Prefrontal D1 signaling and cognitive symptoms of Parkinsons disease

https://www.neurodegenerationresearch.eu/survey/prefrontal-d1-signaling-and-cognitive-symptoms-of-parkinsons-disease/

Principal Investigators

NARAYANAN, NANDAKUMAR

Institution

UNIVERSITY OF IOWA

Contact information of lead PI
Country

USA

Title of project or programme

Prefrontal D1 signaling and cognitive symptoms of Parkinsons disease

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,584,329.36

Start date of award

15/09/2014

Total duration of award in years

3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Neurobehavioral Manifestations, time interval, Parkinson Disease, cognitive process, Ramp

Research Abstract

DESCRIPTION (provided by applicant): Cognitive symptoms of Parkinson’s disease are emerging as an enormous public health problem. Up to 80% of PD patients will suffer

debilitating cognitive symptoms in the course of their disease. In PD patients, cognitive impairments predict a malignant disease course leading to loss of employment, independence, driving deficits, nursing home placement, and death. Because PD is strongly associated with aging, this problem will surge as our society ages. There are few treatments that improve PD-related cognitive symptoms. Thus there is a critical need to develop new, mechanistic treatments for cognitive symptoms of PD. A challenge in developing new treatments is that there is a knowledge gap about the mechanism of PD-related cognitive symptoms. Cognitive deficits in PD patients include impaired working memory, attention, reasoning, planning, and timing. One elementary cognitive task in which PD patients are reliably impaired is interval timing. In this task, subjects are presented with a stimulus, and estimate its duration over several seconds. Interval timing is an ideal window into cognition in PD because this task depends on dopamine and can be readily studied in animal models. Elucidating the neural circuitry of interval timing could help close the knowledge gap about cognitive dysfunction in PD. Our preliminary data strongly implicate D1-type dopamine receptors on pyramidal neurons in the prefrontal area of the cerebral cortex in interval timing. However, it is unclear precisely how prefrontal neurons influence interval timing. Here we combine highly selective and specific techniques such as optogenetics, focal drug infusions, and neuronal ensemble recordings to systematically interrogate the neural activity of prefrontal D1 neurons in great detail, and to map the projections of these neurons. In Aim 1, we determine how prefrontal D1 neurons control interval timing. In Aim 2, we determine which projections of prefrontal D1 neurons control interval timing. Finally, in Aim 3 we rescue interval timing deficits in animal models of PD by stimulating prefrontal D1 neurons and their projections. This work will identify key drivers of a cognitive process impaired in PD patients. Our findings could link a brain region and a receptor system to cognitive processes impaired in PD, and could spur development of targeted pharmacological, genetic, or brain-stimulation therapies. Insights from this work could have relevance for PD as well as for other diseases involving prefrontal dopamine circuits, such as schizophrenia, ADHD, addiction, and Huntington’s disease.

Lay Summary
PUBLIC HEALTH RELEVANCE: Cognitive symptoms in patients with Parkinson’s disease cause morbidity and mortality and have no effective treatments. This proposal explores the mechanism of cognitive dysfunction in animal models with the hope of generating new treatments for cognitive dysfunction in Parkinson’s disease.

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