This Week in The Journal

Cellular/Molecular

Some SALMs Induce Presynaptic Specialization

Won Mah, Jaewon Ko, Jungyong Nam, Kihoon Han, Woo Suk Chung, and Eunjoon Kim

(see pages 5559–5568)

When axons contact target cells, interactions between membrane proteins induce the formation of presynaptic and postsynaptic specializations. Results by Mah et al. suggest that two of the five known members of the synaptic adhesion-like molecule family—SALM3 and SALM5—are involved in this process. When expressed in cultured non-neuronal cells, SALM3 and SALM5 induced presynaptic specialization in contacting axons from excitatory and inhibitory rat hippocampal neurons. Similarly, overexpression of SALM3 or SALM5 in hippocampal neurons increased the number of excitatory and inhibitory presynaptic terminals contacting these neurons. Knockdown of SALM5, in contrast, reduced the number of excitatory and inhibitory synapses contacting neurons. Neither protein induced postsynaptic specialization in contacting dendrites, however. Nonetheless, antibody-induced clustering of SALM3, which contains an intracellular PDZ protein interaction domain, induced clustering of postsynaptic density protein PSD-95 in dendrites; clustering of SALM5, which lacks a PDZ domain, did not affect PSD-95.

Development/Plasticity/Repair

Glutamate Levels Change Effects of Adenosine Receptor Agonists

Shuang-Shuang Dai, Yuan-Guo Zhou, Wei Li, Jian-Hong An, Ping Li, *et al.*

(see pages 5802–5810)

Brain injury increases release of adenosine, leading to activation of adenosine 2A receptors (A_{2A}Rs). In some models of brain injury, A_{2A}R activation promotes inflammation, but in other models it is anti-inflammatory and neuroprotective. Dai et al. show that which effect occurs can depend on glutamate levels. At low glutamate levels, A_{2A}R agonist decreased neuroinflammatory responses of cultured microglia; this effect was blocked by protein kinase A (PKA) inhibitors, but not by PKC inhibitors. In contrast, A_{2A}R agonist potentiated neuroinflammatory responses when glutamate levels were high, and this effect was blocked by PKC inhibitors, but not by PKA inhibitors. After traumatic brain injury in mice, A_{2A}R agonist decreased subsequent brain damage and attenuated neurological deficits when *in vivo* glutamate levels were low (3 h after injury), but A_{2A}R antagonist increased damage. When glutamate levels peaked, 12 h after injury, agonist increased damage and antagonist decreased damage. Blocking glutamate release reversed the latter effects.

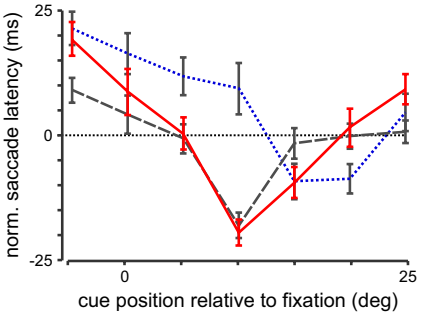
Behavioral/Systems/Cognitive

Attentional Cues Facilitate Motor Planning of Saccades

Aarlenne Z. Khan, Stephen J. Heinen, and Robert M. McPeek

(see pages 5481–5488)

The sudden appearance of a stimulus in the visual periphery directs attention to that location and shortens the latency of subsequent saccades to targets at the same location. Whether the initial stimulus speeds visual processing of the subsequent target or primes the motor system to direct a saccade toward that location has not been investigated. To do so, Khan et al. used a saccade adaptation task: the saccade target was moved while a saccade was in progress, which caused human subjects to unconsciously learn to make a saccade to the final target position. Specifically, subjects learned to make a 10° saccade in response to a target initially presented at 15°. After adaptation, the shortest latency saccades were made when a behaviorally irrelevant stimulus was flashed at the saccade endpoint (10°) rather than at the original target location (15°). These data suggest that the attentional cue facilitates movement planning rather than sensory processing.



In control trials, attentional cues flashed at the saccade target location (10°, black dashed line; or 15°, blue dotted line) shortens saccade latency, whereas cues flashed at other locations can increase latency. After saccade adaptation (red line), cues flashed at the saccade endpoint (10°) shorten latency more than cues flashed at the original target position (15°). See the article by Khan et al. for details.

Neurobiology of Disease

Small Synchronous Clusters Suddenly Expand, Causing Seizure

Premysl Jiruska, Jozsef Csicsvari, Andrew D. Powell, John E. Fox, Wei-Chih Chang, *et al.*

(see pages 5690–5701)

Epilepsy is caused by a variety of molecular and physiological changes, including increased intrinsic neuronal excitability and decreased inhibition. Preventing seizures pharmacologically is difficult, but recognizing the preictal state and understanding how this state progresses to seizure might aid prevention. Jiruska et al. studied this process in rat hippocampal slices under conditions of low calcium, which induces synchronous seizure-like activity. Between seizures, low-amplitude, high-frequency activity was present throughout hippocampal CA1, with synchronous activity occurring in a few, small, localized areas. Just before seizure, one of these areas of synchrony suddenly expanded, first encompassing nearby areas, and ultimately entraining all of CA1. The ability of weak electric fields to trigger seizures increased as the interictal period progressed, suggesting a gradual increase in excitability. Thus, in the preictal period, the brain might become especially sensitive to small perturbations that can switch small clusters of synchronous activity into full-blown seizures.