MULTISCALE ANALYSIS OF SENSORY-MOTOR CORTICAL GATING IN BEHAVING MICE

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Country

USA

Title of project or programme

MULTISCALE ANALYSIS OF SENSORY-MOTOR CORTICAL GATING IN BEHAVING MICE

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,547,474.31

Start date of award

30/09/2015

Total duration of award in years

2

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Basal Ganglia, Motor Cortex, Whole-Cell Recordings, Sensory, Motor

Research Abstract

? DESCRIPTION (provided by applicant): To address the core question underlying the Obama Brain Initiative to better understand the function of complex brain circuits, we propose a multi-scale recording and data analysis project to study the dynamical interactions between sensory cortex, motor cortex, and the basal ganglia in the process of motor planning and execution. The multi-scale approach will involve simultaneous recordings at the cellular, network, and systems level in head-fixed behaving mice trained to perform a rewarded locomotor task. Sensory stimuli delivered to the whiskers will denote GO or STOP cues, and resulting brain processes initiating or suppressing movement will be analyzed. At the cellular level, in vivo whole cell recordings employing autopatcher technology will yield detailed information on the membrane potential trajectory of individual neurons in the sensory and motor cortex in this task. At the network level multiple single unit and local field potential (LFP) recordings will allow the assessment of local population dynamics across multiple layers of cortex and for thalamo-cortical interactions. At the systems level, voltage imaging of the cortical surface using novel transgenic voltage sensing proteins will allow the study of spatio-temporal dynamics of macroscopic activity patterns with a frequency resolution of up to 200 Hz. Recording data simultaneously will allow for a multi-scale analysis of the relations between cellular and network dynamics. For example, the relationship between fluctuations in the field potential and the membrane dynamics of single neurons will be analyzed and is expected to yield important insights into population coding. Similarly, the relation between activity maps obtained with imaging and oscillatory network activity revealed by LFP recordings of cortex is expected to result in important insights into the organization of motor planning. Our work will pay specific attention to the role of beta band (12-35 Hz) oscillations in the control of the observed behavior, because beta oscillations have been implicated convincingly both in cortical sensory processes as well as motor control. Further, beta oscillations are pathologically overexpressed in the basal ganglia of Parkinson’s patients and 6OHDA lessoned rodent animal models of Parkinsonism with a likely source in motor cortex. Thus, our guiding hypothesis is that beta oscillations provide an important scaffold to the communication between brain areas in the process of motor planning and execution. To test the causal relation between beta oscillations and motor processing we will artificially induce beta band activity with ontogenetic stimulation of basal ganglia efferent, sensory cortex, or motor cortex and analyze resulting changes in behavior and brain dynamics in stimulated and non-stimulated areas. Overall, these studies will raise the level of systems neurophysiology of motor processing in the behaving rodent to a new level, and are expected to provide fundamental insights into the organization of brain activity across multiple scales. These insights will be invaluable in studies of pathological brain dynamics in neurological disorders affecting the basal ganglia such as Parkinson’s disease, Huntington’s disease and OCD.

Lay Summary

PUBLIC HEALTH RELEVANCE: The proposed research is relevant to public health because it provides an impactful and innovative study of the circuitry underlying the output from the basal ganglia to the motor cortex and the integration of basal ganglia output with sensory information. Highly debilitating and frequently hard to treat neurological disorders such as Parkinson’s disease, Huntington’s disease and dystonia are caused by dysfunction of this circuitry. The proposed research is expected to provide basic insights into motor circuit function and may reveal new possibilities for treatment of these diseases as well as a better understanding of deep brain stimulation treatments already in use.

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