Inhibition of Action Potential Backpropagation During Postnatal Development of the Hippocampus

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TO THE EDITOR: In their recent article, Fuenzalida and colleagues (2010) describe the contributions not only of glutamate receptors but also postsynaptic action potential (AP) signaling, which underlie spike timing–dependent plasticity (STDP) of Schaffer collateral synapses to CA1 hippocampal neurons. They discuss underlying mechanisms governing dendritic depolarization during STDP and raise an interesting issue regarding why, in some cases, a short burst of APs and not just a single backpropagating AP (bAP) is required to mediate timing–dependent long-term potentiation (tLTP). We would like to highlight the role of GABAergic inhibition affecting dendritic excitability and propose that postnatal development of inhibition can provide one explanation for this discrepancy in the field.

In CA1 hippocampal slices from 2-wk-old rodents, STDP protocols with single postsynaptic bAPs can induce tLTP, in line with robust effects in hippocampal cultures (Bi and Poo 1998). At ≥4 wk, AP bursts are necessary for tLTP in hippocampal slices (Thomas et al. 1998), unless GABA A–mediated inhibition is blocked as the authors report (Campanac and Debanne 2008; Meredith et al. 2003). This observation is supported by calcium imaging of the postsynaptic bAP necessary for STDP. At 2 wk, a single bAP reliably transmits along CA1 apical dendrites to induce a (local) dendritic calcium signal (Spruston et al. 1995). However, at 4 wk, a single bAP leads to failures of calcium signal detection in dendrites more distal than about 250 microns from the cell body (Jaffe et al. 1992). Attenuation of bAP is under GABAergic regulation in distal regions of the CA1 apical dendrite via both γ-aminobutyric acid type B (GABA B; Leung and Peloquin 2006) and type A (GABA A) receptor–mediated inhibition (Tsukuba and Ross 1996). Dendritic GABA A–mediated inhibition increases significantly with CA1 hippocampal development between 2 and 4 wk postnatal age (Banks et al. 2002).

We therefore propose that this difference in the requirement for backpropagation of a single AP or a burst in STDP paradigms can arise from a developmental change in GABAergic inhibition mediated via hyperpolarizing or shunting mechanisms on the apical dendrite. Indeed, at 2 wk GABA A–mediated synaptic inhibition can shift the timing of the postsynaptic AP in CA1 pyramidal neurons at intervals relevant for STDP (Kwag and Paulsen 2009). Thus GABA’s influence on STDP protocols in developing circuitry of the hippocampus will differ with postnatal age and the critical role of dendritic inhibition must be considered in understanding STDP in juvenile and mature neurons in the brain.

R E F E R E N C E S


