FUNCTIONAL NEUROIMAGING

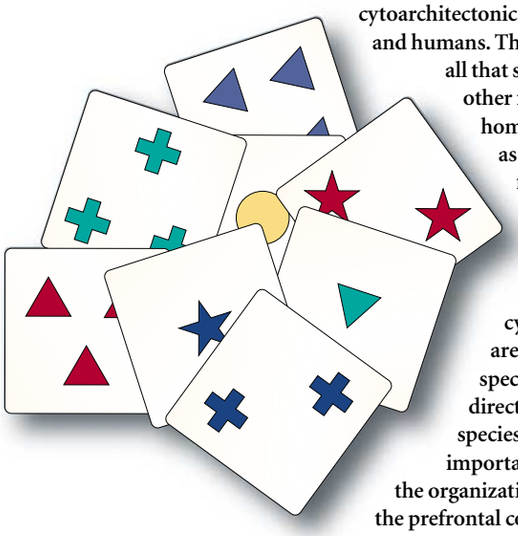
Of monkeys and men

Studies of cortical function in primates have traditionally relied on a combination of electrophysiology in monkeys and functional imaging in humans. But this makes it hard to know how reliably we can extrapolate results from monkeys to humans. Recent technical advances have made it possible to use functional imaging in monkeys, and a new study by Nakahara *et al.* takes advantage of this to revisit a favourite test of cognitive psychologists — the Wisconsin Card Sorting Test (WCST).

The WCST is used to measure behavioural flexibility — subjects have to sort cards by a single feature (for example, colour) and then, without warning, 'shift set' to sort them by a different feature (perhaps the shapes shown on the cards). The group set out to compare directly the brain activation produced by this task in monkey and human brains. The method used to record activation — functional magnetic resonance imaging (fMRI) — was the same for the two sets of subjects, and the task design was also identical.

We know that 'set shifting' involves the prefrontal cortex, because patients with damage to prefrontal cortex often 'perseverate' — they carry on sorting the cards by a particular feature even when they have been told that it is incorrect. So, Nakahara and colleagues used this task to compare the functional organization of the prefrontal cortex in monkeys and humans.

They found that the parts of the prefrontal cortex that were activated by set shifting — which can therefore be considered to be functionally homologous — were in the same cytoarchitectonic areas in monkeys and humans. This might not seem all that surprising, but other functionally homologous areas, such as the frontal eye fields (which are involved in the control of eye movements), are located in different cytoarchitectonic areas in the two species. So, this kind of direct comparison across species will be very important for the study of the organization and evolution of the prefrontal cortex.



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SYNAPTIC PLASTICITY

Tag! You're it!

Several forms of long-term synaptic plasticity require the synthesis of new proteins. Although some of these proteins might be synthesized locally, others have to travel from the cell body to the synapse. At the same time, long-term plasticity shows specificity — only active synapses undergo the plastic change. These two observations have raised a key question: how can the change in efficacy be restricted only to the active inputs if protein synthesis is a cell-wide phenomenon that could affect every synapse? Experiments in *Aplysia* and hippocampal neurons have led researchers to suggest the existence of a 'synaptic tag' that marks active synapses so that, for example, newly synthesized proteins can be appropriately targeted to those contacts. Although the evidence in favour of this idea is compelling, the identity of the tag remains a mystery.

The crayfish neuromuscular junction also shows a form of plasticity that depends solely on presynaptic changes — long-term facilitation (LTF). By studying the mechanisms that underlie LTF and their interaction with another form of plasticity (cyclic-AMP-induced synaptic enhancement), Beaumont, Zucker and colleagues have established that hyperpolarization-activated (I_h) cation channels and actin are key components of a synaptic tag at this synapse.

The authors first showed that the induction of both LTF and cAMP-induced synaptic enhancement required I_h activation, which, in the case of LTF, depended on the electrogenic action of a Na^+/K^+ ATPase and was sensitive to actin depolymerization. But although both forms of plasticity showed I_h dependence, Beaumont *et al.* found that they were not identical: the induction of one of them did not interfere with the induction of the other, as would be expected if they were expressions of the same phenomenon. The authors took advantage of this fact to explore how both forms of plasticity interact, focusing on one question: can the activation of I_h channels by the induction of LTF mark ('tag') synapses so that it is possible to elicit the cAMP-induced enhancement even in the presence of I_h blockers? They found that, indeed, if LTF was induced, then blocking I_h channels during the application of cAMP did not prevent a subsequent synaptic enhancement. Moreover, actin depolymerization was also ineffective in preventing the cAMP-induced enhancement if LTF had been induced as long as one hour earlier.

The physiological meaning of the interaction between these forms of plasticity is uncertain, but the data strongly support the existence of synaptic tags and provide a good lead to their molecular identity. Although long-term plasticity at *Aplysia* and hippocampal synapses seems to require postsynaptic rather than presynaptic tags, it will now be important to test whether similar principles are at work in these other systems.

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