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IN BRIEF

NEURODEVELOPMENTAL DISORDERS

Rescue strategy

Mutations in SH3 and multiple ankyrin repeat domains protein 3 (*SHANK3*) are associated with several neurodevelopmental disorders, but it is not known whether correcting SHANK3 levels in the mature CNS would alleviate synaptic impairments in rodents carrying *Shank3* mutations. Mei ***et al.*** generated a mouse, lacking constitutive expression of *Shank3*, in which the gene could be conditionally knocked-in at specific time points. Knock-in of *Shank3* in these mice during adulthood restored levels of synaptic proteins and corrected physiological impairments in striatal neurons, and rescued impairments in social behaviour. In a different approach, Bidinosti ***et al.*** characterized the dysregulation of phosphoprotein expression that occurs in rat cortical neurons that lack *Shank3* and showed that the expression of CDC-like kinase 2 (CLK2) was upregulated in these cells. Pharmacological inhibition of CLK2 corrected synaptic deficits in brain slices from adult mice carrying a mutation in exon 21 of *Shank3* and rescued impairments in social behaviour in these mice. Together, these findings suggest that adulthood restoration of SHANK3 levels, or restoration of downstream mediators, may be a useful strategy to alleviate some of the synaptic and behavioural impairments associated with *SHANK3* mutations.

ORIGINAL ARTICLES Mei, Y. *et al.* Adult restoration of *Shank3* expression rescues selective autistic-like phenotypes. *Nature* http://dx.doi.org/ 10.1038/nature16971 (2016) | Bidinosti, M. *et al.* CLK2 inhibition ameliorates autistic features associated with SHANK3 deficiency. *Science* http://dx.doi.org/ 10.1126/science.aad5487 (2016)

EMOTION

Waves of fear

Long-range synchronization of neural activity is thought to contribute to fear behaviour. Karalis ***et al.*** show in mice that sustained synchronized 4 Hz oscillations in the dorsal medial prefrontal cortex (dmPFC) and the basolateral amygdala (BLA) predict internally generated freezing behaviour (in the absence of a cue) and cue-induced freezing behaviour following fear conditioning training, but they do not predict periods of passive immobility that occur prior to fear conditioning. Individual neurons in the dmPFC and BLA synchronized their firing to 4 Hz oscillations during freezing behaviour following fear conditioning, and optogenetically driving dmPFC neuronal activity at 4 Hz increased the number of freezing bouts. 4 Hz oscillations in the prefrontal–amygdala circuit may therefore be involved in the initiation and maintenance of fear behaviour.

ORIGINAL ARTICLE Karalis, N. *et al.* 4-Hz oscillations synchronize prefrontal–amygdala circuits during fear behavior. *Nat. Neurosci.* http://dx.doi.org/10.1038/nn.4251 (2016)

GLIA

Identity-driven

Astrocytes are heterogeneous, but how their identity is maintained in the adult brain is not clear. Here, it was shown that in the mature mouse cerebellum, sonic hedgehog (SHH) is produced by neurons. Furthermore, SHH is required for maintaining the molecular characteristics of Bergmann glial cells (BGs; one of two types of cerebellar astrocytes), as selective knockout of the SHH transducer smoothened in BGs reduced the expression of characteristic BG genes. Conversely, induction of SHH signalling in velate astrocytes (the other major astrocyte type in the cerebellum) caused them to become more BG-like. Thus, in the mature CNS, astrocyte identity is flexible and is determined, in part, by neuron-derived cues.

ORIGINAL ARTICLE Farmer, W. T. *et al.* Neurons diversify astrocytes in the adult brain through sonic hedgehog signaling. *Science* **351**, 849–854 (2016)