Calcium imaging of dopaminergic projections to dorsal striatum with single-axon resolution in behaving animals
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Dopamine signaling in the striatum has long been recognized as critical for regulating movement on immediate timescales, and for driving learning-related plasticity over extended timescales. Current theories of dopamine function, derived primarily from midbrain electrophysiological recordings in the midbrain SNc and VTA, propose that dopamine neurons homogenously transmit phasic (hundreds of ms) signals to unpredicted rewards or reward-predictive cues. These signals are believed to enhance representations of environmental stimuli or actions that lead to reward, driving future goal-directed learning and behavior. Regulation of ongoing movement, on the other hand, is believed to be enabled by the ongoing tonic or slowly varying (several seconds) firing within these same neurons. Recent electrophysiological and voltammetric recordings in different striatal subregions have called these theories into question, but lack the combination of fine (micron scale) spatial resolution, striatal projection target specificity, and large sampling region necessary to adequately assess functional dynamics across populations of dopamine axons projecting to specific striatal subregions. To overcome these limitations, we have utilized a new 2-photon calcium imaging approach to measure dynamics across the dopaminergic projection population to dorsal striatum with single axon resolution in behaving mice. This method has revealed phasic, acceleration-locked dopaminergic signals that indicate a role for dopamine in modulating rapid changes in motor output, independently of reward contingencies. Moreover, we have identified significant functional and anatomical heterogeneity in the axonal projection population with respect to acceleration and unpredicted reward signaling. Based on these findings, we propose a new model for dopamine signaling in the striatum that explains the dual roles of dopamine in regulating movement and reinforcement learning.