



*Foundation for Anesthesia  
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## **Dissecting Midbrain Connectivity in Anesthetic Emergence**

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### **Mentored Research Training Grant**

Emergence from general anesthesia is currently a passive process that relies on drug clearance and unknown neural mechanisms. Emergence delirium, a dangerous period of agitation and excitation upon discontinuation of an anesthetic, is a common post-operative complication. Marked by combative behaviors, this phenomenon was first described in the 1960s, occurs in an estimated 10-80% of patients, and still cannot be reliably predicted or modified, highlighting a continued gap in understanding arousal from general anesthesia. Improved understanding of the neural circuitry underlying emergence may provide novel targets for interventions to promote active emergence with minimal agitation, as well as a greater understanding of the mechanisms governing anesthetic drug interactions with brain arousal circuitry. Many studies demonstrate a role for ventral tegmental area (VTA) dopamine in promoting arousal and wakefulness, yet there is relatively little insight into the functional role of VTA circuits during emergence from general anesthesia. It is now well established that the activity of VTA dopamine neurons is modulated by local GABA-releasing and glutamate-releasing neurons, as well as multiple afferent projection circuits. I hypothesize that local VTA microcircuitry is critical during emergence from general anesthesia through neuromodulation of dopaminergic activity. The proposed project will extend mechanistic insight into VTA circuit activity during emergence from anesthesia in a mouse model system and identify the functional relevance of VTA neural circuitry in mediating the transition from anesthetized to awake state.