CDKL5 Program of Excellence
Pilot Grant Program

**Application Title:** Studies of fornical deep brain stimulation and hippocampal memory in CDKL5 mice

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The use of deep brain stimulation (DBS) has revolutionized the treatment for Parkinson’s disease. Over the past decade DBS use has been expanded to a variety of neuropsychiatric disorders such as obsessive-compulsive disorder and Alzheimer’s disease. Recent studies show that DBS in some brain structures (e.g., fornix or entorhinal cortex) enhances spatial memory in patients. DBS is also being applied to treat both motor and neuropsychiatric diseases in children (dystonia and Tourette’s, respectively). The research team has recently demonstrated that chronic fornical DBS rescues learning memory that depends on the hippocampus, a memory center in the brain, in a mouse model of Rett syndrome. DBS also increases adult neurogenesis and the efficacy of information processing between nerve cells in the hippocampus. **CDKL5** is an X chromosome-linked gene associated with early infantile epilepsy and autism spectrum disorders. Cognitive deficits are a key feature of CDKL5 disorder. The researchers propose that fornical DBS targeted to the common neural circuits of memory function across intellectual disability disorders will also improve memory performance in CDKL5 disorders. Using a CDKL5 mouse model, this project will first check the possible alterations of the cellular neural substrate underlying learning and memory. Designed experiments will measure the efficacy of information processing flow between brain cells while animals are in awake, freely-moving state. Then, established DBS treatment will be used to test its effectiveness on learning and memory in CDKL5 mice. Finally, the investigators will determine if the same DBS procedure may improve the neural processing of memory information. The goal of this proposal is to investigate DBS as a possible therapy for CDKL5 disorders and to determine if DBS enhances hippocampal synaptic plasticity. The results of the proposed experiments could have an important impact on both disease research as well future therapeutic interventions of CDKL5 disorders.