The motor network in Parkinsons disease: mechanisms of therapy

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Country

USA

Title of project or programme

The motor network in Parkinsons disease: mechanisms of therapy

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,271,526.61

Start date of award

30/09/2014

Total duration of award in years

2

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Deep Brain Stimulation, Beta Rhythm, Electrocorticogram, Levodopa, Parkinson Disease

Research Abstract

? DESCRIPTION (provided by applicant): Our goal is to understand the motor network in movement disorders and the mechanism of therapeutic interventions in humans, at very fast time scales. Over the past five years we introduced the novel technique of combining subdural

electrocorticography (ECoG) with basal ganglia recording and stimulation in persons undergoing neurosurgical treatment. From ECoG potentials, we can extract information about low frequency rhythms (such as the motor beta rhythm), or about population spiking activity (from high frequency broadband activity). Our prior work in acute intraoperative recording showed that: 1) a major abnormality of the motor cortex in Parkinson's disease (PD) is the excessive coupling of population spiking to the motor beta rhythm; and 2) acute therapeutic deep brain stimulation (DBS) reversibly alleviates this pattern of excessive synchrony. These findings provide a new foundation for understanding the cortical basis for impaired movement and the network mechanisms of antiparkinsonian therapies. However, critical questions remain that cannot readily be studied in the intraoperative setting: Does the mechanism of chronic therapeutic stimulation differ from that of acute stimulation? How do mechanisms of stimulation and levodopa compare? What are the network characteristics underlying dyskinesias? Here, we address these questions using a novel, totally implantable bidirectional neural interface that both delivers DBS and therapy and senses/stores ECoG or local field potentials (Aims 1 and 2). We record and download basal ganglia and cortical potentials at regular intervals in our outpatient clinic under well-defined behavioral conditions with expert characterization of motor function by movement disorders neurologists. In November 2013, we implanted the first such device for multisite (cortex and basal ganglia) recording in a Parkinson's disease patient, under a physician-sponsored protocol. Recording via ECoG has the advantage of excellent signal:noise characteristics and superb spatial and temporal resolution, but given its invasiveness is not amenable to normal controls. Therefore, in Aim 3 we address similar questions using a complementary, noninvasive technique, scalp electroencephalograph (EEG), based on our recent finding that measures of cortical population synchrony unique to PD are detectable by EEG and modulated by both oral levodopa and DBS. This approach allows us to study a large number of subjects and to include normal controls. The impact of these studies will be to: 1) Provide a more detailed understanding of abnormal network synchronization in PD, informing new models that better incorporate cortical function than past models. 2) Provide a mechanistic understanding of the effects of therapeutic DBS on cortical function. 3) Create a foundation for the development of closed loop deep brain stimulation, which could utilize a clinically practical cortical signal for automated control of stimulation parameters. Mechanisms elucidated in this study may be applicable to other network brain disorders where subcortical stimulation shows therapeutic promise.

Lay Summary
PUBLIC HEALTH RELEVANCE: How does Parkinson's disease affect the cortex, and how do therapies such as deep brain stimulation improve cortical function to allow more normal movement? Here, we address these questions by recording changes in brain activity in response to therapies, at multiple time points in our outpatient clinic. This work may lead to improvements in therapy, such as implantable devices that automatically suppress abnormal brain activity using a cortical sensor for feedback control.

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

Database Tags:
N/A