Fourth Quarterly Progress Report

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Feasibility of an Intra-Neural Auditory Prosthesis Stimulating Electrode Array

J.C. Middlebrooks and R.L. Snyder

Kresge Hearing Research Institute
University of Michigan
1301 E. Ann St.
Ann Arbor, MI 48109-0506
jmidd@umich.edu

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1. Introduction

The objective of this research is to evaluate the feasibility of intra-neural stimulation as a means of auditory prosthesis. We are stimulating the auditory nerve with penetrating multi-channel electrode arrays and monitoring the tonotopic spread of activation in the central nucleus of the inferior colliculus (ICC) of cats.

2. Summary of activities for the quarter

In the present quarter, we conducted acute physiological experiments in five cats, using acoustic stimulation and electric stimulation via intra-scalar and intra-neural electrodes. Those experiments concluded our first characterization of intra-neural stimulation using a lateral trans-bulla approach to the nerve. That work includes a first look at tonotopy, thresholds, interference among simultaneously stimulated channels, and temporal integration. We presented results in a podium session at the ARO Mid-Winter meeting in Baltimore, MD, (Feb. 5-9, 2006) and as an invited presentation a EuroConference on Sensation and Perception at the Pasteur Institute, Paris, France, March 9-10, 2006. We submitted for publication a short manuscript describing ICC responses to intra-neural stimulation using a lateral approach. Also in this quarter, we conducted a first test of a guide-tube system that will be used in chronic ICC recordings.

Our results, basis on data from a total of 14 anesthetized cats, demonstrate the following characteristics of activation of the ascending auditory pathway by intra-neural stimulation of the auditory nerve:

- Intra-scalar stimulation produced frequency specific activation of neural populations ranging across the entire range of frequencies represented by characteristic frequencies (CFs) in the ICC. The range of ICC CFs that we could map was limited by the frequency response of our audio system, but with intra-neural stimulation we typically activate ICC loci with CFs <1 kHz and >25 kHz. The map of depth in the auditory nerve to depth along the ICC tonotopic axis is non-monotonic. In the intra-neural array placements yielding the most complete tonotopy, we have observed activation of the middle-turn (mid-frequency) representation, progressing to apical turn (low frequencies), then to basal turn (high frequency) with successive stimulation of distal (deep) to proximal (superficial) intra-neural electrodes.
- Thresholds for intra-neural stimulation are lower than for stimulation with a conventional intra-scalar cochlear implant. We tested single 40-μs/phase biphasic pulses, initially cathodic. Mean thresholds for across 9 cats were 26.2 dB relative to 1 μA for intra-neural stimulation. In contrast, thresholds for intra-scalar stimulation were 50.7 dB for monopolar configuration and 60.3 dB for bipolar configuration. Bipolar intra-scalar is the more appropriate comparison to compare with intra-neural because only bipolar produces spread of excitation that approaches that attainable with intra-neural stimulation. That threshold difference is 34.1 dB, a ~50-fold lower threshold current for intra-neural compared to intra-scalar bipolar stimulation.
- Interference among simultaneously stimulated intra-neural electrodes is markedly reduced compared to intra-scalar electrodes. Stimulation of multiple intra-neural electrodes one at a time results in discrete non-overlapping patterns of ICC activation. Simultaneous stimulation of pairs of those electrodes results in superposition of those activation patterns with the contribution of each electrode clearly evidence and negligible influence of one electrode on the threshold of the other electrode. In contrast, low-level monopolar stimulation of intra-

scalar electrodes results in prominent changes in the threshold and operating range of nearby electrodes (the present results and Middlebrooks, 2004).

- Time constants for paired-pulse temporal integration were shorter for intra-neural stimulation than for intra-scalar stimulation. We measured thresholds as a function of the time interval between pairs of monophasic pulses and fit exponential functions to plots of threshold versus inter-pulse interval. Time constants were ~260 µs for intra-scalar compared to ~130 µs for intra-neural stimulation measured in the same animals. Those time constants are consistent with time constants previously reported for intra-scalar stimulation (504 µs: Dynes, 1996, recording from auditory nerve fibers; and 350 µs: Middlebrooks, 2004, recording from the auditory cortex) and for a single intra-meatal electrode (150 µs: Cartee et al., 2000, recording from auditory nerve fibers). This difference in time constants between stimulation sites suggests a difference in the site of action-potential initiation: spiral ganglion somata in the case of intra-scalar stimulation and axonal in the case of intra-neural stimulation.

We have now submitted for publication a paper describing these basic observations obtained with a lateral approach to the auditory nerve. We generally are pleased with the results, but suspect that the lateral approach to the nerve is not optimal, at least in the cat. We have found it difficult to insert the stimulating probe fully without striking bony obstructions. Indeed, in some animals we have been able to stimulate only apical- and basal-turn fibers and have never located the middle-turn fibers. Also, a single-shank stimulating array, even in the best case that passes transversely through the center of the auditory nerve, permits stimulation only of limited ranges of middle-, apical-, and basal-turn fibers, will no access to fibers located distant to that single traverse. Ideally, one would pass multiple multi-site stimulating arrays into the nerve, but that seems impractical with the lateral approach in the cat. In future experiments, we will attempt to avoid these limitations by approaching the auditory nerve from the inferior cranial fossa and will test a variety of multi-shank stimulating arrays.

In one animal, we tested a prototype of a guide-tube arrangement that will eventually be used for chronic ICC recording. The guide tube consisted of a section of hypodermic tubing containing a space-filling plunger. The guide tube and plunger were beveled to a common tip. The tube and plunger were inserted stereotaxically, and the plunger was removed. A silicon-substrate recording probe fixed in an inner tube then was inserted in the guide tube. Placement of the guide tube was successful in that we could record tonotopically organized ICC units with a tungsten electrode inserted through the tube. Placement of the silicon-substrate probe was unsuccessful, however, in that it could not penetrate the layers of membranes and blood vessels that lie over the inferior colliculus. We intend to modify the guide-tube design to further restrict flexing of the probe.

3. Plans for next quarter:

- Test intra-neural stimulation using an intra-cranial approach to the auditory nerve.
- Modify the ICC chronic guide-tube system and test in one or more animals. We cannot yet complete that system because we require a custom silicon-substrate probe. That probe has been ordered, but there is a ~6-month lead time. Nevertheless, we can test whether or not the system permits silicon-substrate probes to enter the ICC without breaking.

4. References

Caree, LA, van den Honert, C, Finley, CC, Miller, RL (2000): Evaluation of a model of the cochlear neural membrane. I. Physiological measurement of membrane characteristics in response to intrameatal electrical stimulation. Hearing Res. 146:143-152.

Dynes, SBC (1996): *Discharge characteristics of auditory nerve fibers for pulsatile electrical stimuli*. Doctoral Dissertation, Massachusetts Institute of Technology.

Middlebrooks, JC (2004): Effects of cochlear-implant pulse rate and inter-channel timing on channel interactions and thresholds. J.Acoust.Soc.Am. 116: 452-468.

5. Appendix:

- Abstract from a talk at the 2006 ARO Mid-Winter meeting
- Abstract from a talk at a 2006 EuroConference in Paris
- Manuscript of a paper submitted for publication