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Ph.D. DISSERTATION DEFENSE

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Degree:	Doctor of Philosophy
School/Department:	Charles V. Schaefer, Jr. School of Engineering and Science / Biomedical Engineering
Date:	Tuesday, December 12, 2023
Time/Location:	2:00pm, EAS 111
Title:	Gamma Stimulation Modulates the Glial Response to Implanted Microelectrode Arrays
Chairperson:	Dr. George McConnell, Department of Biomedical Engineering, School of Engineering & Sciences
Committee Members:	Dr. Marcin Iwanicki, Department of Chemistry and Chemical Biology, School of Engineering & Sciences Dr. Johannes Weickenmeier , Department of Mechanical Engineering, School of Engineering & Sciences Dr. Shang Wang, Department of Biomedical Engineering, School of Engineering & Sciences

ABSTRACT

Despite continuing technological advances in neural interfaces, challenges with the tissue reaction to chronic brain implants remain. The foreign body response of the brain to an inserted electrode induces sustained inflammation due to the persistent presence of the device and promotes local neurodegeneration. The use of brain stimulation to minimize inflammation is a burgeoning field, and so far, most interventions have been non-invasive. Here, we investigated an invasive method of inflammation-minimizing stimulation for application in individuals with neural electrode implants, e.g., deep brain stimulation and cortical neural prosthetics. We hypothesized that invasive stimulation at the gamma frequency band acutely increases microglial recruitment and chronically reduces astrogliosis at the tissue-electrode interface.

First, we examined the effects of invasive stimulation at the gamma frequency band (i.e., 40 Hz) on glial response by quantification of the acute neuroinflammation at the tissue-electrode interface in the motor cortex to understand the early impact of invasive gamma stimulation. We then applied this knowledge to a 6-OHDA Parkinsonian model and quantified the effects of deep brain gamma stimulation acutely and chronically on neuroinflammation. Lastly, we examined cytokine expression *in vitro* following gamma stimulation to quantify the inflammatory factors underlying the glial changes we observed *in vivo*.

The evidence we present here shows the potential for gamma stimulation to modulate the glial response to invasive implanted electrodes acutely and chronically. Our research suggests that gamma stimulation has potential use for advanced, integrated neuroprosthetic systems that are more effective and reliable in the future.