This Week in The Journal

Aggrecan, Perineuronal Nets, and Plasticity

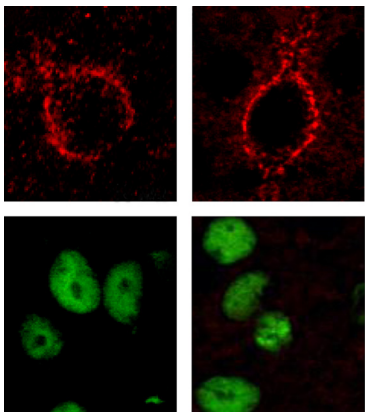
Daire Rowlands, Kristian K. Lensjø, Tovy Dinh, Sujeong Yang, Melissa R. Andrews, et al.

(see pages 10102–10113)

Perineuronal nets (PNNs) are meshworks of extracellular matrix that condense around the soma and proximal dendrites of particular neurons—primarily subsets of fast-spiking parvalbumin-expressing (PV) interneurons. PNNs are composed of long disaccharide polymers that extend from the plasma membrane, interlinked with chondroitin sulfate proteoglycans (proteins with disaccharide side chains) of the lectican family. The nets are more prevalent in some areas of the brain than in others, and their presence is associated with reduced synaptic plasticity. For example, PNNs appear in primary visual cortex (V1) as the critical period for ocular dominance plasticity closes. Moreover, disassembling PNNs reopens the critical period in adult animals. How PNNs regulate plasticity is unclear, but their binding of the chemorepulsive molecule Sema3a might play a role. PNNs also regulate the development and activity of PV-expressing interneurons, limit the diffusion of synaptic proteins, and—because their constituents are negative charged—regulate current flow near the cell membrane. Finally, they appear to protect neurons from oxidative stress.

Although previous work has revealed much about PNN function, most studies have disrupted PNNs using chondroitinase, which digests disaccharide side chains not only on lecticans, but also on other extracellular matrix proteins, complicating interpretation. Therefore, Rowlands, Lensjø, et al. generated mice in which a major PNN lectican, aggrecan, was conditionally knocked out. Brain-wide loss of aggrecan prevented PNN formation and led to reduced expression of PV in interneurons. Moreover, these mice showed better object-recognition memory than controls. Knocking out aggrecan selectively in V1 neurons in adult mice also caused PNN loss. In addition, 4 d of monocular deprivation in these mice produced a shift in ocular dominance that was similar to that seen during the developmental critical period, including both increases in responses to ipsilateral visual stimulation and decreases in responses to contralateral stimulation.

These results indicate that aggrecan is essential for the construction and maintenance of PNNs. They also confirm the importance of PNNs in synaptic plasticity and the maturation of PV interneurons. Still, more research will be required to determine why PNNs form only around a subset of neurons and how exactly they influence plasticity.



Perineuronal nets in V1 are composed of multiple proteins, including cartilage link protein (Ctrl1) and the lectican neurocan (red, top). All components of these nets are disassembled when aggrecan is knocked out (green, bottom). See Rowlands, Lensjø, et al. for details.

Amygdalar Innervation Patterns in Macaque Hippocampus

Jingyi Wang and Helen Barbas

(see pages 10019–10041)

Emotional experiences activate the amygdala, which sends projections to the hippocampus to enhance learning and help animals recognize rewarding and dangerous situations. Although projections from amygdala to hippocampus have been detailed in rodents, which neurons are targeted remains unclear. Furthermore, some evidence suggests the projection patterns differ between rodents and primates, but relatively little is known about the projections in primates. Therefore, Wang and Barbas traced projections from the medial amygdala to the hippocampus in macaques and determined which subregions, layers, and neuron types were targeted.

Afferents from the amygdala terminated throughout the longitudinal extent of the hippocampus, but by far the densest innervation (80% of all boutons) was in the anterior half, particularly in CA1, CA3, and CA1′ of the uncus, the most anterior portion of the hippocampal formation. In these regions, most boutons formed by amygdalar axons were located in the stratum lacunosum-moleculare (SLM), which contains the distal tufts of pyramidal cell apical dendrites; few boutons were found in the lower layers of CA1 and CA3 in the anterior hippocampus. In contrast, amygdalar afferents primarily targeted the pyramidal cell layer and stratum radiatum, which contains the radiating branches of apical dendrites, in the posterior hippocampus.

Boutons formed by amygdalar axons tended to be larger than nearby boutons formed by other excitatory or inhibitory inputs. Although most amygdala terminals were on putative pyramidal neurons, 10–15% of boutons were on presumptive inhibitory neurons, including parvalbumin-expressing neurons, which strongly inhibit pyramidal neurons, and calretinin-expressing neurons, which primarily target other interneurons, and thus disinhibit pyramidal cells. Calretinin-expressing neurons were predominantly located in the SLM and stratum radiatum, and they were more numerous than parvalbumin-expressing neurons, which were found primarily in lower layers.

These results suggest that projections from the amygdala provide strong excitatory input to pyramidal cells via synapses in the SLM of anterior hippocampus. Activation of calretinin-expressing neurons in SLM may further enhance activation of pyramidal cells through disinhibitory mechanisms. Thus, activation of amygdala afferents likely increases the probability of pyramidal cell spiking in response to contextual cues arriving from the entorhinal cortex. This might facilitate learning about emotionally salient situations and enhance retrieval of those memories when similar emotional events occur in the future.

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