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Mitochondrial gene ontology pathways and transcriptional regulators impacted by cocaine self-administration in C57Bl/6 mice

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Exposure to illicit drugs and subsequent chronic use profoundly impacts behavior, neuronal structure and firing, and gene expression through multiple brain regions. Some of these sweeping changes are mediated by and supported by changes in cellular energy homeostasis and mitochondrial function. Recent work has shown that cocaine self-administration significantly alters mitochondrial size in nucleus accumbens medium spiny neurons, and that disruption of proper mitochondrial fission is sufficient to blunt responding for cocaine. Beyond mitochondrial fission, other aspects of the mitochondrial energy cycle are impacted by cocaine exposure. At the transcriptional level, many genes altered by cocaine self-administration are related to cellular metabolism and mitochondrial function. In this study we conducted gene ontology analysis on an RNA-seq data set generated from mice that had undergone cocaine self-administration, with a focus on mitochondrial-related ontology terms. The sequencing data included tissue from the prefrontal cortex, nucleus accumbens, dorsal striatum, ventral pallidum, amygdala, hippocampus, and ventral tegmental area. We found significant representation of transcriptionally regulated genes in metabolism and mitochondrial related gene ontology terms in multiple brain regions. Further, predictive analysis of transcription factor regulation of identified mitochondrial-related genes identified multiple transcription factors across brain regions that may control cocaine-related changes in mitochondrial function. Future work will be needed to validate these predicted targets *in vivo* and understand their role in regulating the cellular and behavioral responses to cocaine self-administration.