IN BRIEF

FEEDING

Sodium intake regulation

Low bodily sodium levels can lead to a rise in sodium appetite but how is the drive to ingest sodium regulated to prevent overconsumption of this mineral? Park et al. found that, in mice, 5-hydroxytryptamine receptor 2C-expressing (5HTR2C$^+$) neurons in the lateral parabracial nucleus (LPBN) increased or decreased their activity when bodily sodium levels were high or low, respectively. Moreover, activation of LPBN 5HTR2C$^+$ neurons suppressed sodium intake, whereas their inhibition induced sodium intake, suggesting that these neurons are key regulators of sodium appetite in mice.

ORIGINAL ARTICLE Park, S. et al. A neural basis for tonic suppression of sodium appetite. *Nat. Neurosci.* https://doi.org/10.1038/s41593-019-0573-2 (2020)

NEURAL DEVELOPMENT

Astrocytic cueing of neuronal migration

Interneurons migrate to the visual thalamus from germinal zones in early development, but the underlying mechanisms are not clear. Here, mice lacking retinal ganglion cells, which send inputs to the lateral geniculate nucleus (LGN), exhibited a low number of LGN interneurons, and this was associated with low levels of fibroblast growth factor 15 (FGF15) in the LGN in development. *Fgf15* deletion similarly reduced LGN interneuron number, suggesting that FGF15 acts as a cue in the migratory process. LGN FGF15 was expressed by astrocytes, indicating that retinal inputs regulate the migration via signalling to astrocytes.

ORIGINAL ARTICLE Su, J. et al. Retinal inputs signal astrocytes to recruit interneurons into visual thalamus. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1913053117 (2020)

DENDRITES

Dendritic motors

The kinesin 1 family of motor proteins (KIF5A, KIF5B and KIF5C) has a well-established role in axonal transport, but its function in dendrites is less clear. This study showed that knockdown of KIF5A or KIF5B had different effects on dendritic spine morphogenesis and transport, and postsynaptic currents in cultured hippocampal neurons. Conditional *Kif5b* knockout in mice reduced dendritic spine number in the hippocampus, impaired excitatory transmission and caused learning and memory deficits. Thus, KIF5s show functional diversity, with a key role for KIF5B in dendrites.

ORIGINAL ARTICLE Zhao, J. et al. Specific depletion of the motor protein KIF5B leads to deficits in dendritic transport, synaptic plasticity and memory. *eLife* https://doi.org/10.7554/eLife.53456 (2020)

NEURODEGENERATIVE DISEASE

Modelling Parkinson disease

Here, the authors generated dopamine neurons from induced pluripotent stem cells derived from people with young-onset Parkinson disease (YOPD). Nearly all the neuronal lines exhibited accumulated α-synuclein, widely implicated in PD, and phosphorylated PKCα (pPKCα). Treatment of these cells with PEP005, a PKC agonist that can promote the lysosomal pathway, reduced α-synuclein and pPKCα levels, but its effect on the former was surprisingly via activation of proteasomal degradation. Thus, elevated pPKCα may be a molecular YOPD phenotype and PEP005 may be a therapeutic candidate.

ORIGINAL ARTICLE Laperle, A. H. et al. iPSC modeling of young-onset Parkinson's disease reveals a molecular signature of disease and novel therapeutic candidates. *Nat. Med.* https://doi.org/10.1038/s41591-019-0739-1 (2020)

Credit: JaCZhou/Getty

NEURAL CIRCUITS

A stand-out loop

The paraventricular thalamus (PVT) is involved in arousal and valence processing. However, how this structure is functionally organized is not clear. Gao et al. molecularly, anatomically and functionally characterized two subpopulations of PVT neurons in mice, one of which forms a thalamo-corticothalamic loop with the infralimbic cortex (IL) that regulates arousal.

Through RNA in situ hybridization, the authors examined the expression of transcripts encoding the dopamine D2 receptor (D2R) along the anteroposterior axis of the PVT. The density of *Drd2*-positive cells was higher in the posterior PVT (pPVT) than in the anterior PVT (aPVT). Notably, the authors found that, whereas D2R$^+$ neurons (which the authors called type I neurons), project to the prelimbic cortex, D2R$^-$ neurons (called type II neurons) project to the IL. Thus, these molecularly defined cell classes are also anatomically distinct.

The authors imaged the Ca^{2+} responses of these two neuron types as mice were exposed to various salient stimuli, including aversive stimuli (such as a tail shock) and rewarding stimuli (such as a female mouse). Type I neurons showed increased and decreased Ca^{2+} fluorescence in response to aversive and rewarding stimuli, respectively. By contrast, aversive and rewarding stimuli both reduced Ca^{2+} fluorescence in type II neuronal cell bodies — and their terminals in the IL — suggesting that type II neurons signal salience to the IL.

Labelled projections from the prelimbic cortex and IL were observed to preferentially innervate the pPVT and aPVT, respectively. In support of a PVT–IL–PVT loop, Ca^{2+} fluorescence in IL neurons projecting back to the PVT (IL^{PVT} neurons) was increased by photostimulation of PVT inputs to the IL (PVT^{IL} neurons). Moreover, IL^{PVT} neurons exhibited reductions in Ca^{2+} fluorescence when mice were exposed to aversive or rewarding stimuli. Optogenetic activation of PVT^{IL} neurons attenuated the reductions in IL Ca^{2+} fluorescence associated with aversive or rewarding stimuli, whereas light suppression of PVT^{IL} neurons did not affect salience-induced IL responses. Therefore, salience inhibits activity in this PVT–IL–PVT loop.

The authors reasoned that this loop could be involved in PVT regulation of arousal. Indeed, chemogenetic activation of type II neurons before the onset of the dark period (when mice are typically more awake) reduced wakefulness and promoted non-rapid-eye-movement sleep. Spontaneous or tail-shock-induced dilation of the pupils — a sign of arousal — was associated with reduced Ca^{2+} fluorescence in IL^{PVT} neurons. Photostimulation of the IL^{PVT} neurons attenuated pupil-dilation responses to tail shocks, suggesting that the IL regulates salience-induced arousal.

Overall, this study reveals a PVT–IL–PVT loop that signals salience and regulates arousal.

Natasha Bray

ORIGINAL ARTICLE Gao, C. et al. Two genetically, anatomically and functionally distinct cell types segregate across anteroposterior axis paraventricular thalamus. *Nat. Neurosci.* https://doi.org/10.1038/s41593-019-0572-3 (2020)