IN BRIEF

LEARNING AND MEMORY

Methylphenidate facilitates learning-induced amygdala plasticity

Tye, K. M. *et al. Nature Neurosci.* **13**, 475–481 (2010)

Methylphenidate (Ritalin) is used to treat attention deficit–hyperactivity disorder, but its mechanism of action is unclear. The authors studied how methylphenidate affected the performance of rats in a cue–reward learning paradigm. Methylphenidate enhanced learning by modulating excitatory synaptic plasticity in cortico-amygdala synapses through increased activation of dopamine receptors in the lateral amygdala. Furthermore, different dopamine receptor subtypes enhanced different aspects of the learning task. These findings suggest a crucial role for dopamine in lateral amygdala-dependent learning.

EPIGENETICS

Dnmt1 and Dnmt3a maintain DNA methylation and regulate synaptic function in adult forebrain neurons

Feng, J. *et al. Nature Neurosci.* **13**, 423–430 (2010)

DNA methyltransferase 1 (DNMT1) and DNMT3A regulate methylation patterns in rapidly dividing cells. Their expression in adult postmitotic neurons suggested that they might have additional functions in the adult nervous system. Here, the authors generated conditional-knockout mice expressing DNMT1 and DNMT3A exclusively in postnatal forebrain neurons. The *Dnmt1–Dnmt3a* double knockout, but not the single knockouts, showed deficits in hippocampal synaptic plasticity and learning and memory, as well as altered gene expression. Thus, DNMT1 and DNMT3A have overlapping functions and are required for the maintenance of DNA methylation in postmitotic neurons.

NEURODEGENERATIVE DISEASE

Caspase activation precedes and leads to tangles

de Calignon, A. *et al. Nature* 31 March 2010 (doi:10.1038/nature08890)

The order of events leading to neurodegeneration in Alzheimer's disease and frontotemporal dementia is debated. Here, the authors use *in vivo* multiphoton imaging to show that, in transgenic mice carrying a mutated human *tau* gene, caspase activation occurs before the formation of fibrillar tau deposits (tangles). Moreover, expressing a construct that mimics caspase-cleaved tau in wild-type mice induced the formation of tau aggregates that included full-length tau. The authors postulate that caspase-cleaved tau initiates tangle formation and then normal tau is recruited to the aggregates.

DEVELOPMENT

A critical role for α4βδ $GABA_A$ receptors in shaping learning deficits at puberty in mice

Shen, H. *et al. Science* **327**, 1515–1518 (2010)

The onset of puberty marks a decline in learning ability. Investigating the underlying mechanisms, the authors showed that α4βδ-containing $GABA_A$Rs are expressed perisynaptically at excitatory hippocampal CA1 synapses at a higher level in pubertal than in prepubertal mice. Pubertal mice show no NMDAR-dependent hippocampal long-term potentiation and impaired hippocampus-dependent learning. These deficits were absent in pubertal mice lacking the δ subunit and could be reversed by allopregnanolone, a $GABA_A$R modulator, suggesting a potential use for this steroid as a 'smart drug' for adolescents.