Hearing the light: Improved frequency resolution of optical vs. electrical inner ear stimulation

Auditory signals, including human speech, are characterized by many features, one important being sound frequency, which is perceived as pitch. In normal hearing people, the cochlea in the inner ear translates different sound frequencies into neural activation at different cochlear locations, establishing a place-frequency code. Unfortunately, ~460 million people worldwide suffer from hearing impairment, mainly caused by damage or loss of sensory cells in the cochlea. In these patients, the place-frequency code can be utilized for artificial hearing by cochlear implants (eCIs; Fig. 1A), which use a few electrodes placed at different locations in the cochlea: By electrically activating neurons of the auditory nerve (which are located just one station behind the damaged/lost sensory cells) at different electrodes, the patient perceives a sound that roughly matches the frequency which is naturally coded at this respective cochlear location. CIs nowadays provide more than half a million patients with an artificial sense of hearing, and even enable speech comprehension in most of these patients. However, despite being considered the most successful neuroprothesis, CIs are still limited in frequency resolution, which normally prevents patients from speech understanding in noise or music appreciation. This limitation originates from the spread of electric current within the cochlea, which naturally is filled by electrically conductive fluids: The generated electric field covers large parts of the cochlea, resulting in activation of many neurons, and thus limiting the precision by which electrical hearing can make use of the place-frequency code. This major bottleneck of eCIs might be overcome by optical stimulation of the auditory nerve, since light can be focused much more conveniently, and thus might activate cochlear neurons with higher spatial precision, resulting in improved frequency resolution (Fig. 1B). However, since the auditory nerve is naturally not responsive to light, it first needs to be modified by using optogenetic tools: viral gene transfer to the inner ear allows the introduction of light-sensitive ion channels into the auditory nerve, rendering it responsive to light.

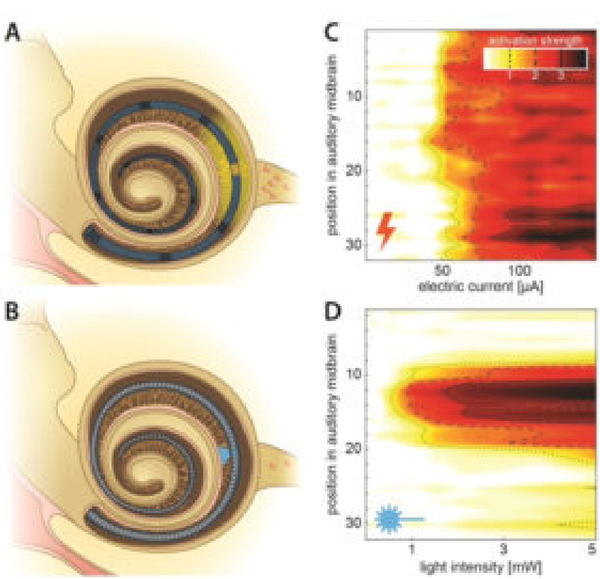

Fig. 1. Artificial activation of the auditory pathway. Illustration of cochlear stimulation by contemporary electrical cochlear implants (eCI; A) and future optical cochlear implants (oCI; B). Auditory nerve stimulation using electric current (eCI) evokes relatively broad activity in the auditory midbrain (C), whereas optical stimulation of the genetically modified cochlea evokes relatively specific responses in the auditory midbrain (D).

To verify the hypothesis of increased precision of optical compared to electrical stimulation of the auditory system, we have used cochlear optogenetics to enable optical stimulation of the auditory nerve in Mongolian gerbils, and subsequently stimulated their auditory nerve using optical fibers that were implanted at different cochlear locations. A different group of gerbils was implanted with clinical-style eCI, and their auditory nerve was activated electrically. While artificially stimulating the cochlea, we recorded neuronal activity in the auditory midbrain as a direct readout of auditory nerve activation: Since the place-frequency code is strongly conserved along the auditory system, cochlear regions coding for a given frequency are wired to corresponding regions in higher brain centers among them the auditory midbrain. In other words, if a given cochlear region gets activated, this activation is passed on along a pre-defined route within the auditory pathway, and by reading out this activity in the auditory midbrain we could infer which cochlear regions have been activated by electrical current or optical illumination. The results obtained from these experiments indeed verified our hypothesis: While electrical stimulation of the auditory nerve activated broad regions of the auditory midbrain (Fig. 1C), optical stimulation led to more confined auditory midbrain activation (Fig. 1D; on average, the increase in frequency resolution of oCI over eCI was more than two-fold). Interestingly, optical stimulation even came close to natural auditory stimulation.

Of course, a long way remains before considering clinical translation of this technology. Nonewithstanding, the demonstrated increase in frequency resolution of optical over electrical auditory nerve stimulation raises hope that future optical cochlear implants might overcome the bottlenecks of nowadays electrical cochlear implants, and provide the patient with more natural hearing restoration.

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