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Review

Auditory midbrain implant: Research and development towards a second clinical trial

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ABSTRACT

The cochlear implant is considered one of the most successful neural prostheses to date, which was made possible by visionaries who continued to develop the cochlear implant through multiple technological and clinical challenges. However, patients without a functional auditory nerve or implantable cochlea cannot benefit from a cochlear implant. The focus of the paper is to review the development and translation of a new type of central auditory prosthesis for this group of patients that is known as the auditory midbrain implant (AMI) and is designed for electrical stimulation within the inferior colliculus. The rationale and results for the first AMI clinical study using a multi-site single-shank array will be presented initially. Although the AMI has achieved encouraging results in terms of safety and improvements in lip-reading capabilities and environmental awareness, it has not yet provided sufficient speech perception. Animal and human data will then be presented to show that a two-shank AMI array can potentially improve hearing performance by targeting specific neurons of the inferior colliculus. A new two-shank array, stimulation strategy, and surgical approach are planned for the AMI that are expected to improve hearing performance in the patients who will be implanted in an upcoming clinical trial funded by the National Institutes of Health. Positive outcomes from this clinical trial will motivate new efforts and developments toward improving central auditory prostheses for those who cannot sufficiently benefit from cochlear implants.

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1. Introduction

There are hundreds of thousands of individuals implanted with a neural device for restoring sensory, motor, or autonomic function as well as for treating neurological and psychiatric disorders (Johnson et al., 2013; Konrad and Shanks, 2010; Navarro et al., 2005). These devices interface with the peripheral or central nervous system, and can be fully implanted into the body or head with wireless capabilities. One of the most successful neural prostheses is known as the cochlear implant (CI), which is designed for implantation into the cochlea for electrically stimulating nearby auditory nerve fibers for hearing restoration (Fig. 1) (Wilson and Dorman, 2008; Zeng et al., 2008). Over 320,000 patients have received a CI, with many of these individuals capable of speech perception and even the ability to converse over the telephone. Children, including infants younger than one year of age, have been implanted with a CI and have been able to integrate into mainstream schools. Therefore, the CI has been remarkably successful in restoring hearing to many deaf individuals, which in turn has guided the development of other neural prostheses for sensory or motor restoration, such as the visual prosthesis or a neural-controlled prosthetic limb (Weber et al., 2012; Weiland et al.,

Abbreviations: A1, primary auditory cortex; ABI, auditory brainstem implant; ACC, core/primary auditory cortex regions; AM, amplitude modulation; AMI, auditory midbrain implant; CI, cochlear implant; CT, computed tomography (imaging); DRNL, dual-resonance nonlinear (model); DSS, dual-site stimulation (within an ICC lamina); IC, inferior colliculus; ICC, central nucleus of inferior colliculus; LFP, local field potential; MGV, ventral division of medial geniculate nucleus; MRI, magnetic resonance imaging; NF2, neurofibromatosis type 2; PABI, penetrating auditory brainstem implant; PSTH, post-stimulus time histogram; R, correlation coefficient; SC, superior colliculus; SSS, single-site stimulation (within an ICC lamina)

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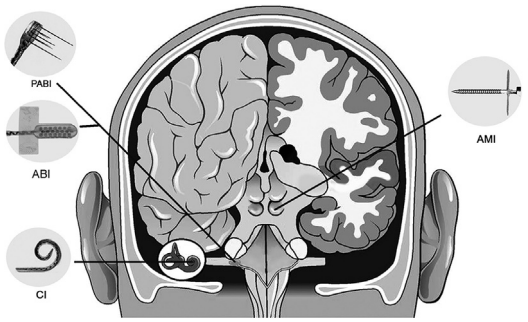

Fig. 1. Different auditory neural prosthetics used in patients for hearing restoration. CI: Cochlear Implant, which consists of an electrode array that is implanted into the cochlea and used for auditory nerve stimulation. ABI: Auditory Brainstem Implant that is used for surface stimulation of the cochlear nucleus. PABI: Penetrating Auditory Brainstem Implant that is used for penetrating stimulation of the cochlear nucleus. AMI: Auditory Midbrain Implant that is used for penetrating stimulation of the auditory midbrain (i.e., the inferior colliculus). There are several companies that build these types of implant devices. The examples shown in this figure are developed by Cochlear Limited (Australia). Figure was taken from Lenarz et al. (2006b) and reprinted with permission from Lippincott Williams & Wilkins.

2011). The monumental achievements of the CI are attributed to the continuous efforts of several visionaries including André Djourno, William House, Blair Simmons, and the 2013 Lasker ~ DeBakey Clinical Medical Research Awardees – Graeme Clark, Ingeborg Hochmair, and Blake Wilson (Eisenberg, 2015; Lenarz, 1998; Mudry and Mills, 2013).

In thinking about the future of auditory prostheses, the question arises as to how hearing performance can be further improved beyond what is possible with current devices, not only for those who are implanted with a CI but also for those who do not have a functional auditory nerve or implantable cochlea. There are exciting efforts towards improving the design of CIs (e.g., new electrode arrays, and binaural or bimodal implants) and activation of the auditory nerve (e.g., current steering techniques, direct nerve stimulation, and optical activation methods) for achieving better performance in noisy environments and with more complex inputs such as music, tonal languages, and multiple talkers. Various technological, modeling, signal processing, physiology, and psychophysics research to achieve these improvements are presented in the other papers in the Lasker Award Special Issue for Hearing Research. The focus of this paper is to present the development and translation of devices for stimulation beyond the auditory nerve within more central auditory structures, particularly the inferior colliculus (IC). Central auditory implants can provide an alternative hearing option for those who cannot benefit from a CI. Furthermore, a major limitation in achieving higher performance with CIs appears to be the limited number of independent information channels available through cochlear stimulation (Friesen et al., 2001). The CI sends current through a bony modiolar wall of the cochlea with scattered flow of electrical charge to a variable distribution and reduced number of auditory neurons associated with deafness. Central auditory prostheses may provide a way for achieving more specific activation of a greater number of frequency channels of information than is currently possible with CIs.

This review will present the rationale for the AMI and the results of the first clinical trial using a multi-site single-shank array. The animal and human studies leading to the development of a new two-shank AMI array will then be presented followed by an update on the second clinical trial.

2. Rationale for the AMI

The CI can provide high levels of speech understanding, at least in quiet environments, for many deaf patients. However, the CI is designed for electrically activating the auditory nerve. For those patients without a functional auditory nerve (e.g., due to a head injury or tumor removal surgery, or being born without a nerve) or without an implantable cochlea to enable array insertion (e.g., due to ossification or head trauma), then the only hearing option is a central auditory implant. The first device, known as the ABI, was implanted as early as 1979 at the House Ear Institute in Los Angeles, California by William Hitselberger and William House. It consisted of two ball electrodes with a fabric backing that was built in collaboration with Douglass McCreery from the Huntington Medical Research Institutes in Pasadena, California. The ABI was positioned onto the surface of the cochlear nucleus. Further details of the development of the first ABIs are provided in Schwartz et al. (2008), Sennaroglu and Ziyal (2012). The ABI was initially designed and justified for patients with a genetic disease known as neurofibromatosis type 2 (NF2), which is usually associated with bilateral acoustic neuromas. Due to removal of these tumors and complete damage of the auditory nerves, the patients became bilaterally deaf and unable to benefit from CIs. Since the cochlear nucleus was already approached during tumor removal, it was then possible to place the electrodes on its surface with minimal added surgical risk. A total of 25 patients were implanted with an ABI by 1992 (Schwartz et al., 2008). Since 1992, the single channel ABI has been developed into a multi-site surface array (Fig. 1) by several implant companies (e.g., Advanced Bionics Corporation, USA; Cochlear Limited, Australia; Med-El Company, Austria; MXM Digisonic, France) and implanted in over 1200 patients worldwide with etiologies no longer limited to NF2 (e.g., those with nerve aplasia/avulsion or cochlear ossification).

The current status of the ABI is that it can achieve high levels of hearing performance in some patients (Behr et al., 2014; Colletti et al., 2014, 2009; Matthies et al., 2014). There appears to be certain types of deaf patients who achieve good hearing performance with an ABI. For example, one study by Colletti et al. (2009) showed that over half of the 48 non-tumor (i.e., non-NF2) adult patients implanted with the ABI achieved reasonable speech perception with a few reaching levels comparable to the top CI patients. These non-tumor patients obtained an average score of 59% on an open-set speech test compared to an average score of 10% across 32 NF2 adult patients. Considering that similar implants, stimulation strategies, and surgical approaches were used for both patient groups in the same clinic, these findings suggested that the limited performance observed in NF2 patients may be related to tumor damage, including surgical damage, of the cochlear nucleus (Behr et al., 2014; Colletti and Shannon, 2005). Even within the non-tumor group, it appeared that those with cochlear ossification or who lost their auditory nerve due to head trauma performed better than those who had cochlear malformations or auditory neuropathy (Colletti et al., 2009). Similar trends have also been observed in children with ABIs in which those with cochlear damage due to ossification or head trauma achieved the best performance over other groups (Colletti et al., 2014).

The fact that the ABI can provide sufficient speech understanding in some patients demonstrates that artificial electrical stimulation even within the brain can restore sufficient hearing function. The question now arises as to how we can further improve central auditory prostheses so that a majority of implanted patients can achieve sufficient hearing performance, especially those with NF2 tumors. There are recent reports indicating that a few NF2 ABI patients are able to achieve speech understanding comparable to