The Chronic FBR and Recording Performance in Aged Rat Cortex using High Density Silicon Recording Arrays

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Statement of Purpose: Chronic use of microelectrode recording devices to monitor motor cortex single unit neural activity offers the potential to control computers and a variety of neuroprosthetic devices. To the best of our knowledge, the development of such recording technology, as well as studies of the FBR to their implantation, have been performed using young animals, even though such devices are likely to be used, at least in part, in the elderly. Available evidence indicates that neuroinflammation is a major cause of inconsistent recording performance of such devices, a condition that may be exacerbated in the aged brain. The goal of this study was to examine recording performance and the FBR to high density microelectrode recording arrays implanted in the aged rat cortex over a chronic time period.

Methods: 4x4 UEAs connected to an Omnetics connector (Omnetics Connector Corporation, Minneapolis, MN) were obtained from Blackrock Microsystems (Salt Lake City, UT). Following ETO sterilization, UEAs were implanted into the cortex of aged male Sprague-Dawley rats (N=5, 70 weeks old at implantation). One week after implantation, and at least weekly thereafter, electrophysiological recordings were obtained from awake, unrestrained animals using a Cerebus recording system (Blackrock Microsystems). Recording data was analyzed offline using Offline Sorter (Plexon, Dallas, TX). Animals were sacrificed 12 weeks after implantation by transcardial perfusion. Arrays were retrieved and the brains post-fixed for 24 hours in 4% paraformaldehyde, followed by equilibration in a 30% sucrose solution. Frozen 30µm horizontal sections were collected and labeled using immunohistochemical markers for inflammation and neuronal tissue.

Results: Isolated single units were obtained from every animal over the entire 12-week implantation period (Figure 1). The average number of units obtained from each animal peaked 4 weeks after implantation (10.5 units/animal) and decreased thereafter. The number of units per electrode showed a strong negative correlation with time ($p<0.001$). While some units were consistently observed week-to-week, many units appeared variable. Average signal-to-noise ratios were highest in week 2 (11.82) and also had a strong negative correlation with time ($p<0.0001$). Histological results indicated a large inflammatory response to the implant, which was greatest near the base of the device and lessoned towards the tips (Figure 2). Similar to what we have previously described in young animals, an area of tissue loss was typically present beneath the implant and tapered with depth (Figure 2).

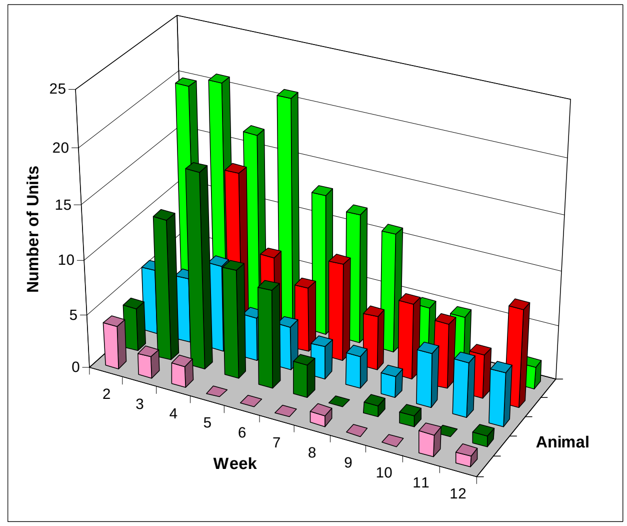

Figure 1. Graphical representation of the number of single units obtained during each week of the study.

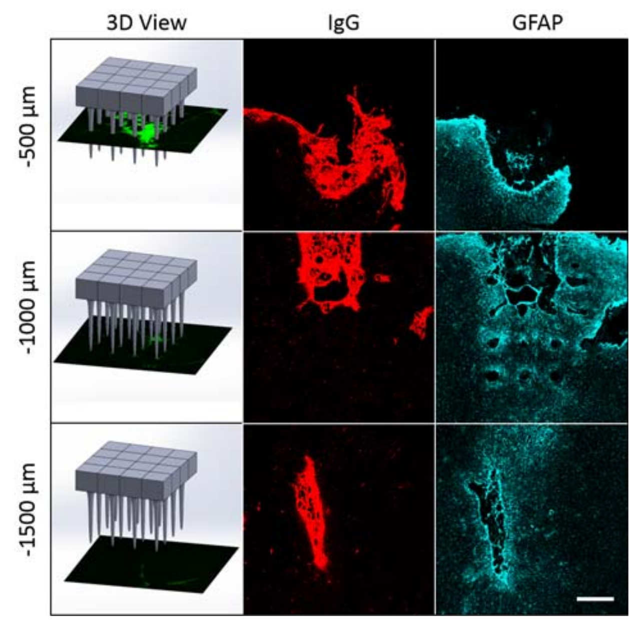

Figure 2. Representative horizontal images taken at varying depths in relation to the array for antisera against IgG, and GFAP. Similar to what we have previously observed in younger animals, an infarct-like area of tissue loss extends deep into brain tissue. Scale bar = 500 µm

Conclusions: This study is the first of its kind to show it is possible to record single unit activity in a freely moving aged rat at a point when animals are dying naturally. Our results indicate that is it possible to obtain these units over a 12 week indwelling period. This work also describes, for the first time, the histological response to high-density recording arrays in aged animals and further supports evidence of areas of extensive tissue loss beneath such penetrating arrays.