This Week in The Journal

Activity-Dependent Regulation of Perineuronal Nets

Gabrielle Devienne, Sandrine Picaud, Ivan Cohen, Juliette Piquet, Ludovic Tricoire, et al.

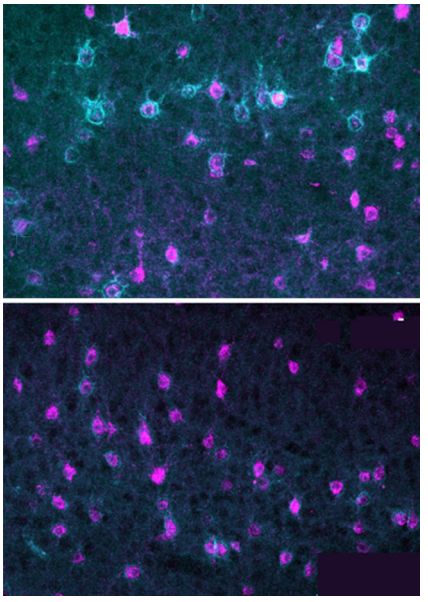
(see pages 5779–5790)

Critical periods of heightened plasticity are a common feature of cortical development. For example, blocking input from one eye during a short window after eye opening greatly reduces that eye's ability to drive neurons in the binocular region of primary visual cortex (V1), but later occlusion does not. The opening of critical periods depends on the maturation of inhibitory interneurons that express parvalbumin (PV neurons), and their closure coincides with the formation of extracellular matrix structures called perineuronal nets that enwrap the somata and proximal dendrites of PV neurons. Enzymatic digestion of perineuronal nets allows ocular dominance plasticity to occur in adult animals, likely in part by reducing inhibition (Lensjø et al., 2017, J Neurosci 37:1269). Consistent with this, reducing PV neuron activity using chemogenetic approaches [specifically, designer receptors exclusively activated by designer drugs (DREADDs)] also reopens the critical period. Because the initial formation of perineuronal nets is regulated by PV neuron activity, Devienne et al. hypothesized that inhibiting PV neurons leads to dismantling of these structures.

To test their hypothesis, the authors expressed the DREADD hM4Di selectively in PV neurons of adult V1. Subsequent administration of the hM4Di ligand hyperpolarized PV neurons and decreased their excitability. This resulted in reduced oscillatory activity in the mid-high gamma range, which is driven by inhibitory interneurons. The balance of excitation and inhibition in V1 as measured with EEG was not altered, however.

Importantly, DREADD-mediated inhibition of PV neurons significantly reduced the density of perineuronal nets in layers IV and V of V1. Notably, the density of perineuronal nets appeared to be reduced particularly around those PV neurons that expressed hM4Di, while the structures surrounding untransfected PV neurons remained intact. Selective inhibition of PV neurons using an ion-channel-based chemogenetic tool (PSAMGlyR) also reduced the density of perineuronal nets around PV neurons, as did selective chemogenetic inhibition of excitatory neurons (which presumably reduced excitatory drive to PV neurons). In contrast, chemogenetic activation of either excitatory or PV neurons had no effect on perineuronal net density.

These results indicate that reducing a PV neuron's activity leads to disassembly of its perineuronal net. Such activity-dependent regulation of perineuronal nets may contribute to plasticity in the adult CNS.



Many PV neurons (magenta) in adult V1 are enwrapped by perineuronal nets (cyan). Suppressing PV neuron activity (bottom) reduces the density of these nets. See Devienne et al. for details.

Activation of Prefrontal Cortex during Hippocampal Replay

Alice Berners-Lee, Xiaojing Wu, and David J. Foster

(see pages 5894–5908)

As rats navigate an environment, hippocampal place cells, each of which represents a specific position in the space, become activated in sequence. These sequences are embedded within cycles of population oscillatory activity in the theta frequency (6–12 Hz). When the animal rests, sequences that occurred during active exploration are replayed during high-frequency oscillatory events called sharp-wave ripples (SWRs). The hippocampus interacts with the prefrontal cortex (PFC) during both theta oscillations and SWRs, but the function of these interactions remains unclear. One hypothesis is that they transfer information from the hippocampus to the PFC for memory consolidation. Alternatively, they may be involved in planning or decision-making. To better understand the function of hippocampal–PFC interactions, Berners-Lee et al. recorded neurons in both structures as rats learned to navigate a Y-maze.

Consistent with previous reports, SWRs contained patterns of spiking similar to those occurring when rats were running in specific arms of the maze. These replay events were linked to activity in ~18% of PFC neurons. Importantly, which trajectory was being replayed in hippocampus during a given SWR could be determined by examining population activity in PFC, suggesting that PFC neurons were activated by hippocampal replay of particular trajectories. Notably, PFC neurons were not similarly activated when rats were actively running along these trajectories.

When rats were actively running, the current trajectory tended to be represented by sequential activation of place cells during the first half of each theta cycle, and trajectories along other arms were represented during the second half of each cycle. PFC neurons that were activated by replay events during SWRs were more often active in the second half of theta cycles than in the first half. Intriguingly, this late-theta activity in hippocampus and the associated activity in PFC could be used to predict which arm of the maze the rat would traverse next.

These data suggest that PFC neurons represent possible future movement, rather than the current location of rats, during both running and rest. This supports the hypothesis that hippocampus–PFC interactions function in planning future actions during navigation.

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