Biotic response to long-term implantation of neural electrodes in the mouse motor cortex

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Neural electrodes are devices implanted in the brain and used to record extracellular potentials for a range of neuroprosthetic and neurotherapeutic applications, including the control of prosthetic limbs or computer-assistive programs. Neural prosthetic devices hold the potential to restore functionality and independence to patients with limited motor functionality.[2,3] However, the long-term reliability of current neural prosthetic devices is limited by diminished signal quality recorded by the electrodes over time.[1,4] The observed signal decline may be attributed to biotic factors that result from the brain's foreign body response to electrode insertion and chronic electrode implantation. Such factors may include ruptured vasculature, glial cell encapsulation, and localized neuronal loss.[5] Typical chronic implantation studies have observed tissue response for different time points up to 12 weeks.[5] However, in human patient trials, the number of single units recorded in a given session has been observed to decrease gradually over a period of six years.[2] To fully understand the effects of foreign body response on the electrophysiological signal recorded from these electrodes, it is important to analyze tissue adjacent to the implant for durations comparable to the timescale of signal decline.

We have applied a sensitive, fluorescence intensity-based method to quantify the cellular response to chronic electrode implantation (3-8 months). Single-shank multielectrode arrays (Neuronexus) were implanted in the mouse caudal forelimb area of the motor cortex. Electrophysiological signal was recorded from the freely-moving animal biweekly until the multi-unit activity firing rate signal declined to ~75% of its initial value, typically 3-8 months post implantation. The brain was extracted, sliced coronally (100 micron), and processed for immunohistochemical staining of cellular proteins (DAPI, GFAP, NeuN, Iba1). We have developed a protocol to create detailed, high-resolution spatial maps of cellular expression. Multiple, overlapping high-resolution z-stacks taken on the confocal microscope (Olympus Ix81 Confocal Laser Scanning Microscope) with a 40x objective were taken over an area ~600 x 600 um centered on the electrode track. The resulting image stacks were aligned using FIJI software and a max projection was calculated. The resulting image was subdivided into a regular grid of small regions (50by50 pixels), and fluorescence data from all pixels was averaged for each mini-region. Using this technique we have been able to measure the cellular composition of the foreign body response that results from chronic electrode implantation.

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