Investigating Behavioral and Neural Effects of Deep Brain Stimulation for Parkinson’s Disease

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Deep Brain Stimulation

DBS is electrical modulation of deep brain structures (e.g. in Basal Ganglia) via chronically implanted electrodes connected to a pulse generator. The electrodes stimulate the neurons at high frequency. In a nutshell, it’s a “pacemaker for the brain”.

Behavior Tasks

Rotation test: drug-induced rotations are measured
- effective DBS attenuates rotations
- DBS significantly reduces rotations relative to prior OFF condition
- no significant difference in the two OFF conditions ($p = 0.145$)

GPI-DBS treats motor asymmetry

Reaction Time Task: measure time to react to cue and time to press lever
- significant increase in MT and RT from naive state
- 4/10 rats had improved MT
- 3/10 rats had improved RT and no rats had an increase in mean RT
- MT correlated with RT ($p < 0.01$)

Neural Recording

We will record from the GPI and Cortex. The relationship between the recorded local field potential (LFP) signals at each structure can be related using a multivariate autoregressive model:

$$y(k) = \sum_{i=0}^{nb-1} \beta_i x(k-i) - \sum_{j=1}^{na} \alpha_j y(k-j) + \epsilon(k)$$

$$\epsilon(k) \sim N(0, \sigma^2)$$

$y(k)$ and $x(k)$ are recorded LFP data at time $kT$, where $T$ is the sampling interval.

Coefficients $\alpha_j$ for $j = 1, ..., na$ and $\beta_i$ for $i = 0, ..., nb - 1$ weight the linear dependence of the output LFP at time $kT$ on the previous $na$ output LFP samples and the previous $nb$ input LFP samples.

Modeling goals:
1. Analytic representation to quantify interactions between nuclei and influence of DBS.
2. Multivariate autoregressive input-output model for data from different nuclei.

Problem Statement

Parkinson’s Disease (PD) is a motor disorder that can be treated by a therapy called Deep Brain Stimulation (DBS). Although DBS is currently used to treat patients, the mechanism of action is not understood.

The goal of this work is to understand behavioral, cognitive and neural effects of DBS, by studying the disease and treatment in the rodent model.

Parkinson’s Disease

PD is a neurological disorder associated with the death of cells that produce dopamine in a particular deep brain structure, the substantia nigra pars compacta (SNc).

There are potential targets structures for electrodes: the globus pallidus internus (GPI) and the subthalamic nucleus (STN).

- 7-10 million people worldwide have PD
- PD is progressive, i.e. the symptoms get worse over time
- the main motor symptoms are rigidity, tremor, slowness and postural instability

“Parkinson’s is a perfect metaphor for lack of control. Every unwanted movement in my hand or arm, every twitch that I cannot anticipate or arrest, is a reminder that even in the domain of my own being, I am not calling the shots.” - Michael J. Fox

Methods

- Adult, male Long-Evans rats are used
- unilateral lesions to kill dopamine cells, i.e., create hemi-parkinsonian model
- unilateral implant of stimulating stereotrode in GPI

The rats will be in the behavior tasks before lesioning, after lesioning (Hemi-Parkinsonian model) and in the lesioned state with stimulation.