

Genetic Effects on the Physiology of a Hippocampal to Hypothalamic Circuit that Regulates Behaviors Comorbid with Substance Use Disorders

The biological mechanisms that underly the effect of genetic variation on substance use disorders (SUDs) and their comorbidities remain elusive. We have been studying a brain circuit that mediates an emotional response related to SUDs, a projection from the ventral hippocampus (vCA1) to lateral hypothalamus (LH). When we optogenetically stimulate this circuit in different inbred mouse lines, we elicit quantitative differences in behavioral performance on a shuttle box avoidance paradigm related to fear. To investigate the physiological mechanisms underlying these behavioral differences, we utilize brain slice electrophysiology to measure intrinsic and optogenetically evoked properties of the vCA1 to LH pathway. Little is known about this pathway, with only a limited number of comparative studies between different inbred lines demonstrating strain differences in hippocampal network oscillation and the expression of neuronal proteins. Utilizing C57Bl/6J and A/J mice, we found differences in spontaneous excitatory postsynaptic currents in neurons in the LH, while other neuronal properties did not show strain specific differences. Overall, a better understanding of the genetic effects on the physiology of the hippocampal to lateral hypothalamus projections will provide mechanistic insight into how genetic effects control SUD associated behaviors.

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