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Traumatic alterations in GABA signaling disrupt hippocampal network activity in the developing brain

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Abstract

Severe head trauma causes widespread neuronal shear injuries and acute seizures. Shearing of neural processes might contribute to seizures by disrupting the transmembrane ion gradients that sub serve normal synaptic signaling. To test this possibility, we investigated changes in intracellular chloride concentration ([Cl -]i) associated with the widespread neural shear injury induced during preparation of acute brain slices. In hippo campal slices and intact hippo campal preparations from immature CLM-1 mice, increases in [Cl -]i correlated with disruption of neural processes and biomarkers of cell injury. Traumatized neurons with higher [Cl -]i demonstrated excitatory GABA signaling, remained synaptically active, and facilitated network activity as assayed by the frequency of extracellular action potentials and spontaneous network-driven oscillations. These data support a more inhibitory role for GABA in the unperturbed immature brain, demonstrate the utility of the acute brain slice preparation for the study of the consequences of trauma, and provide potential mechanisms for both GABA-mediated excitatory network events in the slice preparation and early post-traumatic seizures. © 2012 the authors.

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