



Centre de Neurosciences Psychiatriques

CNP SEMINARS

ANNOUNCEMENT

Friday, March 19, 2021, 11:00 – 12:00

Nr4a1-mediated morphological adaptations in Ventral Pallidal projections to Mediodorsal Thalamus support cocaine intake and relapse-like behaviors.

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Growing evidence suggests the ventral pallidum (VP) is critical for drug intake and seeking behaviors. 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 insights into cocaine-induced transcriptional alterations we performed RNA-sequencing on VP of mice following cocaine self-administration. Gene Ontology analysis pointed toward alterations in dendrite- and spine-related genes. Subsequent transcriptional regulator analysis identified the transcription factor Nr4a1 as a common regulator for these sets of morphology-related genes.

Consistent with the central role of the VP in reward, its neurons project to several key regions associated with cocaine-mediated behaviors. We thus assessed Nr4a1 expression levels in various projection populations. Following cocaine self-administration, VP neurons projecting to the mediodorsal thalamus (MDT) showed significantly increased Nr4a1 levels. To further investigate the role of Nr4a1 in cocaine intake and relapse, we bidirectionally manipulated its expression levels selectively in VP neurons projecting to the MDT. Increasing Nr4a1 levels resulted in enhanced relapse-like behaviors accompanied by a blockage of cocaine-induced spinogenesis. However, decreasing Nr4a1 expression levels completely abolished cocaine intake and consequential relapse-like behaviors.

Together, our preliminary findings suggest that drug-induced neuronal remodeling in pallido-thalamic circuits is critical for cocaine intake and relapse-like behaviors.

Invited by Youna Vandaele
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Related publications

Engeln M et al., (2020) Sex specific role for Egr3 in nucleus accumbens D2-medium spiny neurons following long term abstinence from cocaine self-administration. *Biol Psych.* 1;87(11):992-1000.

Chandra R, Engeln M et al., (2017) Drp1 mitochondrial fission in D1 neurons mediates behavioral and cellular plasticity during early cocaine abstinence. *Neuron.* 96(6):1327-1341

Engeln M et al., (2020) Individual Differences in Stereotypy and Neuron Subtype Translatome With TrkB Deletion. *Mol Psych.* doi: 10.1038/s41380-020-0746-0.

This event will take place on a virtual space on **Friday, March 19th 2021 at 11:00** through the link:

<https://chuv.webex.com/chuv/j.php?MTID=m01ffc971de22cbdee443a85b78418d88>

Meeting number (access code): 183 785 1258

Meeting password: nqG85Q5ptsP