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IN BRIEF

SYNAPTIC PHYSIOLOGY

No clathrin required

Large endocytic vesicles are retrieved rapidly through ultrafast endocytosis, but their fate is unknown. Watanabe *et al.* used the 'flash and freeze' technique to show that at physiological temperatures, stimulation of mouse hippocampal neurons results in clathrin-independent formation of large endocytic vesicles, which transition to the endosome and later bud off in a clathrin-dependent manner to form small synaptic vesicles. Notably, when the same experiment was performed at room temperature, synaptic vesicles were endocytosed by classic clathrin-mediated endocytosis. This might explain some of the apparently conflicting results in the field.

ORIGINAL RESEARCH PAPER Watanabe, S. *et al.* Clathrin regenerates synaptic vesicles from endosomes. *Nature* http://dx.doi.org/10.1038/nature13846 (2014)

NEURODEGENERATIVE DISORDERS

Tangled up

Alzheimer's disease is characterized by neurofibrillary tangles composed of aggregates of truncated and hyperphosphorylated tau protein, but the mechanisms of their formation are understood poorly. The authors showed that in a mouse model of Alzheimer's disease, deletion of asparagine endopeptidase (AEP; a lysosomal cysteine proteinase) reduced tau hyperphosphorylation and cognitive deficits associated with Alzheimer's disease. Adeno-associated viral delivery of degradation-resistant tau had a similar effect, and suggests a role for AEP in tau-associated neurodegeneration.

ORIGINAL RESEARCH PAPER Zhang, Z. *et al.* Cleavage of tau by asparagine endopeptidase mediates the neurofibrillary pathology in Alzheimer's disease. *Nature Med.* http://dx.doi.org/10.1038/nm.3700 (2014)

SYNAPTIC PLASTICITY

Opening a closed window

The mechanisms controlling the opening and closing of critical periods is not known, but Bochner *et al.* found that in adult mice, genetic disruption of paired immunoglobulin-like receptor B (PirB) increased neural plasticity of the visual cortex following monocular deprivation. Furthermore, acute blockade of PirB in layer 5 cortical pyramidal neurons increased spine density and mini excitatory postsynaptic currents, indicative of formation of new functional synapses, and this suggests that PirB contributes to the active repression of plasticity in the mature nervous system.

ORIGINAL RESEARCH PAPER Bochner, D. N. *et al.* Blocking PirB up-regulates spines and functional synapses to unlock visual cortical plasticity and facilitate recovery from amblyopia. *Sci. Transl. Med.* **6**, 258ra140 (2014)

NEUROBIOLOGY OF REWARD

Great expectations

The placebo effect is a powerful example of how expectations can shape experiences. Patients with Parkinson's disease, who have substantial loss of midbrain dopamine neurons projecting to the striatum and prefrontal cortex, show motor improvements after placebo treatment, suggesting that expectation may induce dopamine release. Schmidt *et al.* show that in patients with Parkinson's disease who received a placebo, the expectation of receiving the dopamine precursor L-dopa also increased reward learning, with an efficacy equivalent to that of L-dopa treatment. These findings show that the expectation of receiving dopaminergic treatment can enhance reward learning.

ORIGINAL RESEARCH PAPER Schmidt, L. *et al.* Mind matters: placebo enhances reward learning in Parkinson's disease. *Nature Neurosci.* http://dx.doi.org/10.1038/nn.3842 (2014)