Nature Reviews Neuroscience | Published online3 Jun 2016

IN BRIEF

DEPRESSION

Breaking down ketamine's actions

Ketamine's usefulness as an antidepressant is limited by side effects, including abuse potential and sensory dissociation, and its mechanism of action remains unclear. Here, the authors show that ketamine mediates its antidepressant activity not through NMDA receptor inhibition, as previously assumed, but by boosting AMPA receptor activation. Furthermore, its metabolite (2*R*,6*R*)-hydroxynorketamine is shown to have potent and rapid antidepressant activity in mouse models of depression, and to lack ketamine-related side effects, suggesting a new approach to the development of rapidly acting antidepressants.

ORIGINAL ARTICLE Zanos, P. *et al.* NMDAR inhibition-independent antidepressant actions of ketamine metabolites. *Nature* http://dx.doi.org/10.1038/nature17998 (2016).

NEURODEVELOPMENTAL DISORDERS

Zika virus causes brain defects in mice

The Brazilian Zika virus ($ZIKV^{BR}$) outbreak has been linked to increased incidence of microcephaly; however, *in vivo* evidence for the effects of $ZIKV^{BR}$ on brain development is lacking. The authors show that pups born to SJL mice infected with $ZIKV^{BR}$ during pregnancy exhibit neuronal cell death and reduced cortical thickness as well as altered expression of autophagy- and cell death-related genes. $ZIKV^{BR}$ infection of human-derived neurospheres and cerebral organoids also impaired neural development and increased cell death. These models provide further evidence for the detrimental effects of $ZIKV^{BR}$ on cortical development and might enable the testing of strategies to counter the effects of the virus.

ORIGINAL ARTICLE Cugola, F. R. *et al.* The Brazilian Zika virus strain causes birth defects in experimental models. *Nature* http://dx.doi.org/10.1038/nature18296 (2016).

TECHNIQUES

A CRISPR method of localization

Genome editing using the CRISPR–Cas9 system allows the manipulation of specific genes. Mikuni *et al.* use this approach to insert sequences encoding protein tags into genes of interest in neural progenitors in the embryonic mouse brain, enabling them to map endogenous protein localization in the adult brain with high resolution and specificity. They further show that the system has potential for multiplex labelling, ultrastructual imaging and live imaging of protein dynamics.

ORIGINAL ARTICLE Mikuni, T. *et al.* High-throughput, high-resolution mapping of protein localization in mammalian brain by *in vivo* genome editing. *Cell* http://dx.doi.org/10.1016/j.cell.2016.04.044 (2016).

NEUROENDOCRINOLOGY

Switching on puberty

Puberty onset is coordinated by gonadotropin-releasing hormone (GnRH)-secreting hypothalamic neurons. Here, the authors show that impairing microRNA (miRNA) synthesis causes hypergonadism and sterility in mice. They find that two key miRNAs — miR-200 and miR-155 — target genes that control the activity of the *Gnrh* promoter. By modulating the balance between inductive and repressive signals these miRNAs precisely time the surge in GnRH that drives puberty onset.

ORIGINAL ARTICLE Messina, A. *et al.* A microRNA switch regulates the rise in hypothalamic GnRH production before puberty. *Nat. Neurosci.* http://dx.doi.org/10.1038/nn.4298 (2016).