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## Underlying cellular mechanisms of impulsive behaviors induced by dopaminergic treatments in Parkinson's disease

### Objectifs

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Understanding the implication of the mTOR pathway in the development of impulsive behaviors induced by a dopaminergic anti-parkinsonian treatment in rodents.

### Résumé

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Parkinson's disease (PD) is a well-known neurodegenerative disorder. However, it is also associated with a plethora of neuropsychiatric issues that severely impact the quality of life of the patients. These non-motor symptoms range from depression to impulse control disorders (ICDs). ICDs are a complex group of abnormal impulsive and compulsive behaviors that includes for instance pathological gambling, binge eating or hypersexuality, and that are also called "behavioral addiction". ICDs in PD patients are mainly induced by dopaminergic treatments, such as the agonist pramipexole. In addition, ICDs are associated with a high level of cognitive impulsivity (incapacity to tolerate delays). We have previously shown in the lab that pramipexole in rats also induced a high level of cognitive impulsivity, a behavioral phenomenon that was associated with a dysregulation of the activity of the mTOR pathway in the brain motivational circuit, an intracellular pathway crucial for the control of synaptic plasticity and involved in addictions. The objective of internship will be therefore to further characterize and understand the implication of the mTOR pathway in ICDs in order to provide new therapeutic strategies against this behavioral disorder.

### Méthodes

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This project will combine in rodents, stereotaxic surgery, in situ hybridization, immunohistochemistry, microscopy and animal behavior, transgenic line.

### Références

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**Magnard R**, Vachez Y, Carcenac C, Boulet S, Houeto JL, Savasta M, Belin D and Carnicella S (2018) *Nigrostriatal Dopaminergic Denervation Does Not Promote Impulsive Choice in the Rat: Implication for Impulse Control Disorders in Parkinson's Disease*. *Front behav Neurosci* 12: 312

**Favier M**, Duran T, Drui G, Carcenac C, Savasta M, Carnicella S (2014) *Full reversion of motivational deficits by pramipexole in a rodent model of Parkinson's disease*. *Mov Disord* 7:912-20

**Drui G\***, Carnicella S\*, Carcenac C, Favier M, Bertrand A, Boulet S, Savasta M (2014) *Loss of dopaminergic nigrostriatal neurons accounts for the motivational and affective deficits in Parkinson's disease*. *Molecular Psychiatry* 19(3):358-67

### Domaines d'expertise requis

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Interest for integrated neurophysiology, animal behavior, cellular and molecular biology, immunohistochemistry.

### Contacts

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Contacts

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