Neuron- and Circuit-Specific Mechanisms and Adaptations Regulating Motor Function in Parkinson Disease Models

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Country

USA

Title of project or programme

Neuron- and Circuit-Specific Mechanisms and Adaptations Regulating Motor Function in Parkinson Disease Models

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,916,573.39

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01/04/2009

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3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

pedunculopontine tegmentum, Basal Ganglia, Disease model, Parkinson Disease, Motor

Research Abstract

DESCRIPTION (provided by applicant): The ability to select proper actions is critical for flexible adaptive behavior. In vertebrates, multiple neural systems have evolved to coordinate different aspects of motor selection, execution, and learning. Key among these systems is the basal ganglia, a set of subcortical nuclei that are critical for motor planning and habit learning, and which are also implicated in Parkinson disease (PD), among the most commonly-diagnosed movement disorders. The anatomical connectivity of the basal ganglia is well characterized, and general hypotheses about basal ganglia function and the role of dopamine have been proposed. However, the mechanisms underlying dysfunction of basal ganglia circuits in PD is not well understood. In order to gain new insight into the dysfunction of the basal ganglia, we will target two new understudied aspects of basal ganglia circuitry: (1) the inputs from the thalamus to the striatum, and (2) the outputs from the substantia nigra reticulata/entopeduncular nucleus to the pedunculopontine tegmentum (PPTg). We have obtained compelling preliminary evidence that these regions are involved in motor dysfunction in animal models of PD, and we propose to thoroughly investigate the cellular, synaptic, and circuit mechanisms that underlie this dysfunction. The goal is to identify new therapeutic targets and strategies for treating PD, without the debilitating side effects associated with long-term use of dopamine replacement therapy.

Lay Summary

PUBLIC HEALTH RELEVANCE: The ability to select appropriate actions is critical for survival. Movement disorders such as Parkinson’s disease (PD) are characterized by difficulties selecting or changing actions. This results from dysfunction of neural circuits in the striatum, a core regio of the brain involved in motor planning. Here, we will investigate two new therapeutic targets for treating PD: the thalamostriatal synapse and the pedunculopontine nucleus. Each of these areas is relatively understudied, yet has great potential to lead to new therapeutic strategies for the treatment of 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

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