Thalamic interactions with the striatum

https://neurodegenerationresearch.eu/survey/thalamic-interactions-with-the-striatum/

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Title of project or programme

Thalamic interactions with the striatum

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NIH (NINDS)

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01/06/2013

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2

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Thalamic structure, Parafascicular Nucleus, Corpus striatum structure, Parkinsonian Disorders, Centromedian Thalamic Nucleus

Research Abstract
DESCRIPTION (provided by applicant): The motor dysfunction of Parkinson’s disease is usually described as the result of changes in the activity of basal ganglia-thalamocortical circuits. However, recent research has shown that the heterogeneous family of thalamostriatal projections may also be strongly affected by the disease, and that these changes may

contribute to the development of parkinsonian signs and symptoms. The most substantial thalamostriatal projection comes from the caudal intralaminar nuclei in the thalamus (the centromedian and parafascicular nuclei [CM/Pf]). The CM/Pf-striatal projection gives rise to clusters of axon terminals that target preferentially dendritic shafts of striatal projection neuros, as well as cholinergic interneurons. This projection may be prominently involved in the processing of reward information and in the regulation of vigilance and attention. Another major source of thalamostriatal fibers are the 'basal ganglia receiving' ventral anterior (VA) and ventrolateral (VL) nuclei. Neurons in these nuclei send long un-branched axons to the striatum, with many en passant-type varicosities. The impact of the VL-striatal projections on striatal function is unknown. Postmortem analysis of brain tissue from parkinsonian patients has demonstrated that the source nuclei of the thalamostriatal projection and the organization of their synapses in the striatum are strongly affected by the neurodegenerative process. Neurons in the CM/Pf are particularly affected, with degeneration of more than 50% of neurons early in the course of the disease. We have demonstrated that these aspects of neuron loss are faithfully replicated in MPTP-treated (parkinsonian) monkeys, along with a corresponding decrease in thalamostriatal terminals. In addition, there are extensive changes in the morphology and density of dendritic spines in the striatum, which are the primary recipients of VL input. The functional impact of these changes on striatal activity is not known, but is likely t be substantial, and, given the anatomical and pathological differences, may differ between the two projection systems. We propose to test this hypothesis with a combination of functional and anatomical studies in monkeys. The functional studies (aim 1) will make use of an optogenetic approach that will allow us to selectively activate terminals of the CM-striatal or VL-striatal projections, and to examine the resulting effects on the activity of striatal projection neurons an cholinergic interneurons in awake primates. These studies will first be done in the normal state, and then again after the animals have been rendered parkinsonian by treatment with MPTP. The functional studies will be complemented with quantitative electron microscopic analyses in the same animals, in which opsin expression will be used as an anatomic marker to identify parkinsonism-related changes in the postsynaptic targets of CM- or VL-striatal terminals (aim 2). The proposed studies will help us to gain a more complete understanding of the circuit pathophysiology of parkinsonism, and set the stage for the development of therapeutic strategies to treat Parkinson's disease through influencing specific thalamostriatal interactions.

Lay Summary

PUBLIC HEALTH RELEVANCE: Recent research has shown that the massive thalamostriatal fiber system in the brain is strongly affected by the degenerative process in Parkinson's disease. The proposed studies will examine the impact of the changes on thalamostriatal transmission in primates, using cutting-edge functional and morphological techniques of investigation. These studies will help us to gain a better understanding of the circuit pathophysiology of Parkinsonism, and may lead to the development of new therapeutic strategies to treat Parkinson's disease through influencing specific thalamostriatal interactions.

Further information available at:

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Investments > €500k

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United States of America

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Parkinson's disease & PD-related disorders

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