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Research paper

Factors associated with hearing loss in a normal-hearing guinea pig model of hybrid cochlear implants

Chiemi Tanaka*, Anh Nguyen-Huynh, Katherine Loera, Gemaine Stark, Lina Reiss

Oregon Hearing Research Center, Department of Otolaryngology, Mail Code: NRC04, Oregon Health and Science University, 3181 SW Sam Jackson Park Road, Portland, OR 97239, USA

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A B S T R A C T

The Hybrid cochlear implant (CI), also known as Electro-Acoustic Stimulation (EAS), is a new type of CI that preserves residual acoustic hearing and enables combined cochlear implant and hearing aid use in the same ear. However, 30–55% of patients experience acoustic hearing loss within days to months after activation, suggesting that both surgical trauma and electrical stimulation may cause hearing loss.

The goals of this study were to: 1) determine the contributions of both implantation surgery and EAS to hearing loss in a normal-hearing guinea pig model; 2) determine which cochlear structural changes are associated with hearing loss after surgery and EAS. Two groups of animals were implanted ($n = 6$ per group), with one group receiving chronic acoustic and electric stimulation for 10 weeks, and the other group receiving no direct acoustic or electric stimulation during this time frame. A third group ($n = 6$) was not implanted, but received chronic acoustic stimulation. Auditory brainstem response thresholds were followed over time at 1, 2, 6, and 16 kHz. At the end of the study, the following cochlear measures were quantified: hair cells, spiral ganglion neuron density, fibrous tissue density, and stria vascularis blood vessel density; the presence or absence of ossification around the electrode entry was also noted.

After surgery, implanted animals experienced a range of 0–55 dB of threshold shifts in the vicinity of the electrode at 6 and 16 kHz. The degree of hearing loss was significantly correlated with reduced stria vascularis vessel density and with the presence of ossification, but not with hair cell counts, spiral ganglion neuron density, or fibrosis area. After 10 weeks of stimulation, 67% of implanted, stimulated animals had more than 10 dB of additional threshold shift at 1 kHz, compared to 17% of implanted, non-stimulated animals and 0% of non-implanted animals. This 1-kHz hearing loss was not associated with changes in any of the cochlear measures quantified in this study. The variation in hearing loss after surgery and electrical stimulation in this animal model is consistent with the variation in human patients. Further, these findings illustrate an advantage of a normal-hearing animal model for quantification of hearing loss and damage to cochlear structures without the confounding effects of chemical- or noise-induced hearing loss. Finally, this study is the first to suggest a role of the stria vascularis and damage to the lateral wall in implantation-induced hearing loss. Further work is needed to determine the mechanisms of implantation- and electrical-stimulation-induced hearing loss.

Abbreviations: ABR, Auditory brainstem response; ACE, Advanced Combination Encoder; CAES, Chronic Acoustic Electric Stimulation; CAS, Chronic Acoustic Stimulation; CI, Cochlear implant; CIS, Chronic interleaved sampling; EABR, Electrically-evoked auditory brainstem response; EAS, Electric and acoustic stimulation; HA, Hearing Aid; HC, Hair cell; HL, Hearing loss; IHC, Inner hair cell; IM, Intramuscular; NS, No stimulation; OHC, Outer hair cell; SGN, Spiral ganglion neuron; SV, Stria vascularis, stria vascular

* Corresponding author. Department of Communication Sciences and Disorders, John A. Burns School of Medicine, University of Hawai'i at Mānoa, 677 Ala Moana Blvd., Suite 625, Honolulu, HI 96816, USA. Tel.: +1 808 692 1585; fax: +1 808 566 6292.

E-mail addresses: tanakach@hawaii.edu, chiemit@gmail.com (C. Tanaka), nguyanh@ohsu.edu (A. Nguyen-Huynh), loerakatherine@gmail.com (K. Loera), starkg@ohsu.edu (G. Stark), reiss@ohsu.edu (L. Reiss).

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1. Introduction

Hearing aids (HAs) and cochlear implants (CIs) have become highly successful treatments for hearing loss (HL) and deafness. While these devices benefit many individuals by improving speech recognition, some limitations still exist. For example, high-frequency sensorineural HL is the most common type of HL observed in the clinic, but clinical reports and literature indicate that providing high-frequency amplification in these patients does not always restore speech understanding (Pavlovic, 1984; Kamm et al., 1985; Ching et al., 1998; Hogan and Turner, 1998). At the same time, these patients typically do not qualify for full-insertion CIs because they have too much residual hearing.

The Hybrid CI, also known as electric and acoustic stimulation (EAS), was developed to address the above limitations of the HAs and CIs for these patients (Kiefer et al., 2002; Gantz and Turner, 2003). This is a new type of CI that preserves residual hearing and enables patients to use a hearing aid in the same ear with the cochlear implant after implantation. The use of a shorter, thinner CI electrode array makes it possible to reduce implantation trauma in the low-frequency region of the cochlea, since the array is only inserted into the basal to middle part of the cochlea, leaving the apical cochlea intact. When "soft" surgery techniques are used, low-frequency residual hearing can be preserved. In addition to improving speech recognition in quiet, the Hybrid CI allows patients to perform better in speech recognition in competing background noise (Wilson et al., 2003; Turner et al., 2004, 2008) and musical melody recognition (Gfeller et al., 2006) compared to full insertion CI patients.

However, optimum benefit from Hybrid CIs depends on preservation of residual hearing within the implanted ear. Gantz et al. (2009) reported that 30% of Cochlear Nucleus Hybrid CI recipients had greater than 30 dB of mean low-frequency threshold shifts postoperatively. In their study, HL occurred at different time points ranging from between surgery and CI activation to within 3–36 months after CI activation. Similarly, Gstoettner et al. (2009) reported that 55.6% of the Med-EL Flex EAS recipients (5 out of 9 subjects) showed greater than 10 dB elevations in average pure-tone thresholds from 125 to 750 Hz between 1 month and 17 months after implantation. Santa Maria et al. (2013) also reported progressive changes in hearing preservation over time after implantation. At 0–3 months after implantation, complete, partial, and minimal hearing preservation rates were reported as 42.9%, 50%, and 7.1%, respectively. However, several months after implantation, hearing preservation rates decreased to 22.2%, 66.7%, and 11.1% at 6–12 months and 25%, 12.5%, and 37.5% at 12–24 months after implantation, respectively. These study results suggest that the residual HL can occur anytime after implantation and may be delayed effects of surgical trauma and/or electrical stimulation delivered by the Hybrid CI into the cochlea.

Potential mechanisms of delayed HL related to surgical trauma include direct mechanical trauma to the basilar membrane or osseous spiral lamina (Briggs et al., 2005; O'Leary et al., 1991; Roland and Wright, 2006), or an inflammatory or immune response leading to hair cell death (Eshraghi et al., 2013). Another possibility which has been under-investigated is damage to the lateral wall and the stria vascularis (SV) which could lead to threshold shifts via a reduced endocochlear potential (Wright and Roland, 2013). The formation of fibrosis or new bone growth after implantation can also theoretically cause HL by attenuating the traveling wave (Choi and Oghalai, 2005), and a significant but small correlation has been reported between fibrosis and ABR thresholds (O'Leary et al., 2013).

Another possibility is that electrical stimulation itself contributes to residual HL after implantation. There are few published studies that have directly looked at residual hearing changes with electrical stimulation. Kang et al. (2010) measured residual hearing changes with cochlear implantation and electrical stimulation in both normal-hearing and chemically-deafened guinea pigs, as part of a study looking at electrical stimulation efficacy rather than residual HL. They reported that one of the implanted normal-hearing guinea pigs showed postoperative hearing threshold elevations at 8 and 24 kHz (lower frequencies were not tested), but no corresponding hair cell or spiral ganglion cell pathology. Coco et al. (2007) measured hearing thresholds after long-term cochlear implantation and electrical stimulation in chemically-deafened cats. Electrical stimulation was delivered via a CI for 6 h per day for 5 days per week for up to 252 days. Interestingly, partially deafened animals showed no significant change in acoustic hearing, which contradicts the results from Gantz et al. (2009) in Hybrid CI patients. However, the Coco et al. study (2007) stimulation protocol differed from clinical Hybrid programming in two key ways: electrical stimulation parameters were fixed rather than updated periodically during the experimental period, and electrical stimulation was provided alone without acoustic stimulation.

The goals of this study were to: 1) determine the contributions of both implantation surgery and EAS to hearing loss in a normal-hearing guinea pig Hybrid CI model; 2) determine which cochlear structural changes are associated with hearing loss after surgery and EAS. An animal model was used to reduce the heterogeneity seen in human Hybrid CI patients due to differences in genetic composition, age, medical history, and medication usage, which can confound the interpretation of data, and to allow timely investigation of cochlear structural changes after hearing loss. Guinea pigs serve as an excellent Hybrid CI animal model since their cochleae are easily accessible and large enough to implant multiple electrodes in a commercially available electrode array (Kang et al., 2010). Normal-hearing instead of deafened animals were used to further reduce confounding effects of noise- or chemically-induced hearing loss on the histology. Finally, the chronic stimulation parameters in this model were set up to simulate human Hybrid CI patients as closely as possible.

In this study, we found changes in hearing thresholds both after surgery and chronic acoustic and electric stimulation. Cochlear histology conducted at the conclusion of the study showed significant associations of implantation-induced hearing loss with stria vascularis blood vessel density and ossification, but not hair cell counts, spiral ganglion neuron density, or fibrosis area. No associations were observed for long-term hearing loss after stimulation with any of the histological measures.

2. Material and methods

2.1. Subjects

Eighteen male, 6-week old albino Dunkin-Hartley guinea pigs were purchased from Charles River (Wilmington, MA). Average weight was 524.8 ± 61.9 g. All animal protocols were approved by the Oregon Health and Science University Committee on the Use and Care of Animals and veterinary care was provided by the Department of Comparative Medicine.

2.2. Research design

Three groups of normal-hearing guinea pigs ($n = 18$; $n = 6$ per group) were studied in order to determine the effects of both implantation trauma and chronic electric and acoustic stimulation on hearing. The first group, the Chronic Acoustic Stimulation control group (CAS) consisted of non-implanted guinea pigs that received