## **ASHBi SEMINAR**

Regulating Anxiety: Integrative Physiological and Genetic Mapping of Anxiety-Related Networks in Non-Human Primates

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## Abstract

We investigated neural mechanisms of anxiety and depression using physiological and genetic approaches in non-human primates. We identified the "primate anxiety network" through focal microstimulation, local field potential recordings, and anatomical tracing, revealing a large-scale network including the frontal and cingulate cortices and the striatum, with striosomal structures as central nodes. We hypothesized that these dopamine-regulating circuits mediate pessimistic judgment and motivation, elucidating how anxiety influences decision-making.

To test this hypothesis, we conducted three investigations: (1) **Network analyses** uncovered top-down signals indicating cognitive influence over limbic regions, highlighting a primate-specific system for emotion regulation; (2) **Genome-wide association studies** linked gene expression patterns within the anxiety network to pathological states, highlighting the potential role of the pallidum in depression; (3) **Chemogenetic studies** demonstrated that the ventral striatum–ventral pallidum pathway suppresses motivation under aversive conditions, establishing its causal role in depression-like state.

These studies pave the way for systematically characterizing the mechanisms of the "primate anxiety network." Building on this foundation, we aim to utilize stimulation-induced fMRI to precisely map the network and introduce cell type-specific viral vectors to functionally dissect it. By integrating physiological, genetic, and molecular methods, our work not only bridges primate models with human clinical research but also offers critical insights into anxiety-related circuits, informing the development of novel therapeutics for regulating anxiety and depression.

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