

ASHBi SEMINAR

Causal cortical-basal ganglia mechanisms underlying depression- and anxiety-like behaviors in primates

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Venue **Conference Room Onsite Only***
B1F, Faculty of Medicine Bldg. B



Abstract

Anxiety and depression bias value-based decision-making and motivation, yet the causal circuit mechanisms that generate these maladaptive affective states remain incompletely understood. Using non-human primates, we have established an integrated framework for a primate cortical-basal ganglia network that causally shapes depression- and anxiety-like behaviors.

By combining focal microstimulation, multi-site electrophysiology, and anatomical circuit mapping, we identified a large-scale fronto-cingulo-striatal system in which the striosome compartment of the striatum and its dopamine-regulating pathways play central roles in pessimistic evaluation and motivational suppression. To link circuit architecture with disease biology, we integrated genetic association signals with spatial mapping of psychiatric risk gene expression, revealing a circuit-biased molecular convergence on basal ganglia nodes of the anxiety network, including striatal and pallidal components. Crucially, pathway-selective chemogenetic manipulation demonstrated that inhibition of the ventral striatum-ventral pallidum pathway enhances motivation under aversive conditions, establishing a causal role for this pathway in depression-like motivational states. Together, these findings move beyond correlational network descriptions to define causal circuit-level mechanisms that directly regulate and drive affective decision-making.

Building on this foundation, our lab will advance precise functional dissection of primate circuits using viral strategies that enable cell-type-selective and pathway-selective manipulations, guided by spatial analyses of gene expression linked to psychiatric risk. In parallel, as a translational approach, we will identify anxiety- and depression-related networks using causal microstimulation combined with fMRI and apply transcranial focused ultrasound stimulation to modulate key network nodes in a non-invasive manner.

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