This Week in The Journal

New Regulators of Spine Maturation and Stability

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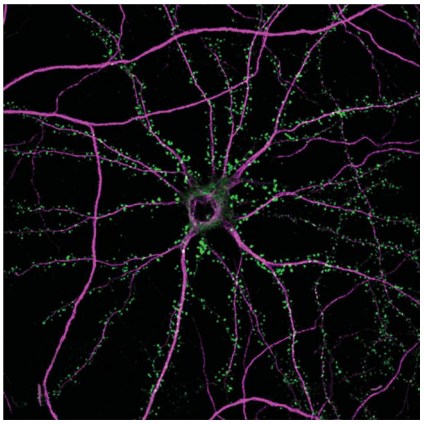
(see pages 526–541)

Dendritic spines are the sites of excitatory input to many neuronal types. Spines start as thin filopodia, but synaptic activity transforms them: first into wide, stubby structures and then into mushroom shapes with large heads and thin necks. If a synapse is inactive for a long period, the spine shrinks and may ultimately disappear. These changes in spine morphology are mediated by remodeling of the underlying actin cytoskeleton, which in turn is governed by a diverse set of actin-binding proteins that promote assembly, disassembly, bundling, or cross-linking of actin filaments. Because the actin-binding protein LASP1 is localized to postsynaptic sites and has been identified as a risk factor for schizophrenia and autism, Myers et al. explored the roles of LASP1 and a closely related protein, LASP2, in spines of cultured hippocampal neurons.

Both LASP1 and LASP2 were enriched in dendritic spines. Knocking down these proteins had different effects depending on the developmental stage of the neurons. Knocking down either protein when dendrites were growing and spines were beginning to form reduced overall spine density while increasing the proportion of thin, filopodia-like spines. Knocking down LASP2 at this stage also reduced the frequency of miniature EPSCs and reduced dendritic branching. Conversely, overexpressing LASP2 increased spine density and dendritic branching, whereas overexpressing LASP1 had no effect.

After dendritic growth was complete and spines had formed but were still maturing, knocking down LASP1 did not affect spine density, but it reduced spine width. In contrast, knocking down LASP2 during this period decreased spine density and width, as well as reducing dendritic complexity. Furthermore, live imaging revealed that LASP2 knockdown increased the movement of spines and dendrite tips. Finally, overexpressing mutant forms of LASP2 lacking either of the two domains required for actin binding mimicked the effect of knocking down the endogenous protein, whereas overexpressing LASP1 mutants had no apparent effect.

These results suggest that LASP1 is involved in spine formation and maturation, whereas LASP2 is involved in stabilization of spines and dendritic branches. Although the effects of LASP2 require its binding to actin, the effects of LASP1 do not. Given that LASP1 is phosphorylated by kinases involved in synaptic plasticity, it may also mediate plasticity-related changes in spine morphology.



LASP2 (green) is concentrated in dendritic spines in cultured hippocampal neurons. See Myers et al. for details.

Amygdala Neurons that Promote Alcohol Consumption

María Luisa Torruella-Suárez, Jessica R. Vandenberg, Elizabeth S. Cogan, Gregory J. Tipton, Adonay Teklezghi, et al.

(see pages 632–647)

The amygdala processes stimuli that have emotional valence and generates appropriate responses. Although best known for its roles in fear and anxiety, the amygdala also governs responses to rewards. Given that alcohol consumption is both rewarding and anxiety reducing, it is not surprising that activation of the amygdala, particularly its central nucleus (CeA), has been linked to alcohol use disorders. The CeA is composed primarily of GABAergic interneurons and projection neurons that produce different sets of neuromodulators and project to different targets. Which subpopulations contribute to alcohol use and abuse remains incompletely understood, but Torruella-Suárez et al. report that neurotensin-expressing CeA neurons are involved.

Alcohol consumption increased fos expression (a marker of neuronal activation) in neurotensin-expressing neurons. When ~50% of these neurons were killed using a genetic targeting strategy, the amount of alcohol mice consumed during a choice test decreased. In contrast, the ablation did not affect anxiety-related behaviors or consumption of plain water or water containing sucrose, saccharin, or quinine.

Most neurotensin-expressing CeA neurons projected to either the bed nucleus of the stria terminalis (BNST) or the parabrachial nucleus (PbN). When optical stimulation of the PbN neurons was given in one of two chambers, mice developed a preference for that chamber, and when stimulation was contingent on nose-poke behavior, mice engaged in more nose poking. When fluid was available, mice licked the delivery spout more often when stimulation was on than when it was off, regardless of whether the fluid was plain water or water flavored with ethanol, sucrose, saccharin, or quinine. However, overall fluid consumption increased only for ethanol, sucrose, and saccharin. Finally, stimulation of PbN-projecting neurons did not increase the consumption of standard chow or sweet food, and in fact decreased the consumption of chow if ethanol was present.

These data suggest that activation of neurotensin-expressing CeA neurons that project to the PbN is inherently reinforcing, promotes short-term fluid intake, and increases the consumption of highly palatable fluids, particularly ethanol, without affecting food intake. Future work should determine which PbN neurons are inhibited by the projections, whether projections to the BNST also influence alcohol consumption, and whether neurotensin or another neurotransmitter released by these neurons mediates their effects.

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