PRIMATE COGNITION

From a Jack to a King

Imagine you are at the theatre and the magician calls you up onto the stage to participate in a simple game. He first offers you two playing cards (Jack and King) and asks you to mentally select one, which you do (Jack), and receive a small reward. A short interval later, he again offers you the same two cards (Jack and King), but this time he asks you to mentally select the one that you did not select earlier to receive another reward. To perform this task, all you have to do is maintain the identity of your first choice in your visual working memory during the delay between the first presentation trial and the second test trial. This requires the maintenance of information in working memory. The only real difficulty you are likely to encounter with this type of test is if the delay between the trials increases beyond your ability to recall the events.

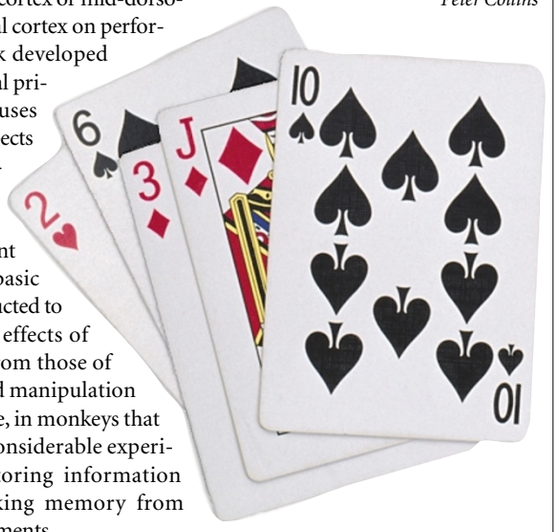
Now imagine that the magician changes the game and offers you five cards (Ten, Two, Jack, Three, Six) and asks you to mentally select a different card on each of five subsequent trials, all of which have a very short delay between each selection. What you would probably do in this situation is memorize all the cards before you make your first selection. You would then have to maintain and monitor the fact that some cards have been selected and some others have not been selected as you make successive choices to avoid selecting the same card on more than one occasion. This type of memory is called self-ordered searching and requires monitoring and manipulation of information in addition to maintenance of information in working memory.

A central question in working memory research concerns how and where in the brain these two components of visual working memory — maintenance and monitoring of information — are processed. One theory suggests that the maintenance of information in visual working memory occurs in the areas of anterior inferotemporal cortex that specialize in processing visual memory and that the more executive processes of monitoring and manipulating that information occur in the mid-dorsolateral region of the prefrontal cortex. However, this is an area of considerable debate in both the experimental primate and functional imaging literatures.

A recent study by Michael Petrides provides strong support for this theory by directly comparing the effects of lesions to either the anterior inferotemporal cortex or mid-dorsolateral prefrontal cortex on performance of a task developed for experimental primates that focuses on these two aspects of visual working memory. A key element of the experiment was that the basic task was constructed to tease apart the effects of maintenance from those of monitoring and manipulation on performance, in monkeys that had acquired considerable experience of monitoring information in visual working memory from previous experiments.

The results demonstrated that increasing the delay during which the information had to be maintained in visual working memory impaired the performance of monkeys after lesions to anterior inferotemporal cortex, but not after lesions to the mid-dorsolateral prefrontal cortex. In contrast, increasing the number of stimuli that had to be monitored impaired the performance of monkeys with lesions to the mid-dorsolateral prefrontal cortex, but not those with lesions to the anterior inferotemporal cortex. Note that even after a single choice the monkeys with mid-dorsolateral prefrontal lesions were impaired as the number of alternatives increased. This demonstrates that their impairment lies in their inability to monitor that stimulus A has been selected, but equally importantly, that stimulus B, C, D and E have not. This double dissociation therefore provides considerable support for theories that posit an executive role for mid-dorsolateral prefrontal cortex in visual working memory. A complete understanding of how the mid-dorsolateral prefrontal cortex manipulates the information in working memory is likely to require similar experimental ingenuity, but it will represent something of a Full House for those working with memory.

Peter Collins



References and links

ORIGINAL RESEARCH PAPER Petrides, M. Dissociable roles of mid-dorsolateral prefrontal and anterior inferotemporal cortex in visual working memory. *J. Neurosci.* **20**, 7496–7503 (2000)

FURTHER READING Owen, A. M. The functional organization of working memory processes within the human lateral frontal cortex: the contribution of functional neuroimaging. *Eur. J. Neurosci.* **9**, 1329–1339 (1997)

ENCYCLOPEDIA OF LIFE SCIENCES Working memory

IN THE NEWS

This year's Nobel prize as reported in *Le Monde*.

The Nobel on Medicine rewards three specialists on the brain

… Paul Greengard has shown that all of the tasks accomplished inside the cell following a signal received at the cell membrane are controlled by signals that proteins address to themselves. These signals essentially consist in the addition (phosphorylation) or excision (dephosphorylation) of chemical groups (phosphates) … resulting in the modification of the spatial structure and function of these proteins. These chemical reactions are accelerated by enzymes (protein kinases and protein phosphatases), the discovery of which has been a great step in understanding the mechanisms responsible for the transmission of cellular signals.

"The brilliant contribution of Paul Greengard has been to show that this phosphorylation mechanism, which had previously been described, is universal and plays a fundamental role in the nervous system", comments Jean-Antoine Giraud (College de France) who spent a few years in Paul Greengard's laboratory. In neurons that respond to dopamine, the transmission of nervous signals by phosphorylation–dephosphorylation cascades is regulated by a central protein, DARPP-32. Like the director of an orchestra, this protein controls the function of numerous other proteins, allowing for the modification of the excitability of rapid synapses, which function in an electrical rather than a chemical manner …

Translated by Raluca Gagescu, Nature Reviews Molecular Cell Biology