Perineuronal Nets in the Prelimbic Cortex

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(see pages 5008–5018)

Perineuronal nets (PNNs) are condensed extracellular matrix structures that form around the cell body and proximal dendrites of a subset of neurons throughout the CNS. In the cerebral cortex, PNNs form drites of a subset of neurons throughout the cerebral cortex, and that PNNs help to maintain perisomatic inhibitory input. Consequently, the disruption of PNNs leads to an imbalance of excitatory and inhibitory input and disrupts gamma oscillations. Whether these effects underlie symptoms of schizophrenia should be examined in future work.

Changes in PV-Expressing Basket Cells in Alzheimer’s Model

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(see pages 5116–5136)

Alzheimer’s disease (AD) is characterized by the accumulation of β-amyloid (Aβ) peptides and tau protein, accompanied by synaptic loss, neurodegeneration, and cognitive decline; but changes in brain activity, including hippocampal hyperactivity and abnormal interactions between the hippocampus and prefrontal cortex, may occur before other symptoms are noticeable. These early changes might stem from deficits in inhibitory transmission, which not only prevents hyperactivity, but also generates synchronous oscillations that are thought to mediate communication between brain areas (Varela et al., 2019, Neurobiol Dis 127:605).

To investigate early deficits in AD, Caccavano et al. examined synaptic function and network activity in the hippocampus of 3-month-old mice harboring five AD-linked mutations (5xFAD mice). These mice had some extracellular Aβ plaques in CA1 and showed mild deficits in a spatial memory task, but they did not yet show synaptic or neuronal degeneration. Because spatial memory formation relies on hippocampal sharp-wave ripples, the authors focused on these events in CA1 of hippocampal slices.

The frequency and amplitude of sharp-wave ripples were greater, but the duration was shorter and the number of incomplete ripples was larger in 3-month-old 5xFAD mice than in controls. To investigate the cellular basis for these changes, the authors assessed the activity of pyramidal cells and three types of parvalbumin-expressing (PV⁺) interneurons. The largest effects were on PV⁺ basket cells. These neurons had a significantly lower spike rate during sharp-wave ripples in 5xFAD slices, likely because the excitatory input was lower than in controls. Furthermore, basket-cell spiking during sharp-wave ripples was confined to a narrower window in 5xFAD mice. In contrast, spike rates were similar in 5xFAD and control pyramidal cells. The number of active pyramidal cells was higher in 5xFAD slices than in controls, however, possibly because of reduced inhibitory input and increases in excitatory input, particularly during sharp-wave ripples. Spiking and synaptic input to bistriated and axo-axonic PV⁺ interneurons of 5xFAD mice were similar to those of controls.

These results suggest that decreased inhibitory input to CA1 PV⁺ basket cells leads to reduced spiking during sharp-wave ripples, possibly shortening ripple duration. Increased excitation of pyramidal cells, along with reduced inhibition during sharp-wave ripples, may explain the increased number of pyramidal cells active during sharp-wave ripples. These larger ensemble sizes might make memory consolidation less precise, thus contributing to impaired spatial memory.

PNNs (green) surround a subset of neurons in the prelimbic cortex, including interneurons that express parvalbumin (blue). PV⁺ neurons with PNNs have longer axon initial segments (magenta) than those without. See Carceller et al. for details.

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