Calcium Imaging Alongside Deep Behavior Learning in Fentanyl Vapor Self-Administration

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The prevalence of opioid use disorder (OUD) and overdose deaths have reached epidemic proportions and constitute a global crisis. In 2019 synthetic opioids, including fentanyl, were being used by 1.2% of the worldwide population and contributed to more than 70% of the record-breaking number of overdose deaths. Fentanyl, which is often used clinically for anesthesia and analgesia, is commonly administered intravenously or by inhalation (smoking/vaping), which results in rapid drug bioavailability in the brain. Technical challenges have contributed greatly to our lack of understanding of the neurobiology of OUD, including limitations of behavioral models, difficulty tracking individual neurons longitudinally in freely behaving animals, and inadequate behavioral analysis tools. Intravenous drug self-administration is considered the “gold standard” model to investigate the neurobiology of OUD preclinically, but it remains difficult to perform in vivo electrophysiology or calcium imaging during drug self-administration due to the tangling of drug catheter and recording cable. This technical challenge was overcome with the development of a noninvasive mouse model of opioid self-administration using vaporized fentanyl that recapitulates key features of OUD. Imaging freely behaving animals is difficult, and conventional single-unit recordings can neither distinguish neuron subtypes nor track individual neurons longitudinally. In contrast, in vivo imaging using miniaturized fluorescence microscope (miniscope) systems allows for examining spatially and temporally coordinated activity in hundreds of individual neurons longitudinally in freely behaving animals. Complex behavioral analysis is infrequently incorporated in preclinical models, which likely contributes to limited translational impact. Recent computational advances in convolutional neural networks, pose estimation, and machine learning analysis has overcome these challenges to provide tools for computational neuroethology. We are leveraging these cutting-edge imaging technologies and behavioral analysis tools to gain a deeper insight into the neuronal ensembles that encode opioid-related behaviors during fentanyl self-administration and relapse.

Keywords: Opioid use disorder, self-administration, relapse, fentanyl, imaging