

## **Tinnitus Research – What Animals Have Taught Us about Tinnitus-Related Activity Patterns in the Brain**

This article continues a series on tinnitus research. In the last article, I introduced the concept of an animal model of tinnitus and how it was verified that animals can indeed perceive tinnitus. I will now summarize what we have learnt from these animal models about how tinnitus might manifest itself in the brain through aberrant activity patterns of nerve cells in the central auditory system (the parts of the brain that are dedicated to the processing of auditory information).

Even in a quiet situation, the nerve cells in the auditory system are not resting. Instead, a lot of them show a considerable amount of spontaneous activity, generating so-called action potentials, little electrical pulses that send messages from one nerve cell to others. However, we do not perceive this normal, healthy spontaneous activity, it signals nothing but silence. The presence of external sounds changes neuronal activity in the auditory system: those neurons that have a preference for the sound are activated, they generate more action potentials to signal the presence of the sound. Moreover, neurons that are tuned to similar sounds, or to features of a complex sound, coordinate their activity and start generating action potentials in synchrony.

In animal models of tinnitus, researchers have recorded the spontaneous activity of neurons in the auditory system, looking for deviations from the normal patterns of spontaneous activity after tinnitus-inducing treatments. Using microelectrodes, they could record the activity of single nerve cells or of small populations of neurons. Such detailed measurements of neuronal activity can only be obtained from animals, brain scanning techniques that are used in humans only measure the average activity of hundreds of thousand of neurons, they are not able to resolve the fine structure of the neuronal activity.

The results from these animal studies indicate that the perception of tinnitus might be related to increased spontaneous activity of neurons in the central auditory system: in animals with tinnitus, the spontaneous neuronal activity was often much higher than in normal control animals. Such elevated spontaneous activity has been found at various processing stages of the central auditory system. Moreover, the neurons were not only more active, they also showed an elevated degree of synchrony in their activity. Thus, the spontaneous neuronal activity was changed such that it was more similar to sound-evoked activity than to normal, healthy, “silence-signalling” spontaneous activity. As a consequence, the altered spontaneous activity could be mistaken as signalling the presence of sound, and thus give rise to the perception of the tinnitus. Interestingly, such neurophysiological correlates of tinnitus have only been found in the central auditory system (i.e. in the brain), but not in the auditory nerve, indicating that tinnitus is generated in the brain, not in the ear.

Further studies have started to unravel how these changes are generated. They found for example that hearing loss leads to a reduction of inhibition in the auditory system, i.e. neurons respond more vigorously to input signals, which could contribute to the development of tinnitus-related brain activity. The functional plasticity mechanisms underlying all of this are still a topic of current investigations. Identifying and understanding these plasticity mechanism might show us a way to revert the pathological changes, and thus to “convince” the hyperactive neurons to return to a normal pattern of spontaneous activity that signals nothing but silence.

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