Accepted Manuscript

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PII: S0142-9612(18)30305-3

DOI: 10.1016/j.biomaterials.2018.04.043

Reference: JBMT 18629

To appear in: *Biomaterials*

Received Date: 12 February 2018

Revised Date: 16 April 2018

Accepted Date: 21 April 2018

Please cite this article as: Eles JR, Vazquez AL, Kozai TDY, Cui XT, *In vivo* imaging of neuronal calcium during electrode implantation: Spatial and temporal mapping of damage and recovery, *Biomaterials* (2018), doi: 10.1016/j.biomaterials.2018.04.043.

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ACCEPTED MANUSCRIPT

In vivo imaging of neuronal calcium during electrode implantation: spatial and temporal mapping of damage and recovery

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1. Abstract

Implantable electrode devices enable long-term electrophysiological recordings for brain-machine interfaces and basic neuroscience research. Implantation of these devices, however, leads to neuronal damage and progressive neural degeneration that can lead to device failure. The present study uses *in vivo* two-photon microscopy to study the calcium activity and morphology of neurons before, during, and one month after electrode implantation to determine how implantation trauma injures neurons. We show that implantation leads to sustained, high calcium levels in neurons within 150μm of the electrode interface. These neurons are morphologically distorted and mechanoporated after implantation, suggesting that calcium influx is related to mechanical trauma. Further, calcium-laden neurites develop signs of axonal injury at 1-3h post-insert. Over the first month after implantation, neuronal calcium activity increases, suggesting that neurons may be recovering. By defining the mechanisms of neuron damage after electrode implantation, our results suggest new directions for therapies to improve electrode longevity.

Keywords: two-photon microscopy; neuron calcium imaging; foreign body response; microelectrode implants; mechanical trauma; brain-computer interface

2. Introduction

Intracortical electrode arrays are necessary tools for recording extracellular action potentials from single neurons in brain-machine interface and basic neuroscience applications [1-5]. Implantation of these devices, however, is an inherently traumatic process that can result in immediate vascular and neural tissue damage, acute and chronic inflammatory glial responses, and progressive local neurodegeneration [6-13]. Neuron loss within the effective recording distance of electrode devices (electrode sites can resolve single neuron activity within 50-140μm [14-16]) is thought to lead to progressive failure of a device's recording quality in rodent [17, 18], cat[19], and primate models [20, 21]. These biocompatibility issues must be surmounted before brain-machine interface technologies can have widespread clinical translation.

One major challenge to biocompatibility is acute tissue damage due to surgical insertion of electrode arrays. Post-mortem studies of stab wounds and acute implantations (1 and 24h) reveal that there is immediate neuronal cell death following implantation, and that the most rapid drop in neuronal cell density relative to

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