



Tinnitus Research update

What key direction is current research taking?

Progress towards finding a cure will be made a lot faster if scientists can work out where and how tinnitus starts. Recent research evidence indicates that tinnitus can either originate in the brain or inner ear (cochlea).

Imaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have been used to demonstrate tinnitus-related activity in the brains of individuals who are able to alter or modify their tinnitus (known as somatic modulation). These tests have shown that areas of the brain that process information from the ears are more active in tinnitus sufferers than in people without the condition. As a next stage, researchers are trying to stimulate these overactive areas of the brain to see whether they can reduce people's perceptions of tinnitus (see section on rTMS below). It is hoped that as these techniques become more widely used, they will increase our understanding of the nature of tinnitus and enable the development of new treatments.

New animal research shows from where, for some tinnitus sufferers at least, the extra brain activity seen in somatic modulation may come. A study of two groups of guinea pigs, one deaf and one with normal hearing investigated nerve cells in one of the first parts of the brain to receive signals from the ear. The area contains 'multi-sensory cells', so called because they can respond to other senses in addition to hearing; for instance they can be activated by the sense of touch. When the nerve that carries touch signals from the face and neck was stimulated, the multi-sensory brain cells became more active in the deaf than in the hearing group. Researchers believe that in the absence of a signal coming from the ear, as in the deaf group, the cells 'over-compensate' and the result is interpreted as sound.

It is now widely accepted that one cause of tinnitus is the release of excessive amounts of the neurotransmitter glutamate by hair cells in the inner ear. Normally, glutamate plays a vital role in communication between nerve cells, making them more likely to send a signal onwards. However, when the cells are subjected to stress - for example by exposure to loud noise or to drugs that are toxic to hair cells - they over-produce glutamate, causing a negative effect known as excitotoxicity. The result is that the original connections between hair cells and the nerves that carry signals from the inner ear on to the brain are destroyed, but can later be replaced by the growth of new ones. These new connections are of a different type to the originals and function differently, becoming over-active when glutamate is released. The over-activity is then perceived as tinnitus.

Research has also indicated that tinnitus could originate in the supporting cells of the cochlea of the inner ear, which are the cells that lie close to the nerve or hair cells. US scientists have discovered that these cells in the developing ear can make their own noise, long before the ears are able to detect sound around them. They have discovered that these cells release a chemical called ATP, which cause the hearing system to generate brain activity in the absence of sound during the early stages of development of the inner ear. If these processes can be reactivated, for example after injury to the cochlea which can cause the release of ATP, it might also explain why people experience tinnitus later in life.

Tinnitus treatments and recent research findings.

- A study at the University of Milan has looked at the link between **tinnitus and hearing loss**. It was already known that most people with hearing loss have some degree of tinnitus but some sufferers of tinnitus appear to have normal hearing. Initial results from the study found that most of those with apparently normal hearing in fact appear to have at least mild hearing loss, especially at higher pitches that are often not tested in a standard audiogram.
- **Hearing aids** are increasingly being used to treat tinnitus as it is thought that tinnitus results where the brain overcompensates for the loss of hearing at particular frequencies. Therefore, providing sufficient input at these should reduce tinnitus. Digital hearing aids alleviate tinnitus more effectively than analogue aids as they can selectively amplify some of the higher frequencies at which tinnitus generally occurs. Scientists at the third meeting of the Tinnitus Research Initiative (TRI) in 2009 called for more research to develop digital hearing aids that can represent these frequencies more effectively and, importantly, using less battery power.

The “open fit” style of hearing aid also seems to be particularly suitable for people with tinnitus and has undergone trials in several centres. Conventional aids can aggravate tinnitus symptoms because they block the ear with an ear mould. With the new design, the canal is left open as the hearing aid is connected into the ear by a thin tube.

- **Cognitive behavioural therapy (CBT)** is a treatment administered by a therapist which seeks to change people's attitudes and behaviour. When used to treat tinnitus it seems to improve patients' quality of life, even when the volume of noise from the tinnitus remains the same. This finding comes from a review of six small trials that gathered data on 285 patients. Tinnitus sufferers reported greater overall satisfaction with their life, compared to a similar group of patients who did not receive CBT treatment. This was in spite of the fact that the CBT failed to produce significant improvements in the subjective (or perceived) volume of tinnitus.
- There is currently a lot of research looking into medications to help tinnitus sufferers and drug companies are interested in finding drugs to suppress it. Many **medications** have been proposed to relieve tinnitus such as lidocaine, benzodiazepines and antidepressant drugs, but so far none has been found to be

truly effective. One drug that shows promise is acamprosate, normally used to treat alcoholism. A randomised controlled trial of 50 people with tinnitus found that the condition improved in 87% of those who received the drug compared with 44% who received a placebo. However, it is not known whether the amount of improvement was great enough to be clinically useful and so further research is needed before the drug can be accepted as a standard treatment.

Another drug which is currently undergoing clinical trials at several centres internationally is called *neramexane*. Initial results from a previous, smaller trial were promising but inconclusive. The current trial will look at potential side-effects and how long any positive effects last.

A review of trials using anticonvulsant drugs to treat chronic tinnitus found just one study with reliable results. The study found that *gabapentin* is not an effective treatment.

Finally, Professor Ana Belén Elgoyhen has presented a promising target for drug development that may be effective for treating hearing loss and tinnitus. A mutation has been discovered in the hair cells of the outer ear of mice that protects the inner ear from noise-induced damage, potentially preventing both hearing loss and tinnitus. Future research will seek to develop a drug treatment that reproduces the effect of this mutation.

- Herbal extracts from the plant **ginkgo biloba** are commonly proposed as a treatment for tinnitus. However, the two most systematic clinical trials, both double-blind and placebo controlled and published in respected peer-reviewed journals, have yielded negative results and suggest that ginkgo biloba extracts are of little more use in the treatment of tinnitus than a placebo. These studies concluded that Ginkgo biloba does not benefit patients with tinnitus.
- A study on **Tinnitus Retraining Therapy (TRT)** reported on 51 patients who were treated for 18 months. 68% of patients reported a reduction in their symptoms relating to tinnitus, such as sleep disturbance, problems with concentration, and inability to relax. 65% thought that their quality of life was improved. Patients who had suffered from tinnitus for less than one year achieved significantly better results than patients who had suffered for a longer period of time. The researchers concluded that TRT is an effective tool in the treatment of tinnitus.

Overall, trials of TRT report success rates of between 70% and 85%. Although these results might appear impressive, there are still no properly controlled clinical studies of efficacy reported in respected scientific journals.

- **Repetitive magnetic transcranial stimulation (rTMS)** is a new, non-invasive approach being developed to reduce tinnitus symptoms. An electromagnet placed on the head uses rapidly changing magnetic fields to generate weak electric currents which excite neurons in the brain.

Preliminary results testing the effectiveness of rTMS in tinnitus patients indicate that it can suppress tinnitus for some people.

Recent pilot studies have been undertaken to determine whether rTMS can reduce patients' perception of chronic tinnitus. One study showed that TMS resulted in partial suppression of tinnitus for six out of 15 subjects. The amount of suppression ranged from 19% to 86% (average 50%). The duration of tinnitus suppression for each of the six subjects was: 20 min, 30 min, 45 min, 60 min, and one and four days, respectively.

A second study tested rTMS for the treatment of tinnitus in 60 patients over a 10-day period. Results showed that there was a remarkable reduction in tinnitus after active stimulation and tinnitus improvement lasted up to three months in some patients. However when treatment was discontinued, the tinnitus returned in all cases.

- An American company has begun pilot studies of a patch designed to be surgically implanted under the skin, above the auditory cortex in the brain of severe tinnitus sufferers. This **cortical-stimulation** device produces electrical impulses controlled by another implant, the size of a pack of cards, which is implanted into the chest of the wearer. All eight patients who were treated with the device over a period of 12 weeks reported an improvement in their tinnitus, but it is not yet known how the device works and further clinical trials are needed.
- Another new therapy is **Neuromonics** which was developed in Australia. It involves music, combining the use of acoustic stimulation with a structured program of counselling and support. It needs independent research to demonstrate its benefits and is not yet available in the UK.
- One of the key themes of the Tinnitus Research Initiative (TRI) meeting in 2009 was the development of treatments that use specially designed sounds to change or even reverse the brain activity that leads to tinnitus. Dr Grant Searchfield and his colleagues at the University of Auckland presented encouraging results from patients who were asked to group sounds that were similar in pitch to their own tinnitus together into one category. After three weeks of training there was both a reduction in the brain activity associated with the categorised sounds, measured using EEG, and a decrease in the level of tinnitus distress experienced by the patients.
- However, a study of **PhaseOut** treatment, by University Medical Centre, Groningen, showed that this treatment was no more effective than stimulating patients with a pure tone. PhaseOut uses a changing cyclic pattern which has been claimed to prolong tinnitus suppression. The study's findings did not support this claim.
- In 2007, eight patients with hearing loss and severe tinnitus were fitted with a **Vibrant Soundbridge®**, an implanted hearing aid that works by vibrating bones in the middle ear and is effective at higher frequencies. German researcher Dr Ebherd Biesinger found in a follow-up study two years later that, when switched on, the *Vibrant Soundbridge®* completely suppressed tinnitus in those patients for whom sound stimulation treatments had been found to work.

The contribution of Deafness Research UK to tinnitus research

Supporting research into tinnitus has been a priority for Deafness Research UK since its inception in 1985.

During the 1990s it gave considerable financial support to Mr Jonathan Hazell of University College London (UCL) for his ground-breaking work to develop Tinnitus Retraining Therapy, a treatment which combines specially designed counselling sessions with sound therapy.

The charity established a Tinnitus Research Group made up of leading UK clinicians and scientists. The group considered how they could encourage more researchers to study tinnitus as there were very few people working in the field. They explored research being undertaken in other medical areas and identified what might be relevant to tinnitus. As a result, research being conducted into the fundamental nature of deafness is now helping to improve our understanding of tinnitus.

The Group encouraged new researchers into the field such as Dr Carole Hackney at Keele University who has discovered that an overproduction of the neurotransmitter glutamate can be linked to tinnitus, a finding central to the development of new drug treatments for the condition (e.g. acamprosate, mentioned above).

Professor Jonathan Ashmore of University College London, who was studying the functioning of the cochlea (inner ear), applied his knowledge to identify what parts of the organ are involved in tinnitus generation. In turn, his work has influenced that of his colleague, Professor Dave McAlpine of the UCL Ear Institute and now one of the world leaders in our understanding of the brain processing mechanisms underlying tinnitus.

In 2007 Dr David Baguley, Director of Audiology at Addenbrooke's Hospital Cambridge, was awarded a Deafness Research UK travel grant which enabled him to spend three months as a visiting Professor at the University of Western Australia where he was based in the Ear Sciences Institute. He worked with scientists interested in the mechanisms of tinnitus and hearing loss, discussing for example, the relationship between tinnitus, hyperacusis and acoustic shock.

In 2008 Deafness Research joined forces with the charity Action for Tinnitus Research (ATR). We started talking to ATR about ways in which we could work together early in 2007. It quickly became apparent that, by combining our resources, we could make an even greater difference to the quality and quantity of tinnitus research being carried out in the UK and radically improve the quality of service offered to tinnitus sufferers. To that end we will be placing even more emphasis on tinnitus research.

In June 2009, Deafness Research UK attended the third conference of the Tinnitus Research Initiative (TRI), a privately funded organisation founded in 2006, dedicated to finding a cure for tinnitus through clinical and scientific research.

TRI held its third conference in Stresa, Italy, bringing an international group of researchers together to discuss past and present results and move the field of tinnitus research forward. Deafness Research UK attended the meeting to share ideas and to find out what has been achieved so far.

Most recently, the results of an important first study into whether there is medical evidence for an effect of caffeine on tinnitus have become available. The research funded by Deafness Research UK and headed by Dr Lindsay St Claire at the University of Bristol wanted to challenge the claim that caffeine makes tinnitus worse because many professionals have supported caffeine withdrawal as a tinnitus therapy, even though no link between the two have been established scientifically.

The research has found that giving up caffeine does not relieve tinnitus and acute caffeine withdrawal might add to the problem. This research provides the first experimental evidence to challenge the theory that caffeine triggers or aggravates tinnitus.

Deafness Research UK is the only national medical research charity dedicated to helping people with deafness, tinnitus or other hearing problems.

Scientists are now predicting that within the next ten to fifteen years there could be a cure for some forms of deafness and much more effective treatments for tinnitus. Deafness Research UK is at the forefront of this work.

You can support us by making a donation or joining the Deafness Research UK League of Friends. For more information call us on 0207 833 1733 or write to:

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