INVESTIGATION OF THE POTENTIAL FOR NEURAL INFLAMMATION INDUCED BY CONTINUOUS PERIPHERAL NERVE STIMULATION

Kara Lane-Lightfoot[1,3] , Alexander Campbell[2,3] and Dr. Shinho Cho[3]
1 Department of Chemistry, Florida State University, FL 32310
2 Department of Cell & Molecular Neuroscience, Florida State University, FL 32310
3 National High Magnetic Field Lab and Florida State University, FL 32310

Introduction:

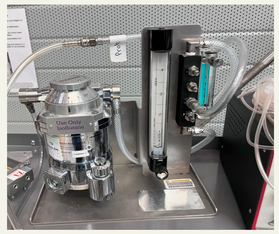
- Neuroinflammation, triggered by autoimmune responses and cellular impairment, contributes to disorders such as Alzheimer's, Parkinson's, and Depression (Mukhara et al., 2020).
- While inflammation is a natural defense mechanism, electrical stimulation may modulate neuroinflammatory responses (Mukhara et al. 2020; Chen et al., 2024).
- Peripheral Nerve Stimulation (PNSt) is used for chronic pain, complex regional pain syndrome, phantom limb pain, and fibromyalgia (Chen et al. 2024; Adair et al., 2020).
- Despite its benefits, prolonged stimulation may negatively impact neuronal health, potentially exacerbating neuroinflammation through central sensory pathway overactivation (Wiart et al., 2007).

Goals:

The goal of this study is to investigate how continuous PNSt affects the somatosensory cortex and thalamus in rats using 21.1 Tesla fMRI. It assesses **Blood Oxygen Level-Dependent (BOLD)** signal changes across brain regions in response to stimulation and examines how variations in stimulation parameters—duration, intensity, waveform, and frequency—correlate with the extent and severity of neuroinflammation induced by long-term electrical stimulation. The findings aim to **optimize neuromodulation therapies** and enhance understanding of sensory-induced neuroinflammation.

Methods:

1. Anesthetize the Sprague Dawley rats with a mixture of isoflurane, oxygen, and atmospheric gases.
2. Connect to the SAM system to monitor and record vitals, including exhalation (via capnograph) and internal temperature.
3. Attach electrodes to the whiskers and forepaws for electrical stimulation.
4. Place the subject in a 21.1 Tesla ultrahigh-field MRI and trigger electrical signals using a PC and Arduino.
5. Record responses through MRI imaging.
6. Assess neuroinflammation post-stimulation using T2-weighted images.



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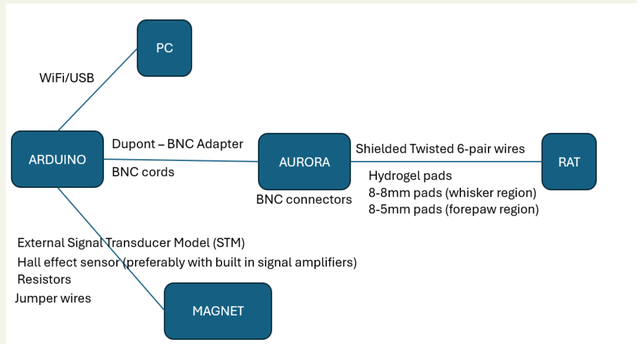
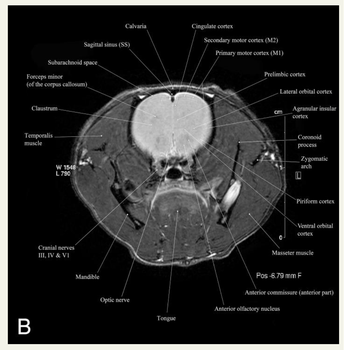


DIAGRAM SHOWING ELECTRICAL SYSTEM SET UP

900 MHz MRI



ANATOMICAL DIAGRAM OF RAT BRAIN

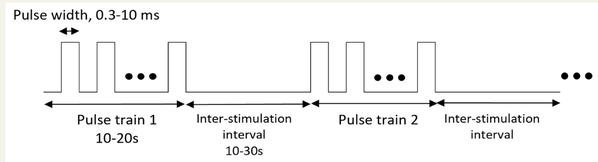


Diagram of Somatosensory Stimulation Protocol. During 15 minutes of functional imaging using Echo-Planar Imaging (EPI), the protocol involves alternating between multiple stimulation pulse trains and inter-stimulation intervals. Each pulse train lasts between 10 to 20 seconds, followed by an inter-stimulation interval of 10 to 30 seconds. This cycle of pulse train and inter-stimulation interval is repeated 18 to 45 times over the 15-minute EPI session. Each pulse train is composed of single bi-phasic or uni-phasic pulses with a width ranging from 0.3 to 10 milliseconds, adjustable based on the stimulator settings. The stimulation amplitude is typically set between 0.5 and 1 mA, and the frequency can range from 1 to 12 Hz. These parameters are manually adjusted to optimize the hemodynamic response observed during the imaging session.

Expected Results/Conclusion:

Ultra-high-field High-resolution rat brain MRI image

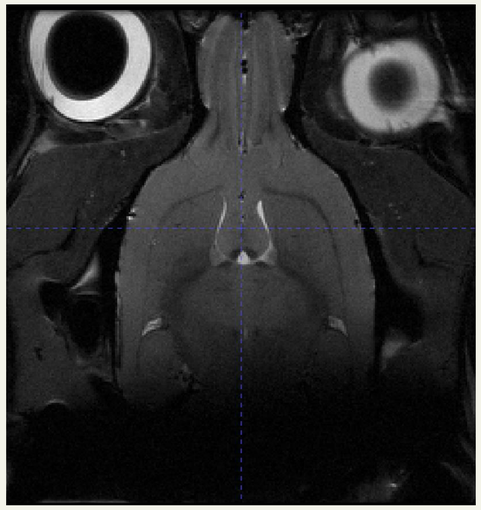


Figure 1: The image presents a coronal slice of a healthy male Sprague Dawley rat brain (150 g body weight). The scan was acquired using a T2-weighted RARE imaging sequence at 21.1 Tesla on a Bruker Paravision 360 system (V3.5). The imaging parameters were as follows: repetition time (TR) = 6000 ms, echo time (TE) = 25 ms, number of averages = 2, echo spacing = 12.5 ms, RARE factor = 4, image resolution = 256 × 256, field of view (FOV) = 25.6 × 25.6 mm, and slice thickness = 0.5 mm. 5 slices.

Neuroinflammation evolved in rat brain

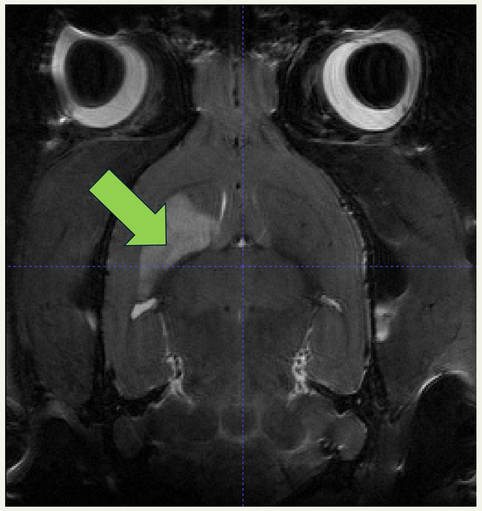


Figure 2 (Expected Results): The image demonstrates the expected result, highlighting neuroinflammation expressed near the thalamus in the left hemisphere (indicated by a green arrow). Prolonged high-energy stimulation of the somatosensory cortex is anticipated to induce neuroinflammation, particularly in the thalamic region. The imaging conditions are identical to those on the left. This image is cited from another research conducted at MagLab, specifically from a study on a progressive Parkinsonian-like pathology neuroinflammation model involving Prostaglandin D2/J2 manipulation.

Research Citations

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