HIGHLIGHTS

IN BRIEF

ADDICTION

The role of withdrawal in heroin addiction: enhances reward or promotes avoidance?

Hutcheson, D. M. *et al. Nature Neurosci.* **4**, 943–947 (2001)

Hutcheson *et al.* investigated whether compulsive drug seeking in heroin addiction is driven by avoidance of withdrawal symptoms, or by enhancement of the incentive value of the drug during withdrawal owing to an alteration in motivational state. In support of the latter idea, they found that rats in heroin withdrawal showed enhanced drug-seeking behaviour only if they experienced heroin during the withdrawal episode. Such experience would have allowed them to learn about the enhanced incentive value of the drug.

SYNAPTIC PHYSIOLOGY

NMDA receptor-mediated Na⁺ signals in spines and dendrites.

Rose, C. R. & Konnerth, A. *J. Neurosci.* **27**, 4207–4214 (2001)

One of the functions of dendritic spines is to compartmentalize signals arising from synaptic transmission. So, for example, calcium transients have been observed in active spines. Rose and Konnerth have now used two-photon sodium imaging to show that synaptic transmission can also lead to local transient increases in sodium concentration, which are mediated by entry of sodium ions through NMDA receptors. This sodium signal might influence the electrical and biochemical characteristics of the spine.

PAIN

Proteinase-activated receptor-2 and hyperalgesia: a novel pain pathway.

Vergnolle, N. *et al. Nature Med.* **7**, 821–826 (2001)

Proteinase-activated receptor 2 (PAR2) is expressed by primary spinal afferent neurons, and PAR2 agonists can cause acute inflammation. Vergnolle *et al.* show that activation of peripheral PAR2s by sub-inflammatory doses of agonists lowers the pain threshold to subsequent thermal or mechanical stimuli. The agonists upregulate Fos expression in the spine, and the hyperalgesia is mediated by a pathway that includes substance P and prostaglandins. Proteinase inhibitors or PAR2 antagonists might therefore be potentially useful for the management of pain.

COGNITION

Electrophysiological correlates of emotion-induced recognition bias.

Windmann, S. & Kutas, M. *J. Cogn. Neurosci.* **13**, 577–592 (2001)

Subjects show a higher rate of false positives for emotional stimuli than for neutral stimuli on recognition tests. Windmann and Kutas studied event-related potentials (ERPs) from subjects in such tasks, and found that there was a marked effect of emotional valence on early prefrontal ERPs for items rated as old. Neutral items rated as old showed a strong old/new difference, whereas negative items did not. The data support the theory that prefrontal cortex may relax the criteria for retrieval of negative stimuli.

DEVELOPMENT

Going off at a tangent

Many of the interneurons that populate the cortex and striatum of the mammalian brain migrate tangentially from a region of the basal telencephalon called the medial ganglionic eminence (MGE). The guidance mechanisms for tangential migration are only just beginning to be understood, and one important question that has emerged is: how do the interneurons destined for the cortex avoid becoming sequestered by the striatum during their journey? Marín *et al.* have provided a possible answer to this question, by showing that the striatum provides an exclusion zone for cortical interneurons.

The authors took MGE tissue from mice expressing green fluorescent protein, transplanted it into the MGE of a wild-type brain slice, and tracked the tangential migration of neurons. This tissue contains a large number of cells that subsequently become GABA-expressing interneurons and migrate to the cortex. The results showed that these cells never enter the striatum, and they also avoid ectopic striatal tissue that is transplanted into the cortex.

What is the molecular basis for this exclusion? Marín *et al.* showed that, during the period when cells are migrating tangentially into the cortex (embryonic day 12–16), the striatum expresses the chemorepellents semaphorin 3A and 3F (Sema3A and Sema3F). The semaphorin receptors neuropilin 1 and neuropilin 2 are expressed in many of the interneurons that migrate into the cortex, but not in those that enter the striatum. To test whether the semaphorins are responsible for excluding the cortical interneurons, the authors transplanted fibroblasts expressing Sema3A, Sema3F or both into the corticostriatal boundary. This prevented interneurons from entering the cortex, and the cells even turned their leading processes away from it. The involvement of neuropilins was confirmed by studying the neuropilin 2 knockout mouse, in which many interneurons fail to reach the cortex and instead colonize the striatum. Also, in slice-culture experiments, expression of a dominant-negative form of neuropilin 1 in migrating interneurons increased the number of cells that entered the striatum.

Marín *et al.* propose that neuropilins and semaphorins are responsible for sorting striatal and cortical interneurons. They suggest that the interneurons destined for the striatum either never express neuropilins, or downregulate them before they begin to migrate. This study not only provides evidence that chemorepulsion is one of the mechanisms that keeps tangentially migrating cortical interneurons on course, but also points to a mechanism that sorts migrating neurons to distinct target zones.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Marín, O. *et al.* Sorting of striatal and cortical interneurons regulated by semaphorin–neuropilin interactions. *Science* **293**, 872–875 (2001)

FURTHER READING Maricich, S. M. *et al.* The role of tangential migration in the establishment of mammalian cortex. *Neuron* **31**, 175–178 (2001)