Invasive Approach to Model Human Cortex-Basal Ganglia Action-Regulating Networks

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Country

USA

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Invasive Approach to Model Human Cortex-Basal Ganglia Action-Regulating Networks

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NIH (NINDS)

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30/09/2016

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3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Deep Brain Stimulation, Basal Ganglia, Structure of subthalamic nucleus, Electrocorticogram, Globus Pallidus

Research Abstract
Project Summary/Abstract Action initiation and withholding are key parts of everyday behavior,

and underlying these is action suppression. This includes (1) suppressing competing actions when selecting one action from alternatives (2) suppressing all responses when presented with conflicting information until a proper decision can be made and (3) suppressing a response when the environment rapidly changes indicating a pre-planned response must be stopped. The literature suggests that these three functions are supported by distinct fronto-basal ganglia (BG) circuits. Yet the evidence for this is only piecemeal as few studies simultaneously record from both cortical and subcortical regions with sufficient spatial, temporal, and spectral resolution while subjects perform multiple tasks. We hypothesize that suppression during selection, conflict and stopping involve dissociable fronto-BG circuits – that different frontal cortical regions causally communicate with different BG regions. We will test this over-arching hypothesis by taking advantage of the unique opportunity of deep brain stimulation (DBS) surgery for Parkinson's disease, to obtain multi-focal cortical and BG recordings across 3 action suppression tasks (self-paced movement, Eriksen Flanker task, and stop signal). We will record across multiple scales – single unit activity, local field potentials, and fMRI – the only way to attain spatio-temporal data sufficient to test the hypothesis. In Specific Aim 1, we aim to demonstrate that spatially, temporally, and spectrally dissociable circuits mediate distinct types of action suppression using the very high spatial and temporal precision of unit activity and local field potentials (LFPs) recorded from the subthalamic nucleus (STN) and globus pallidus internus (GPi) and simultaneously recorded, spectrally rich electrocorticography (ECoG) from 3 cortical regions (pre- and primary motor, pre-supplementary motor, and right inferior frontal gyrus). In Specific Aim 2, we will use invasive brain stimulation to further characterize the separability of these fronto-BG circuits. We hypothesize that DBS-induced patterns of impairment/improvement across different suppression tasks relates to differences in fronto-BG network recruitment relative to the site of stimulation. We will use concurrent fMRI with DBS to evaluate disparate effects of DBS on brain activity across tasks. We will also examine how DBS at different STN foci evokes distinct brain networks using fMRI in patients undergoing asleep MR-guided DBS implants. These studies will guide invasive neurophysiological recordings with intraoperative stimulation during DBS surgery. In Specific Aim 3, we will adapt a dynamic biologically-grounded computational model of action choice to add an action suppression function. We will fit this model to the electrophysiological data and evaluate several computational theories of action withholding and choice. The impact is widespread, including the basic science of action regulation, the role of separate but parallel long-range human brain networks for action regulation, understanding how DBS differentially modulates action suppression functions, and ultimately for circuit-specific implants that modulate human action in various disorders.

Lay Summary

Project Narrative Fluid and appropriate behavior requires suppressing interfering muscles when selecting an action, suppressing all responses when one is in conflict (to buy time to make a decision) and suppressing an action when one needs to stop in hurry. Deficits in these three suppression functions underlie a wide range of neuropsychiatric disorders including Parkinson's disease, Tourette's, and Obsessive Compulsive Disorder. The proposed studies will better characterize how these forms of action suppression relate to parallel but different fronto- basal-ganglia brain circuits, and in so doing illuminate the effectiveness of brain stimulation and neurorestorative therapies.

Further information available at:

Types:

Investments > €500k

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United States of America

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Parkinson's disease & PD-related disorders

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