This Week in The Journal

Astrocytic Phagocytosis in Sleeping and Awake Mice

Michele Bellesi, Luisa de Vivo, Mattia Chini, Francesca Gilli, Giulio Tononi, et al.

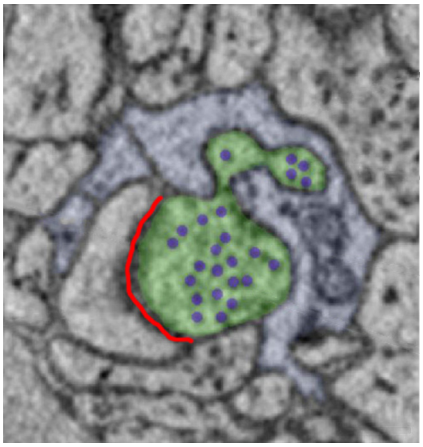
(see pages 5263–5273)

Astrocytes extend processes that approach and surround synapses. When Cajal first described these cells, he hypothesized that their processes extend between synaptic elements to prevent neurotransmission during sleep, and they retract to allow transmission to resume during wakefulness. Although this idea has not gained traction, accumulating evidence indicates that astrocytes contribute to sleep homeostasis and that their functions change across the sleep–wake cycle (Haydon 2017 Curr Op Neurobiol 44:28).

Bellesi and colleagues previously reported that levels of ~1.4% of transcripts in mouse cortical astrocytes differ between sleeping and awake animals and many of the genes that are upregulated during wakefulness are involved in process extension. Consistent with this—but contrary to Cajal's hypothesis—more spine synapses were approached by astrocyte processes in awake mice than in sleeping mice. The authors suggested that the extension of astrocyte processes toward synaptic clefts reflected the need for greater glutamate uptake during wakefulness, when synapses are more active. They now propose another role for these processes: phagocytosis of synaptic elements.

Bellesi et al. examined the morphology of astrocytes and microglia from the frontal cortex of mice that were killed after periods of normal sleep, spontaneous wakefulness, acute (8 hours) sleep deprivation, or chronic (4.5 days) sleep restriction. They found that astrocytic phagocytosis of neuronal components increased during prolonged wakefulness. Indeed, astrocytic processes containing phagocytosed neuronal material were found significantly more often in sleep-deprived mice than in mice that had been sleeping, and more often in chronically sleep-restricted than in acutely sleep-deprived mice. Most of the phagocytosed material (~75%) consisted of parts of axons and axonal boutons, but dendritic spines were also engulfed. Components of large synapses were more likely to be phagocytosed than those of average-sized synapses. Additional studies indicated that chronic, but not acute, sleep deprivation also increased microglial phagocytosis of synaptic terminals.

These data suggest that astrocytes begin to phagocytose large synapses after long periods of extended wakefulness. This may contribute to homeostatic plasticity by preventing runaway potentiation of strong synapses that are repeatedly activated during wakefulness. Future work should investigate whether blocking astrocytic phagocytosis exacerbates or attenuates cognitive impairment associated with sleep deprivation.



Electron micrograph showing an astrocytic process (light blue shading) phagocytosing a portion of a presynaptic bouton (green shading). Red indicates the axon–spine interface. See Bellesi et al. for details.

Properties of Thalamocortical EPSPs *In Vivo*

Madineh Sedigh-Sarvestani, Leif Vigeland, Ivan Fernandez-Lamo, M. Morgan Taylor, Larry A. Palmer, et al.

(see pages 5250–5262)

Most cells in Layer IV of primary visual cortex (V1) are "simple cells", which have elongated receptive fields comprising adjacent ON and OFF subregions. These cells respond most strongly to lines with a matching orientation. When Hubel and Wiesel first described V1 simple cells, they hypothesized that the response properties were generated by convergent input from a select set of neurons in the lateral geniculate nucleus (LGN) that respond to light or dark spots in the same region of visual space. This hypothesis is supported by analyses of correlated spiking in LGN and V1 neurons: monosynaptically connected cells usually have the same sign (responding to light or dark) and have overlapping spatial receptive fields (Alonso 2005 J Neurophysiol 94:26). Because those studies only examined spiking, however, they did not exclude the possibility that synapses also form between LGN and V1 cells that have different response properties, but these synapses are too weak to evoke consistent spiking.

To investigate this possibility, Sedigh-Sarvestani et al. accepted the challenge of recording *in vivo* responses to visual stimuli both extracellularly in LGN and intracellularly in V1 in anesthetized cats. They used spike-triggered averaging of EPSPs to identify monosynaptically connected LGN–V1 pairs. Consistent with previous results, the probability of connection increased with the amount of receptive-field overlap. Nonetheless, many cells with highly overlapping receptive fields were not connected, and some cells with unmatched on/off responses were connected. Notably, mismatched connections were found more often with fast-spiking (presumably inhibitory) than with regular-spiking (presumably excitatory) V1 neurons. Surprisingly, the mean amplitude of thalamocortical EPSPs was much smaller *in vivo* than estimated from *in vitro* recordings. Moreover, EPSP amplitudes were similar in regular- and fast-spiking neurons and were not correlated with the overlap of LGN- and V1-cell receptive fields.

These results confirm that V1 simple cells receive inputs primarily from LGN neurons that have overlapping spatial receptive fields and similar response properties. But they also indicate that response similarity does not determine thalamocortical synaptic strength. The latter finding suggests that Hebbian plasticity does not exert a strong influence on LGN–V1 connection strength in adult cats. How the precise wiring is established is an important question for future research.

This Week in The Journal was written by Teresa Esch, Ph.D.