Neurophysiological mechanisms underlying parkinsonian motor signs

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Contact information of lead PI
Country

USA

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Neurophysiological mechanisms underlying parkinsonian motor signs

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15/05/2016

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5

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Parkinsonian Disorders, neurophysiology, Motor, Basal Ganglia, Globus Pallidus

Research Abstract

? DESCRIPTION (provided by applicant): The goal of this study is to identify the specific neurophysiological changes that occur within and across key nodal points of the

pallidothalamocortical motor circuit with the onset of Parkinson’s disease and how these evolve as motor signs become increasingly more severe. This will be done by simultaneously recording and comparing the activity from populations of neurons across multiple nodal points in the basal ganglia thalamo-cortical motor circuit at rest and during movement during normal, mild, moderate and severe stages of parkinsonism in the same monkeys using sequential, low dose administration of the neurotoxin 1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine (MPTP). Structures that will be examined include the primary and supplementary motor cortices, the premotor cortex, the internal and external segments of the globus pallidus (GPi and GPe, respectively), the subthalamic nucleus (STN), and the motor thalamus including ventralis anterior, ventralis lateralis pars oralis, and ventralis posterior lateralis pars oralis. Specific ims 1 and 2 will characterize changes in synchronized oscillations, bursting patterns, receptive field properties and phase amplitude coupling across basal ganglia- cortical and thalamo-cortical regions, respectively, with the animal at rest and during both passive movement and the performance of a trained motor task. Specific aim 2 will further examine the differential role of subnuclei of the motor thalamus in the development of bradykinesia/akinesia, rigidity and tremor through the application of discrete, fiber-sparing lesions. Specific aim 3 will use LFP recordings across the pallidothalamocortical circuit to characterize changes in effective connectivity between the pallidum, STN, motor thalamus and PMC, SMA and MC as a function of parkinsonian state. By examining the direction and strength of changes in effective connectivity at rest and during movement at different stages of PD we will be able to clarify the type, location and evolution of changes in effective connectivity as parkinsonian motor signs develop and progress in severity. A better understanding of the role of individual motor circuits and the types of physiological changes that occur within these circuits and how they relate to the development of individual motor signs will provide the rationale for the development of new targets, and technology therapies such as deep brain stimulation, transcranial electrical stimulation and gene therapy that are directed at restoring a more normal pattern of activity in the basal ganglia thalamic circuit.

Lay Summary

PUBLIC HEALTH RELEVANCE: The goal of this study is to identify the specific changes in the activity of neurons in cortical and subcortical brain regions that are associated with the onset and progression of individual motor abnormalities associated with Parkinson’s disease (PD). People with PD develop specific problems with movement manifested, including slowness (bradykinesia), stiffness (rigidity), and uncontrollable rhythmic movements in the extremities and face (tremor), that worsen over time. The results of this study will provide the understanding necessary for the refinement of current and development of future therapies, e.g. deep brain stimulation and gene therapy, directed at modulating the neuronal activity in the basal ganglia thalamic circuit responsible for the development of PD motor symptoms.

Further information available at:

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United States of America

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