Longitudinal changes to neural and vascular morphology near an implanted neural electrode

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IMPLANTED neural electrodes enable investigators to record electrical signals from the nervous system. Neural implants are used in medical devices for neurodiagnostic or neurotherapeutic indications, including neuroprosthetic devices for patients who have lost physical mobility [1]. The insertion of an electrode into the brain elicits both acute and chronic changes to local tissue, as evidenced by abnormal physiological response, increased neurotransmitter levels and foreign body response in the tissue. Recent work using in vivo two-photon imaging has shown that an acute microglial response to electrode insertion into the brain [2]. However, little is known regarding the temporal dynamics of the effect of penetrating electrodes on surrounding neurons and vasculature in cortical tissue. This is in part because examining neural processes and neurovascular features below the surface of the brain in vivo over time remains a significant challenge. To determine the effect of the electrode on local tissue health, optical imaging methods were utilized to visualize changes to neurons and vasculature in the local vicinity of the implant electrode array.

We employed two photon microscopy (TPM) and optical coherence tomography (OCT) to investigate neural morphology and vasculature, respectively, in the caudal forelimb area (CFA) of the mouse primary motor cortex. Wild-type C57bl/6 or transgenic mice expressing YFP under the Thy-1 promoter (H line, Jackson Labs) were anesthetized with isoflurane for the surgical implantation procedures. A tungsten (FHC, Inc.) or silicon-based (Neuronexus) microelectrode array was inserted through a craniotomy into the cortex at a 25 degree angle, avoiding disruption of major surface vasculature. A small window of cover glass and a metal head bar were secured with cyanoacrylate.

Using TPM, we are able to visualize the dynamics of neural processes in the motor cortex through a cranial window in transgenic mice expressing YFP in a sparse subset of cortical neurons. Preliminary experiments demonstrate the feasibility of performing electrophysiological recording and two-photon imaging sessions in the same animal for up to 8 weeks. In a parallel set of experiments, we use OCT to image the vasculature structure and blood flow dynamics near to the implanted electrode on both acute and chronic timescales. Through these experiments, we hope to identify correlations between the dynamics of neural processes, vascular remodeling and electrophysiological function. Understanding the local tissue response to the implantation of electrodes will bring insight into the factors that predict neural implant reliability, and provide an important contribution to the development of safe and reliable neural implant devices.

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