This Week in The Journal

Development/Plasticity/Repair

ADAM17 Promotes Oligodendrocyte Progenitor Proliferation

Javier Palazuelos, Howard C. Crawford, Michael Klingener, Bingru Sun, Jason Karelis, et al.

(see pages 11884–11896)

Many secreted signaling molecules are transported to the cell surface as membrane-associated precursors that remain inactive until they are cleaved by members of the a disintegrin and metalloproteinase (ADAM) family of proteins. This cleavage releases the active ectodomain. Shedding of ligands for the epidermal growth factor receptor (EGFR) is induced by ADAM17. Palazuelos et al. demonstrate that through this role, ADAM17 regulates proliferation and survival of oligodendrocyte progenitor cells (OPCs) in the CNS. As expected, knocking out ADAM17 selectively in postnatal OPCs reduced shedding of EGFR ligands, resulting in reduced activation of EGFRs in subcortical white matter. Furthermore, ADAM17 knock-out reduced proliferation of OPCs, accelerated their exit from the cell cycle, and increased apoptosis of both OPCs and immature oligodendrocytes. Together, these changes led to a reduction in myelination, as indicated by lower levels of myelin proteins in subcortical white matter and altered locomotor activity. EGFR overexpression rescued the effects of ADAM17 depletion on OPC proliferation and survival.

Systems/Circuits

Music Lessons Improve Syllable Discrimination

Nina Kraus, Jessica Slater, Elaine C. Thompson, Jane Hornickel, Dana L. Strait, et al.

(see pages 11913–11918)

The correlation between musical training and academic success is widely known. Numerous studies have documented stronger cognitive skills, as well as differences in gray-matter volume and music-induced neural activity in musicians compared to nonmusicians. The extent to which such differences preceded or resulted from music training remained unclear for many years, but accumulating evidence from longitudinal studies suggests that music training can indeed alter cognitive processes, particularly those involving auditory processing. Kraus et al. now add to this evidence. They randomly assigned children to one or two years of instruction in an established community music program and measured auditory brainstem responses to two similar syllables before and after training. Only those children who had undergone two years of training showed improvement in neurophysiological discrimination of the syllables. Given that such neurophysiological distinction has been linked to improved reading and hearing in noise, the results indicate that music training might be able to improve language skills.

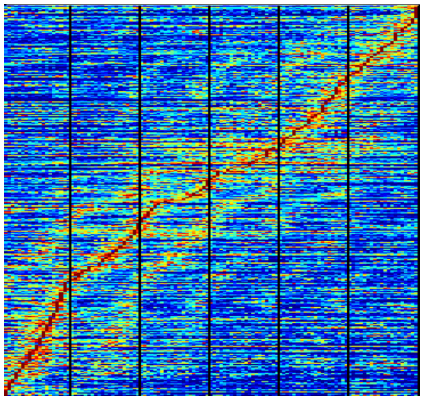
Behavioral/Cognitive

Time Passage Is Reflected in Sequential Activation of Neurons

David A. Crowe, Wilbert Zarco, Ramon Bartolo, and Hugo Merchant

(see pages 11972–11983)

We perceive the passage of time on many scales, from years to subsecond intervals. Encoding of short intervals is essential for accurately performing sequential behaviors, such as tapping a rhythm. To investigate how the nervous system encodes short durations, Crowe et al. recorded neurons in the medial premotor cortex (MPC) while monkeys synchronized tapping to auditory or visual stimuli and then continued tapping at the same frequency in the absence of cues. Many MPC neurons appeared to be tuned to serial order, firing most during a particular intertap interval. The activity of these neurons also varied within each interval and peaked at similar times in sequential intervals. Neurons in a partially overlapping population were tuned to the length of the intertap interval, firing more during longer than during shorter intervals, for example. Thus, the pattern of active neurons rapidly changed throughout each trial. Interestingly, serial order neurons appeared to represent a certain proportion of the intertap interval, rather than an absolute time period.



Average normalized firing rate of different MPC neurons with activity significantly related to serial order, aligned to the time bin of peak activity. Occurrence of taps is indicated by vertical lines, and each intertap interval was divided into 20 bins. See the article by Crowe et al. for details.

Neurobiology of Disease

AMPK Mediates Effects of Aβ on Synaptic Plasticity

Tao Ma, Yiran Chen, Valerie Vingtdeux, Haitian Zhao, Benoit Viollet, et al.

(see pages 12230–12238)

Depletion of cellular ATP leads to activation of AMP-activated protein kinase (AMPK). AMPK helps cells conserve energy in part by activating eukaryotic elongation factor 2 kinase (eEF2K), which halts protein translation by phosphorylating and thus inactivating eEF2. AMPK activity is elevated in brains of Alzheimer's disease (AD) patients, and this may be related to the abnormal energy metabolism and protein synthesis regulation observed in AD. Because protein synthesis is required for many forms synaptic plasticity, Ma et al. hypothesized that AMPK also contributes to the detrimental effects of β-amyloid (Aβ) peptides on long-term potentiation (LTP) and depression (LTD). Indeed, an AMPK antagonist prevented Aβ-induced inhibition of LTP and enhancement of LTD in mouse hippocampal slices and rescued LTP in AD-model mice. Furthermore, Aβ did not impair LTP in mice lacking a catalytic subunit of AMPK. Like AMPK, eEF2 phosphorylation was elevated in AD patients' brains and in hippocampus of AD-model mice, and inhibiting eEF2K prevented Aβ-induced impairment of LTP in wild-type mice.