Evaluation of a conformable Auditory Brainstem Implant in Mouse

Osama Tarabichi1, 2, Nicolas Vachicouras, Vivek Y. Kanumuri1, 2 Amélie Guex, Ariel E. Hight, Stéphanie Lacour, M. Christian Brown1, 2, Daniel J. Lee1, 2

1Eaton Peabody Laboratories, Massachusetts Eye and Ear Infirmary, Boston, MA
2Department of Otolaryngology, Harvard Medical School
3Ecole Polytechnique Federale de Lausanne (EPFL)

INTRODUCTION

Auditory Brainstem Implant Limitations (ABI): The ABI is a neuroprosthetic device placed on the surface of the cochlear nucleus (CN) to provide hearing sensations to deaf patients who are not eligible for cochlear implantation (Otto et al. 1998). The ABI bypasses a damaged or absent auditory nerve or cochlea to electrically stimulate the CN (Hitselberger et al., 1984). Current spread and subsequent poor spatial specificity of neuronal activation is thought to be a main contributor to poor hearing performance among ABI users (Shannon et al. 1990). Furthermore, these patients exhibit side effects (facial twitching, dizziness) due to activation of neighboring non-auditory axons of passage (Herrmann et al., 2015). Side effects can be severe enough to render a device unusable in some patients. The ABI system in clinical use consist of a rigid "paddle" containing 21 surface contacts that does not conform to the curved surface of the brainstem. This rigid configuration means that some electrodes will have minimal contact with the brainstem resulting in high thresholds and spread of current to surrounding structures.

Advantages of Conformable Arrays: Conformable arrays that take the shape of the neural surface they reside on can now be fabricated in light of recent developments in the field of neuroprosthetics (Guex et al., 2015; Minev et al., 2015). These arrays are composed on a silicone based flexible polymer. They can be coated with conductive polymers to reduce high impedance associated with small electrode size, allowing for a considerable density of electrodes. Micro-LEDs can also be incorporated in these arrays for optogenetic stimulation of the cochlear nucleus, a modality that has the potential to provide superior spatial resolution of stimulation. They have been tested in primate and rodent models (Capogrosso et al., 2016; Borton et al., 2014). In rodent models of the ABI, our group has shown that conformable electrical ABIs can generate even thresholds and robust responses at the level of the inferior colliculus (IC) (Guex et al., 2017). Furthermore, the elastic properties of the materials closely match those observed in neural tissue and they may reduce inflammatory responses at the neural interface (Minev et al., 2015).

Development of a chronic ABI mouse model: These new arrays are on the verge of clinical translation, however they have not been evaluated long-term in chronic ABI animal models. Testing the durability and safety of this novel electrode technology is a crucial step before introducing it to the clinical realm. Herein we test the functionality and durability of these arrays in an in vivo, chronic ABI mouse model. We also report preliminary data that shows that micro-LED implants can drive evoke activity in the central auditory pathway.

METHODS

Array Fabrication: Conformable arrays (Figs. 1A, 2) were fabricated at the Ecole Polytechnique Federale de Lausanne (EPFL) Laboratory for Soft Bioelectronic Interfaces (LSBI). Electrodes and interconnects were embedded in a silicone based flexible polymer called polydimethylsiloxane (PDMS). Electrodes were coated in a platinum elastomer mesocomposite to overcome high impedance associated with small electrode size while maintaining conformability. Micro-LED arrays were embedded in the flexible polymer polyimide. Optically evoked recordings: A 16-channel silicone-recording probe (Neuronexus) was then advanced into the right central nucleus of the IC (ICC). Placement in the ICC was confirmed by observing tonotopically organized responses to a range of pure tone stimuli (8-45 kHz). Micro-LED array was placed on the surface of the cochlear nucleus and 1 ms light pulses were delivered at 4 Hz.

RESULTS

Optically evoked recordings: A 16-channel silicone-recording probe (Neuronexus) was then advanced into the right central nucleus of the IC (ICC). Placement in the ICC was confirmed by observing tonotopically organized responses to a range of pure tone stimuli (8-45 kHz). Micro-LED array was placed on the surface of the cochlear nucleus and 1 ms light pulses were delivered at 4 Hz.

Figure 1: Conformable mouse ABI array. A) 3-channel ABI designed for surface placement on dorsal cochlear nucleus of a mouse (100 µm diameter contacts). B) Micro-LED array and design illustration. 2. LED's are placed in a configuration that allows them to be placed along the tonotopic axis of the CN.

Figure 2: Chronic recording of eABRs: eABR waveforms and impedance measurements from a representative experiment. eABR's and electrochemical impedance measures were recorded at post-op week 2, 3 and 4. Stable impedance in electrode 2 allowed for robust stimulation of the central auditory pathway as seen by the generation of electrically evoked waveforms that resemble those correlated with IC responses in acute experiments.

Figure 3: Preliminary results demonstrate the ability of an optical array to evoke multiunit spiking in acute preparations. A) Micro-LED array drives robust multiunit spiking (200 Hz). B) Peristimulus time histogram of evoked activity in the ICC in over thirty trials in optogenetically modified mouse. B) Peristimulus time histogram of evoked activity in the ICC in over thirty trials in a wild-type mouse.

SUMMARY/ CONCLUSIONS

- A method to chronically implant a conformable ABI array in mouse was developed. The functionality of these implants over a period of one month was demonstrated. In other neural systems, these materials can remain durable and functional for months (Borton et al., 2014; Capogrosso et al., 2016).

- In acute experimental preparations, both electrical and micro-LED arrays were fully functional as demonstrated by eABRs and multiunit firing in IC. Preservation of eABR responses were noted for up to four weeks post implantation in the electrical ABI model. Reduction or loss of evoked potentials were associated with sharp increases in electrode impedance likely due to electrode failure or displacement. Future work will focus on developing a chronic optical ABI model.

- This work represents a key step in bringing our technology closer to clinical translation. The knowledge gained from animal work similar to this will be instrumental in developing a next generation human ABI. Future studies will aim to compare behavioral detection thresholds of auditory and electrical stimulation to determine whether meaningful hearing perception is achieved.

REFERENCES

[References...]

Acknowledgements: Supported by the Barstow Foundation program for translational neuroscience.

Contact Details: Osama Tarabichi osama.tarabichi@meei.harvard.edu