Postsynaptic Effects of GABAergic Synaptic Diversity: Regulation of Neuronal Excitability by Changes in IPSC Variance

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GABAergic synaptic inputs to principal cells are heterogeneous in terms of their anatomical, molecular and physiological properties. Whether diversity in GABAergic synaptic inputs affects the efficacy of GABAergic inhibition is not understood. Here we show that alterations in the heterogeneity of IPSCs, even without alteration in the mean amplitude or kinetics of IPSC populations arriving at single cells, can significantly modify the effects of GABAergic inputs on neuronal excitability.

The effects of IPSC diversity were examined in a computational model that incorporated experimentally measured values for spontaneous IPSCs and CA1 pyramidal cell electrophysiological properties. The simulations showed that increased variance in the conductance or decay of IPSCs, even without changes in the mean, could potently modulate the firing rate of the postsynaptic cells. The actual direction of the IPSC variance-induced modulation in postsynaptic cell discharges depended on the mean conductance and mean decay time constant of the IPSCs, as well as on the degree of depolarization and firing of the postsynaptic cell. Further analysis of the underlying mechanisms determined that these effects of IPSC variance on neuronal excitability could be entirely predicted from the non-linear actions of IPSCs on action potential generation.

These data show that the degree of heterogeneity of the GABAergic synaptic inputs to principal cells can modulate the efficacy of GABAergic inhibition. The results have interesting implications for our understanding of the evolution of the diversity of interneurons in cortical and hippocampal circuits, as well as for the unraveling of novel forms of GABAergic plasticity that may take place in various forms of neurological diseases.