Cellular Responses to Micromachined Neuroprosthetic Device Insertion into the Brain

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Insertion of prosthetic device is elicits reactive responses from both nervous tissue and vasculature that prevent successful integration of these devices. Their chronic use is limited due to glial encapsulation that electrically isolates devices from cellular networks. We examined time-dependent changes of reactive responses in neocortex, hippocampus, and thalamus using immunohistochemistry and confocal microscopy. Results show dramatic differences in the magnitude of cellular response in different brain regions and time-courses. These experiments will provide important new information for the design of improved biomaterials and nano/micro-device to control dynamic biological events in the central nervous system.

Keywords: Neuroprosthesis, Silicon neural probe, Reactive responses, Immunohistochemistry

Nano/Micro-fabrication of neuro-prosthetic devices for electrical stimulation and recording from the central nervous system (CNS) provides tremendous potential for furthering our understanding of CNS function and treating disease and injury[1]. However, the success of these devices is presently limited by biological responses associated with their insertion and long-term residence. The previous study reports that the tissue responses have two discrete phases. The early-phase response is due to the injury produced by device insertion. The prolonged-phase response is initiate and continuously promoted by tissue/prosthesis interactions.

While these reactive responses are well characterized in cortex, the responses of other regions are unknown[2]. Responses to inserted devices are particularly relevant to deep-brain stimulating electrodes, which are currently used in treating a number of neurological disorders.

We examined time-dependent changes in neocortex, hippocampus, and thalamus using immunohistochemistry and confocal microscopy (Fig. 1).

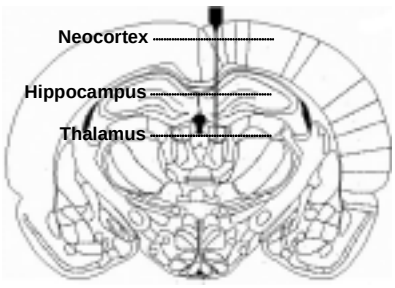

Fig. 1 Schematic view of probe location

Fig. 2 SEM view of silicon multichannel microelectrode

Device shafts were 5 mm long and 50 μm x 128 μm in cross-section (Fig. 2). Antibodies to GFAP (astrocytes), laminin (vasculature), and CD11b (microglia) were used to assess reactive responses around insertion sites at 1 hr, 24 hrs, 1 wk, and 6 wks. Results show dramatic differences in the magnitude of cellular responses in different brain regions. Immuno-reactivity in the hippocampus was stronger than in other regions (Fig. 3). In thalamus, staining for GFAP and laminin were relatively less intense, while CD11b was comparable. Laminin expression in all regions extended considerable distances from probe sites at 1 hr, and decreased at later times.

These data suggest that soluble signals may control the extent and magnitude of responses in different brain regions. Many prosthetic devices currently under development are organized into multishank arrays, which may result in overlapping spheres of influence and elevated responses between shanks. We are testing this hypothesis in neocortex, hippocampus, and thalamus using comb electrodes with different spacing between shanks. This study was supported by the International Collaboration Program of NBS-ERC/KOSEF and NIH/NIBIB, R01-EB-000359.

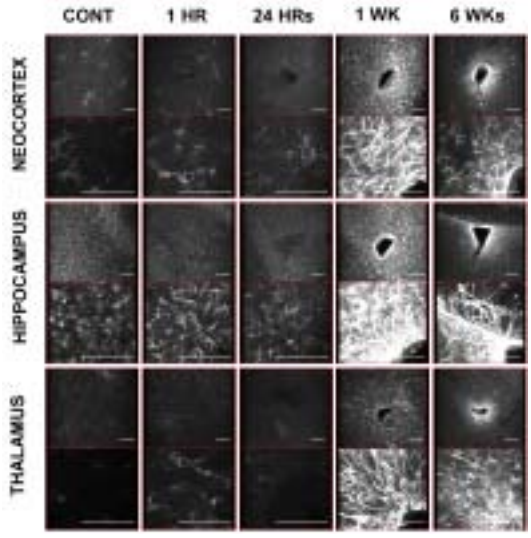

Fig. 3 Immunoreactivity of GFAP post probe insertion. Scale bars = 100 μm

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