EXPLORING THE NEURAL BASIS OF MOTIVATION

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Background: Optimal decision-making is highly dependent on the value attributed to the outcome but also individual motivational status. Evidence has highlighted the nucleus accumbens (NAc) as a core brain region in the neural circuitry underlying motivation. Major inputs to the NAc includes the canonical dopaminergic projections from the ventral tegmental area (VTA), which in turn is tightly controlled by the laterodorsal tegmentum (LDT). Interestingly, LDT also directly projects to the NAc, though the nature and biological role of such connections remains completely unknown.

Aims: Characterize LDT-(VTA)-NAc circuit, and identify the role of these inputs in motivation in control animals and in a model of prenatal exposure to glucocorticoids (iuGC model) that presents motivational deficits.

Method: Neuroanatomical characterization of the rodent circuit using viral transynaptic markers. This neuroanatomic study was complemented by an electrophysiological characterization of LDT-NAc projections *in vivo* in control and iuGC animals. We also optogenetically modulated LDT-VTA-NAc projections in order to evaluate their impact in motivation in rodents.

Results: We showed that LDT-VTA projections are altered in iuGC model, and these changes underlie its motivational deficits[2]. Next, we showed that optogenetic activation of LDT-NAc projections have a pro-motivation and rewarding effect in rats[1]. Moreover, we demonstrate that optogenetic activation of LDT-NAc cholinergic projections is sufficient to recapitulate this behavioral effect. Optogenetic activation of LDT-NAc glutamatergic projections also enhanced motivation but to a lesser extent, whereas activation of GABAergic inputs decreased motivational drive[1].We have also shown that optical activation of D2 neurons in the NAc enhances motivation and requires dopamine release from VTA dopaminergic terminals that then act on dopamine receptor D1 and D2[3]. Additionally, we found that activation of either NAc D1 or D2 neurons can drive reward or aversion, depending on the pattern of stimulation[4].

Conclusions: LDT-VTA-NAc projections play an important role in motivation in rodents, and iuGC exposure impacts this circuitry.

Keywords: Motivation, Reward, Nucleus accumbens, Neuronal circuit

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