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MEETING ABSTRACT

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Cocaine differentially regulates plasticity-related microRNAs in the ventral vs. dorsal striatum

Benoit FORGET*, Arthur GODINO, Vincent KAPPES, Alexandra GARCIA, Radhia KACHER and Jocelyne CABOCHE

Laboratory of Neuroscience, Université Pierre et Marie Curie; INSERM-UMRS 1130; CNRS-UMR 8246, Paris, France

Chronic cocaine exposure induces long-lasting alterations in the brain’s reward circuitry through modification of neuronal plasticity, a phenomenon that may contribute to the development of addiction. MicroRNAs (miRNAs) are emerging as central regulators of gene expression in the brain and have an important role in modulating neuronal plasticity, but their involvement in processes related to cocaine addiction is still not fully understood.

Here, we report that a subset of plasticity-related miRNAs are differentially upregulated between the nucleus accumbens (NAcc) and the dorsal striatum in response to either acute or chronic (sensitization procedure) cocaine treatment in mice, without modifications in the expression of genes involved in their processing. We also investigated under the same conditions the expression of potential target genes of specific miRNAs that were regulated by cocaine. In parallel we demonstrate using in vitro pharmacological and in vivo genetic approaches the potential implication of the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) signaling cascade—a canonical cocaine-activated pathway—in the regulation of miRNA levels by neuronal stimulation. Finally, since the dopamine D1 receptor is centrally involved in mediating the effects of cocaine in the striatum and is essential for cocaine-induced behavioural sensitization, we analyzed the same subset of miRNAs specifically in D1-containing striatal projection neurons in the NAcc using a combination of viral vectors and fluorescent-activated cell sorting (FACS) strategy in mice chronically treated with cocaine.

Better deciphering the role of gene expression regulators like miRNAs in specific neuronal populations in the striatum could help improve our understanding of the long-lasting changes that cocaine induces in the brain’s reward circuitry and thus provide bases for the development of novel efficient therapeutic tools for drug addiction.

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*Submitting author e-mail: benoit.forget@upmc.fr