

# The Auditory Midbrain Implant: a New Deep Brain Stimulator for Hearing Restoration and Tinnitus Therapy

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DEEP brain stimulation (DBS) has been successfully used to treat an increasing number of neurological disorders. While new therapies are continuously being investigated, the lead itself has remained relatively unchanged. In contrast, auditory neuroprostheses such as the cochlear implant (CI) or the auditory midbrain implant (AMI) have been continuously improving, with smaller leads than the traditional DBS that can safely deliver complex electrical stimulation patterns. Similar in design to the CI, with a single linear array, the AMI provides DBS for those patients that cannot benefit from CI stimulation. The AMI targets the inferior colliculus (IC), specifically the well-defined frequency organization of its central region (ICC). Each electrode resides in a different frequency layer of the ICC and thus can employ a similar stimulation strategy as the CI. The AMI has been shown to improve overall hearing capabilities, but speech understanding has been limited, likely due to insufficient temporal cues [1]. While the implant can provide frequency cues, the repeated stimulation of the same neural population causes strong suppressive and refractory effects [2]. In order to achieve improved speech understanding, the second generation AMI will consist of two parallel linear arrays, as we have shown that co-activating the ICC by electrically stimulating two neural populations within each frequency layer circumvents this refraction and elicits enhanced activity in the primary auditory cortex (A1) [2]. Prior to clinical trials, our primary goal is to determine target locations and stimulation strategies that maximize transmission of neural signals to the cortex for restoring speech perception.

In addition to hearing restoration, the AMI has the potential to treat other auditory neurological disorders, such as tinnitus [3], which is a phantom auditory percept that is disturbing and even debilitating for millions of individuals in the U.S. alone. Stimulation of the dorsal region of the IC (ICD), which is known to modulate ICC activity, may suppress the hyperactivity and increased neural synchrony observed during tinnitus [4]. As many of the AMI patients selected for the second generation AMI also have tinnitus, we can directly assess IC stimulation effects on tinnitus suppression in humans. Therefore, our secondary goal is to identify areas of ICD that can effectively suppress tinnitus.

Multi-site electrode arrays were used in two protocols to electrically stimulate and record neural responses in ketamine-anesthetized guinea pigs. In Protocol #1 for the hearing restoration component, the arrays were inserted into the ICC and A1. Two electrical pulses were presented on two sites in the same ICC layer and the evoked activity in A1 was recorded. In Protocol #2 for the tinnitus component, arrays were positioned across ICC and ICD. Spike activity in ICC was recorded in response to broadband noise stimulation and electrical stimulation of the ICD to identify any changes in neural activity. For both protocols, histological techniques were performed to produce 3-D reconstructions of the midbrain and all site locations. For Protocol #1, we found that co-activation of rostral-lateral areas of the ICC elicits greater A1 enhancement (i.e., activity beyond a linear summation of individual pulses) than caudal-medial areas. These rostral-lateral areas correspond to neurons with shorter latencies, more precise time-locking, and more spatially synchronized activity to acoustic tones. Thus, we have identified a location within the ICC that may be optimal for hearing restoration. For Protocol #2, we were able to show that stimulation of all locations across ICD could induce suppression within the ICC. Since tinnitus has been linked to hyperactivity within the central auditory system, including the ICC, we may be able to target just a few locations within ICD to sufficiently suppress the tinnitus percept.

From these animal studies, we have demonstrated that the AMI can effectively activate the IC for potentially restoring hearing and suppressing tinnitus. Given the smaller size and increased number of electrodes in conjunction with the recent developments in current steering techniques, the AMI is capable of more sophisticated and precise stimulation strategies than the traditional DBS lead, and thus it could potentially be used for other neurological applications beyond auditory therapies.

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