IN BRIEF

PSYCHIATRIC DISORDERS

GluN2B mediates ketamine's antidepressant effect

The cellular mechanisms underlying the rapid antidepressant effects of the NMDA receptor (NMDAR) antagonist ketamine are not well understood. Miller et al. showed that mice lacking the NMDAR subunit GluN2B from principal cortical neurons showed reduced despair-like behaviour and that ketamine had no antidepressant effects in these mice. Ketamine increased excitatory synaptic transmission in prefrontal cortex slices from control mice; this effect was mimicked in untreated slices lacking GluN2B, and ketamine had no additional effect on synaptic transmission in these slices. Furthermore, the authors showed that GluN2B-containing NMDARs are tonically activated by ambient glutamate, which could explain why the nonselective NMDAR antagonist ketamine seems to have a GluN2B-selective effect. These data indicate that a suppression of tonic GluN2B activation in cortical neurons could underlie the antidepressant effects of ketamine.

ORIGINAL RESEARCH PAPER Miller, O. H. *et al*. GluN2B-containing NMDA receptors regulate depression-like behavior and are critical for the rapid antidepressant actions of ketamine. *eLife* http://dx.doi.org/10.7554/eLife.03581 (2014)

🔁 GLIA

Glial ankyrins function at the junction

The mechanisms involved in the assembly and maintenance of paranodal axon-glial junctions that flank nodes of Ranvier are not completely understood. Rasband and colleagues showed that the scaffolding proteins ankyrin B (ANKB) and ankyrin G (ANKG) are enriched on the glial, rather than the neuronal side of paranodal junctions in the peripheral nervous system (PNS) and CNS, respectively. Experiments in mice lacking ANKB or ANKG in myelinating glia (Ankb-cKO mice and Ankg-cKO mice, respectively) showed that ANKB is not required for paranodal junction assembly, function or maintenance in the PNS, but that ANKG is important for rapid junction assembly during CNS myelination. In the CNS of Ankg-cKO mice, ANKB could partially compensate for the loss of paranodal ANKG. In a second paper, Rasband and colleagues show that another ankyrin, ANKR, is expressed in myelinated axons and that ANKR can substitute for ANKG in its role in Na⁺-channel clustering at nodes of Ranvier. These studies provide new insight into the functional roles of ankyrins at nodes and paranodes.

ORIGINAL RESEARCH PAPERS Chang, K.-J. et al. Glial ankyrins facilitate paranodal axoglial junction assembly. Nature Neurosci. <u>http://dx.doi.org/10.1038/nn.3858</u> (2014) | Ho, T. S.-Y. et al. A hierarchy of ankyrin-spectrin complexes cluster sodium channels at nodes of Ranvier. Nature Neurosci. <u>http://dx.doi.org/10.1038/nn.3859</u> (2014)

NEUROGENESIS

Fat cells send messages to the brain

The adipocyte-secreted protein adiponectin (ADN) has anti-inflammatory and antidiabetic peripheral effects, similarly to exercise. Investigating a possible link between the effects of exercise and ADN on the brain in mice, Yau *et al.* showed that ADN can pass the blood–brain barrier and that running increased hippocampal ADN levels. Peripheral or central ADN administration reduced depression-like behaviour and promoted hippocampal cell proliferation. Running had the same effects, but not in mice lacking ADN. *In vitro*, the proliferation-promoting effect of ADN was mediated by ADN receptor 1. These data indicate that ADN mediates the neurogenesispromoting and antidepressant effects of exercise.

ORIGINAL RESEARCH PAPER Yau, S. Y. et al. Physical exercise-induced hippocampal neurogenesis and antidepressant effects are mediated by the adipocyte hormone adiponectin. Proc. Natl Acad. Sci. USA 111, 15810–15815 (2014)