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Neuroscientist 2010 16: 114

DOI: 10.1177/1073858409360185

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GABAergic neuronal hubs and hippocampal development

Network dynamics and topology have recently been used to study patterns of connectivity within networks as diverse as the Internet, social sciences, and biology. Small-world and scale-free models suggest that, when applied to neural circuits, although most neurons display local connectivity, a small number of hub neurons, characterized by long-range connections that link large numbers of cells, can confer synchronicity on the network. Thus, the presence of hub neurons, which act as superconnected nodes, has been postulated as a substrate for widespread neural synchronization. However, whether the postulated hubs are, in fact, present within neural assemblies has not been determined. Now Bonifazi and others (2009) report that, using network dynamics imaging, online reconstruction of functional connectivity, and targeted recordings in rats and mice, developing hippocampal neurons can be seen to follow a scale-free topology that includes the presence of functional hubs. Using multibeam two-photon excitation of hippocampal slices together with fluorescent probes to study multi-neuron activity, they determined that connectivity within the networks was distributed as a power law. Interestingly, these investigators found that phasic stimulation of a small

number of cells, which they designated "hub-neurons," induced rhythmic synapse-driven synchronizations, or giant depolarizing potentials. Noting that these hub-neurons are GABAergic interneurons with long axonal arborizations, they next performed paired recordings to show that hub-neurons have lower action potential thresholds and receive more EPSPs. Finally, using cell-attached and whole-cell recordings, they present evidence that firing of hub-neurons is indeed involved in spontaneous synchronization. The authors posit that two distinct classes of hub-neurons, the first displaying long axons spanning regions with sparse collaterals, and the second showing a basket-like morphology with a dense but local arborization pattern, play a crucial role at early development stages, when GABA exerts a complex role. These novel findings may propel future investigations not only on CNS development, but also on mechanisms underlying physiological and pathological network oscillations.

Bonifazi P, Goldin M, Picardo MA, Jorquera I, Cattani A, Bianconi G, and others. 2009. GABAergic hub neurons orchestrate synchrony in developing hippocampal networks. *Science* 326:1419–23.

MHCI molecules and ocular dominance plasticity

Nervous system development and immunological interactions both rest upon highly specific molecular interactions between cells. Nonetheless, it came as a surprise when major histocompatibility complex class I (MHCI) genes were discovered within CNS neurons, via a screen for genes regulated by neural activity. MHCI genes represent a large (50+) family. Now Datwani and others (2009) show that two of these genes, H2-Kb and H2-Db, are required for retinogeniculate refinement during development of the visual system. Using knockout mice, they show that ocular dominance plasticity is enhanced in the absence of H2-Kb and H2-Db. H2-Kb and H2-Db signal both through the T-cell receptor, and also via a molecule called PirB (paired immunoglobulin-like receptor B), an innate immune receptor that is also expressed within neurons in the visual cortex. Datwani and others show that mice lacking PirB show a similar phenotype of enhanced

ocular dominance. Building upon these observations, these investigators demonstrate that H2-Kb and H2-Db are expressed in the lateral geniculate nucleus as well as the visual cortex, and show that protein localization correlates strongly with synaptic markers. In the aggregate, the experiments presented in this study provide strong evidence for signaling via neuronal MHCI receptors that enables activity-dependent remodeling of brain circuits during critical periods of development. This elegant work provides strong evidence for a role of MHCI-PirB signaling in the regulation of strength and stability of synaptic connections.

Datwani A, McConnell M, Kanold P, Micheva K, Busse B, Shamloo M, and others. 2009. Classical MHCI molecules regulate retinogeniculate refinement and limit ocular dominance plasticity. *Neuron* 64:463–70.

Neuronal avalanches and dynamic range in cortical networks

Abundant evidence indicates that the cortex is spontaneously active, and suggests that its spatiotemporal organization reflects past inputs and modulates future network output. The interplay between spontaneous and stimulus-evoked activity within the cortex raises the question of whether particular types of spontaneous activity are generated by cortical networks, in a manner that is optimized for input processing. Shew and others (2009) now argue that “criticality” and neuronal avalanches (which arise during development, are homeostatically maintained for weeks in isolated cortex, and constitute the dominant form of ongoing cortical activity in awake subhuman primates) optimize input processing, and test this prediction in experiments, using cortical slice cultures on planar microelectrode arrays. They show that cortical networks that generate neuronal avalanches benefit from an optimal dynamic range, which maximizes ability to

respond to a range of stimuli. They derive a “network tuning curve” that describes stimulus processing as a function of distance from criticality, by changing the ratio of excitation and inhibition within these cultures, and show that, when closest to criticality as indicated by neuronal avalanches, dynamic range is maximized. These results experimentally confirm theoretical predictions about the computational advantage of operating at, or close to, criticality. The authors interpret these interesting results as suggesting that, in functional terms, a balance between excitation and inhibition is achieved at a point where dynamic range is maximized and cortical networks function at criticality.

Shew W, Yang H, Petermann T, Roy R, Plenz D. 2009. Neuronal avalanches imply maximum dynamic range in cortical networks at criticality. *J Neurosci* 29:15595–600.