component analysis revealed that *Zfp189* preferentially influenced the pink module over other modules, confirming the relationship between *Zfp189* and the pink module that was indicated by WGCNA.

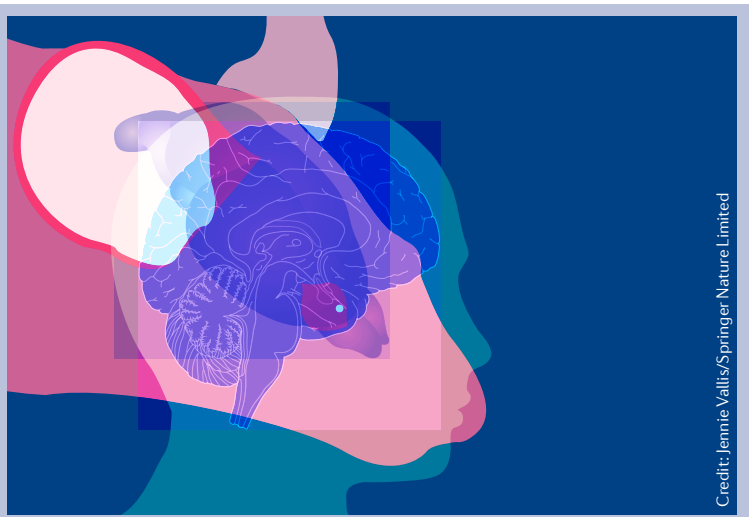
Next, using in silico approaches, the authors identified cyclic AMP response element binding protein (CREB) as a potential upstream regulator of pink module genes. CREB is implicated in MDD and in animal models of depression, and they also observed, by analysing published data, that phosphorylated CREB–*Zfp189* binding is reduced upon CSDS and that antidepressants reversed this reduction, further suggesting that CREB acts upstream of the pink module. Indeed, mice in which *Creb1* was knocked out in PFC neurons, but not control mice, had behavioural deficits after a subthreshold social defeat procedure; overexpressing *Zfp189* rescued this effect. Additionally, *Zfp189* levels were reduced in *Creb1* knockout mice, suggesting that *Zfp189* is upregulated by CREB in PFC neurons.

In fact, CREB may directly interact with *Zfp189*, as CRISPR-mediated targeting of constitutively active CREB selectively to the *Zfp189* promoter in PFC neurons induced *Zfp189* expression and increased resilience to CSDS-induced behavioural impairments as compared with controls. Targeted CREB–*Zfp189* interactions also induced the expression of pink module genes in mice exposed to social defeat. Thus, in mice, CREB–*Zfp189* interactions in the PFC drive a transcriptional network that increases resilience to stress.

As the authors found *ZNF189* mRNA to be reduced in the PFC of post-mortem brains from individuals with MDD compared with control brains, and *CREB1* and *ZNF189* mRNA levels were most highly correlated in control brains, CREB- *ZFP189* interactions in the PFC may be reduced in MDD as well as in CSDS.

Katharine H. Wrighton

ORIGINAL ARTICLE Lorsch, Z. S. et al. Stress resilience is promoted by a Zfp189-driven transcriptional network in prefrontal cortex. *Nature Med.* https://doi.org/10.1038/s41593-019-0462-8 (2019)



Credit: Jennie Vallis/Springer Nature Limited

types, some divergent gene expression was observed, particularly among neurotransmitter receptors, ion channels and extracellular matrix components. As these genes have important roles in neuronal function and connectivity, these differences are likely to be functionally relevant.

These findings show conserved aspects of mouse and human cortex, but also potentially crucial differences, suggesting potential problems with hypotheses about human brain function that are generated on the basis of mouse data and emphasizing the importance of studying human cortical tissue directly when possible.

Sian Lewis

ORIGINAL ARTICLE Hodge, R. D. et al. Conserved cell types with divergent features in human versus mouse cortex. *Nature* https://doi.org/10.1038/s41586-019-1506-7 (2019)

IN BRIEF

CEREBRAL CORTEX

Aversive adaptations

The capacity to adapt behaviour in response to threats is essential for survival and requires both the integration of internal and external stimuli and the selection and execution of appropriate responses. Gehrlach et al. show that, in mice, the posterior insular cortex (pIC) has a central role in the detection and integration of aversive emotional and bodily states and regulates related motivated behaviours in a top-down manner through its projections to subcortical brain regions.

ORIGINAL ARTICLE Gehrlach, D. A. et al. Aversive state processing in the posterior insular cortex. *Nat. Neurosci.* **22**, 1424–1437 (2019)

CELL BIOLOGY OF THE NEURON

A platform for coordinated signalling

Super-resolution imaging studies have revealed the presence of a membrane-associated periodic skeleton (MPS) structure, composed of actin, spectrin and associated proteins, in the axons and dendrites of neurons; however, the function of the MPS is unclear. Zhou et al. used stochastic optical reconstruction microscopy (STORM) in cultured mouse neurons to show that, upon extracellular stimulation, the MPS serves as a signalling platform for the co-localization of various signalling molecules, enabling the transactivation of receptor tyrosine kinases and induction of downstream signalling pathways.

ORIGINAL ARTICLE Zhou, R. et al. Membrane-associated periodic skeleton is a signaling platform for RTK transactivation in neurons. *Science* **365**, 929–934 (2019)

TECHNIQUES

Accelerating reconstruction

Obtaining a map of brain connectivity at the single-neuron level is an ongoing goal in neuroscience; however, current axonal tracing methods are limited by the time required to manually reconstruct projections from stacks of microscopy images. Winnubst et al. have now boosted the efficiency of this process through the development of a semi-automated pipeline for brain-wide two-photon imaging and neuronal reconstruction. Using this approach in mice, they have created an online database of over 1,000 reconstructed neurons, identified projection cell types and provided insight into the principles of brain connectivity.

ORIGINAL ARTICLE Winnubst, J. et al. Reconstruction of 1,000 projection neurons reveals new cell types and organization of long-range connectivity in the mouse brain. *Cell* https://doi.org/10.1016/j.cell.2019.07.042 (2019)

NEURAL REPAIR

Reprogramming astrocytes for repair

Previous studies have shown that reactive glial cells in the cortex can be reprogrammed to produce neurons after injury in vivo, but whether these induced neurons can adequately replace or compensate for the lost neurons is unknown. Mattugini et al. find that virally driven expression of two proneural factors, neurogenin 2 and NURR1, in mouse cortical astrocytes located in the cortical grey matter is sufficient to reprogram the cells into neurons after a stab wound injury. Importantly, the induced neurons exhibited molecular and morphological hallmarks of cortical pyramidal neurons that were appropriate to the cortical laminae in which they were located and formed long-distance axonal projections to relevant downstream brain regions.

ORIGINAL ARTICLE Mattugini, N. et al. Inducing different neuronal subtypes from astrocytes in the injured mouse cerebral cortex. *Neuron* https://doi.org/10.1016/j.neuron.2019.08.009 (2019)