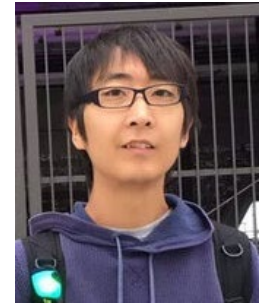


Brain wide neuronal ensembles engaged by opioid

石井 健太郎先生

Acting instructor, Stuber Lab

Center for the Neurobiology of Addiction, Pain, and Emotion
Department of Pharmacology, University of Washington



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Opioid use disorder is a worldwide societal problem and public health burden. The number of prescription opioids and related deaths has been increasing for a decade. The consumption of opioid drugs starts as reinforcing, gradually becomes more dependent and then results in a negative emotional state when the drug is withdrawn. Understanding how the brain functions as a system before, during and after the development of opioid addiction is essential for the discovery of more efficient treatments. Here, we utilized an unbiased approach to map the whole brain response to opioids and opioid withdrawal using tissue clearing and light sheet microscopy methods. Furthermore, by using genetic tools that allow activity dependent labeling, we compared the input-output structure of the neurons which are recruited during opioid administration or withdrawal. Overall, our results highlight that the brain utilizes different sets of neural circuits depending on the stage of addiction.