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Our lab has been investigating the connectivity of the inhibitory synaptic circuit within the hippocampus, with the goal of furthering our understanding of the inhibitory circuit and its role in clinically relevant disorders such as epilepsy. We have been using electrophysiological and neuropharmacological techniques to focus primarily on the role of the inhibitory neurotransmitter GABA in driving the connectivity of the inhibitory circuit in the hippocampus, its importance in regulating synaptic transmission and its contribution to the generation of the synchronous discharges associated with epilepsy.

Excitatory synaptic responses mediated by GABA-A receptors in the hippocampus depolarize interneurons within the inhibitory circuit

In these studies, we examined the synaptic connectivity within the inhibitory GABAergic network in the hippocampus using in vitro intracellular recordings in hippocampal slices. In the presence of the convulsant 4-aminopyridine (4AP), both excitatory and inhibitory circuits displayed synchronized firing patterns. Further investigation led to the novel discovery that, within the inhibitory circuit, synaptic activation of GABA-A receptors on interneurons initiated a sustained recurrent GABA-mediated *depolarization* that resulted in synchronized interneuron firing throughout the inhibitory circuit. Thus, GABA can mediate *excitatory* synaptic responses among interneurons, and this novel depolarizing GABA-A-mediated response provides a mechanism to synchronize recruitment of additional GABAergic interneurons via their recurrent collaterals. Paired recordings from pyramidal, granule and hilar interneurons demonstrated that, although GABA was functioning in an excitatory capacity among interneurons, the congregate output of this depolarizing GABA-mediated synchronization was an enhanced inhibitory response (a large synchronized IPSP) in principal cells.

Gap junction coupling within a distinct subpopulation of hilar interneurons.

In this series of studies, we examined the interconnectivity of distinct subpopulations of interneurons within the hippocampus inhibitory circuit using single unit and paired intracellular recordings and anatomical techniques. Our previous studies found that, in the presence of 4AP, interneurons burst fire synchronously, producing synchronized inhibitory postsynaptic potentials (sIPSPs) in pyramidal cells. Three different hilar interneuron subpopulations contributing to the sIPSP were identified based on their projection properties, morphology synaptic connectivity and firing patterns. One subpopulation of spheroid interneurons was connected synaptically by a novel non-ionotropic glutamate, non-GABA-mediated depolarizing mechanism. A distinct population of oviform interneurons displayed burst firing that was synchronized by gap junctions and, when selectively activated, produced isolated synchronized GABA-B mediated responses in CA3 cells. Carbenoxolone also abolished all synchronized IPSPs in CA3 cells elicited by 4AP in the presence of ionotropic glutamate receptor blockers, suggesting that gap junctions among interneurons are essential for initiating the synchronized interneuron oscillatory network firing in 4AP.