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Neuron

Thalamic Regulation of Sucrose Seeking during Unexpected Reward Omission

Highlights

- Neurons in aPVT, but not pPVT, regulate sucrose seeking only during reward omission
- Neurons in aPVT respond differently during availability versus omission of reward
- Projections from aPVT to NAc decrease sucrose seeking only during reward omission
- Projections from aPVT to amygdala increase sucrose seeking only during reward omission

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In Brief

Do-Monte et al. demonstrate that aPVT neurons fire differently when cued reward is available versus omitted. Distinct aPVT efferents bidirectionally regulate sucrose seeking only during reward omission. Whereas aPVT-NAc projections decrease reward seeking, aPVT-amygdala projections increase reward seeking. Photoactivating aPVT neurons abolishes reward seeking.

Do-Monte et al., 2017, Neuron *94*, 388–400
April 19, 2017
http://dx.doi.org/10.1016/j.neuron.2017.03.036

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Thalamic Regulation of Sucrose Seeking during Unexpected Reward Omission

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http://dx.doi.org/10.1016/j.neuron.2017.03.036

SUMMARY

The paraventricular nucleus of the thalamus (PVT) is thought to regulate behavioral responses under emotionally arousing conditions. Reward-associated cues activate PVT neurons; however, the specific PVT efferents regulating reward seeking remain elusive. Using a cued sucrose-seeking task, we manipulated PVT activity under two emotionally distinct conditions: (1) when reward was available during the cue as expected or (2) when reward was unexpectedly omitted during the cue. Pharmacological inactivation of the anterior PVT (aPVT), but not the posterior PVT, increased sucrose seeking only when reward was omitted. Consistent with this, photoactivation of aPVT neurons abolished sucrose seeking, and the firing of aPVT neurons differentiated reward availability. Photoinhibition of aPVT projections to the nucleus accumbens or to the amygdala increased or decreased, respectively, sucrose seeking only when reward was omitted. Our findings suggest that PVT bidirectionally modulates sucrose seeking under the negative (frustrative) conditions of reward omission.

INTRODUCTION

Cues in the environment that are associated with rewarding or aversive outcomes induce changes in emotional states (Flagel et al., 2011; Namburi et al., 2015; Robinson and Berridge, 2013). While the neural encoding of such changes has long been attributed to the amygdala (Esber et al., 2015; Madarasz et al., 2016; Peck and Salzman, 2014; Sears et al., 2014; Stillman et al., 2015; Tye et al., 2008), emerging evidence suggests that the paraventricular nucleus of the thalamus (PVT) contributes to the regulation of emotional responses (Choi and McNally, 2017; Haight and Flagel, 2014; Hsu et al., 2014; Kirouac, 2015). PVT neurons are activated by contexts/cues associated with reward (Choi et al., 2010; Igelstrom et al., 2010; Li et al., 2016; Matzeu et al., 2017; Schiltz et al., 2007) or aversion (Beck and Fibiger, 1995; Do-Monte et al., 2015b; Penzo et al., 2015; Yasoshima et al., 2007; Zhu et al., 2016). This pattern of activation to stimuli with opposing valence suggests that distinct PVT circuits are recruited to modulate different responses. PVT is broadly connected with regions implicated in motivation, including the prefrontal cortex, the nucleus accumbens (NAc), and the amygdala, and receives extensive hypothalamic projections related to feeding (Lee et al., 2015; Li and Kirouac, 2008, 2012; Moga et al., 1995; Vertes and Hoover, 2008). These connections place PVT in a unique position to integrate positive and negative emotional states in response to cues (for a review, see Do Monte et al., 2016).

Findings from previous studies investigating the role of PVT in reward seeking have been inconclusive. Increased food seeking has been reported following PVT lesions (Haight et al., 2015) or PVT excitation (Barson et al., 2015; Labouèbe et al., 2016), and differing effects on food consumption have been described depending on whether the manipulations were made in the anterior PVT (aPVT) or posterior PVT (pPVT; Bhatnagar and Dallman, 1999; Nakahara et al., 2004; Stratford and Wirtshafter, 2013). These discrepancies may reflect antero-posterior differences, as well as different functions of distinct PVT efferents; however, the projections of PVT regulating reward seeking remain to be determined.

Here, we used a cued sucrose-seeking task to assess the role of PVT and its efferents in reward seeking under conditions of opposing emotional valence: (1) when reward was available during the cue as expected (positive outcome) or (2) when reward was unexpectedly omitted during the cue (negative outcome). Using pharmacological inactivation, unit recording, and optogenetic manipulation of PVT and its outputs, we identified a specific role of aPVT and its projections to the nucleus accumbens and the amygdala in the regulation of reward seeking, specifically during negative outcomes.

RESULTS

Unexpected Reward Omission Increases Sucrose Seeking and Induces Anxiety

Rats previously trained to press a bar for sucrose pellets on a variable reward schedule were given 3 days of cued sucrose seeking in which the availability of reward was signaled by a light (30 s)