Project Title:

High throughput AI-guided Behavioral Classification for Mouse Model of Tourette's Syndrome

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Project Abstract/Proposal Summary:

Tourette's syndrome (TS) is a type of childhood-onset tic disorder. The etiology involves disruptions in the cortico-striatal-thalamic-cortical (CSTC) circuit from genetic and environmental risk factors. My lab has previously identified a new potential etiology through somatic mobile element insertions (MEIs), which could disrupt synaptic genes in TS patient's brains. In one TS patient, we validated two LINE1 (L1) insertions, found in *GABRB3*, encoding the beta3 subunit of the $GABA_A$ receptors and *CFAP47*, encoding a cilia-associated protein. These two insertions were somatic and identified in ~1% of brain cells. Previous studies on pharmacology and transcriptomics in organoid cultures, suggested disruptions in *GABRB3* and *CFAP47* could contribute to tic-like behaviors.

More detailed functional analysis for the role of somatic mutations in TS brains relies on explicit annotations of the tic behaviors in animal models such as rodents. However, no systematic paradigms for classifying tics exits, due to the unknown TS etiology, the complexity of the tic-like behavior, and the close similarity to seizure-led muscle contractions. Here, we will develop an AI algorithm to characterize Tourette Syndrome-specific behaviors in rodent models during live recording. Specifically we will carry out:

Aim1: Induce TS and epilepsy behaviors in mouse with a low dosage of 0.2 ug picrotoxin (PTX) and high dosage (0.4ug) injection into the striatum, respectively.

Aim2: Develop an AI model to classify tic-like behaviors (low PTX dosage) or epileptic behaviors (high PTX dosage);

Aim 3: A pilot study to co-investigate EEG, EMG signal, and tic-like behaviors in rats.

The finished algorithm will help to validate new risk factors for TS, such as somatic disruptions in the GABA pathways, which can lead to the development of more effective and targeted treatment. In addition, the algorithm can also serve as an efficient benchmark in screening new drugs in future studies.