Understanding the effects of deep brain stimulation on cortical processing

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Contact information of lead PI
Country

USA

Title of project or programme

Understanding the effects of deep brain stimulation on cortical processing

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,984,604.59

Start date of award

01/06/2014

Total duration of award in years

3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Deep Brain Stimulation, Parkinsonian Disorders, Parkinson Disease, Globus Pallidus, Structure of subthalamic nucleus

Research Abstract
DESCRIPTION (provided by applicant): Parkinson’s disease (PD) is characterized by abnormal

firing activity throughout the cortex and basal ganglia. Although much research has focused on the altered function in the basal ganglia, recent studies suggest that the key neural activity changes associated with PD symptoms may actually be coming from and/or driven by cortex. Therefore, a better understanding of how PD impacts cortical network activity is needed to develop more effective treatments options. Deep brain stimulation (DBS) is an established therapy for PD but its therapeutic mechanisms of action is still unclear. Clinically-effective DBS can be achieved with either subthalamic or globus pallidus stimulation. How each type of stimulation modulates motor cortical processing is unclear, but their mechanisms of action likely differ. A better mechanistic understanding of how these two types of DBS alter cortical network function will enable researchers to optimize DBS delivery in terms of where to implant the electrodes and what stimulation patterns will most effectively improve motor cortical processing. In this study, non-human primates will be chronically implanted with intracortical microelectrode recording arrays in three different motor cortical processing areas likely to be most affected by DBS. Unit spiking and waveform activity as well as local field potentials will be recorded during various motor tasks to characterize cortical network activity in the normal state. Then the animals will be made moderately Parkinsonian on one half of their body using the neurotoxin MPTP. Changes in cortical network activity between the normal and Parkinsonian state will be characterized. Detailed computational models of the cortical microcircuit representing a cortical column will be used to identify potential mechanisms responsible for the changes in the cortical activity patterns seen experimentally in the animals. Specifically, the cortex model's inputs and inter-neuronal connectivity weights will be iteratively refined until the simulated network behavio matches what was seen experimentally in the animals in the normal and Parkinsonian states. The Parkinsonian cortical microcircuit model will then be expanded to include inputs from DBS applied to the subthalamic nucleus and to the globus pallidus. Model simulations will be run with DBS applied at a wide variety of novel stimulation patterns. Simulated DBS patterns that are most effective at returning the cortical activity to a more normal state will be identified and the be tested experimentally in the Parkinsonian monkeys. In turn, cortical activity patterns recorded experimentally during DBS will be used to validate and further refine the computational model. This combined experimental and modeling approach will advance our understanding of the cortical network changes associated with PD as well as identify potential mechanisms by which different types of DBS can more effectively modulate this cortical network activity to improve motor function.

Lay Summary

PUBLIC HEALTH RELEVANCE: Parkinson's disease affects one to two percent of people over the age of 60, and the chance of developing Parkinson's disease increases with age. Deep brain stimulation is used clinically to relieve motor symptoms in Parkinson's disease, but its delivery has not been optimized due to a lack of understanding of its mechanism of action. A better understanding of how deep brain stimulation modifies motor cortical processing will enable us to optimize its delivery potentially improving symptom relief and reducing unwanted side effects while also reducing power consumption.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

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Parkinson's disease & PD-related disorders

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2016

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N/A

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