LETTER

The dopamine puzzle

Recently, Brischoux et al. (1) proposed that dopamine neurons in the ventral part of the ventral tegmental area (VTA) respond to aversive stimuli. Classically, VTA dopamine neurons were regarded as responding to unexpected rewards, as implicated in reinforcement learning (2). Along with other recent studies (e.g., ref. 3), a complementary role of dopamine neurons in aversive learning is emerging. Aversive dopamine signaling points to a new role of dopamine in drug abuse. Most drugs (like nicotine or cocaine) are neurotoxins, evolved by plants to deter herbivores. It appears paradoxical that they activate herbivore reward circuitry (4). So far, drug-induced increases in dopamine were regarded as a neural correlate of reward. However, the new findings (1, 3) allow an alternative interpretation, namely that the drug-induced increase in dopamine is part of an aversive reaction to toxic substances (4). To test this hypothesis, the anatomical identification of the targets of aversion-related dopamine neurons and their separation from the reward-learning circuit is crucial. Overlapping circuits would call for revisiting the reinforcement-learning hypothesis (5). Separate circuits would mark dopamine as a key player in both reward and aversive learning. However, given the anatomical proximity of the targets of aversive- and reward-related dopamine, their interaction could be a basis for economic decision-making by weighing costs vs. benefits. To better understand mechanisms underlying drug abuse, a next step is to clarify whether addictive drugs increase dopamine levels in the reward- or in the aversive-learning circuit or in both.

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