Chronic physiologic and behavior changes induced by novel STN DBS patterns for PD

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Country

USA

Title of project or programme

Chronic physiologic and behavior changes induced by novel STN DBS patterns for PD

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 2,437,566.97

Start date of award

15/02/2016

Total duration of award in years

1

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Structure of subthalamic nucleus, Deep Brain Stimulation, behavior change, Parkinson Disease, Parkinsonian Disorders

Research Abstract
? DESCRIPTION (provided by applicant): Deep brain stimulation (DBS) has revolutionized the

treatment of Parkinson’s disease (PD), with therapeutic benefit observed for many of its cardinal motor signs when key nodal points of the pallidothalamocortical circuit are chronically stimulated using high-frequency, isochronal electrical pulses. Almost three decades later, these stimulation parameters have largely gone unchanged despite significant advances in our understanding of the changes in underlying neural activity that accompany the development and progression of parkinsonian motor signs. Several recent theories suggest that the development of synchronized oscillations within the dopamine- depleted pallidothalamocortical `motor’ circuit alter functional interactions between the basal ganglia and motor cortical structures, and are associated with the emergence and progression of motor signs. In line with these theories, novel stimulation paradigms have been proposed that may not only be more effective at mitigating these pathological changes but also induce therapeutic benefit that outlasts stimulus delivery. To date, only a limited number of studies have attempted to address the therapeutic potential and mechanisms of these novel paradigms. The current proposal will evaluate and characterize one such paradigm, coordinated reset (CR) DBS developed by Tass, which involves the application of randomized bursts of stimulation across spatially distinct regions of the subthalamic nucleus (STN) in order to desynchronize pathological neural activity across the pallidothalamocortical circuit. Using an established preclinical model of PD, we will determine the magnitude and time course of CR DBS’ effects on individual parkinsonian motor signs, both during treatment as well as following its discontinuation, and compare those to changes observed during traditional STN DBS. In addition, we will use chronic recording arrays implanted in the motor cortex and basal ganglia to assess the changes synchronized oscillatory neural activity that occur across the pallidothalamocortical circuit coincident with improvement in and recurrence of individual parkinsonian motor signs. This study will provide insight into the therapeutic potential and mechanisms of CR and traditional DBS while improving our understanding of the relationship between neural activity within and across key nodal points of the pallidothalamocortical circuit and the manifestation of parkinsonian motor signs.

Lay Summary
PUBLIC HEALTH RELEVANCE: Many patients with advanced Parkinson’s disease who no longer respond adequately to medications can be treated successfully with deep brain stimulation (DBS), a therapeutic approach that currently requires the continuous delivery of high-frequency electrical impulses to specific brain regions in order to maintain control of motor symptoms. In this study, we will use a preclinical animal model with Parkinson-like motor signs to investigate the therapeutic potential of a new approach to DBS, while characterizing and comparing its effect on neural activity in key structures within the brain to traditional DBS. We will use our findings to develop an overall DBS strategy that may provide a more stable and beneficial therapeutic effect than current approaches for patients with PD.

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