Disruption and Repair of Cortical Excitatory-Inhibitory Balance

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Presentation Abstract Summary The fine tuning of inhibition to excitation is important for spike generation, network activity, synaptic plasticity, and seizure generation. Over the course of development, excitatory-inhibitory (E:I) balance is refined in an experience-dependent manner. In some forms of epilepsy, as E:I balance is disrupted, synaptic plasticity might help repair epileptic circuits. Here we examine how spike-timing-dependent plasticity (STDP) calibrates E:I balance across multiple inputs to neurons in mouse auditory cortex and human temporal lobe tissue from epileptic patients. We simultaneously monitored multiple synaptic inputs onto cortical pyramidal neurons and induced synaptic modifications at one set of inputs. Manipulations at paired inputs resulted in heterosynaptic modifications at the strongest excitatory and inhibitory inputs and increased overall E:I balance. In both mouse auditory cortex and human temporal lobe, heterosynaptic modifications were abolished by inhibiting calcium release from internal calcium stores, providing a mechanism for regulating heterosynaptic plasticity. Our results show that heterosynaptic plasticity can rapidly normalize excitation and inhibition in neurotypical and epileptic circuits and suggest that manipulation of the excitatory-inhibitory relationship at the network level might be a promising therapeutic approach for epilepsy.

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