assay. The mice spent more time in the chamber associated with the pHFS than in a chamber in which they received no stimulation. In a social-reward CPP task, mice that freely explored a two-chamber arena in which one chamber included another mouse spent more time in the 'social' chamber, and optogenetic silencing of hippocampus→NAc projections when mice were in either chamber did not affect this. However, the optogenetic silencing when the mice were in the social chamber reduced the animal's later preference for the chamber that previously contained the target mouse. Therefore, LTP at hippocampus→NAc synapses may be intrinsically rewarding, and activity at these synapses may be necessary for forming reward-related memories.

Previous work has shown that chronic stress reduces excitatory drive to the NAc, and that this leads to anhedonia. Here, LeGates et al. exposed mice to chronic multimodal stress to induce an anhedonic-like state (indicated by a reduced preference to sucrose). Compared with unstressed controls, D1R-expressing MSNs in slices from stressed, anhedonic-like mice exhibited weaker synapses and strongly reduced ability to undergo LTP. pHFS also failed to induce CPP in stressed animals. Strikingly, the anhedonia-like behaviour and the synaptic and CPP deficits in these animals were all reversed by chronic (but not acute) treatment with the antidepressant fluoxetine (a selective serotonin-reuptake inhibitor). These data imply that stress may induce anhedonia by impairing hippocampus→NAc synaptic function and LTP.

Overall, this study demonstrates an important role for LTP at hippocampus→NAc synapses in contextual reward-related memories. These findings may be relevant to disorders of reward processing, such as depression and addiction.

Natasha Bray

ORIGINAL ARTICLE LeGates, T. A. Reward behaviour is regulated by the strength of hippocampus–nucleus accumbens synapses. *Nature* https://doi.org/10.1038/s41586-018-0740-8 (2018)

indicating that both lemniscal L4 and paralemniscal POm inputs are required for RPS-induced LTP in L2/3 pyramidal cells.

Normally, L2/3 pyramidal cell activity is in part controlled by parvalbumin (PV)-expressing interneurons in perisomatic regions and by somatostatin (SST)-expressing interneurons in distal dendritic regions. PV and SST interneurons, in turn, are controlled by vasoactive intestinal peptide (VIP)-expressing interneurons. The VIP–SST connections are a well-characterized disinhibitory microcircuit for L2/3 pyramidal cell apical dendrites, which is also the main location of POm inputs.

To investigate the contribution of these interneurons, the authors stimulated POm and L4 and found that this increased VIP and decreased SST interneuron activity. Reducing SST interneuron activity with DREADDS increased the amplitudes of L4- and POm-evoked L2/3 depolarizing postsynaptic potentials. In contrast, reducing VIP interneuron activity decreased POm-evoked post-synaptic potential amplitudes and increased inhibitory input to L2/3 pyramidal cells, suggesting that normally these interneurons disinhibit L2/3 neurons.

Finally, to test if this POm–VIP–SST circuit plays a role in plasticity the authors reduced SST interneuron activity during RPS and found that this did not affect the production of LTP, suggesting that disinhibition gates LTP induction. Moreover, reducing VIP interneuron activity during RPS prevented LTP, showing that VIP interneuron-dependent disinhibition is necessary for LTP.

Overall, these findings reveal that L2/3 pyramidal cell synaptic plasticity is gated by higher-order thalamocortical inputs and local disinhibition. This might be a mechanism by which higher-order thalamic relays can shape the future processing of first-order sensory information.

Sian Lewis

ORIGINAL ARTICLE Williams, L. E. & Holtmaat, A. Higher-order thalamocortical inputs gate synaptic long-term potentiation via disinhibiton. *Neuron* https://doi.org/10.1016/j.neuron.2018.10.049 (2018)

IN BRIEF

SLEEP

Too hungry to sleep

Starvation suppresses sleep, but the mechanisms are not well understood. Here, mice that were food-deprived for 24 hours showed increased wakefulness at the expense of sleep, and increased firing and FOS expression in neurons of the paraventricular thalamus (PVT). Most of these neurons expressed calretinin (PVT^{CR+}) and projected to the bed nucleus of the stria terminalis (BNST). Optogenetic activation of PVT^{CR+} terminals in the BNST promoted wakefulness, and chemogenetic inhibition of these neurons decreased wakefulness. Overall, these findings indicate that the PVT^{CR+}–BNST pathway is crucial for starvation-induced arousal.

ORIGINAL ARTICLE Hua, R. et al. Calretinin neurons in the midline thalamus modulate starvation-induced arousal. *Curr. Biol.* https://doi.org/10.1016/j.cub.2018.11.020 (2018)

MYELIN

All wrapped up

The role of cell adhesion molecules (CAMs) in oligodendrocyte–axon contact and myelination is not well understood. Overexpression of the membrane-bound extracellular domain of the CAM CADM4 (CADM4-ED) in cultured oligodendrocytes resulted in an increased number of axoglial contact sites but reduced myelin maturation compared with controls. Overexpression of CADM4-ED in mice resulted in hypomyelination of axons and inappropriate myelination of soma. These results indicate a key role for axoglial CAMs in proper myelin targeting and maturation.

ORIGINAL ARTICLE Elazar, N. et al. Axoglial adhesion by Cadm4 regulates CNS myelination. *Neuron* https://doi.org/10.1016/j.neuron.2018.11.032 (2018)

NEURODEGENERATIVE DISORDERS

Seeds of change

Some people who were treated with cadaveric human growth hormone (cHGH) and who developed Creutzfeldt–Jakob disease also developed deposits of amyloid-β protein (Aβ), pathology more commonly associated with Alzheimer disease (AD). As AD brain homogenates can seed Aβ deposits in mice, the authors hypothesized that the cHGH used might have been contaminated with Aβ as well as prions. Indeed, certain cHGH batches were contaminated with $Aβ_{40}$ and $Aβ_{42}$, and intracerebroventricular injection of these contaminated samples into mice expressing a mutant humanized amyloid precursor protein resulted in Aβ plaque formation and development of cerebral Aβ–amyloid angiopathy.

ORIGINAL ARTICLE Purro, S. A. et al. Transmission of amyloid-β protein pathology from cadaveric pituitary growth hormone. *Nature* https://doi.org/10.1038/s41586-018-0790-y (2018)

SLEEP

From sleeping to waking

Noradrenergic locus coeruleus (LC-NE) neurons are involved in sleep-to-wake transitions and the maintenance of wakefulness, but a definitive role for noradrenaline has not been established. Here, the dopamine β-hydroxylase gene (*Dbh*) was disrupted selectively in mouse LC-NE neurons in vivo using CRISPR–Cas9 technology. This protocol considerably reduced noradrenaline in the LC. Bilateral LC-specific *Dbh* disruption decreased the total wake period of these animals compared with controls and reduced arousal in response to a stressful stimulus, suggesting noradrenaline is involved in the maintenance of wakefulness induced by salient stimuli.

ORIGINAL ARTICLE Yamaguchi, H. et al. In vivo cell type-specific CRISPR knockdown of dopamine beta hydroxylase reduces locus coeruleus evoked wakefulness. *Nat. Commun.* https://doi.org/10.1038/s41467-018-07566-3 (2018)