RESEARCH HIGHLIGHTS

IN BRIEF

CEREBRAL CORTEX

Cortical reconstruction

The fine anatomical relationships between brain cells remain mostly unknown. This study examined the connectivity of a 1,500 µm³ volume of mouse neocortex. More than 2,000 29-nm coronal brain sections were generated with an automatic tape-collecting ultramicrotome and used in scanning electron microscopy, and the neocortical volume was reconstructed from the resulting images. 1,700 synapses were found in this volume, but there were many more incidences of axons touching spines without forming synapses, indicating that the close proximity of axons to spines does not predict connectivity. **ORIGINAL RESEARCH PAPER** Kasthuri, N. et al. Saturated reconstruction of a volume of neocortex. *Cell* **162**, 648–661 (2015)

LEARNING AND MEMORY

Demethylated learning

Lysine-specific histone demethylase 1A (LSD1) targets histone H3 lysines to regulate transcription. Wang *et al.* found that, *in vitro*, a neuronal LSD1 isoform (LSD1n) targeted a different substrate: histone H4 lysine 20 (H4K20). *Lsd1n* knockout (*Lsd1n^{-/-}*) mouse neurons showed increased H4K20 methylation and impaired gene transcription following neuronal activity, and *Lsd1n^{-/-}* mice showed deficits in two learning and memory tasks. Thus, LSD1n may promote activity-induced transcription in neurons and thereby regulate memory formation.

ORIGINAL RESEARCH PAPER Wang, J. et al. LSD1n is an H4K20 demethylase regulating memory formation via transcriptional elongation control. Nat. Neurosci. <u>http://dx.doi.org/10.1038/nn.4069</u> (2015)

CIRCADIAN RHYTHMS

The rhythm regulator

The small ventral lateral neurons (sLNvs) are the main clock neurons in fruitflies and show circadian changes in excitability and axonal terminal width, which are at their greatest at dawn. This study revealed that sLNvs also show circadian changes in axon volume, suggesting the involvement of an actin-related mechanism. Indeed, levels of Rho1 — a GTPase implicated in actin dynamics — exhibited circadian oscillations in sLNvs, and overexpressed Rho1 maintained axon terminals in a retracted state, leading to arrhythmic circadian behaviour and impaired regulation of downstream clock neurons. Thus, oscillatory Rho1 activity is a key circadian regulator in fruitflies.

ORIGINAL RESEARCH PAPER Petsakou, A., Sapsis, T. P. & Blau, J. Circadian rhythms in Rho1 activity regulate neuronal plasticity and network hierarchy. *Cell* http:/dx.doi.org/10.1016/j.cell.2015.07.010 (2015)

NEUROTRANSMITTER RECEPTORS

Recoding the pathways

In the ventral striatum, motivated behaviour is understood to be encoded through a direct pathway, in which medium spiny neurons (MSNs) project from the nucleus accumbens (NAc) to the ventral mesencephalon (VM), and an indirect pathway, in which NAc MSNs project to ventral pallidum (VP) neurons, which target the VM. The direct and indirect pathway MSNs are thought to express dopamine D1 and D2 receptors, respectively. However, using an optogentic approach, Kupchik *et al.* show that activation of D1- or D2-MSNs in the NAc core can elicit inhibitory currents in the VP, opposing the idea that the indirect pathway is simply coded by D2 receptors.

ORIGINAL RESEARCH PAPER Kupchik, Y. M. *et al.* Coding the direct/indirect pathways by D1 and D2 receptors is not valid for accumbens projections. *Nat. Neurosci.* <u>http://dx.doi.org/10.1038/nn.4068</u> (2015)