This Week in The Journal

Adult-Born Granule Cells Grow More Spines and Bigger Boutons

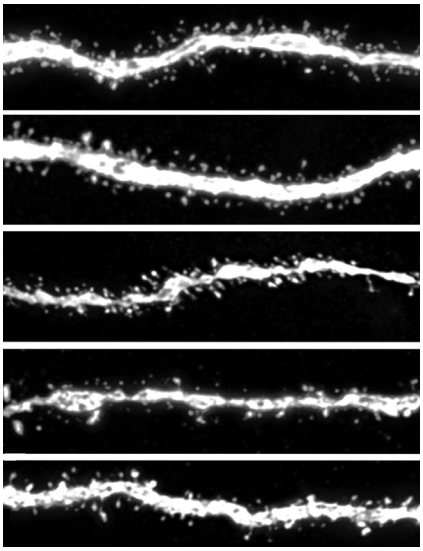
John Darby Cole, Delane F. Espinueva, Désirée R. Seib, Alyssa M. Ash, Matthew B. Cooke, et al.

(see pages 5740–5756)

New neurons are generated in the dentate gyrus of rodents and other mammals well into adulthood. Many of these neurons migrate to the granule cell layer; develop axons, dendrites, and spines; and become incorporated into the dentate circuitry. This incorporation is facilitated by elevated excitability of maturing newborn neurons relative to fully mature neurons. Eventually, adult-born neurons come to resemble neurons generated during the early postnatal period (Jahn and Bergami, 2018, Cell Tissue Res 371:23), but Cole, Espinueva, et al. add to accumulating evidence that adult-born neurons retain unique properties throughout their lifetime.

To investigate the development of adult-born neurons in rats, the authors labeled neurons born when rats were 1 d or 9, 12, or 14 weeks old and examined neuronal morphology when the rats were 16 weeks old. They also labeled neurons generated when rats were 8 weeks old and examined them 24 weeks later. As expected, dendrites grew longer as neurons aged. Unexpectedly, however, some distal dendrites appeared immature even in 24-week-old adult-born neurons, suggesting that dendritic growth was ongoing. The number of dendritic spines also increased over time, peaking when neurons were 7 weeks old. Notably, spine density was significantly greater in 7- and 24-week-old adult-born neurons than in 16-week-old neonatally born neurons. The size of presynaptic boutons formed by adult-born neurons also increased with age, peaking at 24 weeks, when the boutons were much larger than those of neonatally born neurons. Axonal boutons of adult-born neurons also had more, and longer, filopodia (which form synapses with inhibitory interneurons in hippocampal area CA3) than those of neonatally born neurons.

These results indicate that adult-born granule cells continue to develop for longer than previously appreciated, ultimately generating more spines, larger presynaptic boutons, and more bouton filopodia than neonatally born neurons. This may give adult-born neurons a more prominent role in hippocampal circuits—particularly in shaping inhibition—than might be expected based on their relative number. Indeed, modeling work suggested that adult-born neurons may account for 10% of spines in the dentate gyrus when rats are 1.5 years old. Future work should determine whether persistent morphological differences between adult-born and neonatally born granule cells are accompanied by persistent functional differences.



Adult-born mouse granule cells have more spines when they are 7 (top two panels) or 24 (middle panel) weeks old than neurons born on the day of birth have when they are 16 weeks old (bottom two panels). See Cole, Espinueva, et al. for details.

Suppression of Perirhinal M-Current Aids Recognition Memory

Anastasia Kosenko, Shirin Moftakhar, Marcelo A. Wood, and Naoto Hoshi

(see pages 5847–5856)

The M-current is a noninactivating voltage-gated potassium current that is active at subthreshold membrane potentials and opposes depolarization. It is mediated by K_V7 channels, which are expressed widely in the nervous system. It is called the M-current because it is suppressed as a consequence of activation of muscarinic acetylcholine receptors (mAChRs), leading to a transient increase in neuronal excitability. It has since been shown to be suppressed after activation of other G_q-coupled receptors as well.

M-current suppression is thought to contribute to the ability of acetylcholine to enhance learning, but little direct evidence of such a role has been reported. To provide this evidence, Kosenko et al. assessed the effects of knocking in a mutant form of $K_V7.2$ that has normal M-currents at baseline, but lacks a site required for M-current suppression. Mutant mice behaved similarly to wild type when exploring an open field and walking on a rotating rod. They also performed similarly to controls in object location memory and contextual fear-conditioning tests. In contrast, long-term object recognition was impaired in knock-in mice; whereas wild-type mice explored a novel object more than one presented the previous day, knock-in mice spent similar amounts of time investigating novel and previously presented objects. Knock-in mice were also impaired on a long-term social-odor-recognition task. Importantly, object-recognition memory deficits were prevented by administering a K_V7 channel blocker before or immediately after training, but not by administering the blocker just before testing the next day.

These results suggest that M-current suppression and the resulting increase in neuronal activity are essential for consolidation of memories that depend on the perirhinal cortex (object and social-odor recognition), but not on those that depend on the hippocampus (location and contextual fear memory). If this is true, the authors reasoned, then preventing M-current suppression should reduce activity in perirhinal cortex, but not in hippocampus, after training on the respective tasks. Indeed, c-fos labeling in perirhinal cortex was lower after training in K_V7 knock-in mice than in controls, whereas c-fos labeling in hippocampus was similar in mutant and control mice. Furthermore, blocking K_V7 restored perirhinal activation after training. Altogether, these results support a role for M-current suppression in learning that depends on the perirhinal cortex.

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