Electrophysiological mapping of networks dynamics in basal ganglia in normal and Parkinsonian conditions using optogenetic control of specific neuronal pathway.

https://www.neurodegenerationresearch.eu/survey/electrophysiological-mapping-of-networks-dynamics-in-basal-ganglia-in-normal-and-parkinsonian-conditions-using-optogenetic-control-of-specific-neuronal-pathway/

Principal Investigators

MALLET Nicolas

Institution

IMN Bordeaux

Contact information of lead PI
Country

France

Title of project or programme

Electrophysiological mapping of networks dynamics in basal ganglia in normal and Parkinsonian conditions using optogenetic control of specific neuronal pathway.

Source of funding information

ANR

Total sum awarded (Euro)

€ 324,168

Start date of award

01/10/2014

Total duration of award in years

4

Keywords
Research Abstract
The basal ganglia circuits form a complex loop of nuclei that connect the cortex to the thalamus and are critically important for motor and cognitive behaviors. During motor behaviors, basal ganglia circuits are involved in many aspects such as the selection and the initiation of motor

plans but also the suppression of unwanted actions. The importance of basal ganglia circuits in movement is perhaps best illustrated by the consequences of their dysfunction and the devastating motor impairments that appear following the dopamine loss occurring in Parkinson Disease (PD). Akinesia/bradykinesia is one of the main symptoms in unmedicated PD and it describes the inability to start/the slowing down of movement. Furthermore, prolonged levodopa (L-DOPA) therapy, the ‘gold standard’ treatments for PD, inevitability leads to unbearable side effects which are the exact opposite of PD, that is a paradoxical hyperkinetic behavior characterized by frequent abnormal and involuntary movements also known as L-DOPA induced dyskinesias (LIDs). These LIDs cannot be suppressed voluntary and are very debilitating for patients. Altogether, in PD, both movement initiation and cancellation processes can be altered at different time course of the disease but which of the multiple basal ganglia neuronal pathways directly underlie those alterations is not known.
Specialized electrical activities known as ‘synchronized oscillations’ are used for network dynamics and are important for optimal communication in healthy brain circuits. Oscillations can be distinguished by their characteristic frequencies. In both humans and animals, the emergence of distinct oscillations is correlated with different motor outcomes. For example, in the healthy brain motor system, the so-called ‘beta’ oscillations (15-30 Hz) accompany the maintenance of postural sets and are linked with ‘anti-movement’ functions. Conversely, ‘gamma’ oscillations (40-80 Hz) are associated with the initiation of new motor actions, linking them to ‘pro-movement’ functions. Importantly though, if synchronized oscillations are not properly controlled in space and time, they could become counterproductive or truly pathological. Indeed, excessive synchronization of neuronal activity is recognized as a critical functional change accompanying Parkinsonism. Interestingly, different frequencies have been associated with the different symptoms of PD. More specifically, excessively synchronized oscillations at beta frequencies have been associated with akinesia, whereas pronounced gamma oscillations expression has been correlated to the paradoxical hyperkinetic behavior visible during the LIDs. Therefore, abnormally synchronized oscillations might be responsible for both hypokinetic and hyperkinetic behaviors in PD. With this in mind, it is now especially timely and important to go beyond correlational analysis. Here, using newly developed method, I will dissect the causal relationship between basal ganglia circuits and their involvement in abnormal motor behavior of rodents. I will employ a multidisciplinary approach combining cutting edge optogenetic toolboxes, electrophysiology, and behavior to investigate how targeted neuronal pathway causally influence network dynamic in basal ganglia and behavior. Altogether, this strategy will give us valuable insights into the neuronal processes that underlie ‘Start’ and ‘Stop’ signals within BG.
The goal and ambition of this project is to provide a critical step towards the identification of new candidate therapies that can be used to reduce the severity of PD and LIDs. Hence, my research proposal will be at the interface of basic neuroscience and clinical research, with the ultimate goal of translating discoveries from bench to bedside. Furthermore, this study will greatly increase our understanding of how basal ganglia and their partner circuits work together to influence behavior.

Further information available at:

Types:
Investments < €500k

Member States:
France

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A