DYNAMIC REPRESENTATION OF APPETITIVE AND AVERSIVE STIMULI IN NUCLEUS ACCUMBENS MEDIUM SPINY NEURONS

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Background: The nucleus accumbens (NAc) is an essential brain region in encoding reward and aversion. Pivotal in vivo electrophysiological recordings report that NAc neurons innately respond to appetitive stimuli, such as sucrose, and to aversive stimuli, like mild foot shock. Interestingly, most neurons exclusively respond to positive or negative valence stimuli, though some neurons respond to both. In addition, NAc neurons also respond to reward/aversion-predictive cues, and accumbal activity is crucial for cue-outcome associations, i.e. Pavlovian conditioning. The NAc is mainly composed of GABAergic medium spiny neurons (MSNs), segregated into those expressing dopamine receptor D1 (D1-MSNs) or D2 (D2-MSNs). The classical model in the field proposed a functional opposition at the level of these two striatal subpopulations, with D1-MSNs encodeing reward and D2-MSNs encodeing aversion. Yet, this model fails to explain recent data that favors a model where the two subpopulations work together to drive rewarding/aversive behaviors.

Aims: Here, we aim to define the involvement of NAc D1- and D2-MSNs in encoding stimuli of opposing valence and cue-outcome associative learning.

Method: To achieve our goals, we used 1-photon imaging (miniaturized microscope) coupled with a genetically encoded calcium indicator to record and track the activity of NAc D1- or D2-MSN in mice, while they were exposed to stimuli of opposing valence and during appetitive and aversive learning (Pavlovian conditioning).

Preliminary results: We observed a robust variability in the representation of stimuli by individual neurons of each population within session, and a drift in activity across days. Nevertheless, D1- or D2-MSN population activity was sufficient to discriminate between positive and negative stimuli and predicting cues. Optogenetic manipulation of either population delayed appetitive associative learning. We demonstrate that D2-MSNs, in contrast with D1-MSNs, play a pivotal role in the process of aversive extinction learning. Together, these results propose a model of population-level encoding of positive and negative valence stimuli within the two major NAc subpopulations, which act cooperatively to encode appetitive/aversive behaviors.

Keywords: Nucleus accumbens, Reward, Aversion, D1-MSNs, D2-MSNs

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