

Memory: Dissociating multiple memory processes

Adrian M. Owen

Memory depends upon a network of interconnected and functionally related cortical and subcortical areas including, at the very least, the prefrontal cortex and the medial temporal lobe structures. Evidence is now emerging to relate these neuroanatomical regions to specific aspects of mnemonic processing.

Address: MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge, CB2 2EF, UK.

Current Biology 1998, 8:R850–R852
<http://biomednet.com/elecref/09609822008R0850>

© Current Biology Ltd ISSN 0960-9822

Cognitive psychologists have for many years sought to dissociate memory processes into multiple functional units or ‘systems’. This often takes the form of dichotomies, such as long-term versus short-term (or more recently ‘working’) memory, declarative (conscious or explicit) versus procedural (implicit) memory, and semantic (knowledge) versus episodic (experiences) memory. Even within these groupings, further distinctions are often drawn, for example, between spatial and non-spatial working memory. Until recently, however, attempts to map these putative functional models onto specific neural systems or anatomical regions within the brain have met with limited success.

It has been known for many years that bilateral lesions of the limbic region of the temporal lobe, namely the amygdala, the hippocampus and the cortex that surrounds these structures — the entorhinal cortex, perirhinal cortex and parahippocampal gyrus — produce a severe amnesic syndrome, characterised by an inability to store new information about facts and events. Although the prefrontal cortex was also implicated in memory processes as early as 1936, with the pioneering work of Jacobsen [1], it is only more recently that this region has emerged as a primary contributor to many aspects of mnemonic processing.

There are three reasons for this development. First, electrophysiological recording studies in the monkey have identified neurons within the prefrontal cortex that respond preferentially during the delay period of memory tasks (reviewed in [2]). Importantly, visual-form-specific neurons with activity that is sustained during a delay have also been found in the inferior temporal cortex (area TE), and in the perirhinal and entorhinal regions of the anterior-medial temporal lobe. Second, recent studies in patients with neurosurgical excisions of the frontal cortex (for example [3]), and in monkeys with discrete prefrontal lesions (reviewed in [4]), have demonstrated that damage to this area can impair performance on certain types of

memory task, while sparing performance on others. Finally, since the emergence of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) as useful tools for investigating cortical functioning *in vivo* in humans, numerous cases have been reported of specific activation, during various types of memory task, in regions of the frontal lobe that were previously assumed not to be involved in mnemonic processing.

Two recent studies [5,6] have optimised the second of these two imaging techniques, using event-related fMRI to investigate memory-encoding processes in humans. Brewer and colleagues [5] scanned subjects while they were making simple decisions about whether each of a series of novel pictures depicted an indoor scene or an outdoor scene. Thirty minutes after scanning, the subjects were given an unexpected memory test for the pictures viewed while they were in the scanner, and their memory for each picture was judged as ‘remembered’, ‘familiar, but not well remembered’ or ‘forgotten’. The extent to which a stimulus was remembered well was found to correlate with activity in the right frontal lobe and bilaterally in the parahippocampal gyrus during encoding.

Wagner and colleagues [6] have also used event-related fMRI to study memory encoding while subjects performed an incidental task, judging whether each of a series of visually presented words was concrete, such as ‘ticket’, or abstract, such as ‘courage’. Twenty minutes after the scanning session, the subject’s memory for the words was tested and, as in the study by Brewer and colleagues [5], each word was classed as ‘remembered (high confidence)’, ‘remembered (low confidence)’ or ‘forgotten’. Greater activation was observed during the presentation of words that were remembered well, compared with that during the presentation of words that were forgotten, in the left prefrontal cortex, fusiform gyrus and left parahippocampal region of the temporal lobe. The restriction of the activity associated with this word-encoding task to the left cerebral cortex, unlike that observed during the picture-encoding task employed by Brewer and colleagues [5], is entirely consistent with the known dominant role for this hemisphere in language processes.

The results of both of these fMRI studies [5,6] imply that the degree of activation in both the prefrontal cortex and in the parahippocampal region of the temporal lobe relates to how well a given stimulus is encoded, and so predicts whether it will be remembered or forgotten. In the primate brain, widespread cortical and subcortical projections converge upon the parahippocampal gyrus

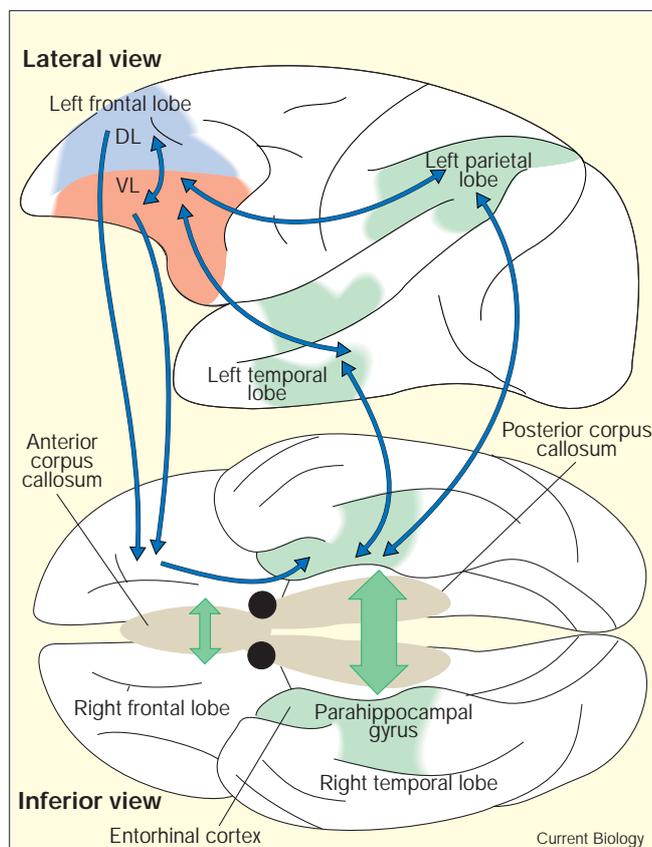
(Figure 1), which projects, via the entorhinal cortex, to the hippocampus itself. The parahippocampal gyrus thus occupies a pivotal position within the medial temporal lobe structures [7]. Furthermore, Goldman-Rakic and colleagues [8] have described several multi-synaptic connections between the frontal cortex and the medial temporal lobe structures, which suggests that there may be a reciprocal functional relationship between these areas in certain aspects of mnemonic processing.

This issue has recently been tackled by Hasegawa and colleagues [9], who used an elegant set up involving monkeys with partial 'split brains' to investigate the complementary roles of frontal and temporal lobe regions in memory retrieval. The monkeys were required to memorize associations between pairs of patterns, which were sequentially presented to just one cerebral hemisphere (by restricting the display to one visual hemifield). Although monkeys with lesions to the posterior corpus callosum and associated fibres (Figure 1), which interconnect left and right temporal and occipital sensory areas, were able to learn this task as well as unoperated control monkeys, they were unable to use the information to facilitate learning when stimulus presentation was switched to the opposite hemisphere. This suggests that memories acquired through visual stimulus-stimulus associations are transferred between cerebral hemispheres via the posterior callosal fibres but not via more anterior regions of the corpus callosum, which interconnect the frontal lobes and remained intact in the operated monkeys (Figure 1).

Once the monkeys with posterior callosal lesions had relearned the associations with the second hemisphere, Hasegawa and colleagues [9] modified the memory task such that the cue and choice stimuli were presented sequentially to opposite hemispheres. The lesioned monkeys were able to perform this task as well as controls, suggesting that, in these animals, one hemisphere could still instruct the other, via the intact anterior corpus callosum, to select the correct choice specified by the cue. In contrast, when the lesion was extended to include anterior regions of the corpus callosum which interconnect the frontal lobes, performance fell to chance, although the same monkeys were still able to perform the task normally if the cue and choice stimuli were presented to just the one hemisphere.

The results of this study [9] clearly imply that the prefrontal cortex and regions of the temporal lobe interact closely, but that they are disproportionately involved in different aspects of memory processing. In particular, the prefrontal cortex would seem to be more important for 'executive' or 'organisational' aspects of performance, and the temporal lobe for more basic mnemonic processes, such as information storage. Thus, although learned associations did not transfer via the anterior corpus callosum, implying that these associations are 'stored' in posterior

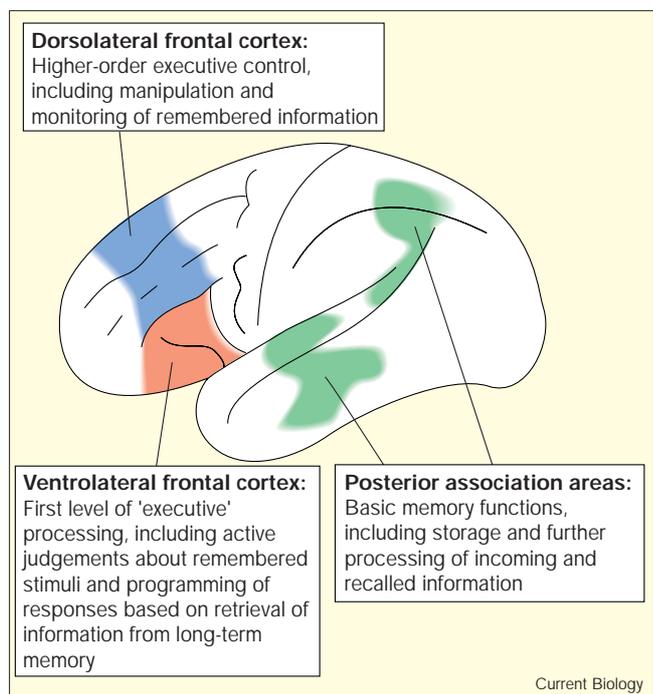
Figure 1



The brain of the macaque monkey, showing the anatomical relationships between key regions implicated in mnemonic processing, notably the parahippocampal gyrus, the ventrolateral prefrontal cortex (VL) and the dorsolateral prefrontal cortex (DL). Green arrows represent the interhemispheric connections between the frontal lobes and posterior temporo-occipital sensory areas that are mediated by anterior and posterior sectors of the corpus callosum, respectively. Blue arrows represent some of the known functional interactions between posterior cortical association areas and the frontal lobe. Information within sensory-specific and multimodal posterior association areas in the parietal and temporal cortices (green) may be fed forward for further processing via bidirectional projections to the ventrolateral frontal cortex (red), which is closely connected to the mid-dorsolateral frontal cortex (blue). Not shown are the direct and indirect (via ventromedial frontal cortex) connections between the dorsolateral frontal cortex and the memory system of the medial temporal lobe. (Adapted from [4].)

neocortex, the prefrontal cortex still appeared to be able to 'direct' memory retrieval from more posterior cortical regions via the anterior corpus callosum.

A general theoretical framework for understanding the relationship between regions of the prefrontal cortex and more posterior cortical association systems in mnemonic processing has recently been proposed [4]. According to this model, basic memory functions, including storage and further processing of incoming and recalled information,

Figure 2

The lateral surface of the human brain, showing the anatomical locations of the posterior cortical association areas (green), the ventrolateral frontal cortex (red) and the dorsolateral frontal cortex (blue), and their proposed roles in mnemonic processing.

are carried out within sensory-specific and multimodal posterior 'association areas' in the parietal and temporal cortices (Figure 2). Neural activity in these areas is thus considered to underlie, not only perceptual processing and the long-term storage of information, but also the short-term retention and integration of new or recently recalled information. The frontal lobes may receive and act upon this information via bidirectional connections between the posterior cortical association areas and the ventrolateral frontal cortex, which in turn is closely connected to the mid-dorsolateral frontal cortex, or via direct connections between dorsal regions of the frontal cortex and the medial temporal lobe (Figure 1).

According to the model [4], the ventrolateral frontal cortex thus constitutes a first level of interaction between posterior regions and the entire lateral frontal cortex. In this capacity, the ventrolateral frontal cortex is assumed to be critical for various 'executive' or 'organisational' processes, such as comparisons between, or judgements about, remembered stimuli, and the active organisation of responses based on conscious, explicit retrieval of information from long-term memory. In contrast, the mid-dorsolateral frontal cortex is assumed to provide a second level of memory processing, only being recruited when the active manipulation or 'monitoring' of remembered information

is required. Evidence to support this model [4] has come from lesion studies in monkeys [10] and from functional neuroimaging studies in humans [11].

The more recent studies discussed above [5,6,9] provide some additional support for this distributed neural model, by which normal mnemonic processing depends on a close functional interaction between sensory-specific and multimodal posterior association areas and the lateral frontal cortex. For example, in the imaging study by Wagner and colleagues [6], successful word encoding was associated with greater activity in the parahippocampal gyrus and in ventrolateral regions of the frontal lobe, a finding that is entirely consistent with an assumed role for both of these regions in short-term retention and integration of information into long-term memory. Further insights into precisely what these roles might be is provided by Hasegawa and colleagues [9], who have successfully dissociated posterior storage functions from prefrontal executive control.

Memory depends very much on the perspicuity, regularity, and order of our thoughts. Many complain of the want of memory, when the defect is in the judgement; and others, by grasping at all, retain nothing. Thomas Fuller, 1608–1661.

References

- Jacobsen CF: **Studies of cerebral function in primates I. The functions of the frontal association areas in monkeys.** *Comp Psychol Monogr* 1936, 13:1-60.
- Rushworth MFS, Owen AM: **The functional organisation of the lateral frontal cortex: conjuncture or conjecture in the electrophysiology literature?** *Trends Cogn Sci* 1998, 2:46-53.
- Owen AM, Morris RG, Sahakian BJ, Polkey CE, Robbins TW: **Double dissociations of memory and executive functions in working memory tasks following frontal lobe excisions, temporal lobe excisions or amygdalo-hippocampectomy in man.** *Brain* 1996, 119:1597-1615.
- Petrides M: **Frontal lobes and working memory: evidence from investigations of the effects of cortical excisions in nonhuman primates.** In *Handbook of Neuropsychology Vol 9*. Edited by Boller F and Grafman J. Amsterdam: Elsevier; 1994:59-82.
- Brewer JB, Zhao Z, Desmond JE, Glover GH, Gabrieli JDE: **Making memories: brain activity that predicts how well visual experience will be remembered.** *Science* 1998, 281:1185-1187.
- Wagner AD, Schacter DL, Rotte M, Koutstaal W, Maril A, Dale AM, Rosen BR, Buckner RL: **Building memories: remembering and forgetting of verbal experiences as predicted by brain activity.** *Science* 1998, 281:1188-1191.
- Amaral DG, Witter MP, Insausti R: **The entorhinal cortex of the monkey: a summary of recent anatomical findings.** In *Brain Mechanisms of Perception and Memory: From Neuron to Behavior*. Edited by Ono T, Squire LR, Raichle ME, Perret DI, Fukuda M. New York: Oxford University Press; 1993:228-240.
- Goldman-Rakic PS, Selemon LD, Schwartz ML: **Dual pathways connecting the dorsolateral prefrontal cortex with the hippocampal formation and parahippocampal cortex in the rhesus monkey.** *Neuroscience* 1984, 12:719-743.
- Hasegawa I, Fukushima T, Ihara T, Miyashita Y: **Callosal window between prefrontal cortices: cognitive interaction to retrieve long-term memory.** *Science* 1998, 281:814-818.
- Petrides M: **Impairments on non-spatial self-ordered and externally ordered working memory tasks after lesions of the mid-dorsal part of the lateral frontal cortex in the monkey.** *J Neuroscience* 1995, 15:359-375.
- Owen AM, Evans AC, Petrides M: **Evidence for a two-stage model of spatial working memory processing within the lateral frontal cortex: a positron emission tomography study.** *Cerebr Cortex* 1996, 6:31-38.