Press Release

No. 018e, 5 February 2021

Synaptic diversity broadens the range of sound we can hear

Hearing occurs when sensory hair cells in the inner ear convert sound into neural signals transmitted to the brain. The sensory hair cells have about a dozen communication points with the auditory nerve fibers, called synapses. Scientists from the Institute for Auditory Neuroscience at the University Medical Center Göttingen discovered that the synapses of a single sensory hair cell process sound information differently. This diversity contributes to processing of a wide range of sound volumes. Published in The EMBO Journal.

(mbexc/umg) Hearing is one of our most important senses. In fact, hearing disorders are very common: according to the World Health Organization (WHO), about 466 million people (five percent of the world's population) suffer from hearing loss that requires treatment. Understanding the elementary processes of hearing is an important prerequisite for developing better methods for treating hearing loss in the future. For example, it needs to be clarified how our ears do cope with processing a wide range of sound volumes, such as the noise of rustling leaves in a gentle breeze and the loud music in a rock concert. Hearing aids and cochlear implants have limited success in making this wide range of volumes accessible to people with hearing impairment.

First author Dr. Özge Demet Özçete Institute for Auditory Neuroscience, CRC889. Photo: private

Dr. Özge Demet Özçete and Prof. Dr. Tobias Moser, scientists at the Institute for Auditory Neuroscience of the University Medical Centre Göttingen, focused on the first communication point between the sensory hair cells and the nerve fibres to investigate this question. They found that the about fifteen synapses of inner hair cells have different sensitivity and response properties. By combining for the first time imaging calcium signals and transmitter release, they found that synapses of a single hair cell have different sensitivities, and respond differently to the same stimulation. Their conclusion: these synaptic differences help the cell to diversify its output, which might be needed for the processing a wide range of sound volumes.

The study was funded by the Göttingen Cluster of Excellence Multiscale Bioimaging: from molecular machines to networks of excitable cells (MBExC) and the Collaborative Research Center Cellular Mechanisms of Sensory Processing (CRC 889). The research results have been published in The EMBO Journal.

University Medical Center Göttingen, Georg-August-University, Press- and Public Relations
Stefan Weller, Von-Siebold-Straße 3, D-37075 Göttingen, Germany, phone +49-551-39-61020, 39-61022, 39-61024
fax +49-551-39-61023, presse.medizin@med.uni-goettingen.de, www.umg.eu
Editor University Medical Center Göttingen, Georg-August-University, Executive Committee

Press Release

Original publication:

Özçete ÖD, & Moser T (2020) A sensory cell diversifies its output by varying Ca^{2+} influx-release coupling among presynaptic active zones for wide range intensity coding, The EMBO Journal (2020) e106010.
https://doi.org/10.15252/embj.2020106010

Research results in detail

Sound waves are collected by the outer ear, travel through the little bones in the middle ear, and reach to the cochlea in the inner ear. In the cochlea, the vibrations caused by the sound waves deflects the hair bundles of inner hair cells, activating their ion channels, and thereby electrically charging it. This electrical charging of the cell, called receptor potential, activates the synapses at the base of the cell. The strength of the receptor potential correlates with the loudness of sound. At the synapse, the receptor potential activates channels that let calcium enter the cell, and the calcium acts as a messenger to trigger release of neurotransmitters from the synaptic vesicles. These neurotransmitters activate the auditory nerve fibres, and thereby the sound information is transduced and conveyed further to the brain.

In their study, the scientists investigated whether the sound information, contained in the receptor potential of inner hair cells, is diversified via synapses with different properties. By using electrophysiological and imaging techniques, the researchers studied the calcium signalling and neurotransmitter release at the inner hair cell synapses. These synapses showed differences in their release of neurotransmitters in response to the same stimulation. The differences in the output of the cell emerged from heterogeneity of calcium signals and the calcium dependence of release, which in turn depends on the molecular organization of these synapses.

In addition, the scientists gained new insights regarding the spatial organization of synapses within the inner hair cell: the synapses on one side (pointing away from the centre of the cochlea) of the cell released at weaker potentials, and typically had a tighter calcium channel-release coupling compared to the ones on the other side (pointing toward the centre of the cochlea) of the cell (Figure).

"Using imaging, we were able for the first time to study the coupling of calcium channels and neurotransmitter release at individual synapses, even analysing multiple synapses of an inner hair cell," says Dr. Özge Demet Özçete, first author of the publication. "Our previous work had already revealed initial evidence for diversity in the calcium signals of hair cell synapses. The additional information on transmitter release that we have now obtained allows us to relate this phenomenon to sound-induced nerve cell responses", says Prof. Dr. Tobias Moser, senior author of the publication. In this way, we in the Cluster of Excellence MBExC combine the

University Medical Center Göttingen, Georg-August-University, Press- and Public Relations
Stefan Weller, Von-Siebold-Straße 3, D-37075 Göttingen, Germany, phone +49-551-39-61020, 39-61022, 39-61024
fax +49-551-39-61023, presse.medizin@med.uni-goettingen.de, www.umg.eu
Editor University Medical Center Göttingen, Georg-August-University, Executive Committee

molecular imaging of individual sensory cell synapses to the function of the neural network that enables us to perceive hearing," says Moser.

Three subtypes of synapses

By using a machine learning clustering method, the investigators found three putative synapse subtypes within an inner hair cell. This provided a potential link to the classical observation in auditory physiology: The synapses that are active at weaker potentials might drive the auditory nerve fibres that are especially sensitive to the sound. The collaborative work of the auditory nerve fibres with different sound sensitivities is believed to be important for processing a wide range of sound volumes.

*The **Göttingen Cluster of Excellence Multiscale Bioimaging: From Molecular Machines to Networks of Excitable Cells (MBExC)** is funded since January 2019 in the framework of the Excellence Strategy of the German Federal and State Governments. The overall goal of MBExC is to understand the relationship between heart and brain diseases, to link basic and clinical research, and thus to develop new therapeutic and diagnostic approaches with social implications. The **Collaborative Research Center 889,** funded by the German Research Foundation since 2011, investigates the cellular mechanisms of sensory processing.*

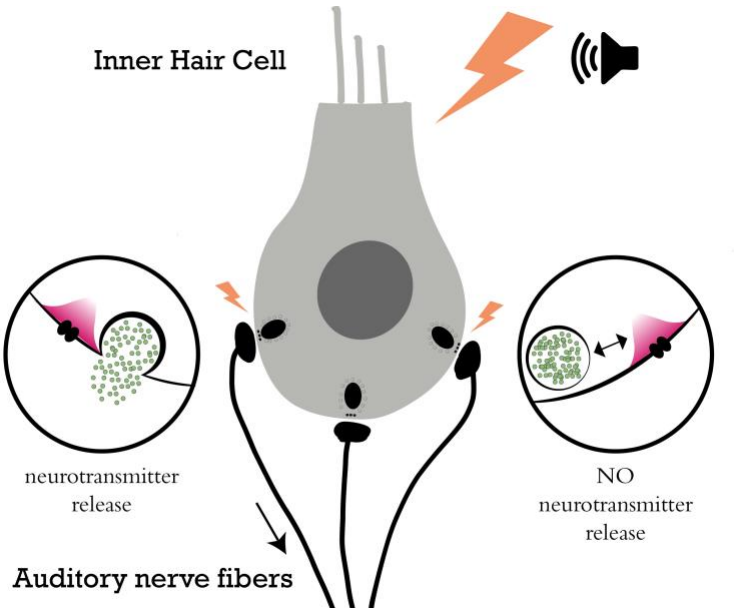

Figure Legend:
Inner hair cell splits the sound loudness information at synapses with diverse coupling of calcium channels and neurotransmitter release sites. The receptor cells of the cochlea, so called inner hair cells, get activated by sound vibrations. This

University Medical Center Göttingen, Georg-August-University, Press- and Public Relations
Stefan Weller, Von-Siebold-Straße 3, D-37075 Göttingen, Germany, phone +49-551-39-61020, 39-61022, 39-61024
fax +49-551-39-61023, presse.medizin@med.uni-goettingen.de, www.umg.eu
Editor University Medical Center Göttingen, Georg-August-University, Executive Committee

activation leads to the electrical charge of the cell. This electrical charge, called receptor potential, activates the calcium channels at synapses at the base of the cell. The calcium entry to the cell triggers release of neurotransmitter glutamate from synaptic vesicles and thereby transmit the sound information to the auditory nerve fibres. In their study, the investigators found that synapses on the abneural side (right side on the illustration) of the inner hair cell were active and released neurotransmitters at weaker potentials than the ones on the neural side (left side). The underlying mechanism of such a diverse output was the heterogeneous voltage dependence of calcium channels and their coupling to neurotransmitter release. Such diversification of the sound information might help with the processing of a wide range of sound volumes.

FURTHER INFORMATION
Institute for Auditory Neuroscience:
http://www.auditory-neuroscience.uni-goettingen.de/
Cluster of Excellence MBExC: https://mbexc.de/
Collaborative Research Center (CRC) 889: www.sfb889.uni-goettingen.de

Contact:
University Medical Center Göttingen, Georg-August-University
Institute for Auditory Neurosciences
Prof. Dr. Tobias Moser
Robert-Koch-Str. 40, 37075 Göttingen
Phone: 0551 / 39-63071
tmoser@gwdg.de

University Medical Center Göttingen, Georg-August-University, Press- and Public Relations
Stefan Weller, Von-Siebold-Straße 3, D-37075 Göttingen, Germany, phone +49-551-39-61020, 39-61022, 39-61024
fax +49-551-39-61023, presse.medizin@med.uni-goettingen.de, www.umg.eu
Editor University Medical Center Göttingen, Georg-August-University, Executive Committee