Session 211 - Astrocytes: Synaptogenesis, Synaptic Plasticity, and Neuron-Interaction

Add To Itinerary

211.28 / D33 - Active dendritic conductances regulate the impact of gliotransmission on rat hippocampal pyramidal neurons

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Presenter at Poster
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Authors
*S. ASHHAD, R. NARAYANAN;
Indian Inst. of Sci., Bangalore, India

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S. Ashhad: None. R. Narayanan: None.

Abstract
Glial cells in the brain actively communicate with neurons through release of transmitter molecules that result in neuronal voltage deflections, thereby playing vital roles in neuronal information processing. An important manifestation of this is the N-methyl-D-aspartate receptor (NMDAR)-dependent slow inward currents in neurons. Although a significant proportion of information processing in neurons is performed in their dendritic arborization, the intra-neuronal spatial dynamics of these events or the role of active dendrites in regulating their amplitude and spatial spread have remained unexplored. Here, we employed somatic and/or dendritic recordings from rat hippocampal pyramidal neurons and demonstrate that a majority of NMDAR-dependent spontaneous slow excitatory potentials (SEP) originate at dendritic locations and are significantly attenuated through their propagation across the neuronal arbor. We substantiated the astrocytic origin of SEPs through paired neuron-astrocyte recordings, where we found that specific infusion of inositol trisphosphate ($InsP_3$) into either distal or proximal astrocytes enhanced the amplitude and frequency of neuronal SEPs. Importantly, SEPs recorded after $InsP_3$-infusion into distal astrocytes exhibited significantly slower kinetics compared to those recorded after proximal infusion. Furthermore, employing neuron-specific infusion of pharmacological agents and morphologically realistic conductance-based computational models, we demonstrate that dendritically expressed hyperpolarization-activated cyclic-nucleotide-gated and transient potassium channels play critical roles in regulating the strength, kinetics and compartmentalization of neuronal SEPs. Finally, through the application of subtype-specific receptor blockers during paired neuron-astrocyte recordings, we provide evidence that GluN2B- and GluN2D-containing NMDARs predominantly mediate perisomatic and dendritic SEPs, respectively. Furthermore, in replicating experimentally observed somatodendritic SEP amplitudes in morphologically realistic conductance-based models, we arrived at a testable prediction that the density of extrasynaptic NMDARs should increase with dendritic distance from the soma. Our results add a significantly complex dimension to neuron-glia interactions by unveiling an important role for active dendrites in regulating the impact of gliotransmission, and suggest astrocytes as a source of dendritic plateau potentials that have been implicated in localized plasticity and place cell formation.