

Transcriptional adaptations in the ventral pallidum following cocaine self-administration

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Growing evidence suggests that the ventral pallidum (VP), a major structure in the reward circuit, is critical for drug intake and seeking behavior. Receiving dense projections from the nucleus accumbens as well as dopamine inputs from the midbrain, the VP plays a central role in the control of motivated behaviors. Repeated exposure to cocaine is known to alter VP neuronal firing and neurotransmission. Surprisingly, there is limited information on the molecular adaptations occurring in VP neurons following cocaine intake. To provide insight into cocaine-induced transcriptional alterations we performed RNA-Seq on VP of mice that underwent 10 days of cocaine self-administration (0.5mg/kg/infusion) followed by twenty-four hours of abstinence. We observed differential gene expression in 363 genes between animals that self-administered cocaine and saline controls. Among them, various transcription factors and histone modifying enzymes, including FosB, Nr4a1, Nr4a3, Egr3, Mef2, HDAC2, and Kdm7a displayed increased expression in VP in the cocaine group. Further a number of Nr4a1 transcriptional targets including Plk2, Rap1gap and Grin2b, which are important for synaptic and structural plasticity, were similarly increased after cocaine self-administration. These transcriptional changes in VP were confirmed with qRT-PCR. Our future studies will use cell-type specific molecular profiling to investigate which VP projection neuron population displays the altered transcriptional changes we observed after cocaine self-administration. Further, we will investigate Nr4a1 and gene targets in VP neuron populations to determine if these molecules are important for cocaine intake and VP neuron structural plasticity. Altogether, our work can provide crucial information on the molecular substrates of cocaine intake behavior by identifying transcriptional profiles in VP after cocaine self-administration.