Credit: Jorg Greuel/Getty

centre of the arena and increases in plasma corticosterone, but sucrose consumption during the shock sessions reduced these effects. Therefore, rewarding stimuli may attenuate stress responses via effects on PVN CRF neurons.

Yuan et al. examined patch-clamp recordings of spontaneous excitatory and inhibitory postsynaptic potentials (sEPSCs and sIPSCs) of PVN CRF neurons in brain slices from control mice and mice exposed to a foot shock plus either water or sucrose. Foot shock led to an increase in sEPSC frequency and amplitude, but sEPSCs in slices from mice that were given sucrose as well as the foot shock had similar amplitudes to those in control slices. Intriguingly, the frequency and amplitude of sIPSCs in PVN CRF neurons were increased in the foot shock plus sucrose group compared with both other groups. Repeated foot shocks promoted bursting activity in these cells, but sucrose consumption reduced the frequency and proportion of intra-burst spikes in the PVN CRF neurons of repeatedly foot-shocked animals. Thus, rewards suppress stress-induced excitation and bursting in PVN CRF neurons.

Together, these results demonstrate that PVN CRF neurons are activated and inhibited by stressors and rewards, respectively. In line with a role in integrating valence signals, Yuan et al. used afferent-tracing techniques to show that these neurons receive inputs from many stress- and reward-related regions.

Natasha Bray

ORIGINAL ARTICLES Kim, J. et al. Rapid, biphasic CRF neuronal responses encode positive and negative valence. *Nat. Neurosci.* https://doi.org/10.1038/s41593-019-0342-2 (2019) | Yuan, Y. et al. Reward inhibits paraventricular CRH neurons to relieve stress. *Curr. Biol.* https://doi.org/10.1016/j.cub.2019.02.048 (2019)

the netrin receptor DCC in motor axon growth cones. In an explant assay, they found that motor axons lacking p190 grew towards a source of netrin 1, whereas those taken from control mice were unresponsive to netrin 1.

This finding suggested that p190 silences netrin 1 attraction in motor neurons to ensure accurate axon pathfinding. The authors hypothesized that the loss of p190 may cause motor axons to be inappropriately attracted to netrin 1 expressed at the pial surface (where it acts to guide commissural axons) and thus disrupt spinal cord exiting. In support of this idea, mice lacking both p190 and netrin 1 exhibited normal spinal exit. The distal muscle-targeting deficits observed in mice lacking p190 were not rescued by the removal of netrin 1, however, indicating that an alternative function of p190 is involved in this stage of pathfinding. Interestingly, in vivo structure—function analyses revealed that, whereas guidance within the limb was dependent on p190's classical RhoGAP function, a 'non-canonical' RhoGAP-independent activity of p190 regulated motor axon exiting.

Next, the authors considered the mechanism by which p190 might silence netrin 1 attraction during spinal exit. They identified a specific interaction between p190 and the intracellular domain of DCC that restricts the recruitment of the molecular effectors of DCC signalling to the receptor complex, suggesting that p190 might act to prevent signalling downstream of netrin 1–DCC binding.

This study highlights the importance of regulatory mechanisms that suppress responses to irrelevant signals, or 'noise', in a cell's environment. In the case of axon pathfinding, such suppression must be temporary and reversible, to allow the responsiveness of axons to different cues to change as they progress toward their destination; further work is required to identify the mechanisms that gate p190's effects in a time and context-dependent manner.

Katherine Whalley

ORIGINAL ARTICLE Bonanomi, D. et al. p190RhoGAP filters competing signals to resolve axon guidance conflicts. *Neuron* https://doi.org/10.1016/j.neuron.2019.02.034 (2019)

IN BRIEF

NEURAL REPAIR

The mechanics of neural regeneration

The mechanisms underlying neuronal outgrowth after injury are poorly understood. In a *Drosophila* model of neuronal injury, knockout of the gene encoding the fly mechanosensitive ion channel Piezo (DmPiezo) in non-regenerating neurons resulted in substantial axon regrowth not observed in wild-type flies. In a mouse sensory neuron injury model (corneal sensory nerve laser ablation), conditional knockout of the gene encoding PIEZO1 (the mammalian homologue of DmPiezo) drove a relative increase in axon regeneration compared with controls. Thus, PIEZO channels may have an evolutionarily conserved role in inhibiting axon regeneration.

ORIGINAL ARTICLE Song, Y. et al. The mechanosensitive ion channel piezo inhibits axon regeneration. *Neuron* https://doi.org/10.1016/j.neuron.2019.01.050 (2019)

NEUROPSYCHIATRIC DISORDERS

Lightening depression

How light therapy ameliorates depression is not well understood. Here, tracing techniques revealed that the circuit responsible for this effect involves M4-type retinal ganglion cells (RGCs) that project via a disynaptic circuit onto GABAergic neurons in the thalamic ventral lateral geniculate nucleus and intergeniculate leaflet (vLGN/IGL). Projections of these neurons in turn inhibit excitatory neurons of the lateral habenula (LHb). Depressive-like behaviours evoked by chronic exposure to aversive stimuli or social defeat stress were attenuated following activation of this RGC–vLGN/IGL–LHb pathway or by visual light.

ORIGINAL ARTICLE Huang, L. et al. A visual circuit related to habenula underlies the antidepressive effects of light therapy. *Neuron* https://doi.org/10.1016/j.neuron.2019.01.037 (2019)

NEURAL REPAIR

The ins and outs of microglia

In a zebrafish spinal-root injury model that involves complete severing of a peripheral nerve from the cord, microglia were observed using time-lapse imaging to leave the spinal cord and enter the periphery. Once there, they phagocytose debris from the injury site and re-enter the spinal cord in a morphologically changed state, and were observed to emigrate as far as the brain. This emigration required glutamate-mediated activation of NMDA receptors and was regulated by heterotypic interactions with macrophages. These data reveal that rather than being confined to the CNS, microglia can exit and re-enter central regions.

ORIGINAL ARTICLE Green, L. A., Nebiolo, J. C. & Smith, C. J. Microglia exit the CNS in spinal root avulsion. *PLOS Biol.* https://doi.org/10.1371/journal.pbio.3000159 (2019)

AGEING

Reawakening the aged brain

The olfactory bulb (OB) of mice contains neural stem cells (NSCs) that can differentiate into various interneuron subtypes. Here, transcriptomic analysis showed that quiescent NSCs (qNSCs) in young and old mice exhibit similar transcriptional profiles, but that the proportion of qNSCs increases with age. As qNSCs are more resistant to injury-induced activation, they are less able to promote repair in aged brains. The increased proportion of qNSCs with ageing seems to result from locally secreted inflammatory mediators and increased expression of antagonists of WNT signalling.

ORIGINAL ARTICLE Kalamakis, G. et al. Quiescence modulates stem cell maintenance and regenerative capacity in the aging brain. *Cell* https://doi.org/10.1016/j.cell.2019.01.040 (2019)