MedicalXpress

Study identifies key cellular mechanisms behind the onset of tinnitus

May 10 2012

Researchers in the University of Leicester's Department of Cell Physiology and Pharmacology have identified a cellular mechanism that could underlie the development of tinnitus following exposure to loud noises. The discovery could lead to novel tinnitus treatments, and investigations into potential drugs to prevent tinnitus are currently underway.

Tinnitus is a sensation of phantom sounds, usually ringing or buzzing, heard in the ears when no external noise is present. It commonly develops after exposure to loud noises (acoustic over-exposure), and scientists have speculated that it results from damage to nerve cells connected to the ears.

Although hearing loss and tinnitus affect around ten percent of the population, there are currently no drugs available to treat or prevent tinnitus.

University of Leicester researcher Dr Martine Hamann, who led the study published in the journal *Hearing Research*, said: "We need to know the implications of acoustic over exposure, not only in terms of hearing loss but also what's happening in the brain and central nervous system. It's believed that tinnitus results from changes in excitability in cells in the brain - cells become more reactive, in this case more reactive to an unknown sound."

Dr Hamann and her team, including PhD student Nadia Pilati, looked at

cells in an area of the brain called the dorsal cochlear nucleus - the relay carrying signals from nerve cells in the ear to the parts of the brain that decode and make sense of sounds. Following exposure to loud noises, some of the nerve cells (neurons) in the dorsal cochlear nucleus start to fire erratically, and this uncontrolled activity eventually leads to tinnitus.

Dr Hamann said "We showed that exposure to loud sound triggers hearing loss a few days after the exposure to the sound. It also triggers this uncontrolled activity in the neurons of the dorsal cochlear nucleus. This is all happening very quickly, in a matter of days"

In a key breakthrough in collaboration with GSK who sponsored Dr Pilati's PhD, the team also discovered the specific cellular mechanism that leads to the neurons' over-activity. Malfunctions in specific potassium channels that help regulate the nerve cell's electrical activity mean the neurons cannot return to an equilibrium resting state.

Ordinarily, these cells only fire regularly and therefore regularly return to a rest state. However, if the potassium channels are not working properly, the cells cannot return to a rest state and instead fire continuously in random bursts, creating the sensation of constant noise when none exists.

Dr Hamann explained: "In normal conditions the channel helps to drag down the cellular electrical activity to its resting state and this allows the cell to function with a regular pattern. After exposure to loud sound, the channel is functioning less and therefore the cell is constantly active, being unable to reach its resting state and displaying those irregular bursts."

Although many researchers have investigated the mechanisms underlying tinnitus, this is the first time that cellular bursting activity has been characterised and linked to specific potassium channels. Identifying the

potassium channels involved in the early stages of tinnitus opens up new possibilities for preventing tinnitus with early drug treatments.

Dr Hamann's team is currently investigating potential drugs that could regulate the damaged cells, preventing their erratic firing and returning them to a resting state. If suitable drug compounds are discovered, they could be given to patients who have been exposed to loud noises to protect them against the onset of tinnitus.

These investigations are still in the preliminary stages, and any drug treatment would still be years away.

The research was funded by a Research Councils UK fellowship to Dr Hamann, a grant from the Wellcome Trust and a PhD studentship from GlaxoSmithKline, with follow-up investigations funded by a three-month grant from Deafness Research UK. Further pharmaceutical research will be carried out by the University of Leicester in collaboration with Autifony Therapeutics Ltd via a Medical Research Council Case studentship due to start in October 2012.

Vivienne Michael, Chief Executive of Deafness Research UK, said "We're pleased to hear about this progress in such a debilitating hearing impairment. The charity continues to fund research into better treatments for tinnitus, with the ultimate aim of a cure. Our free information leaflets offer immediate help to sufferers and our national helpline provides additional support. Regularly tinnitus generates the most requests for help."

Provided by University of Leicester

onset-tinnitus.html