Interactions within and between the basal ganglia and thalamocortical circuits in function and dysfunction

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Country

United Kingdom

Title of project or programme

Interactions within and between the basal ganglia and thalamocortical circuits in function and dysfunction

Source of funding information

MRC

Total sum awarded (Euro)

€ 2,166,487

Start date of award

01/07/2013

Total duration of award in years

5.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords
Research Abstract
This research programme will provide fundamental new insights into the mechanisms and functions of neuronal network activity in the basal ganglia. We place special emphasis on

explaining how mutual interactions between these nuclei, as well as key inputs from the cerebral cortex and thalamus, orchestrate the activity patterns that are generated therein. In particular, experiments are designed to elucidate when, why and how specialised types of network activity, such as synchronised oscillations, are either advantageous or counter productive for the operation of these circuits in the intact brain. We will define the factors controlling the temporal and spatial boundaries of synchronised activity in these circuits that must be in place for normal information processing and behaviour to occur. As an important corollary of this, we will also dissect the cellular substrates and network mechanisms supporting the inappropriate synchronisation of activity that emerges in these circuits following the chronic loss of dopamine from the brain, as occurs in idiopathic Parkinsons disease and its animal models. We will use novel and advanced electrophysiological, anatomical and analytical techniques to achieve these aims: we will record neuronal activity from several sites in the basal ganglia, cortex, and thalamus simultaneously using high-density multi-electrode arrays. Time- and frequency-domain analyses of the extracellular data derived from such large-scale recordings will enable us to elucidate the potential circuit interactions underlying activity. Further mechanistic insights will be provided by selective pharmacological challenge, by intracellular recordings of single neurons and by optogenetic and pharmacogenetic circuit perturbations. In some experiments, single neurons will recorded extracellularly and then selectively labelled using a juxtacellular procedure, allowing the post-hoc identification of the structural and neurochemical substrates underlying activity. We will utilize two complementary in vivo preparations, anaesthetised rodents and behaving rodents (rats and mice). This multidisciplinary approach will enable us to reveal the importance and mechanisms of neuronal network activity at several functional levels. In elucidating the functional and dysfunctional roles played by synchronised oscillations and other activities in the basal ganglia and their partner thalamocortical networks, this programme will significantly progress our understanding of how these circuits work together to influence behaviour. Moreover, the advances made will place us in a much stronger position to provide a rational basis for the development of new therapeutic interventions that are able to more effectively counteract abnormal brain activities and provide improved symptomatic relief in disease.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

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