CL^{EGR2+} neurons immediately before tones considerably reduced auditory population responses.

In the other study, Jackson et al. used a retrograde virus approach to specifically target claustral neurons projecting to the prefrontal cortex (PFC) in mice (CL → PFC neurons). Optogenetic stimulation of these CL → PFC afferents led to a strong overall inhibition of pyramidal neurons and inhibitory neurons in the PFC. In acute slices, claustrum-stimulated inhibitory responses of prefrontal pyramidal cells were blocked by glutamate receptor antagonists, suggesting that the claustrum inhibits pyramidal cells through inhibitory interneurons. In line with this notion, fast-spiking parvalbumin-expressing (PV^+) interneurons (FS neurons) and neuropeptide Y-expressing interneurons (NPY neurons) were strongly depolarized following photostimulation of CL → PFC afferents.

By analysing pyramidal cell inhibitory postsynaptic potentials (IPSPs), Jackson et al. deduced that 43% of IPSPs driven by claustrum activation were probably mediated by NPY neurons, whereas 35% were mediated by FS neurons and 22% by co-innervation by FS and NPY neurons. Pharmacogenetic silencing of PV^+ neurons (including FS neurons) or NPY neurons greatly reduced the inhibitory responses of pyramidal cells to claustral stimulation. Notably, when NPY neurons were silenced, claustral stimulation even led to excitation of pyramidal cells, suggesting that claustrocortical excitation of pyramidal cells is usually prevented by NPY cell-mediated inhibition.

Together, these studies show that the claustrum provides inhibition to the PFC and auditory cortex, thus shedding light on how the claustrum may regulate cortical function.

Natasha Bray

ORIGINAL ARTICLES Atlan, G. et al. The claustrum supports resilience to distraction. *Curr. Biol.* https://doi.org/10.1016/j.cub.2018.06.068 (2018) | Jackson, J. et al. Inhibitory control of prefrontal cortex by the claustrum. *Neuron* https://doi.org/10.1016/j.neuron.2018.07.031 (2018)

replaced by homomeric GluA1 AMPARs. Sequential confocal microscopy of anti-GluA2 IgG pretreated hippocampal neurons revealed decreased surface expression of GluA2, which was blocked by inhibiting endocytosis during pretreatment. This indicates that anti-GluA2 IgG induces GluA2-containing AMPAR internalization.

The authors examined whether human anti-GluA2 IgG also affected AMPAR signalling in brain tissue by delivering this fraction into mice by intrahippocampal injection. Confocal microscopy of hippocampal slices from these animals revealed downregulation of synaptic GluA2 after injection. Although the treatment did not affect the peak amplitude of electrically evoked EPSCs in granule cells of the dentate gyrus, there was a decrease in the number of single channels and a rise in the conductance of these channels. In addition, when slices from injected mice were treated with a non-GluA2-containing AMPAR inhibitor, there was a decrease in mEPSC amplitudes. A similar decrease was also observed in slices from anti-GluA2 IgG-treated GluA1 knockout mice, which could not compensate for any effects on AMPARs by incorporating GluA1 homomers. Together, these findings again indicate that anti-GluA2 IgG treatment affects AMPAR properties in a way that is consistent with a decrease in GluA2-containing and rise in non-GluA2-containing receptors.

The authors next examined long-term potentiation (LTP) in the Schaffer collateral–CA1 hippocampal pathway after treatment, as LTP is thought to be a key mechanism underlying hippocampal-dependent memory. IgG fraction treatment impaired a postsynaptic component of LTP. Mice that received anti-GluA2 IgG by passive transfer into the brain also showed deficits in memory in an object recognition task.

Together, these data indicate that autoantibodies against GluA2 induce changes in AMPAR subunit composition, which may alter receptor properties, and impair LTP and memory.

Darran Yates

ORIGINAL ARTICLE Haselmann, H. et al. Human autoantibodies against the AMPA receptor subunit GluA2 induce receptor reorganization and memory dysfunction. *Neuron* https://doi.org/10.1016/j.neuron.2018.07.048 (2018)

IN BRIEF

SPATIAL NAVIGATION

Planning a path

Spatial navigation involves co-ordination between action planning by the prefrontal cortex and spatial representation of the environment in the hippocampus. In this study, when rats performed an alternating arm choice task in a T maze, the coordination of the timing of spikes between neurons in the medial prefrontal cortex (mPFC), the thalamic nucleus reuniens (NR) and the hippocampal CA1 was found to increase; co-ordinated firing between supramammillary nucleus (SUM) and CA1 neurons also increased. Silencing of SUM neurons decreased spike-time coordination in the mPFC-NR-CA1 circuit and impaired representations of the trajectory of travel in NR and CA1, suggesting that SUM modulates the communication of action planning information from the mPFC to downstream targets.

ORIGINAL ARTICLE Ito, H. T. et al. Supramammillary nucleus modulates spike-time coordination in the prefrontal-thalamo-hippocampal circuit during navigation. *Neuron* **99**, 576–587 (2018)

TECHNIQUES

Catching waves

Measurement of changes in intra-axonal calcium with high temporal and spatial resolution has been technically difficult. Now, a technique has been developed that enables the genetically encoded calcium indicator GCaMP6 to be transported into axons, where calcium fluctuations can be monitored with high signal-to-noise ratio, brightness and stability. This approach was used to measure layer-specific axon activity in mouse cortex at deeper cortical levels than was previously possible.

ORIGINAL ARTICLE Broussard, G. J. et al. In vivo measurement of afferent activity with axon-specific calcium imaging. *Nat. Neurosci.* **21**, 1272–1280 (2018)

NEURODEGENERATIVE DISEASE

Untangling tau structure

The human form of tau exists in isoforms that contain either three (3R) or four (4R) microtubule-binding repeats. Tau can also form filamentous aggregates, which are a hallmark of Alzheimer disease and Pick disease. In this study, cryo-electron microscopy was used to investigate tau structure in these aggregates. The folded structure of tau that aggregates in patients with Pick disease was found to be distinct from that found in patients with Alzheimer disease, which might contribute to the distinct neuropathological phenotypes of these disorders.

ORIGINAL ARTICLE Falcon, B. et al. Structures of filaments from Pick's disease reveal a novel tau protein fold. *Nature* **561**, 137–140 (2018)

NEURONAL CELL BIOLOGY

Novel inhibition

Recent technological advances have enabled ever more detailed characterizations of neuronal subtypes. Here, immunohistochemistry and unbiased single-nucleus RNA sequencing was used to identify several human cortical GABAergic neuronal subtypes that possess distinct molecular signatures and transcriptomes. One notable subtype had 'rosehip'-like axonal boutons and inhibited backpropagating action potentials in pyramidal neuron dendrites; these neurons are thus likely to be involved in local regulation of dendritic computation.

ORIGINAL ARTICLE Boldog, E. et al. Transcriptomic and morphophysiological evidence for a specialized human cortical GABAergic cell type. *Nat. Neurosci.* **21**, 1185–1195 (2018)