Selective Stimulation and Measurement in the Cochlear Nucleus with the Spike Microelectrode Array

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Abstract- **Current prosthetic devices to restore hearing sense of patients with bilateral acoustic neuromas aren't always effective, because we don't have sufficient knowledge of the auditory pathways and the Cochlear Nucleus (CN) functions to stimulate the Cochlear Nucleus functionally. Our goals are to enhance our understanding of such functions and to develop effective stimulating strategies of the CN. In this paper, we fabricate the spike microelectrode array with 16-sites in 1.3mm-square area for stimulation and measurement of the CN and show its feasibility through rats' experiments. In the experiments, spatiotemporal responses in the CN are recorded with the electrode. Electrical stimulation at different sites with different current amplitudes exhibits different spatiotemporal patterns on the Auditory Cortex. These results will provide useful information to study the auditory pathways and the CN functions and to develop stmulating strategies.**

***Keywords*- microelectrode, cochlear nucleus, electrical stimulation, Auditory Brainstem Implant**

I. Introduction

The auditory brainstem implant (ABI) that restores hearing by direct stimulation of the Cochlear Nucleus (CN) with an electrode array has been clinically applied. Few patients, however, benefit from the use of the device [1]-[4]. One possible reason for this poor efficacy of ABI is lack of the knowledge about auditory pathways, especially concerning the CN functions. Accordingly, the CN has not been effectively stimulated. Conventional studies about the CN with glass pipet needle or single microelectrode have enhanced our knowledge about specific function of individual neurons or interaction between nearby neurons. However, little is known about overall functions of the CN [5]-[10]. In order to clarify these functions, spatiotemporal information obtained by multi-point electrodes may be useful. In addition, it is useful to study responses in the central nerve system to the electrical CN stimulation because those data demonstrate how activation of discrete portions in the CN affect the processing in the central nerve system.

In order to study auditory pathways and develop effective stimulating strategies, we have developed the system that can measure and stimulate neuronal activities at multiple sites in the CN and can record them on the Auditory Cortex (AC). So far, we have developed the surface microelectrode that measures spatiotemporal patterns on the AC [11]. In this paper, we describe a spike microelectrode array for multi-point recording and stimulation in the CN. In rats' experiments with the electrode, we measure spatiotemporal responses to the auditory stimulation and stimulate the CN. These experiments show the utility of the system and present results.

II. Materials and Methods

A. Electrode fabrication

A spike microelectrode array must be long and slender enough to reach the CN located in a relatively deep position of the rats' brain. The electrode, shown in Fig.1, is designed to have 16 stimulating and recording sites in 1.3mm-square area. The spike microelectrode array is fabricated by three steps as shown in Fig.2: Substrate fabrication (1), Assembly of the electrode array (2), and Tip processing (3).

In substrate fabrication process, a glass mold is etched to make 100μm wide and 100μm deep trenches at 400μm intervals with polystyrene sandblast processing. The pattern of trenches was copied on the substrate by pressing the mold (1). In assembly process, 100μm diameter tungsten rods are aligned in the trenches of the substrate to make a single layer. After assembly of each layer, 4-layers are pressed and bonded (2). In tip processing, the tips are aligned to the same height with electro-discharging, in which 200 volts were applied between each tip and the 1-M NaOH water solution. The tip shapes are modified by electro-polishing at 2 volts in the 1-M NaOH water solution (3). A polishing period and the reciprocation stroke determine the tip diameter (between 2-3μm and 100μm) and the tip tapers, respectively (Fig.1 (b)). Finally, liquid polyimide is coated on the tips to make the insulation layers, and insulation at the tips is removed by electro-discharging (Fig.1 (c)). 1.27mm pitch sockets for integrated circuit are employed for wiring, in which other edges of tungsten rods are directly inserted and soldered.

B. Animal preparation

All experiments were performed in accordance with the guideline of the Animal Experiments Committee of the University of Tokyo. Fig.4 shows a schema of the experimental setup. Adult albino rats with normal ABR weighting 200-300g were used. Each animal was anesthetized with Ketamine (50mg/kg) and Xylazine (7mg/kg). The cerebellum was exposed and partly removed to expose the CN. The spike microelectrode array was introduced to the CN at about 50μm depth. The AC was also exposed and the surface microelectrode was mounted on the AC with keeping the dura mater intact. Fig.3 shows the surface electrode that has 32 recording-sites in 2mm-square area [11]. Sockets of integrated circuits were positioned at vertex, and at 7mm anterior to vertex, as reference and ground electrode, respectively.

C. Experimental protocol

1) Auditory Evoked Potentials in the CN: 16-Auditory Evoked Potentials (AEPs) in the CN were recorded with the spike microelectrode array. The auditory stimuli were alternating clicks at 90dB SPL delivered through a speaker located 20cm in front of the rat's head. 32-AEPs were amplified and filtered with a band-pass of 50-1500Hz. Each signal was averaged over 15 trials.

2) Electrically Evoked Potentials on the AC: The CN was stimulated with the spike microelectrode array, and 32-Electrically Evoked Potentials (EEPs) on the AC were measured with the surface electrode. Preceding CN stimulation, AEPs were also measured in the CN. In this protocol, the spike microelectrode

This paper was supported by the Organization for Pharamaceutical Safety and Research (OPSR) of Japan.

Report Documentation Page

Report Date	Report Type	Dates Covered (from... to)
25 Oct 2001	N/A	-

Title and Subtitle Selective Stimulation and Measurement in the Cochlear Nucleus With the Spike Microelectrode Array	**Contract Number**
	Grant Number
	Program Element Number
Author(s)	**Project Number**
	Task Number
	Work Unit Number
Performing Organization Name(s) and Address(es) Graduate School of Engineering The University of Tokyo Tokyo, Japan	**Performing Organization Report Number**
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group PSC 802 Box 15 FPO AE 09499-1500	**Sponsor/Monitor's Acronym(s)**
	Sponsor/Monitor's Report Number(s)

Distribution/Availability Statement
Approved for public release, distribution unlimited

Supplementary Notes
Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, October 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom.

Abstract

Subject Terms

Report Classification unclassified	**Classification of this page** unclassified
Classification of Abstract unclassified	**Limitation of Abstract** UU

Number of Pages
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array with 4-sites was employed for the stimulation and recording and each site was labeled A, B, C, and D in order from a caudal site to a rostral site. In addition, 32-AEPs on the same area of the AC were measured as reference. The electrical stimuli were monopolar and biphasic charge-balanced constant-current pulses with a total duration of 200μs and an amplitude ranging from 150 to 200μA. Evoked Potentials are presented as described above.

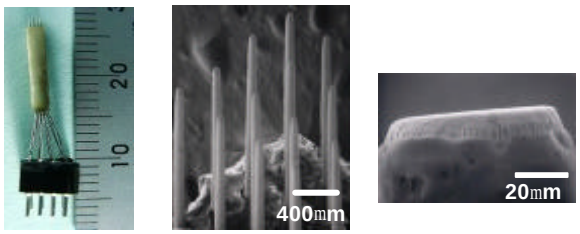

Fig. 1 Photo of the spike microelectrode array. (a)Whole view. (b)Tip view. (c)Magnification of the tip.

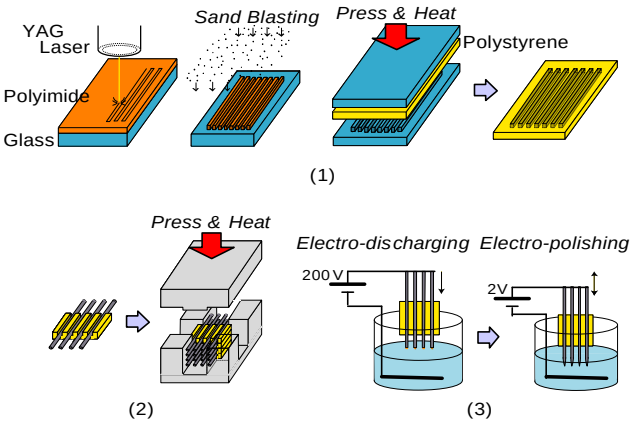

Fig. 2 Process flow of the spike microelectrode array. (a)Substrate fabrication. (b)Assembly of the electrode array. (c)Tip processing

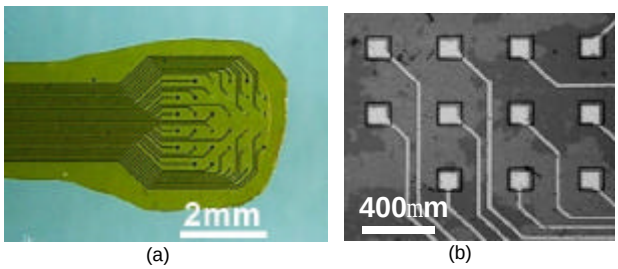

Fig. 3 Photo of the surface microelectrode. (a)Whole view. (b)Tip view.

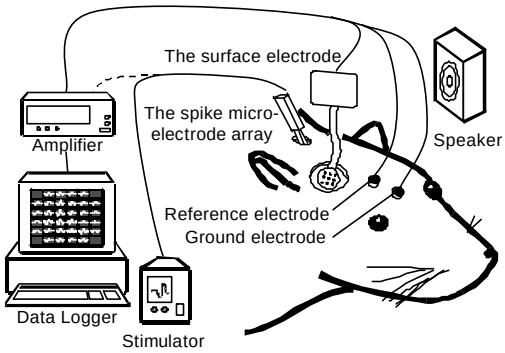

Fig. 4 Schema of the experimental setup

III. Results

Fig.5 (a) shows 16-AEPs in the CN acquired with the spike microelectrode array. Time-series AEPs distributions patterns, based on the data of Fig.5 (a), are shown in Fig.5 (b). The large responses were recorded at 3 spots of each figure.

Fig.6 (a) shows 32-AEPs on the AC detected with the surface electrode as reference to following EEPs. Fig.6 (b) shows time-series AEPs distribution patterns. Different responses at each site are observed, and large responses travel from the rostro-ventral area to the caudro-dorsal area. Fig.7 shows 4-AEPs in the CN acquired with the 4-spike microelectrode array. In case of B, C, and D, large responses over 100μV are recorded, whereas site A exhibits far smaller response than others. Then, 32-EEPs were recorded. The stimulation of A didn't elicit significant EEPs, while that of B, C, and D result in large responses. Fig.8 (b) and (d) shows 32-EEPs in response to the CN stimulation at site B and D, respectively. Red and blue lines indicate differences in stimulating amplitude: red, 150μA; blue, 200μA. EEPs elicited by the C stimulation were almost the same as those by D. Fig.9 (b), and (d) show time-series EEPs distribution patterns. The stimulation at site B elicited large responses at the rostro-ventral area of the AC, while D elicited large responses at the caudro-dorsal area.

Fig.10 shows the average amplitude of largest peaks recorded at each recording site of the AC, when stimulating with different amplitude (150μA, 200μA) at different sites (B, C, and D)

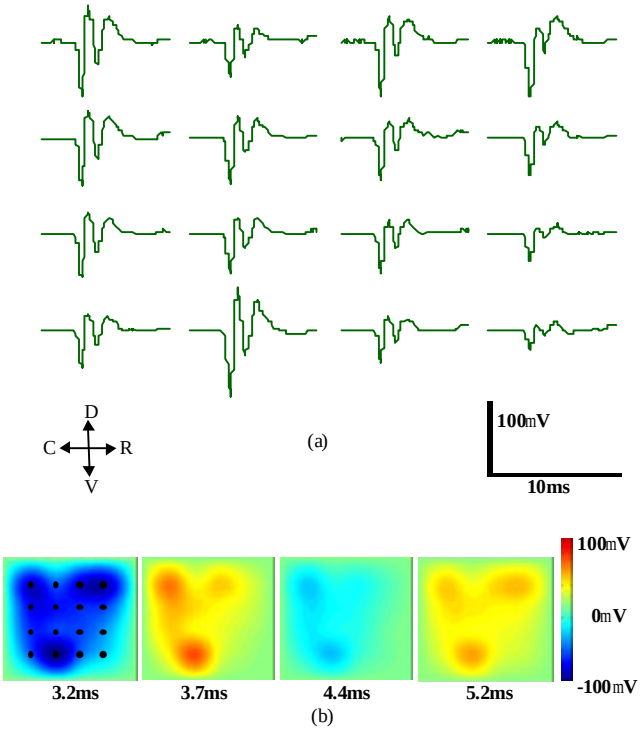

Fig. 5 AEPs acquired with the spike microelectrode array in the Cochlear Nucleus (a) and their color-coded potential distribution patterns at each latency (b). Black dots in the distribution pattern correspond to the location of recordingsites. (Abbreviations:D:dorsal, V:ventral, R:rostral, C:caudal)

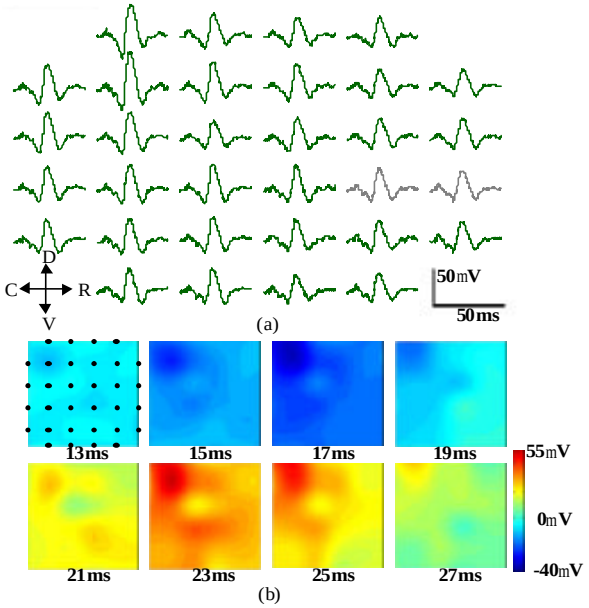

Fig.6 AEPs acquired with the surface microelectrode on the Auditory Cortex in response to Click sounds (a) and their color-coded potential distribution patterns at each latency (b). Gray lines, whose recording sites weren't available, are average responses of surrounding sites.

Fig.7 AEPs acquired with the 4-spike microelectrode array in the Cochlear Nucleus

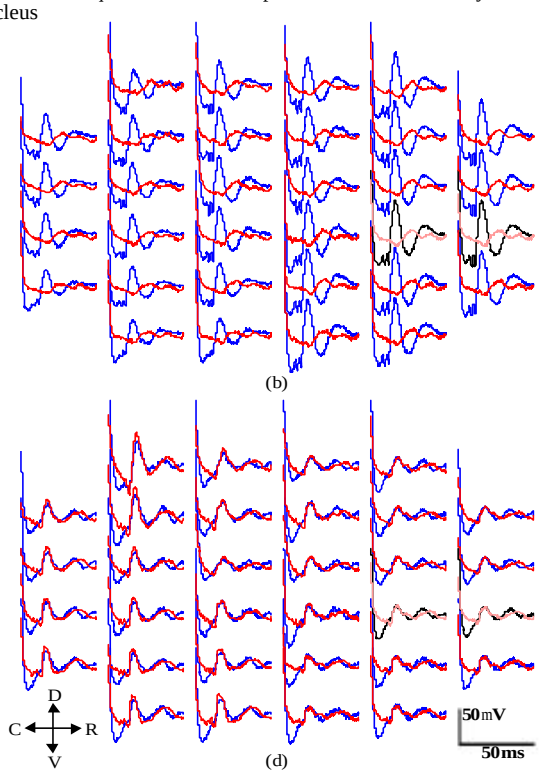

Fig.8 EEPs acquired with the surface microelectrode on the Auditory Cortex in response to electrical stimulating B site (b), and D site (d). Red and blue lines correspond to responses to the stimulation at 150μA and 200μA, respectively. Pink and black lines, whose recording sites were not available, are average responses of the surrounding sites.

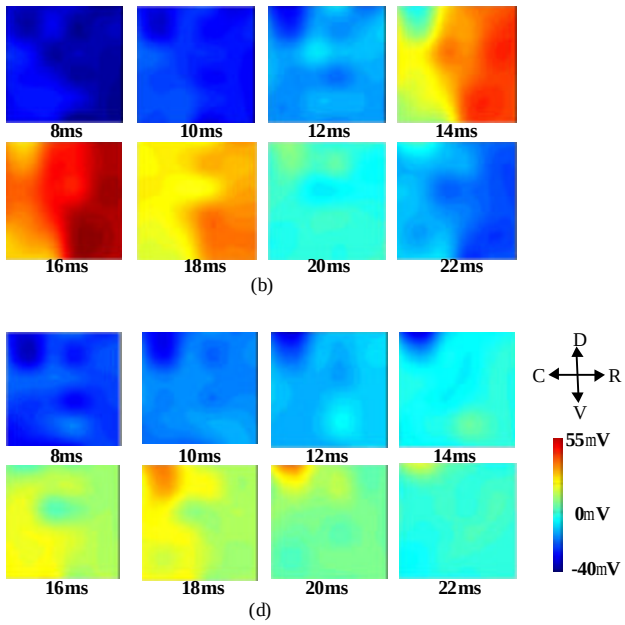

Fig.9 Color-coded potential distribution patterns on the Auditory Cortex at each latency in response to electrical stimulating site-B (b), D (d).

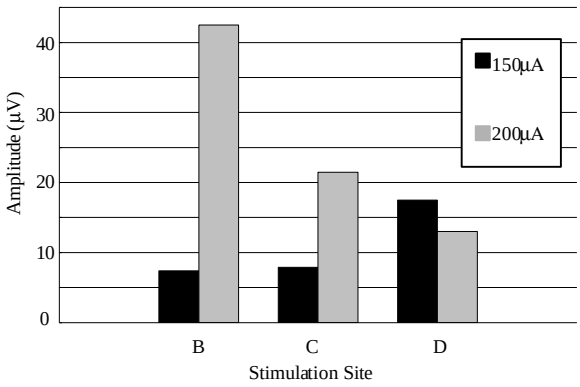

Fig.10 The avarage amplitude of largest peaks recorded at each site of the surface microelectrode on the Auditory Cortex

IV. Discussion

The feasibility of the spike microelectrode array was demonstrated through multi-point recording and selective stimulation in the CN. In the last decade, multi-point electrodes based on MEMS technology have been reported and their feasibility have been documented through multi-point recording and stimulation experiments [12]-[15]. Compared with these multi-point electrodes, the spike electrode array is easier to fabricate and to make the array as demanded in particular experiments such as whole shape, tip diameter, probe interval, total number of probes, probe material, and coating, while the spatial resolution is almost the same as that of the silicon-electrodes. For instance, the tip diameter should be a few micros for counting firing rate and should be thicker for measuring field potentials of relatively large areas.

Present experiments exhibit: 1) significant spatiotemporal

activities in the CN can be recorded in response to the auditory stimulation; 2) electrical stimuli at different sites or different amplitudes result in different responses on the AC.

Three strongly activated areas in the CN as shown in Fig.5 (b) may correspond to the PosteroVentral Cochlear Nucleus (PVCN), the AnteroVentral Cochlear Nucleus (AVCN), and the Dorsal Cochlear Nucleus (DCN), according to the cerebral atlas. These nuclei have different features: DCN is thought as primary auditory pathways which have fine-tune tonotopic organization; AVCN is thought as non-primary auditory pathways that just relay afferent signals; PVCN has the feature of both DCN and AVCN [16]. However, since these functions were examined by single neuron recordings, little is known how they interact in signal processing and how each nucleus affects the central auditory pathways. Therefore, to measure spatiotemporal activities of both the CN and the AC may be useful in order to enhance further understanding of these CN functions.

Our present results show that electrical stimulation at various portions of the CN may contribute to our understanding of the auditory pathways as well as the CN functions. AEPs on the AC show two strongly activated areas of the caudro-dorsal portion and the rostro-ventral portion, which may correspond to the primary auditory area (AI) and anterior auditory field (AAF) as reported by Horikawa [17]. The AAF was activated by stimulation at site B or C, while the AI was activated by stimulation at D as shown in Fig.7. In addition, when stimulating D, different stimulating amplitudes caused different responding potentials in the AI, but caused no significant changes in the AAF. These results indicate that specific portions of the CN might project to specific fields of the AC. Stimulating amplitude also suggests interesting characteristic of the auditory pathways; EEPs amplitudes evoked by the stimulation at B or C increased as stimulating amplitude increased, while those by D decreased. When stimulating D, possibly, activation in the peripheral portions may cause inactivation in the central auditory pathways. These results suggest we should consider, when developing new generation ABI, inhibitory effects.

Although these data are still preliminary, they will provide useful information for understanding the CN functions and the interaction between the CN and the central auditory pathways.

V. Conclusion

This paper described the spike microelectrode array for multi-point neural stimulation and recording and showed its feasibility. In recording experiments, spatiotemporal patterns of Auditory Evoked Potentials in the Cochlear Nucleus (CN) were obtained with 16-sites microelectrode. In stimulating experiments, selective stimulation of the CN with 4-sites microelectrode was demonstrated through Electrically Evoked Potentials on the Auditory Cortex recorded with the surface microelectrode. These results could help to understand the complex organization of the CN and overall auditory pathway functions, and to develop effective stimulating strategies of the CN.

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