PHYSIOLOGICAL AND HISTOPATHOLOGICAL EVALUATION OF CHRONICALLY IMPLANTED MICROELECTRODE ARRAYS

E. Fernandéz[1], M. Avilés[1], F.J. García-DeQuiros[1], E.M. Maynard[2], D. Warren[2], I. Aranda[1], R. Climent[1], R.A. Normann[2]

[1]Institute of Bioengineering. Univ. Miguel Hernández, Alicante, Spain; [2]Department of Bioengineering. Univ. Utah, Salt Lake City, USA

Purpose

Intracortical electrodes could provide new directions of therapy for several central nervous system disorders. The high spatial specificity achieved using arrays of penetrating electrodes is essential for accessing the organization of the nervous system at a level that is not possible with electrodes implanted on the surface of the brain. One of the major prerequisites for such clinical applications is that the organism accept these devices and that the stimulation through multiple penetrating electrodes will be safe.

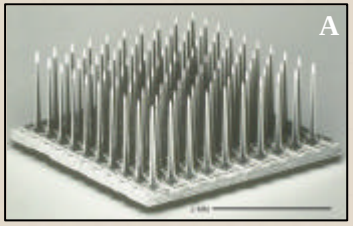
This study investigates the implantation of intracortical microelectrode arrays in cerebral cortex and the problems associated with this procedure on a long-term basis.

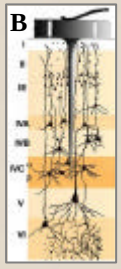
Methods

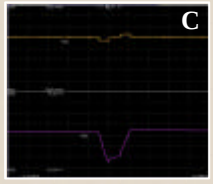
We used arrays of 100 or 25 penetrating silicon electrodes (Utah Electrode Array (UEA)), designed to focally stimulate or record cortical neurons located in a single layer up to 1.5 mm beneath the surface of the cerebral cortex. The arrays were inserted on the visual cortex of Halothane anaesthetized animals (cats, rabbits and rats) in a sterile surgical environment with the help of a pneumatically actuated impulse inserter.

The UEA was connected to a 100-channel amplifier and a digital signal processor based data acquisition system (Bionic Technologies, LLC). A programmable, battery powered miniaturized stimulator (Biomedical Technologies SL) was used to inject different currents into single electrodes. Microelectrode impedances were measured and stored by the stimulators.

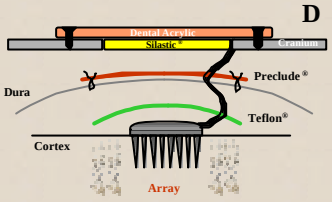
After several time intervals (ranging from 12 hours to 9 months) the animals were sacrificed. The microelectrode arrays were explanted and the implant site and surrounding tissue removed and processed histopathologically. The explanted arrays were studied by scanning electron microscopy.



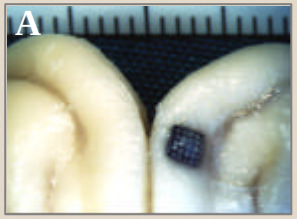


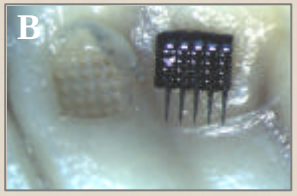


(A) Scanning electron micrograph of the UEA. (B) Schema of a transverse section of the cortex with an implanted microelectrode. (C) Waveform of the biphasic current pulse and electrode voltage. (D) Side schematic of the array implant site

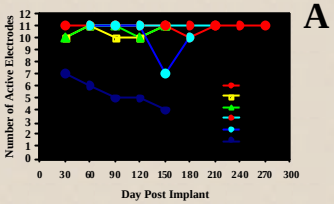


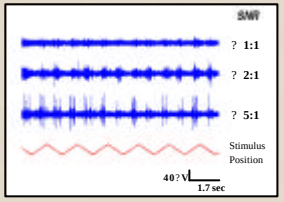
Results





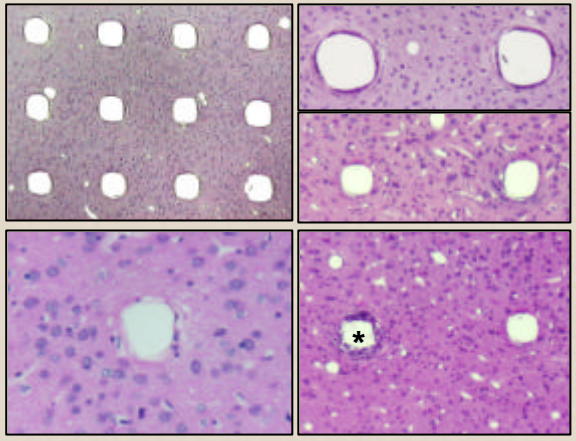
Explanted microelectrode array. (A) Position of 25-electrode array near primary visual cortex in a cat. Note the size of the electrode array relative to the size of the gyrus. (B) Explanted electrode array after 148 days of implantation. Note the absence of fibrous tissue in between the electrodes of the array.





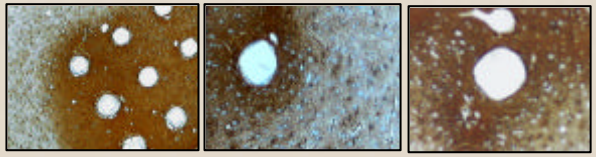
(A) Number of viable electrodes as a function of the time after implant. (B) Cortical visually evoked responses fall into three categories: well isolated single-units (bottom trace), multi-units with occasional single-units; and field potentials from distal units. Responses were evoked by a light bar, moving across the animal's visual field in a triangle wave sequence (lower trace).

Histological changes (H&E stain).



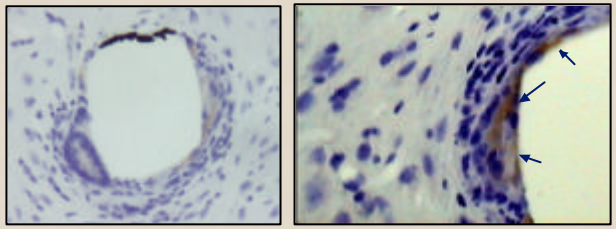
Light micrograph of tissue implanted with the UEA. Neurons in close proximity to the tracks appear normal although 6-8% of the electrode tracks (asterisk) show signs of an ongoing chronic response. Notice the thin fibrous encapsulation around microelectrode tracks.

Proliferation of reactive astrocytes (GFAP stain).

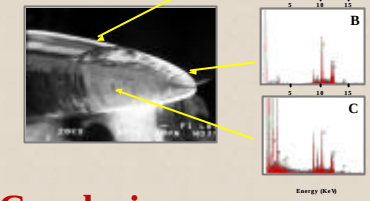


Astrocytes are observed in the vicinity of the tracks. There is an increased diffuse GFAP production in an area of 100-150 ?m around microelectrode tracks although neurons near the electrode tips appear normal.

Proliferation of macrophages (CD68 stain).



Scanning Electron Microscopy (SEM)



Response of the electrodes to long-term chronic implantation: SEM image after 6 months of implantation. The quantification using microanalysis shows places with normal silicon (A), places with a normal platinum-iridium surface (B) and places where the platinum-iridium deposit is lost (C).

Conclusions

- The Utah Electrode Array can be used to chronically record single and multiple unit neural activity. This verifies that intracortical microelectrodes can be implanted and chronically reside in close proximity to fully functional neurons.
- Intracortical microelectrodes are well tolerated by the central nervous system. In some electrode tracks there are a chronic inflammatory response characterized by astrocytes and macrophages which proliferate in the vicinity of the tracks. We have not found differences among arrays implanted in cats, rabbits and rats.
- These data suggest that multiple intracortical microelectrodes could be used for a long-term stable and safe clinical neuroprosthesis, although more studies regarding surface preparation of the microelectrode insulation, possible damage of neural tissues by permanent charge injection and the more effective means of stimulating cortical tissue are needed.