE

Don McFerran

Although there are many management strategies for helping people with tinnitus, none of them offer a cure and both patients and clinicians remain frustrated by this lack of an effective solution. There are various on-going strands of research searching for this elusive cure, including such disparate modalities as transcranial magnetic stimulation and sound therapy. However, top of the list for most tinnitus sufferers is the hope that a pharmaceutical solution for the condition will be developed: a 'pill for tinnitus.'

A literature search unearthed about a score of publications in the last year that have addressed drug research for tinnitus. At first glance, this research seems disjointed, almost random. However, closer evaluation reveals that there are a few common themes. Firstly, research is divided into human research and animal research. Within the human studies are systematic reviews of previous drug research, case reports of potentially interesting drugs and proposals for the use of new classes of drugs. More excitingly, there are trials that have tested drugs on people with tinnitus. These include direct drug treatment of subjective idiopathic tinnitus, treatment of subgroups of tinnitus patients and use of drugs as adjuvants to potentially enhance the effectiveness of other types of treatment.

These human tinnitus drug trials have tested compounds that occur both within the field of conventional medicine and within complementary and alternative medicine (CAM). There have also been some studies looking at the treatment of particular conditions, such as Ménière's disease, where tinnitus is just one part of the symptom complex: these studies are beyond the scope of this brief article and will not be considered further. Animal studies have determined whether particular drugs are effective in controlling tinnitus in animal models of the condition and have also been used in an effort to better understand the pathophysiology of tinnitus.



HUMAN TRIALS

Systematic reviews of drug treatments for tinnitus

Jufas and Wood explored whether benzodiazepines are effective in the management of tinnitus [1] and carefully considered the side-effect profile of these potent drugs. They found that there was some evidence suggesting that clonazepam can be helpful but the relevant studies all had methodological shortcomings. Diazepam was ineffective and there was equivocal evidence regarding alprazolam. They identified one study suggesting that oxazepam may be helpful. Overall, the authors concluded that the evidence to support benzodiazepines for treating tinnitus is poor and due to the safety profile of these drugs, caution should be exercised in their usage.

Miroddi *et al* investigated trials [2] that had used the hormone melatonin either as a stand-alone drug or in combination with other drugs, namely sulodexide or sulpiride, in the management of tinnitus. They found significant biases in the studies, such that they could not comment on whether or not melatonin improves tinnitus. They did find some evidence suggesting that melatonin may help sleep disturbance in tinnitus patients. Given the high prevalence of sleep problems in people with tinnitus, this is an area deserving of further research.

Case reports

McCormick and Walega reported a case of a patient who developed tinnitus after an episode of acute otitis

media [3]. The patient found that his tinnitus was exacerbated by neck movements and trials of various treatment modalities including acupuncture and chiropractic therapy proved ineffective. Cervical epidural injection of steroids gave him significant improvement, lasting from a few weeks to several months at a time. It is impossible to make generalisations from a single case report, but as the authors of this work point out, many patients with tinnitus have a somatic component to their symptomatology. Commonly this is related to jaw or neck movements and is a rather under researched topic.

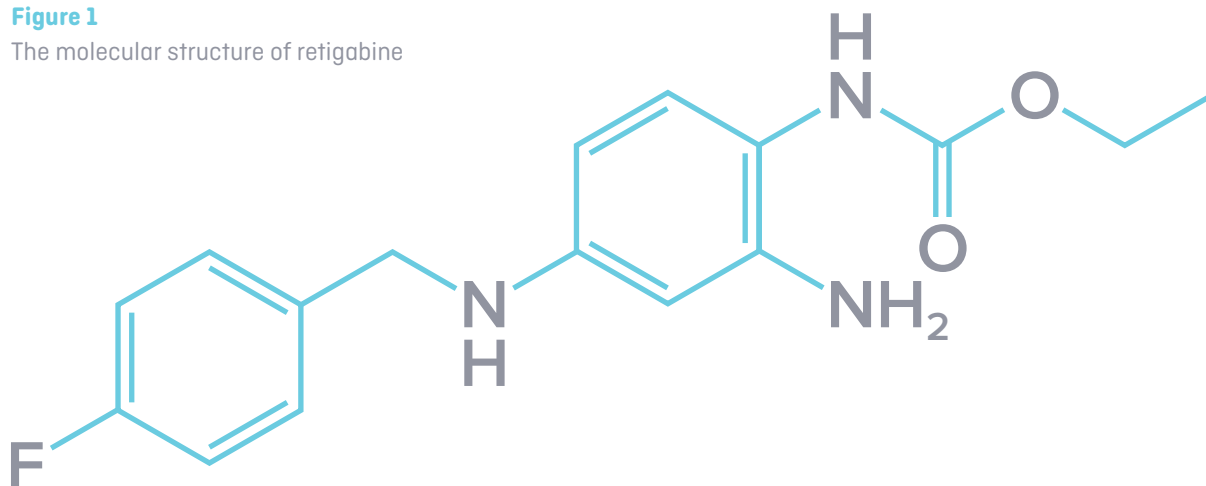
Gopal *et al* reported use of the antioxidant L-carnitine in a 41-year-old woman with tinnitus [4]. Tinnitus improved and various audiometric tests showed marginal improvement. Once again, it is important not to draw conclusions from single case reports but this is an interesting observation that merits further experimental scrutiny.

Proposals for new tinnitus drugs

There has been considerable recent interest in drugs that modify potassium channels that are ion channels present in both central and peripheral neurones. Down-regulation of these channels has been suggested as being part of the pathogenesis of various conditions including neuropathic pain, epilepsy and tinnitus. Patient groups have highlighted the possibility that the antiepileptic drug retigabine, which acts upon

Figure 1

The molecular structure of retigabine



potassium channels, may improve tinnitus (Figure 1). Unfortunately, this compound has significant side effects, particularly the risk of causing permanent visual impairment, and is unlikely ever to enter widespread tinnitus usage. Langguth *et al* review this topic in depth [5]. Kalappa *et al* report on the development of a new drug produced by adding fluorine to part of the retigabine molecule [6]. In experimental trials, this new compound seems to be more potent and less toxic than retigabine with regard to both epilepsy and tinnitus. Clinical trials are planned. Hagenow and Stark report on the possibility of using drugs that antagonise histamine H4 receptors to treat tinnitus [7]. The rationale for this is somewhat tenuous and this proposal is very much at an early stage.

Specific drug trials in humans

Randomised controlled trials (RCT) are considered the most scientifically rigorous way of evaluating drug therapies, either using a placebo (placebo-controlled RCT) or a previously tested therapy (positive-control RCT) to compare with the drug being tested. There have been several recent trials using RCT design to investigate drugs for the treatment of tinnitus.

The first of these RCTs used an interesting combination of oral gabapentin and lidocaine, injected intradermally in the external auditory canal [8]. The rationale for using gabapentin is that this drug, which is a structural analogue of gamma amino butyric acid (GABA), has been reported to help some people with tinnitus though a previous systematic review [9] concluded that the evidence is inadequate to recommend its usage. Lidocaine and certain other

local anaesthetic agents have long been recognised as been able to temporarily suppress tinnitus in the majority of patients when given as an intravenous bolus injection. Such injection, however, carries a risk of significant side effects and is not a viable therapeutic option. The researchers in this trial divided 72 patients into three groups, which received gabapentin tablets and intradermal saline, gabapentin and intradermal lidocaine or placebo and intradermal saline. Notably they did not allocate a group to placebo tablets and intradermal lidocaine. The primary outcome measure for the trial was the Tinnitus Handicap Inventory (THI) questionnaire [10] and results from this tool suggested that gabapentin and intradermal lidocaine improve tinnitus more than gabapentin and intradermal saline or placebo and intradermal saline. While encouraging, this was a small-scale trial and further work in this area is required.

The second RCT considered the use of trimetazidine [11]. This is a drug used for treating angina that has cytoprotective anti-ischaemia properties. It has been tested in various otological conditions including Ménière's disease and vertigo and according to the authors of this paper from Turkey, it is widely prescribed for tinnitus. As chronic subjective idiopathic tinnitus is not generally considered to be associated with ischaemia or inflammation the rationale for its use seems somewhat tenuous. The primary outcome measure was the THI questionnaire with secondary measures on a visual analogue scale (VAS) of loudness. The trial found no significant difference between trimetazidine and placebo, leading the researchers to conclude that it is ineffective in treating tinnitus.

Another RCT trial design was used in the on-going series of trials of AM-101 [12]. This is an experimental drug that has been revealed to be esketamine, the S(+) enantiomer of ketamine, the commonly used anaesthetic agent. Ketamine has a complex mode of action, interacting with many receptors, ion channels and enzymes. In the management of tinnitus, it is being used for its ability to act as an antagonist of NMDA glutamate receptors. One theory of tinnitus pathogenesis is that following acute cochlear damage, cochlear glutamate levels are high and this has the potential to trigger tinnitus. The research team has proposed that by blocking NMDA receptors in the acute phase (within three months of tinnitus onset) tinnitus initiation can be halted. The drug is administered in a gel as an intra-tympanic injection. Several trials have been conducted and further trials are in progress. This particular study examined the optimum dosage regime and concluded that three injections over three consecutive days were best. Various outcome measures were used including patient reports of tinnitus loudness and annoyance, the Tinnitus Handicap Questionnaire (THQ) [13] and audiometric tinnitus loudness matching and minimum masking level. Arguably, the team have invalidated the THQ results by omitting one of the items of the questionnaire. The authors stress that this trial was not powered to determine statistical significance of efficacy between treatment groups. In the event, the trial demonstrated some relatively modest benefit of AM-101 over placebo for some but not all outcome measures.

Treatment of subgroups of tinnitus patients

Although tinnitus is often regarded as a single entity, there may well be different pathophysiological processes in different patients and looking for a single solution may be an impossible aim. Trying to find patients with particular types of tinnitus and offering them a tailored solution may be a more appropriate strategy.

Singh *et al* conducted a randomised controlled pilot study of a North Indian population of tinnitus patients whereby participants received intramuscular injections of vitamin B12 or saline [14]. Outcome measures were the Tinnitus Severity Index questionnaire [15] and a VAS of tinnitus loudness. 42.5% of patients were found to be vitamin B12 deficient and this subgroup showed statistical improvement of their tinnitus measures when their deficiency was corrected. Vitamin B12 deficiency in first world countries varies from $\leq 3\%$ in young people to 6% in those aged over 70, whereas figures of 70% to 80% have been reported in India [16]. This study potentially has enormous importance for regions such as India

with high levels of vitamin B12 deficiency. There is probably less likelihood that it is going to be an important factor in UK tinnitus clinics though perhaps clinicians should be screening people in high-risk groups such as the elderly or those with a vegetarian diet.

Another study from India on a subgroup of tinnitus patients was reported by Hameed *et al* [17]. They describe their trial as quasi-experimental and no control group was used. Ninety-eight patients with raised serum cholesterol were given dietary advice and atorvastatin. In 51%, the cholesterol level normalised whereas in 48% it remained elevated. Tinnitus measures improved in 70.5% of the responsive group but only 4.2% of the unresponsive group. However, the study used a non-validated questionnaire and the researchers did not quantify their definition of improvement.

Drugs tested as adjuvants to other therapies

Various drugs have been investigated as potential neuroplasticity enhancers and in a small RCT Krings *et al* explored the use of D-cycloserine to aid a computer-assisted cognitive therapy program for patients with tinnitus [18]. Using the Tinnitus Functional Index questionnaire (TFI) [19] as their primary outcome measure, the researchers found that the drug was well tolerated but demonstrated no tinnitus benefit. However, it did statistically improve cognitive difficulties.

Using a non-RCT design Lin *et al* reported a small case series of patients who were treated with what was described as Western anti-tinnitus treatment, namely peripheral vasodilators and thiamine [20]. Ten subjects were also given a Chinese herbal treatment, Chai-Hu-Jia-Long-Gu-Mu-Li-Tang (CHJLGMLT) whereas 11 were not given adjuvant therapy. Various tools were used to evaluate outcome with the THI chosen as the primary measure. Benefit was demonstrated in the group that received the Chinese medicine but as in all retrospective case series studies, caution must be exercised interpreting the results.

ANIMAL STUDIES

Two studies from the same department examined the possible role of cannabinoids in tinnitus. The first paper, by Zheng, Reid and Smith was a trial of two cannabinoids in rats [21] with the animals divided into four groups. One group received cannabinoids and was exposed to acoustic trauma; the second group received cannabinoids and sham treatment; the third group received the drug vehicle but no active cannabinoids and was exposed to acoustic trauma; the final group

“Application of AM-101 to the round window reduced the loss of ribbon synapses in noise-exposed animals, suggesting a mechanism by which AM-101 might help people with acute tinnitus”

received the drug vehicle and sham treatment. Results show that the cannabinoids in the study increased the risk of the rats that were exposed to noise developing tinnitus. The researchers extrapolate this finding to suggest that humans who use cannabis as a recreational drug may be increasing their risk of tinnitus but go on to point out that cannabis contains over 400 chemicals but only two were tested in this study. The other paper from the same department was a review article discussing the biological effects of cannabinoids in the central auditory system and speculating upon the possible relationship with tinnitus [22]. No clear conclusion was reached.

Bing *et al* reported an animal study that investigated the use of AM-101 [23] (see page 39 for further details regarding this drug). Ribbon synapses are specialised neuronal synapses that allow very rapid, precise and sustained transmission of information. They are present in sensory organs, particularly the retina, cochlea and vestibular system. Loss of ribbon synapses was used in this experiment as a correlate for deafferentation. Application of AM-101 to the round window reduced the loss of ribbon synapses in noise-exposed animals, suggesting a mechanism by which AM-101 might help people with acute tinnitus.

The same department that described animal studies on cannabinoids also published an article regarding the use of a melanocortin agonist [24]. Observations that there is microglial activation in the cochlear nucleus of animals that have developed tinnitus following noise exposure, have prompted the hypothesis that

inflammatory processes in the central auditory system may be part of tinnitus pathogenesis. Melanocortins have anti-inflammatory properties but use of an experimental melanocortin receptor subtype 4 agonist did not protect against tinnitus.

Song and Lou found increased levels of two proteins in the brains of rats that had developed tinnitus after administration of salicylate [25]. This process was reversed by the administration of GM1, a ganglioside. Gangliosides are a family of complex molecules produced by the body and occur on the surface of cells, particularly within the nervous system. GM1 has important functions regarding neuronal repair and plasticity. Based on the results of their trial the authors suggest that GM1 should now be explored as a possible tinnitus treatment.

Lobarinas *et al* described a study investigating the use of cyclobenzaprine in a rat model of noise-induced tinnitus [26]. Cyclobenzaprine is a molecule that chemically resembles tricyclic antidepressants and is used to treat muscle spasms. The authors reported that this compound is effective in transiently suppressing tinnitus in rats and go on to discuss the mechanisms by which the drug may be having this effect.

Conclusions

Interest in trying to find the pharmacological solution to tinnitus remains strong and last year has seen a fascinating portfolio of research into the topic. Although there has been no breakthrough, there have been some interesting findings and pointers towards further trials.

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DR MIKE MULHERAN

Lecturer

University of Leicester

Mike obtained his PhD in 1990 in Experimental Models of Tinnitus at the University of Keele.

He has continued to be involved experimental and clinical projects since then. He collaborated with GSK on developing putative tinnitolytics and identifying possible therapeutic drug targets for tinnitus.

His current research interest has an applied synaesthetic flavour which is establishing whether tinted light can be reliably used to modulate perception of tinnitus.

Outside work he tries to maintain a general interest in all aspects of life and sees merit in using the metaphor of pantomime for a variety of human endeavours.

NIC WRAY

Communications Manager

British Tinnitus Association

Nic Wray has been Communications Manager of the British Tinnitus Association (BTA) since June 2010. She is responsible for the BTA's communications online and in print in addition to providing PR support. In addition to writing a number of the BTA's information leaflets, Nic also edits the BTA's journal, *Quiet*. She sees providing the tinnitus community with information as a key to helping people live well with tinnitus. A graduate of the University of Sheffield, she is an Accredited PR Practitioner.

(T) British Tinnitus Association

A NON-LINEAR PATH: Mike Mulheran talks to Nic Wray

What first made you interested in tinnitus, Mike?

Well, it was perfectly by chance I became interested in tinnitus really. I ended up at the University of Keele in the Department of Communication and Neuroscience as a PhD student back in 1982. This was under Professor Ted Evans, an eminent auditory physiologist of the time. He had a number of experimental PhD projects, one of which was developing models of tinnitus. I plumped for that one.

Since then, I've been involved in tinnitus research on and off and it's been a fascinating subject. Not least because tinnitus as a phenomenon is inextricably linked to so many other questions as to how the nervous system as a whole works.

For example, many neuroscientists would want to ask the question, "How do we actually code the absence of stimuli – or more specifically in the case of the auditory system - silence?" You might think that absence of stimuli in the auditory periphery would be easily coded as an absence of neural activity. But this is not the case – the majority of the many thousands of auditory nerve fibres in our cochlear nerves are very busy in the absence of sound. So a proper understanding of tinnitus needs to include this. The perception of tinnitus - at least in part - is going to be referenced against this normal activity that codes silence in the absence of external environmental auditory stimulus. This line of questioning gives us an insight into how we pick up perceptual signals from the nervous system such as an itch or acute flashes in the eye.

The other thing I have found fascinating is how tinnitus appears to be linked to other serious conditions in the nervous system such as epilepsy and chronic pain. Our knowledge and understanding of these two conditions have been very important in understanding how we might develop drug therapies for the treatment of tinnitus.

Mike, you obviously have a long history with tinnitus - what research are you currently involved in?

Currently, my main job is working as a pharmacology lecturer in the University of Leicester Medical School. But I am fortunate in that I do have some research time for projects in the auditory sciences.

“Tinnitus appears to be linked to other serious conditions in the nervous system such as epilepsy and chronic pain. Our knowledge and understanding of these two conditions have been very important in understanding how we might develop drug therapies for the treatment of tinnitus.”

My main project at the moment is working with colleagues at the Leicester Royal Infirmary ENT Department, and Mr Bannerjee, one of the senior ENT surgeons at Leicester. This is a clinical trial looking at the effect of tinted light on tinnitus (Figure 1). From a previous pilot study we carried out, it appears that some tinnitus patients (about 40%) seem to report that their tinnitus improves with certain tints of light. This seems to be a repeatable phenomenon, but this current trial is specifically designed to see whether these reports are repeatable over the longer term. The study is on-going and we hope to have finished collecting data some time later this year.

I'm also involved with experimental studies here at Leicester in the Auditory Group, headed by Professors Ian Forsythe and Blair Grubb. I developed acute *in vivo* Auditory Brainstem Response (ABR) noise models to complement the work of Ian and Blair, which has synergistically contributed to much work in the group subsequently.

Ian is a basic auditory neuroscientist of long standing and has great expertise in *in vitro* single neuronal recording and his work focuses mainly on single-cell and ion channel physiology. Blair, who has now moved to Liverpool, has very extensive expertise in the

neurosciences with both *in vitro* and *in vivo* methods. Combining expertise has enabled the development of some very interesting models of changes in gene expression following relatively modest noise exposure. The models aim to see what patterns in gene activation occur within the auditory system following acute noise trauma. Acute noise exposure is a common tinnitogenic agent.

A secondary aim is to then see if we can identify novel potential targets for tinnitus therapeutics, for example in identifying what different kinds of drug targets arise following noise trauma. These may be more susceptible to tinnitolytic drugs that would preferentially bind to these new targets and hence attenuate the perception of tinnitus.

How did your research career develop to where it is now?

I initially set out as a young scientist in the hope of a research career with a clear narrative and trajectory. As for many scientists, this linear trajectory did not happen! I have moved around a range of projects but mainly within the auditory field. One project I particularly remember joining in Bradford in the 1990s involved using Fast Fourier Transform analysis of peripheral blood flow to non-invasively predict ovulation.

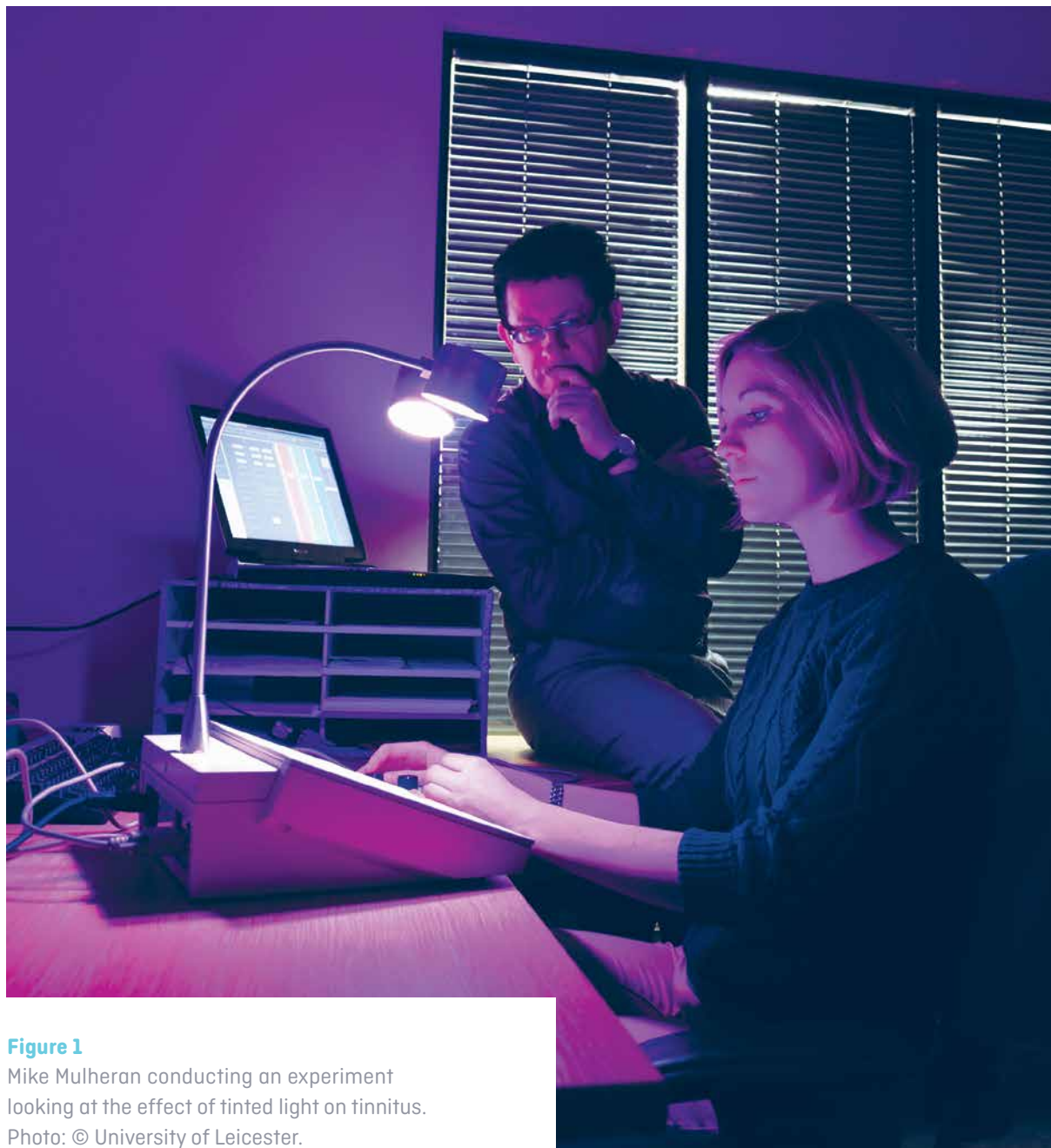


Figure 1

Mike Mulheran conducting an experiment looking at the effect of tinted light on tinnitus. Photo: © University of Leicester.

I then went back into the auditory field working in experimental and clinical ototoxicity with a particular interest in looking at aminoglycoside ototoxicity in patients with cystic fibrosis and people who had recovered from bacterial meningitis. I was also fortunate enough to collaborate on industrial projects with GlaxoSmithKline.

In retrospect, my research career path has not quite been what I had expected and I have found the journey a bewildering mix of excitement,

disappointment and not a little anxiety! For those who remember – it sometimes feels like my having being a contestant in the inter-town game show ‘It’s a Knockout!’

And hopefully without all the foam, although maybe you’ve had the foam! I suppose it’s wise to always expect the unexpected.

I think the key thing is for all researchers to keep an open mind to new opportunities. Often in research, these opportunities can come along and you don’t recognise them for what they are at the time, but

it's important to be open to them. Perhaps even more importantly, it is essential to get along with the colleagues you are working with if you are collaborating.

Wise words. Is there any other advice you would give to others considering a research path in tinnitus?

I've got some general career advice for anyone here going into experimental science and this is particularly relevant to medics thinking of doing research. My advice is that for most projects you will really need to adjust your sense of timescales. This is especially so when coming from a clinical background, where your mind-set is focused on results or 'diagnostic success' being achieved within shorter timescales out of necessity. This is because as a clinician, you will often have an expectation of at least some resolution with any treatment or procedure you've decided upon within days or a few weeks.

In the more 'open loop' environment of experimental sciences, timescales seem to expand exponentially as you begin your search for 'answers'. However, the likelihood of there being a realistic solution or answer, even after years, can sometimes seem to be frustratingly low. Take a look at the tinnitus field! But *mon ami* that's the nature of the beast! The important thing is not to beat yourself up about it and learn to be constructively rather than destructively critical - there is a world of difference!

In addition, I would also advise any budding researcher to make sure that you put time into learning statistics and statistical methods properly. Stats are often seen as the bane of a researcher's life but believe you me, it will pay dividends and help reduce the probability of unnecessary pain of manuscript rejection because you didn't check the experimental design or know how to perform an appropriate test.

Moving away from budding researchers and back to more established ones, what is your favourite piece of tinnitus research?

Favourite piece of tinnitus research? I would genuinely say there are so many pieces of excellent work done in the field that it would be very hard to pick just one. However, I would make mention of the excellent work over the last decade or so done by Susan Shore in her lab at the Kresge Hearing Research Institute at the University of Michigan. I was also very taken by the fundamental studies of Bob Patuzzi on frequency-specific electrocochleography.

I have to say a lot of tinnitus research has also been very well informed by basic neurophysiological research. In this regard, one of the finest examples in scientific method I received was by watching how Nigel Cooper did his work on non-Poisson-like bursting activity in normal auditory fibres. This was akin to seeing what we thought was tinnitus like activity in otherwise normal nerve fibres. Nigel was doing his PhD at the same time as I was doing mine at Keele. He was methodical, consistent and tremendously generous in his time, advice and assistance. Without Nigel, I don't think I would have got through.

Finally, what aspects of tinnitus research give you the most hope for future treatments?

I think eventually, as we begin to systematically conduct clinical trials for a wide range of putative tinnitolytic drugs, we will be able to offer hope to groups of tinnitus sufferers. I believe the voltage gated sodium channel blockers, for example those used as anti-epileptics, have considerable potential for specific tinnitus sufferers.

I also feel that with increased understanding of how cross-sensory modulation of tinnitus works such as somato-sensory stimulus and maybe in combination with the pharmacological approach, would offer hope for the future.

I should also say that in terms of prevention, the simple but effective advice we can give to everyone who suffers from tinnitus - and doesn't suffer from tinnitus - is to avoid excessive noise!

Many thanks Mike; it's been a real pleasure to talk to you.



DR VERONICA KENNEDY
Consultant
Audiovestibular Physician
Bolton NHS Foundation Trust

Veronica Kennedy is an Audiovestibular Physician who leads the Paediatric Audiology Service in Bolton. She was one of the co-authors of the recent first ever Practice Guidance document for the management of tinnitus in children. She has also been involved in the creation of the BTA's series of leaflets on tinnitus aimed at children. She has worked with the BTA for many years providing advice, assisting with information leaflets and participating in courses. Veronica was part of the working group which devised the Tinnitus in Children Practice Guidance, and acted as professional adviser for the BTA series of children's leaflets.

NOT ALWAYS A CONDITION OF THE AGED: Tinnitus in children

Dr Veronica Kennedy

Published scientific literature in 2015 on tinnitus in children covered several themes. These included the prevalence, and risk of developing, tinnitus, investigation of tinnitus, and articles where tinnitus was a symptom accompanying other symptoms in a variety of medical conditions.

There were two papers looking at the prevalence of tinnitus in children. The first was a Polish observational cross-sectional study [1] of 15,199 students aged 7 and 12 years. In this study, 6.0% of the overall children reported tinnitus lasting for 5 minutes or more. A secondary objective was to test the relationship between hearing loss and tinnitus prevalence. The prevalence of tinnitus was found to be significantly related to the degree of hearing loss and age. Children with bilateral moderate hearing loss reported tinnitus significantly more often than children with any other type of hearing loss. Frequency of tinnitus reported by children was equal between sexes. Children with unilateral high-frequency hearing loss reported tinnitus significantly less often compared to other children from the unilateral loss group. The other prevalence paper [2] described the study protocol for an impending systematic review of the prevalence and severity of tinnitus and/or hyperacusis in children and adolescents.

Several papers looked at risks of developing tinnitus. One was a study [3] looking at the association between childhood hearing disorders and tinnitus in adulthood. However, the results of the analyses in this study showed that no childhood hearing disorders were positively associated with tinnitus. The other [4] was more child focused with an interesting - but unsurprising - finding that high school music students are exposed to high sound levels in the course of their academic activity and may be at risk of developing tinnitus. The choice of instrument as well as the music style played a role in this risk. The students in the study reported tinnitus, hyperacusis, diplacusis, and sound distortion. While it was acknowledged that there could be exposure to high sound levels outside the school through other external activities, the authors of the study felt that the students were not entirely aware of the health risks related to exposure to high

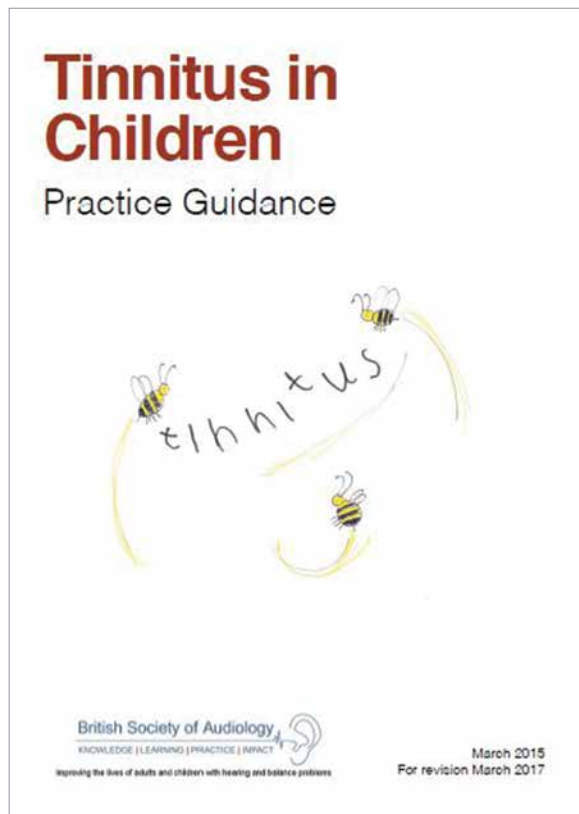


Figure 1

Tinnitus in Children: Practice Guidance [17]

sound pressure levels. This prompted the conclusion that it is important to start intervention in relation to noise risk reduction at an early stage. These findings support the value of the British Tinnitus Association's Plug'em campaign [5] to reduce the impact of noise exposure and protect against tinnitus.

For adults with unilateral tinnitus or unilateral or asymmetric hearing loss, Magnetic Resonance Imaging (MRI) is recommended in order to investigate the possibility of a vestibular schwannoma [6]. The evidence for routine MRI screening in children for vestibular schwannoma seems to be less robust. There was one study in 2015, which looked at the use of MRI in children with auditory or vestibular symptoms [7]. Levi *et al* retrospectively reviewed the results of 65 children referred for a MRI with tinnitus as one of the referral reasons. While the study focused on the 34 who underwent audiometric assessment, findings of an enlarged vestibular aqueduct, a post traumatic extradural haematoma

and an incidental Chiari 1 malformation were noted in those who didn't have a hearing assessment. Of those who had a hearing assessment, nine had a hearing loss. There was no pathology on MRI relating to the vestibulocochlear system or involving the cerebellopontine angle in any of these cases. Four of the nine children where a hearing loss was noted were found to have demyelinating changes on their MRI scan, three being consistent with multiple sclerosis. These three children had a unilateral hearing loss, with neurological symptoms (ataxia, cranial nerve palsies) noted in two.

The remainder of the papers which mentioned tinnitus in children were predominantly case reports or series with most focused on hearing loss. There was one paper where tinnitus was the presenting symptom in two children with a raised intracranial pressure [8]. Both children subsequently developed headaches and one developed double vision. The tinnitus persisted for the 10-12 month follow up period despite treatment of the raised intracranial pressure. Pulsatile tinnitus is a known symptom of intracranial hypertension, however, the tinnitus in these cases was not reported to be pulsatile. Non-pulsatile tinnitus was reported as a symptom in case report of a child presenting with sensorineural hearing loss and intracranial hypertension [9]. This child also had vertigo and a continuous headache. After treatment, his symptoms settled and within the two year follow up, his hearing loss, vertigo and tinnitus symptoms had resolved. Non-pulsatile tinnitus was also part of the presenting symptoms in a series of children with focal epilepsy where the tinnitus accompanied vestibular symptoms suggesting a temporal-parietal ictal origin of the epilepsy [10].

There was one case report which mentioned tinnitus as a symptom in a child with an autoimmune hearing loss [11]. The child also presented with dizziness and subsequently developed a congenital heart block. Another case report described transient tinnitus as part of the presenting otological symptoms accompanying vertigo in a 13 year old with juvenile Ménière's disease [12]. Ewers *et al* published the case of a 15 year old with Lyme disease who presented with tinnitus, taste disturbance, otalgia and subjective hearing loss [13]. The symptoms resolved with antibiotic therapy. Tinnitus was also a symptom reported in a study of children and adults with temporal bone fractures [14]. After a 12 month period, tinnitus was still present in 56% of the patients.

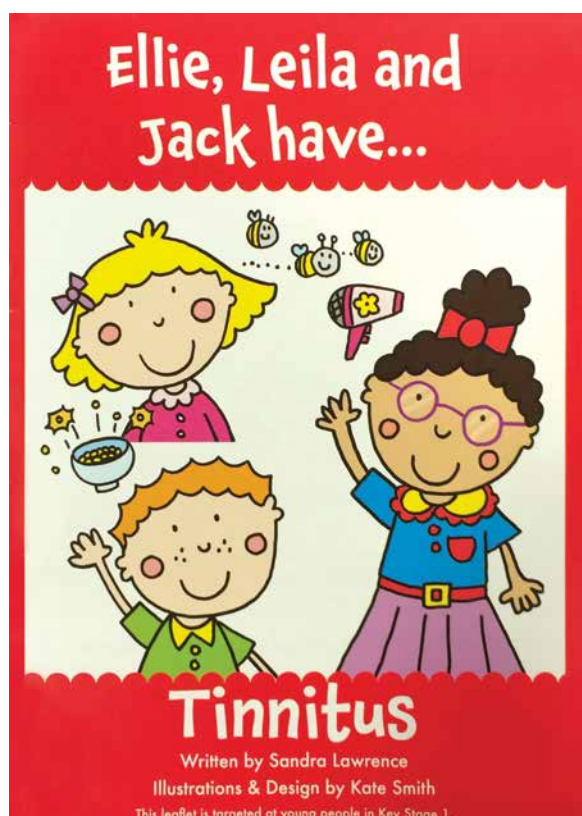


Figure 2

One of the BTA's range of leaflets for children [18]

Showing that tinnitus is not always bad news, a retrospective case series of 37 children with idiopathic sudden sensorineural hearing loss found that the presence of tinnitus, as well as early intervention, was positively associated with hearing recovery [15].

One of the main aims of research is to improve the care of those with tinnitus. Putting this into practice, in 2015, the British Tinnitus Association (BTA) was involved in a number of child focused tinnitus publications. In 2012 the James Lind Alliance had undertaken a Tinnitus Priority Setting Partnership. This non-profit making initiative specialises in bringing patients and clinicians together to identify and prioritise uncertainties, or 'unanswered questions'. The project identified the top ten research uncertainties for tinnitus agreed by patients and clinicians. One of these agreed top ten uncertainties was the need to identify the optimal set of guidelines for assessing children with tinnitus [16]. To help address this uncertainty, in 2015, the Paediatric Audiology Interest Group (PAIG) of the British Society of Audiology (BSA), supported by the BTA, published Practice Guidance for the management of children with tinnitus (Figure 1) [17]. The guidance was based on adult tinnitus guidance principles but underpinned by child friendly practice principles, guidance on the management of conditions in children such as anxiety, and recognition of the changing cognitive and linguistic needs throughout childhood. The guidance provides a toolkit of different assessment and management approaches tailored to the needs of the children and their families and appropriate to different ages and levels of understanding of the child.

Complementing this publication, the BTA was successful in obtaining funding from Awards for All England (Big Lottery Fund) to develop a series of leaflets for children. After wide consultation and the selection of a specialist writer for children and illustrator, information about tinnitus was incorporated into a charming story for the under eights [18], as well as more factual pieces for the 8-11 [19] and 11-16 age groups (Figure 2) [20]. The leaflets were Highly Commended and Commended in the British Medical Association's Patient Information Awards. The BTA also successfully held a number of two day courses in 2015 on the assessment and management of tinnitus in children. The BTA is planning further expansion of its range of resources for children with tinnitus.

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DAVID STOCKDALE

Chief Executive

British Tinnitus Association

David Stockdale has been Chief Executive of the British Tinnitus Association (BTA) since February 2010 where he is responsible for anticipating, shaping and influencing the direction of the charity at strategic and operational levels. He sees supporting the tinnitus community, ensuring a preventative message targets those at risk and increasing research into tinnitus as the BTA's priorities. He is a member of the British Society of Audiology's Tinnitus and Hyperacusis Special Interest Group and the co-author of a number of tinnitus related papers

WHAT DOES THE TINNITUS COMMUNITY WANT FROM RESEARCH?

David Stockdale

What does the tinnitus community want from research?

The British Tinnitus Association (BTA) has a huge interest in following research, identifying the latest theories, following projects and understanding the direction of travel of the leading centres. We commission, follow, lobby, influence and disseminate research across the UK. We always want more high quality research to be undertaken. There are many neglected aspects of the condition that get little attention - and this is within a field we believe is underfunded and undervalued to begin with.

Talking to people with tinnitus

Over the last year, we have been undertaking work to better understand people's hopes and aspirations for research across the tinnitus community, building on the James Lind Alliance Tinnitus Priority Setting Partnership (www.tinnitus.org.uk/JLA) that the BTA led on in 2012 [1][2] (Figure 1). We have been asking people with tinnitus what they want from research. We have done this through our information days, annual conference and when visiting tinnitus support groups. The answer is of course obvious – a cure. If you start to unpick this though, then the answer becomes more nuanced. A cure means different things to different people. For some, it is to never hear the tinnitus ever again. For others, a cure is viewed as being able to live a life undisturbed by tinnitus – which can mean still hearing the sound but not being bothered by it. In some ways, the latter sounds more achievable, but the former offers a far simpler outcome to assess.

When talking with the tinnitus community about research priorities, discussion often focuses on prevention. What are the best ways to prevent tinnitus where possible? This is a priority for people with tinnitus and an area which may be neglected, as it is often not reflected in research output. There is no section on it within this publication. Prevention forms one of the strands of the BTA's education aims, with the development of the Plug'em project and website www.plugem.co.uk (Figure 2).

Figure 1

James Lind Alliance Tinnitus Priority Setting Partnership workshop



The tertiary concern is the necessity to work within the healthcare sector more generally. There is a need for information to aid a better understanding of the condition amongst General Practitioners. Again, this is an area where little work has been produced. Fourthly, the management of tinnitus has been raised as a priority. It can be argued this was further down the list as it could also be considered under 'cure' for some. There is a desire to better understand what treatments that could help people with tinnitus are available now and how to improve access to such treatments. In addition, there is a need to understand what is out there that does not work, is unproven at best or is ineffective. Very little research currently explores those treatments that we have all heard about that are out there and we have a feeling that they are ineffective, and yet are still heavily marketed as alleviating tinnitus.

Interaction with research and dissemination

There is also then an expectation that research results will be disseminated and that it will be done in a timely manner. We would like to see that trials are published using media other than journal articles and conference presentations to disseminate results. There was a desire to see video reports of research and more accessible charts and summarised reports. There is also a desire to know "What next?" "So what?" "What happens after the fanfare of publication?" "How will the

research be used and developed?" Again, to many this is a mystery and a better understanding of this would be of great benefit to the wider tinnitus community and possibly also the research community. We need to democratise access to research. With social media and online publishing widely and cheaply available, there has never been a better opportunity to bring research to the notice of the general public.

There was also concern over the potential for some trials to give the perception that they over promise and under deliver. Many projects start, are terminated early or find no overall change. When there are the means and methods for the tinnitus community to discuss these trials *ad infinitum*, there is a responsibility on the part of the researchers and commissioners to be honest about the possible outcomes - ALL the possible outcomes. It can be a huge blow to the community when trials of the 'new hope' reveal that it is not everything we hoped for. The hope invested by the tinnitus community in some of these trials may be unrealistic, and it is important we all play a part in managing expectations, and we can do this by better communication from the outset. However, hope is what research offers the tinnitus community. Hope that there will one day be a cure, hope that tinnitus can be prevented, hope that there will be better understanding throughout healthcare,

hope that everyone can access improved management options. Hope is vital for people with tinnitus, and the importance of it should not be underplayed. We do need to manage these hopes and expectations correctly. However, we can offer everyone the hope that there is a skilled, dedicated, compassionate research community out there working tirelessly to produce a better future.

Clinicians' perspective

The BTA works extensively with clinicians across the UK. We have just started to develop Regional Tinnitus Networks to better support clinicians offering tinnitus services, based on a model pioneered by our President Dr David Baguley in the East of England. Feedback from this group is that there is far more research than was previously the case. Whilst this is seen as a positive step, sorting through the 'noise' for what is clinically meaningful and relevant is more challenging for busy clinicians. Hopefully this document goes some way to resolving that!

Our challenge to the research community is threefold:

1. Ensure that the results of their research are accessible and available in a range of different formats.
2. Ensure that any promises of what the research offers (both before and after publication) are measured and balanced.
3. Help clinicians identify what is meaningful to them in their roles and to support them translating it into practice.

Most of all though, we want researchers to carry on doing what they are doing, giving the millions out there living with tinnitus hope of a better future.

References

[1] British Tinnitus Association. *James Lind Alliance Tinnitus Priority Setting Partnership*. 2013 available from www.tinnitus.org.uk/JLA [accessed 27 July 2016].

[2] Hall D, Mohamad N, Firkins L, Fenton M, Stockdale D. Identifying and prioritizing unmet research questions for people with tinnitus: the James Lind Alliance Tinnitus Priority Setting Partnership. *Clinical Investigation*. 2013; **3(1)**: 21-28. doi: 10.4155/cli.12.129



Figure 2

The Plug'em campaign www.plugem.co.uk

