Organisation of the Neuronal Networks of the Basal Ganglia

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Title of project or programme

Organisation of the Neuronal Networks of the Basal Ganglia

Principal Investigators of project/programme grant

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- United Kingdom

Source of funding information

Medical Research Council

Total sum awarded (Euro)

3004158.61

Start date of award

01-04-2005

Total duration of award in months

60

The project/programme is most relevant to

- Parkinson's disease
- Huntington's disease

Keywords
Research abstract in English

"The basal ganglia are a group of nuclei situated deep in the brain that are involved in a variety of functions including the control of movement and are of particular clinical importance because of their

involvement in a variety of neurological disorders including Parkinson's disease and Huntington's disease and disorders such as schizophrenia and obsessive compulsive disorder.The overall objective of this project is to provide an advanced level of understanding of the principles of operation of the neuronal networks that constitute the basal ganglia by anatomical and combined quantitative anatomical and physiological approaches. The new knowledge will provide a basis for understanding how cortical excitation of the basal ganglia is transformed into phasic inhibitory output signals and for understanding the role of the so-called indirect pathway network in the expression of basal ganglia function. Specifically we propose to i) elucidate the synaptic organisation of the neostriatum, ii) elucidate the synaptic organisation of the globus pallidus, iii) elucidate the properties and connections of dopamine neurones of the substantia nigra and thalamostriatal neurones, iv) elucidate the properties and connections of neurones of the pedunculopontine nucleus, v) characterise the functional properties of the indirect network in relation to cortical inputs and the output nuclei, vi) identify sites of drug action in the basal ganglia by the localisation of receptors and vii) provide insights into basal ganglia disorders by analysis of animal models of Parkinson's disease and Huntington's disease.

These aims will be achieved by studying the brains of rodents using a multidisciplinary approach. The following techniques will be used. Single and double anterograde tracing with or without retrograde tracing for light and electron microscopy. Multiple immunolabelling for neurotransmitters and receptors will be carried out by techniques that are well established in the Unit. Electrophysiological analyses in vivo, for example, extracellular and intracellular recordings together with recording of local field potentials and cortical EEG, combined with cell labelling, recovery of the neurones and electron microscopy.

The outcome of the research will be to provide an advanced level of understanding of the principles of operation of the microcircuits of the basal ganglia in health and in models of disease. The experiments will yield both qualitative and quantitative data on the synaptic and neurochemical organisation of the neural networks of the basal ganglia. The electrophysiological analyses will reveal the properties of individual neurones and the relationships between neurones. The in vivo electrophysiological analyses will reveal the properties of individual neurones and networks in the expression of basal ganglia function and the role of the cortical input. The experiments will also give clues as to what goes wrong in Parkinson's disease when the dopamine neurons are lost. By elucidating the organisation of the basal ganglia in the normal brain we will be able to understand what goes wrong in disease and identify potential new sites of therapeutic intervention"

Lay Summary