Dissecting Neuromodulatory Circuits and Signaling in Motivated Behavior

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Stress and affective behaviors are largely controlled by specific neurotransmitters and their receptors in the central nervous system. Many of these signals are conveyed through activation of both neuropeptide (i.e. CRF and Opioid) and monoamine (norepinephrine, dopamine, serotonin) receptor systems. These receptors are seven transmembrane spanning G-protein coupled receptors (GPCR) and they can stimulate a variety of signaling cascades following neurotransmitter/neuropeptide release. The Bruchas laboratory uses a multimodal effort to uncover GPCR-mediated neuromodulation from receptor, signaling, circuits, and systems level analysis. Here I will describe our efforts to understand endogenous opioid neural circuits in motivated behaviors and drug addiction (cocaine and nicotine), alongside a recent developments in the laboratory examining less well known neuropeptides in motivation. Finally, I will present our efforts in technology development for dissecting neuromodulation *in vivo*. In this presentation, I will specifically focus on presenting a short background of our prior studies, alongside new unpublished data of a novel brain region subnuclei containing a novel neuropeptide and its cognate GPCR in the paranigral ventral tegmental area (dopamine system) that acts to gate motivated behavior. We find that chemogenetic and optical control of this neuropeptide-GPCR system results in altered motivation, reward and aversion behavior. We also identify a critical corresponding VTA opioid GPCR system that mediates this neuropeptide's effects on motivation. In sum, I will highlight our long terms efforts to better understand how neuromodulatory circuits impact motivated behaviors including addiction, as well as featuring our new technology development efforts associated with these long term efforts.