Basal Ganglia Cortical Coupling and Connectivity Changes in PD and DBS

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Country

USA

Title of project or programme

Basal Ganglia Cortical Coupling and Connectivity Changes in PD and DBS

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 2,599,242.20

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01/07/1999

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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, Parkinson Disease, Coupling

Research Abstract
DESCRIPTION (provided by applicant): Synchronized oscillations in the pallido-thalamo-cortical

circuit have been hypothesized to underlie the development of parkinsonian motor signs by altering connectivity between the basal ganglia and cortical structures. Deep brain stimulation (DBS) improves parkinsonian motor signs; but how it changes basal ganglia cortical interactions remain unclear. The goal of this proposal is to characterize the changes in synchronization and effective connectivity that occur between the basal ganglia and motor and supplementary motor cortices (MC and SMA, respectively) in the parkinsonian state and during therapeutic DBS of the internal segment of the globus pallidus (GPi) and the subthalamic nucleus (STN). A second goal of this study is to examine the feasibility of exploiting the presence of these oscillations in the pathological state for use as biomarkers in the development of a closed loop control system for DBS. These goals will be accomplished by simultaneously recording from populations of neurons in both subcortical and cortical areas at rest and during movement; characterizing the physiological changes in synchronized oscillatory activity and effective connectivity between the basal ganglia and MC and SMA in the parkinsonian state and during therapeutic DBS in the nonhuman primate MPTP model of Parkinson's disease (PD). Putative biomarkers, identified as part of the first phase of the study, will be evaluated as triggers for closed loop stimulation delivery during a goal directed reaching task in the final stuy phase. The results of this study will provide critical new information to help us to understand the changes in interactions that occur across the MC, SMA and basal ganglia network in PD, identify biomarkers that can be used as triggers for closed loop control of DBS and compare the relative effect of STN versus GPi DBS on basal ganglia cortical interactions and as sites for triggers in a closed loop control system.

Lay Summary

PUBLIC HEALTH RELEVANCE: Millions of people in the U.S. and worldwide have been diagnosed with Parkinson's disease (PD), a progressively debilitating disorder characterized by abnormal movement. Fortunately, many patients with advanced disease who no longer respond adequately to medications can be treated successfully with an FDA- approved implantable device that provides electrical stimulation deep within the brain, a therapy known as deep brain stimulation (DBS). DBS is being used for the treatment of a variety of movement as well as psychiatric disorders, with new applications arising at a rapid pace despite all that remains unknown about how it works. While DBS therapy generally is effective for patients with PD, results still vary widely among individual patients. In this study, we will use non-human primates with Parkinson-like motor symptoms to investigate further the therapeutic effect of DBS delivered to two specific areas of the brain (the “”STN”” and “”GPi””) that are known to improve symptoms in both affected non-human primates and patients. Stimulation at these sites causes changes in neuron activity, not only at the site of stimulation, but also in and between other regions of the brain involved in planning and executing movement. We will examine and characterize changes in physiological interactions that occur between structures within the “”motor circuit”” of the brain before and during the development of parkinsonian motor symptoms in animal subjects and subsequently in the absence and presence of DBS therapy. Results from this study will provide significant insights into how communication between key structures within the motor circuit network is altered in the parkinsonian state and how DBS modifies these interactions to produce a therapeutic effect. We will use our findings to develop and assess a DBS strategy that may provide a more continuous and beneficial therapeutic effect than current approaches.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

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