Dopaminergic encoding of counterfactual information in human striatum

https://www.neurodegenerationresearch.eu/survey/dopaminergic-encoding-of-counterfactual-information-in-human-striatum/

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Country

USA

Title of project or programme

Dopaminergic encoding of counterfactual information in human striatum

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 2,271,444.95

Start date of award

01/09/2015

Total duration of award in years

4

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Corpus striatum structure, Dopamine, Essential Tremor, Parkinson Disease, dopamine system

Research Abstract

? DESCRIPTION (provided by applicant): Diseases and disorders directly affected by dopamine systems (e.g., drug addiction and Parkinson’s disease) highlight the importance of these

systems in motivated human behavior and cognition. The dopamine system is known to be a critical component of normal learning, reward processing, and decision-making (reviewed in Montague et al., 2004). Unfortunately, our present knowledge of dopamine systems in human brains is relatively sparse compared to the wealth of experimentation and computational modeling on these systems in rodents and non-human primates. Previously, technological constraints have limited direct experimentation in human brains. This proposal capitalizes on our group's recent technological innovation, which was supported by the NIH R21 mechanism – CEBRA: R21DA024140 – and resulted in the successful completion of the first sub-second measurements of dopamine release in a human brain. Furthermore, these measurements took place during an active decision-making task that was framed by computational models of learning and reward processing (Kishida et al., 2011 and Kishida et al., under review). We propose to pursue three specific aims, which combine our technological advance with active learning tasks designed to probe the role of dopamine in human behavior. Our aims incorporate three learning signals, where actual and counterfactual experience will each be examined in human striatal responses. The proposed work will inform on the controversial role for dopamine in reward/movement interactions. The experiments proposed will yield unprecedented insight into the function of the dopamine system in the humans afflicted with Parkinson's disease and Essential Tremor. With the support of the NIH (R21DA024140), our team successfully developed a complete prototype system for making electrochemical measurements of dopamine delivery in the human brain. Feasibility has been demonstrated by obtaining the first dopamine measurements in the striata of subjects with Parkinson's during a decision-making task. This substantial preliminary work is now ready for a larger scale with specific hypothesis testing about the role of dopamine systems in Parkinson's disease, Essential tremor, and human decision-making and behavior.

Lay Summary

PUBLIC HEALTH RELEVANCE: Experiments and computational models (primarily investigated in rodents and non-human primates) suggest dopamine systems in the brain are essential for normal learning, reward-processing, and ongoing decision- making. This proposal builds upon our group's innovative work, which – for the first time – recorded sub- second measurements of dopamine in human subjects and amalgamated these measurements with computational models of dopamine function. Herein we propose to use this newly developed technology to generate unprecedented insight into the function of dopamine systems directly in humans.

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