UNIVERSITY of WASHINGTON
PSYCHIATRY & BEHAVIORAL SCIENCES
School of Medicine

Erik Sean Carlson MD, PhD

[Faculty Profile]

Summary of Research Program:

I recently joined the faculty after completing Psychiatry residency at UW in June 2014. I was also awarded a KO8 Career Development award from the NIMH (1K08MH104281-01). My goals under this proposal are to establish an independent research program that will begin to address the following questions: Does altered function of specific neuronal population in a specific region of the cerebellum contribute to specific symptom domains relevant to psychiatric illness? What is the molecular and neurophysiological phenotype of these neurons?

The cerebellum is well known for its role in coordinating temporal and sensorimotor processes. A lesser appreciated, but no less important function of the cerebellum is its role in cognition, social function, and affective state. Humans with discrete cerebellar lesions manifest neuropsychiatric symptoms, including: flattened affect, depression, reduced language and social interactions, disturbances of working memory, spatial cognition, attention, and even psychosis in the absence of motor deficits. In persons with schizophrenia, neuroanatomical and clinical markers of cerebellar dysfunction correlate with the severity of negative symptoms. The cerebellum is reciprocally connected with several limbic structures known to play important roles in psychiatric illnesses, including the prefrontal cortex, striatum, ventral tegmental area, amygdala, and hippocampus. Virtually nothing is known about how specific cell types influence cerebellar function or how specific neuronal populations within discrete cerebellar nuclei influence behavior, particularly in cognitive, affective, and social domains. I propose that specific deep cerebellar nuclei (the major output of the cerebellum) are essential for cerebellar-dependent regulation of cognitive functions, social functions and affective state. To test this hypothesis, I have proposed to complete two specific aims. For my first aim, I will determine the impact of reversible silencing of a specific population of neurons in the dentate nucleus of the cerebellum on behaviors related to social function, affective state, and cognition. To accomplish this aim, I will transiently and reversibly inhibit specific populations of D1 receptor expressing neurons in the dentate nucleus of the cerebellum through conditional expression of Designer Receptor Exclusively Activated by a Designer Drug (DREADD), hM4Di. For the second aim, I will determine how D1 receptor positive neurons in the dentate nucleus of the cerebellum respond during behaviorally relevant tasks using in vivo electrophysiology and in vivo calcium imaging. This training grant will provide me with the skills necessary to develop and implement advanced mouse-based pharmacogenetic experiments, and to use in vivo neuronal activity monitoring tools such as electrophysiology and calcium imaging in order to examine how critical neurocircuitry regulates behavioral domains relevant to neuropsychiatric disorders.