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editorial

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# Hearing loss and tinnitus – the hidden healthcare time bomb

Hearing loss and severe tinnitus affect 16% and 1% of the population, respectively; the prevalence of both conditions increases with age. In the next 10 years, the number of individuals over the age of 65 years is set to outnumber those under the age of 5 years for the first time in history [1], and by the year 2040 the number of elderly worldwide is set to soar to 1.3 billion [1]. Such changes in demographics will undoubtedly shape new global approaches to healthcare, with a clear need to address conditions more often faced by the elderly, greatly affecting quality of life but currently dismissed as a 'natural' part of the aging process.

Hearing loss currently costs society billions each year [2], and with major shifts in demographics towards an older population, it is likely to become an even greater economic burden to society in the future. Why then are there no licensed pharmaceuticals available that target this condition? In the past, this might have been due to a lack of knowledge of the basic biology of hearing loss, but the field has made significant advances, and in the past ten years has entered the realm of 'translatable research'. This issue of *Drug Discovery Today*, produced in conjunction with the RNID (see Box 1) and Fight for Sight, highlights the advances made in the understanding of the biology behind hearing and vision loss, and the exciting potential for treatments. This editorial examines how advances in hearing research, could provide answers to the treatment of presbycusis (age-related hearing loss) and tinnitus. With such exploitable markets at hand, industry should view both hearing loss and tinnitus as the next major conditions to target and upon which to capitalise.

## An aging population

Over the past century, the medical field has moved forward in radical leaps and bounds. The combination of advanced biological and technical knowledge has meant that ailments which previously held with it a death sentence are now treatable, and even curable. As such life expectancy has shot up; in the UK today one in four children born can expect to live to 100 years of age (http://www.ageconcern.org.uk/). Although such achievements can surely be marvelled at, society now faces a very different type of healthcare problem, shifting the focus from merely getting us to old age, to maintaining or improving quality of life once old age is reached.

A recent report by the NIH estimates that within 35 years the over-65 year olds will make up 14% of the total world population, double the current proportion [1]. This puts the number at around 1.3 billion [1]. Such a prominent section of society will not stand for the dismissal of age-related conditions as simply a 'natural' by-product of the aging process. In short, society will need to tailor its approach to healthcare, placing greater emphasis on the treatment and cure of age-related conditions; an aged individual might live

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with such an ailment for another 30–40 years, one-third of their total lifespan.

## Sensory impairment: the burden of hearing loss

Sensory impairment is one such group of conditions largely dismissed when experienced by the aged. Although not life-threatening, sensory impairment is often concomitant with more serious conditions. For example, individuals suffering a hearing loss experience diabetes [3,4], stroke [4] and elevated blood pressure [3] more often than those with normal hearing. Hearing loss, as a communication disorder, can result in feelings of isolation and depression, reduced physical and psychological well-being, and social withdrawal [5]. In assessments of global burden of diseases, hearing loss was ranked 13th most disabling in 2002, and is projected to jump to a ranking of 9th by 2030, just two rankings below chronic obstructive pulmonary disease [6].

Presbycusis, or age-related hearing loss (>25 dB HL) is estimated to affect just over 40% of people aged 61–80 years old in its mild form (UK) and a further 20% in its moderate to severe form (>35 dB HL) [7]. Presbycusis is a progressive bilateral sensorineural hearing loss initially affecting high frequencies then spreading to lower frequencies. The onset of presbycusis might be affected by lifelong exposure to excessive noise, ototoxic drug exposure, pathological conditions and genetic predisposition. In this way, the treatment of presbycusis, at least in its primary stages, might be the same as for other forms of sensorineural hearing loss.

The prevalence of tinnitus also increases with age and often coexists with a hearing loss [8]. It is a heterogeneous condition generally described as the perception of sound without an external source, and can be significantly debilitating to the lives of sufferers. Although the majority of those affected by hearing loss and tinnitus are elderly, the underlying pathology of both remains the same across age groups. For example, hearing loss is often associated with the degeneration of sensory hair cells, auditory neurons and supporting structures within the cochlea. Thus, to find treatments for these conditions, a broad approach, irrespective of age, must initially be taken and later applied more specifically within the aging paradigm.

## Current approaches to treatment and advances in the field

One of the major criticisms of the hearing loss and tinnitus research fields, with respect to development of therapeutics, has been the lack of available animal models for basic research and preclinical trials. As Henry Ou's review in this issue of *Drug Discovery Today* demonstrates, such limitations are no longer the case, and a variety of models are now available for use. Traditional animal models remain the tool of choice for studying the life cycle of sensory hair cells, particularly in mammalian systems. An exciting tool for drug discovery and screening is the zebrafish. Research with these small fish has already led to the identification of ototoxic drugs and drugs with potential otoprotective properties.

Various human cell lines have been and are being developed to provide a further tool for research and drug screening. The source of these cells makes their use distinctly advantageous on the road to developing clinically relevant therapies. The development of auditory stem cells for restorative therapeutics is particularly exciting. As Marcelo Rivolta reviews in this issue, human fetal auditory stem cells have recently been isolated, expanded and demonstrably exhibit hair-cell-like phenotypes when differentiated in the presence of retinoic acid (RA) and epidermal growth factor (EGF). Although this type of technology presents the tantalising possibility of 'curing' sensorineural deafness, issues surrounding translation to the clinic must still be addressed.

In addition to the identification of effective drugs that might have restorative or protective modalities of action, drug delivery to the inner ear in itself presents a major challenge (reviewed by Staecker *et al.*, in this issue). One novel approach being examined by most implantable device companies is the potential to deliver drugs locally via their devices. Candidate drugs are being selected that might enhance the functionality of cochlear implants in several ways. These include anti-inflammatory drugs reducing the trauma to the ear upon implantation and antioxidants or gene therapy approaches to prevent further degeneration of auditory cells.

The development of treatments for tinnitus might be seen as far more challenging than that of hearing loss due to the varied aetiology of the condition. Yet despite this, the strong neurological component of tinnitus has made it an attractive target for some larger pharmaceutical companies such as GSK and Merz (see Elgoyhen *et al.*, in this issue). Indeed the recent commercial activity within tinnitus R&D demonstrates how, if companies think creatively, they might be able to adapt existing compounds for treatments in novel areas of unmet clinical need, which present large untapped markets.

## Hearing progress?

Although hearing loss and tinnitus research has made spectacular advances in the past ten years, the lack of research funding and

commercial interest in true translational research programmes are major barriers in the development of much needed treatments. In 2007–2008, hearing loss researchers in the UK only received £6.8 million in funding from the Government's main medical research funding body (MRC). Diabetes, which WHO nominates as having a lower global burden of disease than hearing loss (ranked 20 *versus* 13 for hearing loss [5]), received £21.7 million worth of MRC funding in that same year (personal correspondence with MRC). Such chronic under-funding places the onus on not-for-profits to help cover the short fall.

Few incentives exist for the pharmaceutical and biotechnology sectors to invest in new streams of R&D, where the markets are not yet established. RNID attempts to encourage interest in hearing loss/tinnitus R&D by producing free market reports, which provide companies with essential information on market size, segmentation, value and background biology. For example, the RNID presbycusis market analysis report estimates a current market size of 50.5 million in the USA and EU alone and predicts a novel treatment to be worth US$1.5 billion per annum [6].

Governments and funding bodies have identified aging and quality of life as priority areas, however, although it would seem obvious for hearing loss and tinnitus to be strongly linked to these issues, somehow those links remain as mere weak associations. Governments and industry alike need to recognise that hearing loss is a major contributor to the loss of quality of life amongst the elderly, and one that could be reduced by focussing resources on greater R&D in this field.

Neither hearing loss nor tinnitus is a communicable or life-threatening condition, facts which perhaps further contribute to their 'forgotten' nature. When describing these conditions, what must be stressed is the extreme isolation sufferers experience and the devastating impact on quality of life, both of which might lead to the development of more serious conditions. This issue of *Drug Discovery Today* is decidedly timely, highlighting the necessity for investment in research and technology to aid, cure or halt the progression of sensory impairment, particularly as result of the aging process. Ideally, social responsibility alone should drive this investment but pragmatically, the economic benefit to society as a whole and industry specifically, will, if recognised, see a shift in attitude towards a real expansion within this field with benefits finally reaching the millions affected worldwide.



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