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IN BRIEF

LEARNING AND MEMORY

Childhood problems and solutions

As children grow up, they switch from procedure-based to memory-based strategies for problem solving. However, the changes in brain circuitry underlying this switch are unknown. In a functional MRI analysis of 7–9-year-old children who were asked to solve simple addition problems (such as 3 + 5 =?), the authors found that the switch to memory-based strategies involved an increase in hippocampal activity, a decrease in prefrontal–parietal activity and increased hippocampus–neocortex connectivity. The efficiency of the memory-based strategy continued to improve through adolescence and into adulthood. This finding highlights the importance of functional reorganization in the hippocampus and neocortex during this developmental period.

ORIGINAL RESEARCH PAPER Qin, S. *et al.* Hippocampal-neocortical functional reorganization underlies children's cognitive development. *Nature Neurosci.* **17**, 1263–1269 (2014)

PAIN

Inflammation and pain

Spinal cord injury (SCI) results in inflammatory changes in the brain, but whether these changes underlie the effects of SCI on cognition is not known. Wu *et al.* showed that mice with SCI had memory deficits and depression-like behaviour. These behavioural changes were associated with increased microglial activation and, 12 weeks later, with neuronal loss in the hippocampus and cortex. Cell cycle genes were also upregulated in these brain areas. Chronic increases in cell cycle activation leads to neuronal cell death, and these data suggest that the therapeutic window for treating SCI might be longer than previously thought.

ORIGINAL RESEARCH PAPER Wu, J. *et al.* Spinal cord injury causes brain inflammation associated with cognitive and affective changes: role of cell cycle pathways. *J. Neurosci.* **34**, 10989–1006 (2014)

NEURODEGENERATIVE DISEASE

Hypermethylation raises AD risk

Drugs that modify DNA methylation have been shown to alter Alzheimer's disease (AD) pathology in animal models. Two recent studies therefore investigated whether DNA methylation underlies some of the changes in gene expression that occur in AD, De Jager *et al.* performed gene discovery analysis, comparing autopsied brain tissue from patients with AD with that from control individuals. They found 71 CpG dinucleotides in which the level of methylation correlated with the severity of AD neuropathology. Moreover, several of the genes located near the hypermethylated CpG dinucleotides, including *ANK1*, were members of a group of genes known to confer susceptibility for AD. *ANK1* was the focus of the second, related study. Lunnon *et al.* showed in post-mortem cortical brain tissue from patients with Alzheimer's disease that CpG sites in *ANK1* were hypermethylated (compared with controls). The hypermethylation was associated with neuropathological changes in areas of the cortex typically affected in AD, but not the cerebellum, which is usually protected in AD. Because these DNA methylation patterns were observed in presymptomatic patients as well as those with the disease, they might play a part in both the onset and neuropathology of AD.

ORIGINAL RESEARCH PAPERS De Jager, P. L. *et al.* Alzheimer's disease: early alterations in brain DNA methylation at *ANK1*, *BIN1*, *RHBDF2* and other loci. *Nature Neurosci.* **17**, 1156–1163 (2014) | Lunnon, K. *et al.* Methylomic profiling implicates cortical deregulation of *ANK1* in Alzheimer's disease. *Nature Neurosci.* **17**, 1164–1170 (2014)