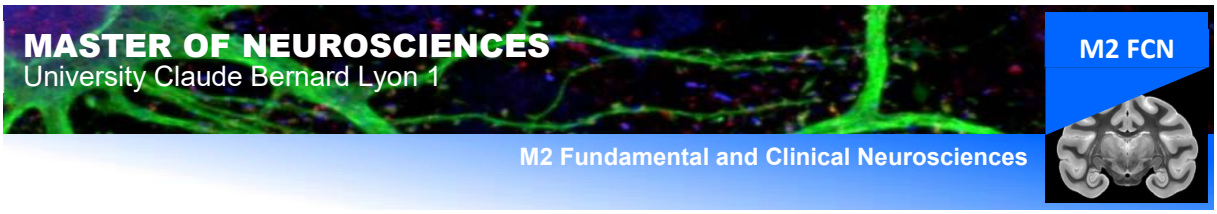

MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2022-2023

(internship from January to June 2023)

Host laboratory: *Institut des Sciences Cognitives – Marc Jeannerod, UMR CNRS 5229,* 67 Bd Pinel, 69 675 Bron

Host team: *Pathophysiology of the Basal Ganglia, http://www.isc.cnrs.fr/*

Internship supervisor: *Benjamin Pasquereau, CRCN CNRS, benjamin.pasquereau@isc.cnrs.fr*

Project title: Serotonergic action of aripiprazole on neuropsychiatric symptoms: a multimodal imaging study on Tourette patients

Project summary: Aripiprazole is a third-generation antipsychotic which nowadays is considered as a first-choice drug for the treatment of numerous patients with neuropsychiatric disorders such as in Tourette disorder (TD). Despite its widespread use, the brain mechanisms that underpin aripiprazole effects remain unclear. In particular, little is known about where and how this treatment acts in the brain to modulate multidimensional neuropsychiatric symptoms or comorbidities such as tics, anxiety, depression and obsessive-compulsive behaviors. Aside its well-known dopaminergic effects on motor functions (i.e., anti-tics), aripiprazole is also assumed to act on both cognitive and affective functions via the serotonin (5-HT) system. But, overall, the serotonergic action of this treatment remains largely unknown. Because *in vitro* studies report a high affinity of aripiprazole for 5-HT$_{2A}$ receptors, in our project, we hypothesize that aripiprazole may crucially operate via 5-HT$_{2A}$ receptors to trigger beneficial effects on psychiatric comorbidities in TD. To localize and characterize the action of aripiprazole in the whole-brain, and more specifically, to clarify the impact of this treatment via 5-HT$_{2A}$ receptors, we propose to perform a multimodal imaging study with TD patients. Neuroimaging data will be collected with a hybrid system that simultaneously combines the positron emission tomography (PET) and the functional magnetic resonance imaging (fMRI). A highly selective PET radiotracer will be used to map the binding of aripiprazole on 5-HT$_{2A}$ receptors, while fMRI will provide detail information regarding the altered brain activities. Together, receptor-specific imaging data will be correlated with clinical scores and task performance to determine whether and how aripiprazole acts on diverse symptoms and cognitive functions. Hence, our findings will bring substantial knowledge about the aripiprazole, the pathophysiology of TD, and the neuronal processes related to the 5-HT system which is involved in many psychiatric disorders.

Please send your proposal to marion.richard@univ-lyon1.fr for publication on the Master of Neuroscience website.

3-5 recent publications :

Pasquereau B, Drui G, Saga Y, Richard A, Millot M, Météreau E, *et al.* (2021): Selective serotonin reuptake inhibitor treatment retunes emotional valence in primate ventral striatum. *Neuropsychopharmacology*. https://doi.org/10.1038/s41386-021-00991-x

Martinez E, Pasquereau B, Drui G, Saga Y, Météreau É, Tremblay L (2020): Ventral striatum supports Methylphenidate therapeutic effects on impulsive choices expressed in temporal discounting task. *Sci Rep* 10: 716.

Martinez E, Pasquereau B, Saga Y, Météreau É, Tremblay L (2020): The anterior caudate nucleus supports impulsive choices triggered by pramipexole. *Mov Disord* 35: 296–305.

Pasquereau B, Tremblay L, Turner RS (2019): Local Field Potentials Reflect Dopaminergic and Non-Dopaminergic Activities within the Primate Midbrain. *Neuroscience* 399: 167–183.

Pasquereau B, Turner RS (2017): A selective role for ventromedial subthalamic nucleus in inhibitory control. *Elife* 6. https://doi.org/10.7554/eLife.31627