Therapeutic effect of DBS of wakefulness brain centers on excessive daytime sleepiness in parkinsonian monkey

Objectives (3 lines max):
The main goal of our study is to apply deep brain stimulation (DBS) to the pedunculopontine region (PPN) in order to treat excessive daytime sleepiness (EDS) on parkinsonian monkeys.

Abstract (10 lines max):
Excessive daytime sleepiness (EDS) with sleep attacks is one of the most common non-motor symptoms in Parkinson’s disease (PD), which highly impairs patients’ quality of life. Current treatment options for EDS in PD are still unsatisfactory. A better understanding in EDS pathophysiology is essential to develop more effective treatments for EDS in these patients. Dysfunction of the brain wakefulness-promoting network might explain EDS in PD. A loss of wake-promoting orexinergic neurons has been reported in post-mortem PD brains. Moreover, dopaminergic (DA) neurons depletion could also play a critical role in the disruption of the wake/sleep cycle and EDS observed in PD. In addition to reproduce PD motor symptoms, the MPTP monkey model of PD also replicates the chronic sleep–wake cycle disruption with, nighttime sleep instability and EDS. These sleep disturbances occur before the emergence of motor symptoms and are concomitant with a breakdown of DA homeostasis, suggesting that progressive DA depletion affects the neuronal activity of the brain regions that regulate wakefulness. Those include the lateral hypothalamus (LH) and one of its targets, the pedunculopontine nucleus (PPN). In parkinsonian patients, PPN deep brain stimulation (DBS) can induce arousal. In this study, we propose to record the neuronal activities of the PPN and LH during sleep in normal and parkinsonian monkeys. Then, we will evaluate and compare the effect of DBS of the PPN and of the LH on EDS and on sleep macrostructure. The results of our study would set the bases for the development of new therapeutic strategies for sleep disturbance and EDS in PD.

Methods (3 lines max):
Monkeys will be rendered progressively parkinsonian with low doses of MPTP. Sleep and motor behaviour will be evaluated. Monkeys will be chronically implanted with a radio-telemeter transmitter for continuous and long-term recording of the polysomnographic signals and with one quadri-electrode within the PPN area and connected to a Brain Radio device (Medtronic, US) in order to record and stimulate these brain regions.

Relevant publications of the team (3 max):
On the Role of the Pedunculopontine Nucleus and Mesencephalic Reticular Formation in Locomotion in Nonhuman Primates.
Goetz L, Piallat B, Bhattacharjee M, Mathieu H, David O, Chabardès S.

Gait is associated with an increase in tonic firing of the sub-cuneiform nucleus neurons.

Requested domains of expertise (few keywords):
Deep brain stimulation, monkey, parkinson's disease, sleep