

A hybrid clinical–research depth electrode for acute and chronic *in vivo* microelectrode recording of human brain neurons

Technical note

MATTHEW A. HOWARD III, M.D., IGOR O. VOLKOV, PH.D., MARK A. GRANNER, M.D., HANNA M. DAMASIO, M.D., MICHAEL C. OLLENDIECK, B.S., AND HANS E. BAKKEN, B.S.

Departments of Surgery (Division of Neurosurgery) and Neurology, University of Iowa College of Medicine, Iowa City, Iowa

✓ For several decades, important scientific information has been gained from *in vivo* microelectrode recordings of individual human cerebral cortical neurons in patients with epilepsy. The experimental methods used, however, are technically complex and require a highly skilled intraoperative team. There are also significant experimental time limitations, as well as constraints on the type of behavioral tests conducted, and the brain regions that may be safely studied. In this report, a new method is described for obtaining *in vivo* microelectrode recordings using a hybrid depth electrode (HDE). High-impedance research recording contacts are interspersed between low-impedance clinical electroencephalographic (EEG) contacts along the HDE shaft. The HDE has the same external physical properties as a standard clinical depth electrode (DE). Following preclinical laboratory testing, 15 HDEs were used in the evaluation of six patients with medically refractory epilepsy. High-quality EEG recordings were obtained in all cases (two acute intraoperative, four from the chronic epilepsy monitoring unit). Action potentials from individual neurons were successfully recorded during all experimental sessions; however, the chronic preparations were clearly superior. Chronic HDEs are placed using a standard stereotactic system, and the locations of recording contacts are documented on a postimplantation imaging study. The quality of the chronic research recordings was excellent over study periods ranging from 5 to 14 days. The patients rested comfortably on the ward and were able to cooperate with complex experimental instructions. Basic neuroscientists participated fully in all aspects of the chronic investigations. The use of an HDE in place of a standard clinical DE may now allow detailed physiological investigations of any brain region targeted for clinical DE implantation.

KEY WORDS • depth electrode • epilepsy • *in vivo* recording • single-unit recording

IMPORTANT information about normal human cerebral cortex function has been provided by neurosurgical investigators conducting microelectrode studies during epilepsy surgery. Using research microelectrodes, these investigators have performed extensive acute physiological studies of lateral temporal lobe cortical neurons in awake humans.^{4–6,8,10,11} These microelectrodes gather research data exclusively and are placed in tissue that will be subsequently resected.

To advance this research, we describe a new hybrid depth electrode (HDE) that was designed to provide simultaneous clinical depth electroencephalographic (EEG) monitoring and microelectrode research recordings in both acute (intraoperative) and chronic (epilepsy monitoring unit) settings. This new method was developed to pro-

vide cortical neuron recordings from multiple human brain sites situated along any trajectory selected for depth electrode (DE) implantation.

Overview of Electrode Design

Metal research microelectrodes are typically thin, rigid wires, such as tungsten, with finely sharpened tips. The HDE described in this report was designed to record in regions of human brain that may not be subsequently resected. To avoid causing additional brain tissue disruption for research purposes only, the HDE does not incorporate any features requiring the passage of microelectrodes beyond the boundaries of a clinical DE. Instead, the exposed ends of the thin flexible wires are positioned

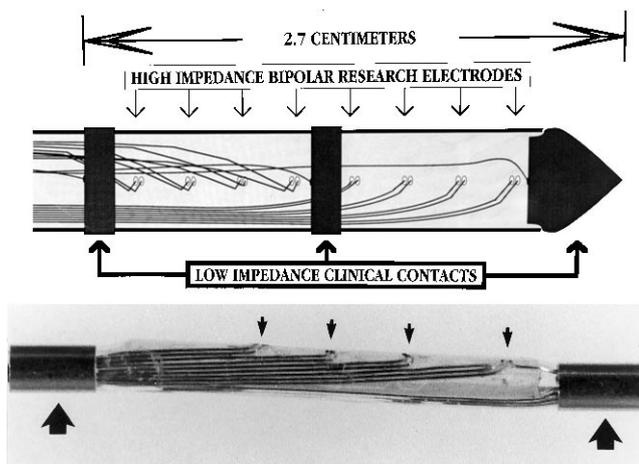


FIG. 1. *Upper:* Schematic diagram depicting a flexible-shaft hybrid depth electrode (HDE). Eight pairs of high-impedance bipolar research recording contacts are interspersed between three low-impedance clinical electroencephalographic (EEG) recording contacts. *Lower:* Photograph demonstrating four pairs of high-impedance bipolar contacts (*small arrows*) positioned between two low-impedance EEG contacts (*large arrows*) on a flexible shaft HDE (1.25 mm outer diameter).

along the shaft of a clinical DE, interspersed between, and flush with, standard clinical low-impedance monopolar EEG contacts. All electrodes described in this report were approved for use in human subjects by the University of Iowa Human Subject Institutional Review Boards.

Flexible Shaft HDE

Each HDE (Radionics, Inc., Burlington, MA) has three low-impedance clinical EEG contacts, as well as multiple bipolar and tripolar microelectrode recording sites (Fig. 1). The shaft is constructed of flexible, tecoflex-polyurethane (1.25 mm outer diameter) through which teflon-coated platinum-iridium high-impedance electrode wires run (50 μm cross-section diameter, 15 Mohm DC resistance). A thin removable stainless steel stylet is used during electrode placement. The flexible HDE has been used for both acute and chronic human recordings. An earlier rigid shaft HDE design was abandoned after only one use.

Recording Arrays

Tripolar recording arrays are used as stereotrodes, as described by McNaughton, *et al.*⁹ Differences in amplitude of action potentials from a single neuron simultaneously recorded from different recording combinations of the tripolar array provide a spatially dependent characteristic for that neuron that allows for more reliable isolation of individual neurons from multiunit data. Signal amplification was performed using eight differential amplifiers (Bak Electronics, Germantown, MD). All data are stored on a multichannel tape recorder (Racal, Herndon, VA) and analyzed offline in our laboratory. The EEG leads from the low-impedance contacts are connected to the clinical EEG monitoring machine.

The HDE's external physical characteristics and technique for stereotactic implantation are the same as for a

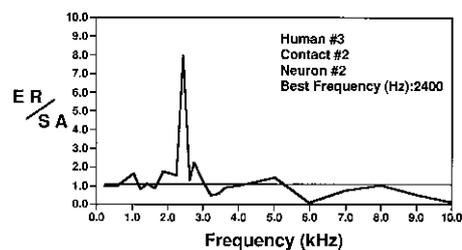


FIG. 2. Graph showing physiological data obtained during an acute recording session using a hybrid depth electrode positioned within a patient's right transverse temporal (Heschl's) gyrus. The graph depicts the frequency response properties of an individual auditory cortex neuron. Pure tones (300 msec duration, 80 dB intensity) were presented through a sound tube in the awake patient's left ear at 1-second intervals. The neuron's responses to tones of 25 different frequencies (30 repetitions each) were analyzed by determining the ratio of the evoked response (ER: rate of action potential firing during the first 50 msec following tone presentation) divided by the spontaneous activity (SA: rate of firing during the 300 msec preceding tone onset) for each frequency tested. The neuron shown displayed frequency-dependent response properties similar to those previously reported in the auditory cortex of experimental animals.¹⁴

standard clinical DE. In the current series, chronic HDEs were placed using a Cosman-Roberts-Wells stereotactic system (Radionics). Localization of chronic HDE recording sites was initially accomplished by correlating postoperative stereotactic computerized tomography data with the preoperative magnetic resonance (MR) images. Subsequently, it has been confirmed that HDEs can be safely located directly with a postimplantation MR image without risk to the patient or loss of electrode recording quality.

Results

Acute Intraoperative Recordings

Two acute HDEs were placed in two epilepsy patients undergoing a right temporal lobectomy. High-quality EEG recordings were obtained from the low-impedance contacts in both cases. Microelectrode recordings from the first case were obtained using the rigid shaft monopolar HDE. Whereas single unit activity could be discriminated from some recording sites, there were significant pulse artifacts and electronic noise. The flexible shaft HDE model was used in the second acute case and recordings showed no evidence of pulse artifact and minimal electronic noise (Fig. 2).

Chronic Recordings

Thirteen chronic HDEs were implanted in four epilepsy patients. Patients were monitored on the epilepsy ward for periods ranging from 5 days to 2 weeks. The low-impedance EEG contacts functioned well throughout the monitoring periods. The first research recordings from the high-impedance sites were obtained 24 hours after implantation, and subsequent recording sessions were conducted for 1- to 2-hour periods each day. During the first postimplantation recording sessions, multiunit neuronal activity was obtained from all implanted HDEs, with no

Hybrid depth electrode recordings

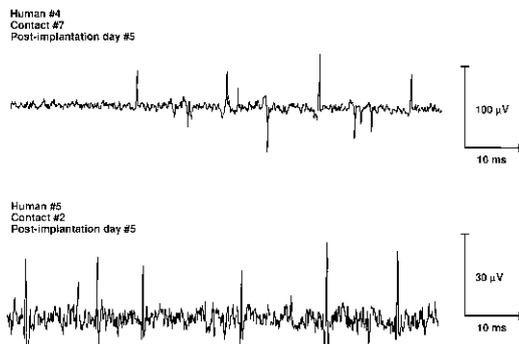


FIG. 3. Representative chronic microelectrode recordings from two different patients 5 days after hybrid depth electrode implantation. This spontaneous neural activity was recorded from bipolar high-impedance contacts. Action potentials from individual units can be discriminated for physiological analysis using a window discriminator.

pulse artifacts and minimal electronic noise. The level of spontaneous neuronal activity was greater than that noted during the acute experiments in humans. Undisturbed recordings were obtained while the patients performed complex auditory discrimination tasks and underwent neuropsychological testing. Examples of microelectrode recording data obtained from chronic HDEs are shown in Fig. 3.

In all chronic cases, microelectrode recording quality steadily improved during the first 4 days after implantation. The signal-to-noise ratio for isolated neurons increased, and action potentials from new units were noted during this early dynamic phase. Beyond this period, the high quality of the microelectrode recordings remained stable.

Stereotrode recordings displayed the same single-unit isolation capabilities described by McNaughton, *et al.*,⁹ in experimental animals. This method was particularly useful for identifying units with low-amplitude action potentials and for following the same unit for several days (Fig. 4). An example of the scientific usefulness of the chronic HDE method is provided in Fig. 5, which depicts the anatomical location and physiological properties of an insular cortex neuron studied 5 days after HDE implantation.

Discussion

In the current report, a new HDE is described that features a series of high-impedance microelectrode recording sites interspersed with standard clinical low-impedance EEG recording contacts. Experimental results in humans demonstrate that high-quality microelectrode recordings of cerebral cortical neurons can be consistently obtained in both acute (intraoperative) and chronic (epilepsy monitoring unit) settings.

Over the last several decades, a small group of investigators has applied acute microelectrode recording methods to the study of normal cerebral cortex physiology in awake humans.^{4-8,10,11,15} These unique research recordings were usually obtained by advancing microelectrodes into brain tissue that was scheduled to be resected.

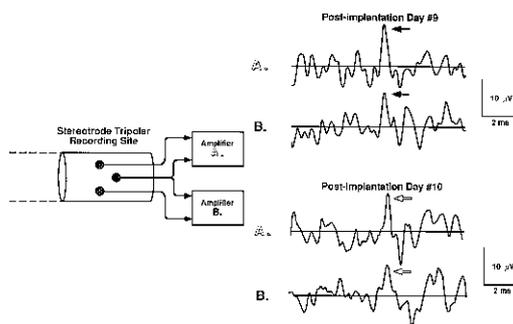


FIG. 4. Schematic diagram of tripolar stereotrode recording method with representative recording data. Two spatially distinct bipolar recordings are simultaneously obtained from the same neurons, thus allowing for enhanced discrimination of single units, as described by McNaughton, *et al.*⁹ Stereotrode recordings of low-amplitude action potentials (arrows) from the same neuron recorded on postimplantation Days 9 (upper) and 10 (lower) are shown. Ratios of action potential peak amplitudes (Channel A/Channel B) provide a consistent spatial characteristic to action potentials from a given neuron. Amplitude ratios (A/B) for the action potentials shown are 1.57 (Day 9) and 1.61 (Day 10).

The HDE described in this report was developed to enable investigators to safely obtain simultaneous microelectrode recordings from multiple human brain regions. By positioning all the research electrodes along the shaft of a clinical DE, it is possible to investigate any brain region situated along the planned DE implantation trajec-

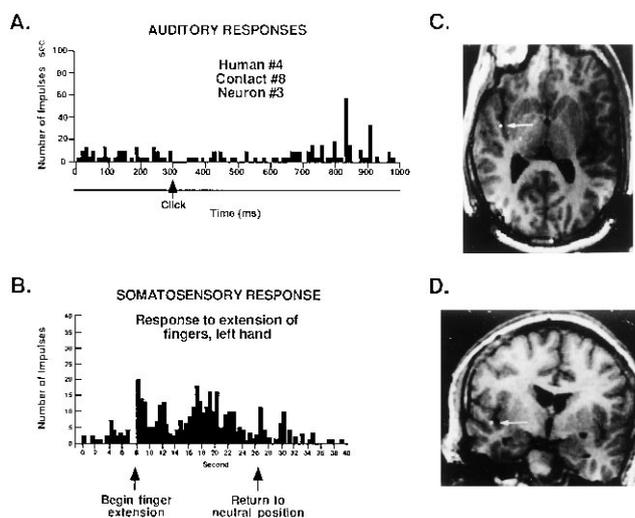


FIG. 5. Physiological and radiological data obtained from a chronic hybrid depth electrode (HDE) recording session. The graphs depict the responses of an individual insular cortex neuron with polymodal sensory receptive fields 5 days after HDE implantation. This neuron displayed slight transient inhibition following click presentation in the left ear (60 dB, 50 repetitions, 1-second intervals), followed by long latency rebound excitation (A). Movement of the left upper extremity evoked a strong excitatory response from the same neuron (B). The location of the HDE contact (arrows) from which this neuron was recorded is shown on the postimplantation axial (C) and coronal (D) reconstructed magnetic resonance images.

tory, including tissue that may not be subsequently resected.¹³

The HDE has a flexible shaft, bipolar research recording contacts, and tripolar stereotrode arrays. It can be used for both acute and chronic recordings. Acute preparations, however, are difficult because of time limitations, the requirement for handling recording equipment in a sterile fashion, and constraints on patient positioning and movement.

Chronic recordings have many important advantages. One improvement is the ability to determine the location of the recording electrode on a postimplantation brain imaging study. Other advantages include a tremendous increase in the amount of time available to perform complex physiological investigations and an improved environment in which to conduct these studies. The quality of chronic microelectrode recordings was excellent and demonstrated steady improvement during the first 4 days after surgery. Unit activity then remained stable for the duration of the monitoring periods. The stereotrode recording sites were particularly useful in identifying individual low-amplitude units and for following the same units for several days.

The HDE differs from the electrodes developed by Babb and coworkers.^{1,2} These investigators passed fine recording wires through a hollow electrode shaft positioned within a patient's amygdala or hippocampus. The recording wires were advanced beyond the end of the shaft into a zone of targeted brain tissue. Bechtereva and collaborators³ also have used fine wire electrodes for chronic human brain research recordings.

If the HDE results described in the current report can be confirmed in large numbers of patients, the potential scientific usefulness of the HDE is great. Chronic recordings from MR image-defined sites are capable of generating large amounts of high-quality, closely controlled physiological data from many individual cortical neurons simultaneously. By placing HDEs into the numerous cerebral locations reported as DE targets, it may be possible to generate cellular physiological maps of normal human brain function that expand on the pioneering functional mapping studies conducted by Penfield and colleagues.¹²

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Address reprint requests to: Matthew A. Howard III, M.D., Division of Neurosurgery, The University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, Iowa 52242.