Neurochemical closed-loop controller for smart DBS

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Country

USA

Title of project or programme

Neurochemical closed-loop controller for smart DBS

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,804,751.38

Start date of award

01/01/2014

Total duration of award in years

3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Deep Brain Stimulation, neurochemistry, Dopamine, Structure of subthalamic nucleus, Corpus striatum structure

Research Abstract

DESCRIPTION (provided by applicant): Deep brain stimulation (DBS) is a well-established therapy approved by the FDA for the treatment of advanced Parkinson’s disease (PD) and

tremor. Additionally, humanitarian device exemptions for dystonia and obsessive-compulsive disorder have been established and studies are underway for depression and epilepsy. Although a highly successful therapy, there remain many challenges to the field. One of such challenges is the large number of surgical targets, stimulation settings, and electrode configurations that have to be attempted in the search for therapeutic clinical outcomes. A wide range of factors such as neurologic state, electrode placement, brain shift, tissue encapsulation, and stimulation parameters can affect the clinical outcomes of DBS. As such, there is a critical need for DBS systems that can compensate for some of these uncontrollable factors. For example, by using the brain's dynamic environment to guide electrode placement and stimulation programming, thereby resulting in a DBS system that can be tailored to individual patients and symptoms. Characterization of electroactive neurochemicals in charge of modulating critical therapeutic neural activity will allow us to use real-time neurotransmitter concentration measurements to identify these optimal locations for electrode placement, as well as to identify optimal stimulation parameters after the electrode has been implanted. We propose to study the neurochemical dynamics of DBS by characterizing striatal dopamine responses evoked by STN stimulation. We also propose using these responses to develop a closed-loop system for modulating dopamine concentration. In Aim 1, we will develop an inexpensive animal model for acute characterization of striatal dopamine release evoked by DBS of the subthalamic nucleus (STN) in anesthetized healthy pigs. In Aim 2, we will use techniques developed using the less-expensive pig model to develop a closed-loop controller for modulating dopamine concentration in healthy anesthetized non-human primates (NHP). Finally, in Aim 3, we will use a NHP model of PD to develop a neurochemically-mediated closed-loop DBS system for sustained therapeutic response in a dynamic environment. Characterization of the neurochemical dynamics of dopamine evoked by DBS represents an important step forward toward understanding the underlying mechanisms of DBS. In the future, closed-loop systems building on the system proposed here will reduce the need for frequent clinical interventions in the form of DBS programming and medication adjustments. Undoubtedly, this technology will have a profound impact on both basic and clinical neuroscience approaches to the treatment of neurologic and psychiatric disease, and will provide the rationale for expanding the neurologic and psychiatric conditions that can be treated with DBS.

Lay Summary

PUBLIC HEALTH RELEVANCE: Deep brain stimulation (DBS) is an effective and well-established therapy, approved by the FDA, for the treatment of advanced Parkinson's disease (PD) and tremor. The objective of this proposal is to get a better understanding of the effects of DBS on the brain's chemistry and to improve existing DBS technology by building a closed-loop controller that can monitor neurochemical activity and use this information to adjust stimulation. These experiments will increase the insight into the mechanisms of action of DBS, resulting in expansion of the neurological and psychiatric conditions that can be treated with DBS. In turn, this will benefit an increasing number of patients and substantially improve their quality of life. Moreover, by monitoring real- time changes in brain chemistry, this controller will reduce unnecessary stimulation, and therefore reduce the amount of medication needed. Furthermore, it will decrease the number of clinical interventions required for programming and medication adjustments, thereby lowering health-care costs.

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