This Week in The Journal

● Cellular/Molecular

Vesicular Glutamate and Monoamine Transporters Cycle Differently

Bibiana Onoa, Haiyan Li, Johann A. Gagnon-Bartsch, Laura A. B. Elias, and Robert H. Edwards

(see pages 7917–7927)

Properties of synaptic glutamate release have been extensively studied by measuring postsynaptic currents. Because this method cannot measure release of metabotropic neurotransmitters, however, considerably less is known about dopamine release properties. To address this question, Onoa et al. compared the behavior of vesicular glutamate and monoamine transporters (VGLUT1 and VMAT2) labeled with pHluorin, a molecule that is quenched when inside synaptic vesicles, fluoresces upon vesicle fusion, and is requenched when recycled into a new vesicle. The transporters were largely colocalized at synaptic boutons in transfected mouse hippocampal and midbrain dopaminergic neurons; but they did not overlap in all midbrain boutons, suggesting they are sorted into separate vesicles. The rate of fluorescence increase upon prolonged stimulation suggested that a smaller proportion of VMAT2 is available for evoked release compared with VGLUT1, and that more VMAT2 resides in the reserve pool. The requenching rate suggested that VMAT2 endocytosis is slower than VGLUT1 endocytosis, but VMAT2 recycling increased during stimulation in midbrain.

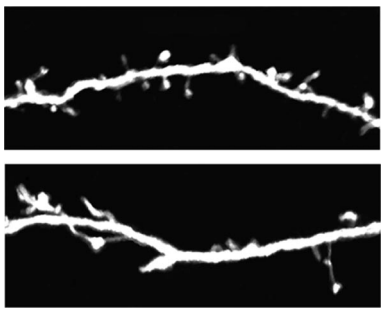
▲ Development/Plasticity/Repair

Spine Maturation Is Delayed in FMRP-Null Dendrites

Alberto Cruz-Martín, Michelle Crespo, and Carlos Portera-Cailliau

(see pages 7793–7803)

Dendritic spines begin as long, thin protrusions that shorten and develop a mushroom shape as they stabilize and mature. This process appears to be disrupted in people lacking fragile X mental retardation protein (FMRP): they have a higher-than-normal density of dendritic spines, and these are abnormally long and thin. Similarly, layer 5 pyramidal cell dendrites in mice lacking FMRP have increased spine density and length. In contrast to these previous studies using fixed tissue, however, Cruz-Martín et al. found no difference *in vivo* in the density or length of dendritic protrusions in layer 2 dendrites in somatosensory cortex of FMRP-null and wild-type mice. In both genotypes, the density of protrusions increased and protrusion length decreased over the first three postnatal weeks. But reduction of protrusion motility and turnover, and the progression to mature spine morphology, were delayed in knock-out relative to control mice, suggesting that FMRP has a role in spine stabilization and maturation.



An inverse agonist of metabotropic glutamate receptors, previously shown to attenuate the effects of FMRP knock-out in adult mice, did not rescue the increased turnover rate in young knock-out mice. The inverse agonist increased protrusion length and motility and decreased protrusion density in 2-week-old knock-out mice (bottom), but not in wild-type mice (top). See the article by Cruz-Martín et al. for details.

■ Behavioral/Systems/Cognitive

Mice Without Sweet Receptors Still Prefer Glucose

Xueying Ren, Jozélia G. Ferreira, Ligang Zhou, Sara J. Shammah-Lagnado, Catherine W. Yeckel, et al.

(see pages 8012– 8023)

Most mammals prefer foods containing sugar to those containing proteins. Even given a choice between glucose-containing water and water containing the sweet-tasting amino acid L-serine, mice drink more glucose solution, suggesting sweet taste alone is not sufficient to drive food preference. Ren et al. have shown this conclusively. During short presentations, mice lacking transient receptor potential channel M5 (TRPM5)—the receptor required for sweet, bitter, and most amino acid tastes—showed no preference for glucose versus isocaloric serine solution. After several hours of continued availability, however, TRPM5-null mice consumed more glucose solution, and they could be conditioned to prefer the location of glucose presentation. Moreover, wild-type mice drank more plain water when paired with intragastric or intravenous glucose infusion than when paired with serine infusion. Across mice, glucose oxidation rate, but not blood glucose levels, was correlated with the number of licks of glucose solution, suggesting glucose metabolism drives the preference.

♦ Neurobiology of Disease

Caloric Restriction Slows Effects of Brain Aging

Erik K. Kastman, Auriel A. Willette, Christopher L. Coe, Barbara B. Bendlin, Kris J. Kosmatka, et al.

(see pages 7940 –7947)

Caloric restriction increases lifespan in every animal species tested, and has been reported to reduce risk of age-related neurological disease, increase survival of adult-born neurons, increase resilience to excitotoxic and oxidative stress, and improve cognitive function. In a continuing long-term study of calorie restriction in adult rhesus monkeys, Kastman et al. now report that calorie-restricted monkeys performed a fine-motor-skill task more quickly than controls and had lower levels of non-heme iron accumulation—an indicator of aging—in globus pallidus and substantia nigra. Whether caloric restriction has similar beneficial effects in humans and whether such effects would be outweighed by negative consequences has yet to be determined. Given that calorie-restricted diets, which typically involve a 30% reduction in caloric intake, will not be attractive to most people, determining what mediates the beneficial effects of calorie restriction in animals will likely be required to develop strategies for extending brain health in humans.