

Abstract

Isocortical circuits in healthy, cognitively normal mammals are noteworthy for their ability to perform complex and flexible tasks. This intellectual and behavioral capacity is supported by a key feature of emergent dynamics: the healthy mammalian cortex is stably organized around “criticality”, a computational regime that maximizes computation, such as information capacity and dynamic range. Criticality has long been hypothesized as a principle for efficient computation in many domains (e.g., neuronal and artificial neural networks), and has been shown to be an endpoint of homeostatic processes in neurons. In contrast to normal development and function and based on extensive preliminary data, we hypothesize that the panoply of genetic mutations that cause Autism Spectrum Disorder and Intellectual Disability (ASD/ID) result in aberrant cognition and behavior by way of undermining criticality. We propose to evaluate critical dynamics in primary sensory cortices, higher order association cortices, and subcortical structure in three mouse models of ASD/ID. We will take advantage of our ability to conduct continuous, single neuron- and spike time- resolution recordings in multiple regions of freely behaving animals (Aim 1). In addition, we will assess the viability of known mechanisms of homeostatic plasticity in ex vivo slices containing the same circuits (Aim 2). This work is part of a larger, emerging vibrant collaboration between four laboratories at Washington University. The support required to conduct these physiological and computational experiments will bolster multiple applications for federal funding in the next two years.