

Optical Sensors Reveal Local Regulation of Dopamine Release during Motivated Behavior

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Dopamine has critical roles in both learning from rewards, and motivation to obtain more rewards. The learning role is widely considered to involve encoding of reward prediction errors (RPEs) by phasic bursts of dopamine cell firing in the ventral tegmental area (VTA). How dopamine is regulated to achieve motivational functions is less clear. Dopamine release in nucleus accumbens (NAc) has been found to ramp up as animals approach rewards, as if encoding the increased motivation associated with reward expectation. We recently took advantage of a new generation of optical sensors (dLight), developed by Lin Tian and colleagues at UC Davis, to show that this approach-related increase in NAc dopamine occurs without any changes in VTA dopamine cell firing (Mohebi et al. 2019 *Nature*). This suggests that dopamine release is being locally regulated instead. To explore the mechanisms of this regulation, and the impact of dopamine release on NAc circuitry, we have been using a multiplexed photometry approach combining a red-shifted version of dLight together with GCaMP expression in specific cell types and/or optogenetic manipulations.