Integrative Neuroscience and Cognition Center (INCC-UMR 8002)

Monday, March 18th 2019 at 11:00h

Amphi WEISS (1st floor)
Centre Universitaire des Saints-Pères
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Neuronal populations and genes involved in drug addiction

Motivational processes are under the critical influence of the ventral part of basal ganglia, comprising several interconnected nuclei (as striatum, globus pallidus and ventral tegmental area (VTA)). Addictive drugs increase extracellular DA levels in the ventral striatum, Nucleus Accumbens (NAc), and share this ability despite varied pharmacological properties and mechanisms of action. A major goal in the field of drug addiction has been to uncover the molecular mechanisms underlying addiction-associated neuroadaptations. It has been hypothesized that one such mechanism is the regulation of gene expression7, and there have been numerous studies that have documented altered expression of genes in the NAc. We discovered that Maged1 (*Melanoma antigen genes d1)* has a mandatory role in behaviours related to drug addiction in BG. Mice lacking *Maged1* are insensitive to the behavioural effects of cocaine as assessed by locomotor sensitization, conditioned place preference (CPP), and drug self-administration. Electrophysiological experiments in brain slices and conditional KO mice demonstrated that *Maged1* is critical for cortico-accumbal neurotransmission. Further, expression of *Maged1* in the prefrontal cortex and amygdala, but not in dopaminergic or striatal neurons, is required for cocaine-induced extracellular DA release in the NAc as well as cocaine-mediated behavioural sensitization and acute cocaine effect respectively. This work identifies *Maged1* as a critical molecule involved in cellular processes in BG and behavioural models of addiction.

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