Hearing with light: Optogenetics for Auditory Research and Prosthetics

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(umg) Hearing impairment is the most common human sensory deficit and has major socioeconomic impact. Hearing can be partially restored to the deaf by cochlear implant (CI), which bypass the cochlear dysfunction via direct electric stimulation of spiral ganglion neurons (SGNs). CIs enable open speech comprehension in most users, but the quality of hearing is low. This results from low frequency and intensity resolution of coding due to the wide spread of electrical current from each electrode contact. CI users have problems to understand speech in background noise and typically do not appreciate music. An international research team led by scientists of the University Medical Center Göttingen proposes to overcome this fundamental problem of CI by establishing many independent coding channels via spatially confined optical stimulation of channelrhodopsin (ChR)-expressing SGNs by tens of microscale light emitters along the tonotopic axis of the cochlea (cochlear optogenetics). They obtained proof of principle in rodents where they activated the auditory pathway with blue light stimulation of ChR-expressing SGNs and this way could restore auditory activity in deaf mice.
Original publication (advanced online, in the press)
Victor H Hernandez, Anna Gehrt*, Kirsten Reuter*, Zhizi Jing*, Marcus Jeschke, Alejandro Mendoza Schulz, Gerhard Hoch, Matthias Bartels, Gerhard Vogt, Carolyn W Garnham, Hiromu Yawo, Yugo Fukazawa, George J Augustine, Ernst Bamberg, Sebastian Kügler, Tim Salditt, Livia de Hoz, Nicola Strenzke, Tobias Moser (2014) Optogenetic stimulation of the auditory pathway. Journal of Clinical Investigation.
The WHO estimated that in 2005 there were 278 million people in the world with disabling hearing impairment (HI). So far, a causal treatment is not available for its most common form: sensorineural HI. Therefore, hearing aids and auditory prostheses represent the only means to restore auditory function in most hearing impaired subjects. Cochlear implants (CIs) bypass the dysfunctional sensory organ of Corti in the cochlea via direct electric stimulation of spiral ganglion neurons (SGNs). CIs enable open speech comprehension in the majority of deaf or profoundly hearing impaired users. However, users of current CIs suffer from poor comprehension of speech in noisy environments and typically do not appreciate music. This is largely attributed to the wide-spread current around an electrode contact which leads to channel-crosstalk and limits the number of useful frequency channels to less than ten. Information coding by CIs is also limited with respect to sound intensity: the dynamic range of their output is typically below 10 dB. Increasing the frequency and intensity resolution of auditory coding with CIs is a crucial objective for improving speech comprehension. Optical stimulation is expected to dramatically increase the frequency resolution of CIs, because light enables spatially confined stimulation of SGNs, and therefore promises to overcome the limitations of current CIs (Fig. 1). In addition, activation of smaller populations of neurons can also enhance the dynamic range of coding e.g. by varying recruitment of neighboring channels.
"Because light can be conveniently focused, optical stimulation promises the use of tens to hundreds of independent stimulation channels. This innovation has the potential to fundamentally improve the discrimination of sound frequency and intensity by CI users. However, before translation into the clinic can be achieved, cochlear optogenetics will already be of enormous use in auditory research.", says Dr. Tobias Moser of the Department of Otolaryngology at the University Medical Center Göttingen, the corresponding author and team leader. The research of the team is part of the BMBF-funded Göttingen Focus for Neurotechnology as well as of the DFG-funded Göttingen Center for Nanoscale Imaging and Molecular Physiology of the Brain (CNMPB).
HOW TO MAKE COCHLEAR NEURONS SENSITIVE TO LIGHT?
In order to render the neurons light sensitive the scientist used the novel optogenetic approach of expressing the light-gated microbial ion channel channelrhodopsin. To do so the team also used harmless viral vectors similar to those presently used in clinical trials on gene-therapy of blindness. They then implanted micro-light emitting diodes (µLED) and laser-coupled micro-fibers for optical stimulation.
RESULTS
"Optogenetic activation of the auditory pathway works in rodents! We could detect light-evoked nerve impulse of individual SGNs and summed activity of pathway" says Anna Gehrt, author of the study and clinician-scientist at the Department of Otolaryngology: "Using optogenetically-evoked potentials we could demonstrate an activation of the auditory pathway in mouse models of human deafness ". Finally, the team achieved a first assessment of the frequency selectivity of optogenetic stimulation in comparison to electrical stimulation. The results agree with the predictions of a mathematical model: optical stimulation achieved better frequency selectivity than amenable to electrical stimulation.
"Much remains to be done to translate cochlear optogenetics into clinical rehabilitation of hearing impairment. says Dr. Moser. To further develop the approach the Göttingen team also collaborates with scientists of the Freiburg Fraunhofer Institute for Applied Physics and the University of Freiburg, who develop multichannel opttical cochlear implants with more than 100 µLEDs within the BMBF funded project "Light-Hearing". Dr. Moser identifies further hurdles to take: cochlear optogenetics requires fast channelrhodopsins that can drive spiking of SGN up to a few hundreds per second. With the introduction of Chronos, a rapidly gating and light sensitive channelrhodopsin characterized by the Boyden lab at MIT, Cambridge, MA this now seems within reach. Moreover, biosafety of gene transfer and optical stimulation need to be demonstrated.
Fig. 1 Electrical versus optical stimulation of the cochlea:
Top: in electrical CIs usually 12-24 electrodes are used to stimulate SGNs. Current spread leads to activation of a large population of neurons along the tonotopic axis, thereby limiting the frequency resolution and dynamic range of electrical coding.
Bottom: optical stimulation promises spatially confined activation of SGNs allowing for a higher number of independent stimulation channels and, thereby, improving frequency and intensity resolution.
Graph: umg
FURTHER INFORMATION
Websites of the laboratories of Dr. T. Moser und Dr. N. Strenzke at University Medical Center Göttingen: http://www.innerearlab.uni-goettingen.de

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