Journal of Neuroscience & Clinical Research

Review Article

A SCITECHNOL JOURNAL

Biological Mechanism of Cochlear Implant Technology in Humans

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Abstract

The World Health Organization reports that hearing loss was the most common form of sensory impairment in humans, affecting 360 million persons worldwide, with a prevalence of 183 million adult males and 145 million adult females. The most common source of hearing loss is sensorineural hearing loss, characterized by disfunctions of the sensory organ: the cochlea and its associated structures. These dysfunctions may be genetic or acquired. In the latter case, it can be due to environmental factors such as chemical agents or noise exposure, or to age related senescence. In patients with sensorineural hearing loss, the functions of the cochlear cells and tissues are lost. Nevertheless, some auditory neurons survive, and the role of the cochlear implants is to stimulate them directly by shunting the cochlea. In this case, the hearing of patients with profound hearing loss can be successfully rehabilitated with cochlear implants capable of encoding and delivering the spectral and the temporal information of sound to the surviving auditory neurons. In this review, we summarize the physiological mechanisms involved in hearing loss and hair cell apoptosis, the role of cochlear implants in cochlear neuron stimulation, and the clinical advantages and disadvantages related to this cochlear device implantation.

Keywords

Cochlear implant; Hearing loss; Inner ear; Electrical stimulation; Multichannel electrode

Biology of Hearing Loss

The mammalian inner ear is a sensory organ capable of perceiving sound over a range of pressures and differentiating both infrasonic and ultrasonic frequencies in different species. In human hearing, sound pressure waves travel down to the ear canal and cause the vibration of the eardrum. These vibrations are transmitted to the cochlea *via* 3 small bones: the malleus, the incus, and the stapes, all located in the middle ear. The movement of these bones allows the oval window to move and to conduct the movement into the cochlea. The cochlea is then responsible for transducing the mechanical vibration into action potential that will propagate towards the part of the brain responsible for hearing which allows perceiving a sound.

The cochlea is a spiral structure divided along its length by a membrane, called the basilar membrane. It is large and flexible at its apex, and narrow and stiff at its base. This longitudinal stiffness gradient makes the basilar membrane react differently depending on the frequency of the incoming sound. For sounds with energy in the low-frequency range, vibrations are maximal at the apex, while for sounds with energy in the high-frequency range, vibrations are maximal at the base. This results in a tonotopic organization of the acoustic input along the cochlea [1]. The organ of Corti, located on the basilar membrane, houses two different subtypes of sensory cells arranged along the duct: three rows of outer hair cells and one row of inner hair cells, those are the true sensory hair cells [2]. Each one possesses dozens of hairs which bend back and forth with the vibration of the basilar membrane. This bending of the hair depolarizes the cell, which releases neurotransmitters onto the afferent nerve fibers, provoking an action potential transmitted to the auditory brain structures. More than 90% of the afferent fibers originate at the inner hair cells. Each fiber has synaptic contact with one inner hair cell which is innervated by around 10-20 fibers. The outer hair cells are innervated by only 10% of the afferent nerve fibers, and many outer hair cells converge on a single fiber. These dendrites forming synaptic contact with hair cells compose the spiral ganglion, a nervous structure that transmits electrical signals from the cochlea to the central nervous system. One tiny change in one of these structures or systems can lead to sensorineural hearing loss (SNHL).

As mentioned before, in 2012, the World Health Organization reported that hearing loss was the most common form of sensory impairment in humans, affecting 360 million persons worldwide [3]. The most common source of hearing loss is sensorineural hearing loss, which accounts for about 90% of reported hearing loss and emerges from disfunctions of the sensory organ: the cochlea and its associated structures. These disfunctions may be genetic; 40 genes have been identified to cause deafness [4] or acquired. In this case, it can be due to environmental factors such as chemical agents or noise exposure, or to age related senescence [5].

It is well established that mitochondria are responsible for ATP production, and that this process induces an increase of reactive oxygen species (ROS) such as superoxide anion, hydrogen peroxide, and hydroxyl radical, playing an essential role in cell signaling [6]. Under normal conditions, ROS produced by the mitochondria are easily metabolized by endogenous antioxidant mechanisms such as catalase, superoxide dismutase, glutathione, and balance cell homeostasis. However, the aging process, pharmacological treatment, or external factors, can alter this balance. This imbalance is called oxidative stress [7]. Several publications confirm that the mitochondrial ROS overproduction plays a key role in hearing loss by activating hair cell apoptotic pathways [8]. More precisely, intracellular damage caused by noise, or ototoxic agents such as aminoglycosides or cisplatin, seems to share a final common pathway *via* the cytochrome c translocation and caspase activation, leading to hair cell death [9].

In patients with SNHL, the function of the basilar membrane and the sensory cells is lost. Nevertheless, some auditory neurons survive, and the role of the cochlear implants (CI) is to stimulate them directly by shunting the cochlea. In this case, the hearing of patients with profound hearing loss secondary to ototoxic agents can be rehabilitated successfully with CI capable of encoding and delivering the spectral and the temporal information of sound to the surviving auditory neurons [10,11].

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Received: April 03, 2018 **Accepted:** April 12, 2018 **Published:** April 28, 2018

The Roles of Implants

The CI is a small and complex electronic device allowing the perception of sound to persons suffering from profound to severe hearing loss. This is the most successful neuroprothesis employed by more than 300,000 users worldwide [12]. Its role is to bypass cochlear dysfunction by stimulating the spiral ganglion neurons (SGN), allowing the electrical signal to be transmitted to the auditory brain areas.

The implant possesses four different components divided in two parts: an external portion located behind the ear and a second portion located under the skin during a surgery. The external portion is composed of a microphone which selects sounds from the environment, and a speech processor which selects and arranges sounds collected by the microphone. The internal portion of the CI is composed of a transmitter whose role is to receive the signals from the speech processor and convert them into electric impulses, and an electrode array. This is a group of electrodes that collects the electric impulses from the transmitter and sends them to different regions of the cochlea to stimulate the auditory nerve in a tonotopic manner, and mimics cochlear hair cell function [13]. This type of stimulation reproduces the capability of the cochlea to analyze the frequency and the amplitude of the sound along the spiral [14] and this is possible due to multichannel CIs inserted in the scala tympani, one of the three fluid-filled compartments of the cochlea. Each electrode stimulates a precise location of the cochlea which means that a multichannel CI is able to stimulate different subpopulations of neurons, leading to a precise analysis of the stimulation. The electrodes situated at the base are activated in the presence of high frequency sounds whereas the electrodes located at a more apical position are activated in the presence of low frequency sounds [15].

Different strategies are developed to improve speech perception. The three most used are spectral peak coding (SPEAK), continuous interleaved sampling (CIS) and advanced combination encoders (ACE). In brief, the SPEAK strategy delivers the signal at a moderate rate of stimulation, around 250-300 pulses/s, while selecting the number and the location of the electrodes to be stimulated according to the intensity and frequency of the incoming sound. The CIS strategy delivers the signal at a higher rate of stimulation, around 600-1800 pulses/s, for a small number of channels. Lastly, the ACE strategy combines the advantages of the two previous ones by using high rates of stimulation with a dynamic electrode selection and a large number of available electrodes [16]. The CIS strategy is currently used by all CI manufacturers [17].

Implant Technology

The first reported electrode implantation was performed in 1961 in Los Angeles, California by audiologist William House and neurosurgeon John Doyle. A single electrode was placed in the scala tympani *via* an opening anterior to the round window [18]. The patient reported perceiving sound, and a five-wire electrode system was inserted three months later. Unfortunately, 11 days later the implant had to be removed due to a non-bio-compatibility. Twenty years later, the first CI was commercialized, and the first child – a 10-year-old genetically deaf boy - was implanted by William House [19]. The Food and Drug Administration approved the first multichannel cochlear implant as medically safe for use in adults in 1984 and in children in 1990. As of December 2012, approximately 324,200 registered devices have been implanted, and roughly seven cochlear implants per million individuals are sold each year.

Nowadays, an increasing number of cochlear implants are being developed by these four major actors: Cochlear Limited (Australia) which possesses 53% of the market share, MedEl Corporation (Austria), Advanced Bionics (USA) and Neurelec (France) [20]. Despite the impressive development of technologies and materials, the success of an implant depends on multiple factors, particularly the ability to regain an effective language, which depends on the age of the patient at the time of implantation, and the age at which deafness starts. Thus, if a patient became deaf after the development of a spoken language, the possibility to maintain an appropriate speech capacity is high. However, in babies born deaf, it has been shown that children who receive a cochlear implant before a substantial delay in spoken language (around 12-16 months) are more likely to develop age-appropriate spoken language [21]. The benefits are greater if the patient has access to an effective auditory training program resulting in improvement in speech processing and music perception [22]. Biologically, performance after implantation is better in patients with higher residual spiral ganglion nerves [23], suggesting that the structure of the cochlea and the number of remaining nerves are important to the success of the cochlear implant.

After implantation, the brain slowly learns to use the electrical information encoded by the CI to extract the information from the acoustic environment. This process lasts many years prior to the initial activation of the CI. It is necessary for the comfort of the patient to detect the psychological threshold, as well as the maximum comfortable level of stimulation. Over time, changes in these indicators, electrode failures, or extrusion and unwanted stimulations require reprogramming of the speech processor [14]. That is why an implanted patient needs a consistent follow-up to ensure a good functioning of its implant. Reprogramming is traditionally performed in clinics, as it requires special equipment and software, but nowadays remote CI programming exists and is a safe, viable, and user-friendly improvement in terms of CI reprogramming [24].

Clinical Benefits and Disadvantages of CI

Despite constant improvements, many patients continue to report difficulties using their CI, especially in noisy environments and regarding the perception of music. This is mostly due to the wide spread of currents around each electrode leading to channel crosstalk, possible tonotopic shifts, and warping in the frequency-to-place mapping of spectral information [25]. It appears that even the best listeners are unable to use more than 10 channels of spectral information, no matter how many are present. Thereby, CI users have a mean pitch direction discrimination of three semitones, compared to one semitone for normal hearing individuals, underlying the difficult recognition of melodies: CI users recognized melodies 25.1% of the time, compared to 87.5% of the time for normal hearing listeners [26].

To diminish this wide range of currents around the electrodes, manufacturers are working on optical stimulation, since light can be focused and might improve the frequency resolution of sound encoding. In this way, infrared neural stimulation improves spatial selectivity when compared with electrical stimulation [27,28]. Based on this work, a proof of principle has been presented for optogenetic stimulation of the cochlea, and neurons of the auditory cortex, as well as a flexible µLED-based multichannel CI [29]. In the future, the combination of these technologies could offer both a better perception of music and better speech recognition in a noisy environment.

CIs have external parts which are exposed to the environment, making them more vulnerable to damage caused by water, extreme

temperatures or moisture. This forces the user to remove their CI during exposure to water for instance while swimming or perspiring during physical exercise. This means that users are "disconnected" from external sounds during these periods, leading to exclusion or dangers (eg. not hearing a car while running) [14]. To fix these issues, manufacturers are working on completely immersed cochlear implant with battery and speech processors implanted under the skin of the skull. Even with this technical progress the totally implanted CI will need an external device for battery charging and program switching, but it will allow the user to engage in activities without caring about their implant.

Finally, to enhance the chances of regaining quasi-normal hearing, some researchers are focusing on developing a way to use the CI as a delivery device by adding a microcannula on it. This will allow the administration of compounds directly into the cochlea, close to the targeted cells, while continuing to stimulate the SGN [30].

The cochlear implant represents huge technical progress, allowing hundreds of thousands of users to regain a sense of hearing. Even if there are areas to be improved for the development of a CI capable of melody discrimination and speech recognition in noisy environments, children born deaf can develop a language and live a quasi-normal life thanks to currently available CIs. Manufacturers continuously strive to develop devices which are more and more sophisticated, which will enable millions of people to have access to a solution to their hearing loss.

References

1. Macherey O, Carlyon RP (2014) Cochlear implants. Curr Biol 24: R878-R884.
2. Stöver T, Diensthuber M (2011) Molecular biology of hearing. GMS Curr Top Otorhinolaryngol Head Neck Surg 10: 06
3. WHO (2012) WHO global estimates on prevalence of hearing loss. Mortality and burden of diseases and prevention of blindness and deafness. Geneva, Switzerland.
4. Matsunaga T (2009) Value of genetic testing in the otological approach for sensorineural hearing loss. The Keio J Med 58: 216-222.
5. Marie A, Larroze-Chicot P, Cosnier-Pucheu S, Gonzalez-Gonzalez S (2017) Senescence-accelerated mouse prone 8 (SAMP8) as a model of age-related hearing loss. Neurosci let 656: 138-143.
6. Niethammer P, Grabher C, Look AT, Mitchison TJ (2009) A tissue-scale gradient of hydrogen peroxide mediates rapid wound detection in zebrafish. Nature 459: 996.
7. Du Z, Yang Q, Liu L, Li S, Zhao J, et al. (2015) NADPH oxidase 2-dependent oxidative stress, mitochondrial damage and apoptosis in the ventral cochlear nucleus of D-galactose-induced aging rats. Neurosci 286: 281-292.
8. Gonzalez-Gonzalez S (2017) The role of mitochondrial oxidative stress in hearing loss. Neurol Disord Therap.
9. Cheng AG, Cunningham LL, Rubel EW (2005) Mechanisms of hair cell death and protection. Curr Opin Otolaryngol Head Neck Surg 13: 343-348.
10. Nichani J, Bruce IA, Mawman D, Khwaja S, Ramsden R, (2013) Cochlear implantation in patients deafened by ototoxic drugs. Cochlear Implants Int 14: 207-212.
11. Firszt JB, Koch DB, Downing M, Litvak L (2007) Current steering creates additional pitch percepts in adult cochlear implant recipients. Otol Neurotol 28: 629-636.
12. Moser T (2015) Optogenetic stimulation of the auditory pathway for research and future prosthetics. Curr Opin Neurobiol 34: 29-36.
13. Zeng FG, Rebscher S, Harrison W, Sun X, Feng H (2008) Cochlear implants: system design, integration, and evaluation. IEEE Rev Biomed Eng 1: 115-142.
14. Roche JP, Hansen MR (2015) On the horizon: cochlear implant technology. Otolaryngol Clin North Am 48: 1097-1116.
15. Wilson BS, Dorman MF (2008) Cochlear implants: current designs and future possibilities. J Rehabil Res Dev 45: 695.
16. Pasanisi E, Bacciu A, Vincenti V, Guida M, Berghenti MT, et al. (2002) Comparison of speech perception benefits with SPEAK and ACE coding strategies in pediatric Nucleus CI24M cochlear implant recipients. Int J Pediatr Otorhinolaryngol 64: 159-163.
17. Caldwell MT, Jiam NT, Limb CJ (2017) Assessment and improvement of sound quality in cochlear implant users. Laryngoscope Investig Otolaryngol 2: 119-124.
18. Mudry A, Mills M (2013) The early history of the cochlear implant: a retrospective. JAMA Otolaryngol Head Neck Surg 139: 446-453.
19. House WF, Berliner KI, Eisenberg LS, Edgerton BJ, Thielemeir MA (1981) The cochlear implant: 1980 update. Acta Otolaryngol 91: 457-462.
20. Hainarosie M, Zainea V, Hainarosie R (2014) The evolution of cochlear implant technology and its clinical relevance. J Med Life 7: 1-4.
21. Nicholas JG, Geers AE (2007) Will they catch up? The role of age at cochlear implantation in the spoken language development of children with severe to profound hearing loss. J Speech Lang Hear Res 50: 1048-1062.
22. Fu QJ, Galvin JJ 3rd. (2007) Perceptual learning and auditory training in cochlear implant recipients. Trends Amplif 11: 193-205.
23. Seyyedi M, Viana LM, Nadol JB Jr. (2014) Within-subject comparison of word recognition and spiral ganglion cell count in bilateral cochlear implant recipients. Otol Neurotol 35: 1446.
24. Ramos A, Rodriguez C, Martinez-Beneyto P, Perez D, Gault A (2009) Use of telemedicine in the remote programming of cochlear implants. Acta Otolaryngol 129: 533-540.
25. Friesen LM, Shannon RV, Baskent D, Wang X (2001) Speech recognition in noise as a function of the number of spectral channels: comparison of acoustic hearing and cochlear implants. J Acoust Soc Am 110: 1150-1163.
26. Kohlberg G, Spitzer JB, Mancuso D, Lalwani AK (2014) Does cochlear implantation restore music appreciation. Laryngoscope 124: 587-588.
27. Moser T (2015) Optogenetic stimulation of the auditory pathway for research and future prosthetics. Curr Opin Neurobiol 34:29-36.
28. Richter CP, Rajguru SM, Matic AI, Moreno EL, Fishman AJ, et al. (2011) Spread of cochlear excitation during stimulation with pulsed infrared radiation: inferior colliculus measurements. J Neural Eng 8: 056006.
29. Jeschke M, Moser T (2015) Considering optogenetic stimulation for cochlear implants. Hear Res 322: 224-234.
30. Salt A, Hartsock J, Gill R, Smyth D, Kirk J, et al. (2017) Perilymph pharmacokinetics of marker applied through a cochlear implant in guinea pigs. PloS One 12: e0183374.

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