

SURC 2015 Presentation Proposal

A Blueprint of the Striatal Medium Spiny Neuron Population in an Animal Model of Obsessive Compulsive Disorder

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Obsessive Compulsive Disorder (OCD), a neuropsychiatric disorder that affects 1-3% of the world's population, is characterized by recurring anxiety-inducing thoughts relieved by the execution of stereotyped motor behaviors. Experimental evidence in humans and mice indicates that: (1) a specific neuronal circuit, the Cortico-Striatal-Thalamo-Cortico (CSTC) pathway, shows patterns of hyperactivity in OCD; (2) there is a strong association between loss-of-function mutations in the gene encoding the neuronal glutamate transporter EAAC1 and OCD. Consistent with these findings, our own data indicates that mice lacking EAAC1 (EAAC1^{-/-} mice) exhibit repetitive behaviors reminiscent of OCD-like behaviors. Within the CSTC pathway there is a brain region (the striatum) that controls anxiety and motor behaviors and that has high expression levels of EAAC1. The majority of the striatum is composed of neurons, called medium spiny neurons (MSNs), which express either D1 or D2 dopamine receptors. The traditional view of MSNs is that D1-MSNs control movement initiation and D2-MSNs control movement termination, but recent evidence indicates that the functional heterogeneity of D1- and D2-MSNs is more pronounced than previously thought. Here we propose to use functional and molecular biology experiments to determine the presence of different MSN subtypes within D1 and D2-expressing cells, in both wild type mice and in mice lacking EAAC1. We have successfully set up an experimental design that combines patch-clamp electrophysiology recordings with single-cell RT-PCR, and this will be instrumental to attain our goal. These findings will provide the first blueprint of the MSN population in the striatum, and will contribute new mechanistic insights into the cellular and molecular basis of OCD.

Keywords: Obsessive-compulsive disorder, glutamate transporters, synapses, dopaminergic neurons