3D Spatiotemporal Profiling of Adrenergic and Cholinergic Transmission

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Norepinephrine (NE) and acetylcholine (ACh) mediate cell-to-cell communication in the central and peripheral nervous systems. Due to their importance in regulating many complex brain functions, dysregulation of NE/ACh transmission is linked to many disorders, including Alzheimer's disease, ADHD, depression, and addiction. Despite the significance of NE/ACh in pathophysiological conditions, the precise regulations and exact functional roles of NE/ACh transmission remain poorly understood, due to the limitations of available tools for monitoring NE/ACh (Aston-Jones and Cohen, 2005) (Jacob and Nienborg, 2018). Recently developed single fluorescent protein modulation-based genetically-encoded sensors for NE (GRABNE) and ACh (iAChSnFR) allow live imaging of adrenergic and cholinergic transmissions (unpublished). In this project, I further developed imaging and analysis methods that permit 3D spatiotemporal visualization of adrenergic and cholinergic action at nanoscale resolution. Specifically, I analyzed adrenergic and cholinergic transmission release probabilities and release site numbers by directly visualizing real-time, dynamic NE release in mouse basolateral amygdala (BLA) and ACh release in the medial entorhinal cortex (MEC). My analysis found distinct neurotransmitter properties, supporting different functional roles of adrenergic and cholinergic transmission in fine tuning attentional performance and maintaining attention, respectively, disproving traditional theories on neuromodulatory transmission, and revealing the downsides of current pharmacotherapies while suggesting new, more effective treatment strategies.

Awards Won:

Second Award of $1,500