## P2.085

### BRAIN-WIDE NEURAL DYNAMICS OF POST-STROKE RECOVERY INDUCED BY OPTOGENETIC STIMULATION

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**Abstract**

**Background:** Post-stroke optogenetic stimulations can promote functional recovery. However, the circuit mechanisms underlying recovery remain unclear. Elucidating key neural circuits involved in recovery will be invaluable for translating neuromodulation strategies after stroke. Here we employed optogenetic functional magnetic resonance imaging (ofMRI) to map brain-wide neural circuit dynamics after stroke, in mice treated with and without optogenetic excitatory neuronal stimulations (OST).

**Method:** Male mice expressing channelrhodopsin (ChR2) in ipsilesional M1 (iM1) layer V excitatory neurons were used. ofMRI were performed on pre-stroke and post-stroke days (PD) 3, 15 and 29. OST were given daily from PD5-15. Sensorimotor tests were conducted one day prior to each ofMRI session. Mice underwent transient middle cerebral artery occlusion (intraluminal suture model, 30 minutes). Stimulated mice received 10 days of OST and no stim group (mice without OST). The effects of selective optogenetic stimulation of the cortico-thalamic circuit on recovery was also investigated. The expression of plasticity marker GAP43 and synaptophysin were examined.

**Result:** Our results show that optogenetic excitatory neuronal stimulations in iM1 promote motor performance after stroke. ofMRI mapping data revealed key circuits disrupted by stroke, including cortico-cortico, cortico-thalamic, transcallosal and cortico-cerebellar circuits. iM1 stimulations restored activation of the ipsilesional cortico-thalamic and cortico-cortical circuits, and the extent of activation was correlated with functional recovery. Furthermore, stimulated mice exhibited higher expression of axonal growth associated protein 43 in the ipsilesional thalamus and showed increased synaptophysin$^{+}$/channelrhodopsin$^{+}$ presynaptic axonal terminals in the cortico-thalamic circuit. Importantly, selective stimulation of the cortico-thalamic circuit was sufficient to improve functional recovery.

**Conclusion:** Our findings demonstrated early involvement of cortico-thalamic circuit as an important mediator of post-stroke recovery. Our study also highlighted several stroke-disrupted circuits (i.e. transcallosal and cortico-cerebellar circuit) as potential brain stimulation targets for stroke recovery.

**Keywords:** optogenetic brain stimulation, stroke recovery, cortico-thalamic, functional MRI

## P2.086

### HIPPOCAMPAL POTENTIALS EVOKED BY NETWORK-TARGETED STIMULATION VARY BY THETA PHASE

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**Abstract**

Although stimulation targeting the hippocampus indirectly via its network can impact hippocampal memory function, the mechanisms governing its effects are not fully understood. For example, though CA3 excitability and entorhinal connectivity vary with hippocampal theta phase, it is not known whether phase has an impact on network stimulation efficacy. To address this question, we tested whether corticocortical evoked potential (CCEP) amplitude in the human hippocampus varies according to local theta phase at the time of stimulation. Intracranial local field potential data were collected from individuals with epilepsy undergoing medically necessary stereotactic electroencephalographic recording (sEEG) ($n = 7$ participants, 23 hippocampal sEEG contacts). Biphasic bipolar direct electrical stimulation (1Hz, 5mA) was delivered via sEEG contacts in the lateral-temporal node of the hippocampal network. Lateral-temporal stimulation consistently yielded CCEPs in ipsilateral hippocampus with distinct early (N1) and late (N2) negative components. We hypothesized that component amplitudes would vary periodically with local theta phase at stimulation onset. Further, we hypothesized that stimulation would evoke maximum component amplitude when delivered at theta trough and minimum amplitude at peak. We found significant circular-linear correlation between theta phase and mean amplitude during both N1 ($P<0.002$) and N2 ($P<0.01$; computed via permutation testing). Control analyses on stimulation-free epochs indicated that the periodic stimulation effects were not merely due to a relationship between phase and future amplitude. Contrary to our hypothesis, N2 amplitude was significantly greater in peak trials than trough trials, an effect which persisted even after correcting for the stimulation-free amplitude predicted by phase at stimulation onset ($P<0.02$). These findings suggest that local theta phase predicts the magnitude of evoked hippocampal response by stimulation of lateral temporal afferents. These findings are relevant to understanding mechanisms for control of hippocampal function via network-targeted stimulation.

**Keywords:** hippocampus, CCEP, theta, phase

## P2.087

### VAGUS NERVE STIMULATION USING MICRO-MAGNETIC STIMULATION

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**Abstract**

**Introduction:** Vagus Nerve Stimulation (VNS) has become an important alternative to pharmacotherapy in neuropsychiatric disorders. The typical approach in VNS is electrical stimulation which stimulates the entire vagus nerve by positioning electrodes in galvanic contact with the nerve supplying with two different voltage potentials. Due to this non-selectivity, some unintended side effects, like bradyarrhythmias following stimulation of efferent cardiac fibers, were reported. We hypothesize that producing a focal time-varying magnetic field to the vagus nerve could excite a targetted afferent nerve bundle selectively, reducing the side effects while maintaining the therapeutic response.

**Method:** In the first set of experiments, the vagus nerve was collected from male Wistar rats, and TEM imaging was done to understand the spatial distribution of A-fibers. A numerical simulation of the electromagnetic field generated by micro-coil was performed to assess the stimulation efficacy of the rat's vagus nerve. In the second set, we performed magnetic VNS in anesthetized rats while monitoring the animals' physiological parameters (arterial blood pressure, respiration, and ECG). The magnetic stimulation device was electrically insulated to avoid electrical stimulation using Parylene C conformal vacuum coating. A conventional electrical VNS was also used for the comparison.

**Results:** The simulation results estimated that the focal stimulation of the A-fiber bundle in the vagus nerve could be achievable. The preliminary results showed that the magnetic stimulation produced a partial physiological response compared to the electrical stimulation by reducing the cardiac side effects during the magnetic stimulation. In terms of efficacy, magnetic stimulation was shown to alter the respiratory rate through afferent fiber activation.

**Discussion and conclusion:** Current data indicated the potential application of the vagus nerve stimulation with reduced side effects using magnetic stimulation.

**Keywords:** Magnetic stimulation, VNS, A-fibers, Micro-coil

## P2.088

### REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION PROMOTES IMPROVEMENT IN PHYSICAL ACTIVITY AMONG BREAST CANCER SURVIVORS

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