Neuronal Activity in MC and SMA during STN and GPi DBS in the Parkinsonian Monkey

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Neuronal Activity in MC and SMA during STN and GPi DBS in the Parkinsonian Monkey

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1

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Structure of subthalamic nucleus, Globus Pallidus, Deep Brain Stimulation, Parkinsonian Disorders, Motor Cortex

Research Abstract

DESCRIPTION (provided by applicant): The motor cortex (MC) and supplementary motor area

(SMA) are components of a subcortical-cortical and cortical-cortical network intimately involved in motor control, in mediation of the development of motor signs in Parkinson's disease (PD), and the improvement in motor function during deep brain stimulation (DBS). Yet, the role of these cortical motor areas in the development of motor signs and pathophysiology of PD remains ill-defined. Similarly, the effects of DBS in the subthalamic nucleus (STN) and internal segment of the globus pallidus (GPi) on neuronal activity in the MC and SMA are largely unknown. To date, there are only a few studies in parkinsonian animals that have examined neuronal activity changes in the MC and SMA and fewer still that have performed these studies during DBS in the STN or GPi. The current proposal will characterize these changes in the MPTP monkey model of PD and those neuronal activity changes that occur in the MC and SMA during DBS (STN and GPi) both at rest and during passive and active movement. We will determine if specific neuronal activity changes correlate with improvements in motor symptoms detected during DBS. In addition, we will use chronically implanted microarrays to assess the changes in cortical activity on each side of the brain during chronic unilateral stimulation correlating them to coincident changes in motor signs on both the ipsilateral and contralateral sides of the animal. This study will provide new insights into the pathophysiology of PD, provide a greater understanding of the cortical mechanisms underlying the improvement in motor symptoms during DBS and investigate the cortical mechanisms that underlie improvement in ipsilateral motor signs during unilateral stimulation. Results from this study will allow us to beter determine which neuronal patterns of cortical activity correspond to the development of, and improvement in, motor signs and provide specific rationale for designing programming algorithms directed at modifying cortical activity to optimize clinical outcomes in PD patients treated with DBS and form the basis upon which closed loop programming methods could be developed.

Lay Summary

Millions of people in the U.S. and worldwide have been diagnosed with Parkinson's disease, a progressively debilitating disorder characterized by abnormal movement function. Fortunately, many patients with advanced disease who no longer respond adequately to medications have been successfully treated with an FDA- approved implantable device that provides electrical stimulation deep within the brain, a therapy known as deep brain stimulation (DBS). While DBS may significantly reduce symptoms in many cases, there is still much that is unknown about the way it works, especially under different conditions. Our goal is to obtain a better understanding of how DBS works in and between specific regions of the brain to improve movement function and to apply this knowledge to optimize DBS therapy for patients affected by movement disorders, such as Parkinson's disease. In this study, we will use non-human primates with Parkinson-like symptoms to examine the effects of chronic stimulation in two specific areas of the brain that are known to improve symptoms in both affected non-human primates and patients. Stimulation in these areas causes activity changes in and between cortical regions of the brain involved in planning and executing physical movement. A longitudinal study of the changes in cortical activity in relation to changes in the rate and quality of specific movements under different stimulation conditions and locations will provide a basis upon which new DBS therapies may be developed or improved.

Further information available at:

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