Supplementary Note

Selective Tonic/Phasic Dopamine Modulation of Limbic and Cortical Drive of Nucleus Accumbens: Control of Goal-Directed Behavior

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A model of tonic/phasic dopamine release in the accumbens

It has been suggested that tonic dopamine (DA) release maintains the basal level of DA concentration in the NAcc. Since D2 receptors have high affinity for DA, such basal levels of DA continuously activate these receptors. In this condition, limbic and cortical information processing may be balanced in the NAcc (Supplementary figure 1a). Electrophysiological studies of DA neurons in primates report that encountering an unexpected reward or a signal that predicts such reward evokes burst firing in these neurons. Burst firing causes phasic DA release in their terminal fields. Phasic DA release activates D1 receptors, and shifts the balance of information processing in favor of limbic inputs (Supplementary figure 1b). At the same time, increasing tonic DA release results in further attenuation of PFC inputs, filtering out weak, information-irrelevant cortical inputs (Supplementary figure 1b). Thus, phasic and tonic DA release sets a condition in which neural ensembles are formed by limbic and cortical coincidence detection in NAcc neurons, which is proposed to mediate goal-directed behaviors. In contrast, the omission of an expected reward or aversive stimulus causes a suppression of tonic DA neuron spike firing. In this condition, tonic DA release in the NAcc is reduced, decreasing D2 receptor stimulation and shifting the balance in favor of PFC inputs (Supplementary figure 1c). We have previously shown timing-dependent PFC and limbic input interaction in the NAcc, in which we reported that asynchronous PFC inputs preceding limbic inputs dampened subsequent limbic inputs. Therefore, suppression of
tonic DA release and consequently a decreased D2 receptor stimulation would result in closing the gate of NAcc outputs by dampening NAcc neural activity, allowing PFC inputs to become predominant (Supplementary figure 1d). This inhibition of inappropriate responses with reduction of tonic DA release in the NAcc may be the mechanism for set shifting. Therefore, increased hypothalamus (HPC) afferent drive of the NAcc with D1 activation by phasic DA release may be crucial for learning a response strategy\textsuperscript{11,12}, whereas PFC inputs into the NAcc with D2 inactivation by suppression of tonic DA release may underlie the ability to switch to a new strategy for achieving a goal\textsuperscript{13-15}. DA has been implicated in the induction of synaptic plasticity in a number of brain regions including the PFC\textsuperscript{16}, amygdala\textsuperscript{17}, and the HPC\textsuperscript{18}. It is possible that D1 activation by phasic DA release or D2 inactivation by suppression of tonic DA release may induce synaptic plasticity at HPC or PFC inputs into the NAcc as a mechanism for learning or selecting a response strategy toward achieving a goal (Y. Goto & A.A. Grace, Biol. Psychiatry 55, 8S, 743, 2004).

Supplementary references


