RESEARCH HIGHLIGHTS

IN BRIEF

NEURODEGENERATIVE DISORDERS

Tackling TAUxicity

It has recently been shown that acetylation of soluble tau oligomers is increased in the brains of people with mild-to-moderate Alzheimer disease (AD). This study shows that, in a mouse model of AD and also in human AD, acetylation of tau at the K174 residue is a key pathological change that increases tau accumulation. In a mouse model of frontotemporal dementia, inhibition of tau acetylation reduced tau accumulation and behavioural deficits, suggesting that inhibiting tau acetylation might have therapeutic potential in these disorders.

ORIGINAL RESEARCH PAPER Min, S. W. *et al.* Critical role of acetylation in tau-mediated neurodegeneration and cognitive deficits. *Nat. Med.* <u>http://dx.doi.org/10.1038/nm.3951</u> (2015)

NEUROPHARMACOLOGY

Old and young

The involvement of dentate gyrus (DG) neurogenesis in the antidepressant action of selective serotonin reuptake inhibitors (SSRIs) is not known. The effects of the SSRI fluoxetine on the hypothalamic–pituitary–adrenal axis and on anxiety-like behaviours were reduced in mice following deletion of serotonin 1A receptor (5-HT1AR) from mature DG granule cells (DGGCs), but not in mice lacking 5-HT1AR selectively in new, adult-born DGGCs. Conversely, selective expression of 5-HT1ARs exclusively in DGGCs resulted in normal behavioural, neuroendocrine and neurogenic responses to fluoxetine, suggesting that DGGCs expressing 5-HT1AR are sufficient to mediate the effects of this drug.

ORIGINAL RESEARCH PAPER Samuels, B. A. et al. 5-HT1A receptors on mature dentate gyrus granule cells are critical for the antidepressant response. *Nat. Neurosci.* http://dx.doi.org/10.1038/nn.4116 (2015)

COMPUTATIONAL NEUROSCIENCE

Mind over matter

Brain-machine interface technology needs to be improved before it can be more widely used as a solution for limb paralysis. Prosthesis-connected electrode microarrays were implanted in the brains of two people with amyotrophic lateral sclerosis. Brain activity occurring during imagined finger movements was decoded with an algorithm and was used to control the movement of a computer cursor. The performances of the patients in this task were improved using the new algorithm compared with when they were tested using the previously available algorithm.

ORIGINAL RESEARCH PAPER Gilja, V. et al. Clinical translation of a high-performance neural prosthesis. Nat. Med. http://dx.doi.org/10.1038/nm.3953 (2015)

LEARNING AND MEMORY

Neurotrophic memory

G protein-coupled oestrogen receptor 1 (GPER1) is expressed in hippocampal dendritic spines and axon terminals, but its role in long-term depression (LTD) is not known. Here, 17β -estradiol (E2) activation of GPER1 in CA3 resulted in the release of brain-derived neurotrophic factor and the local translation of activity-regulated cytoskeleton-associated protein (ARC). This increase in ARC levels led to the internalization and proteasome-mediated degradation of GluA1-containing AMPA receptors, and LTD, thus revealing a novel way in which E2 can mediate synaptic plasticity in the hippocampus.

ORIGINAL RESEARCH PAPER Briz, V. *et al*. A novel form of synaptic plasticity in field CA3 of hippocampus requires GPER1 activation and BDNF release. *J. Cell Biol.* **210**, 1225–1237 (2015)