Asymmetric frontal activation during episodic memory: what kind of specificity?

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Over the last decade functional brain imaging techniques, such as positron emission tomography (PET) and magnetic resonance imaging (MRI), have become an important addition to the traditional lesion method in the longstanding effort to identify neural substrates of various cognitive functions. A major advantage of these techniques is that they allow study of the intact neural network subserving a specific process, thereby avoiding possible confounds associated with the study of damaged brains; for example, neural reorganization. In addition, it can be difficult, if not impossible, to make inferences based on lesion studies about the effect of the lesion on specific component processes. One example of this problem comes from the study of episodic memory. Patients with medial temporal lobe lesions are known to be severely impaired on episodic memory tests, but it is not clear whether such a lesion is affecting the ability to properly encode and store new episodes or whether it is primarily compromising retrieval operations. Functional neuroimaging can address this problem by allowing the separate study of encoding and retrieval processes.

In an early review of relevant PET studies, Tulving and colleagues noted that preferential brain regions were consistently involved in episodic memory. Strikingly, activation patterns associated with encoding processes generally included left prefrontal regions, whereas retrieval-related activations tended predominantly to involve right prefrontal regions. These results suggested that different neural systems mediate encoding and retrieval processes, and they formed the basis for the ‘hemispheric encoding/retrieval asymmetry’ (HERA) model. According to this model, left prefrontal cortex is differentially more involved in retrieval of information from semantic memory, and in simultaneously encoding new aspects of the retrieved information into episodic memory, than is the right prefrontal cortex. The right prefrontal cortex is differentially more involved in episodic memory retrieval than is the left prefrontal cortex.

In a subsequent review, additional studies were considered. These included encoding tasks involving intentional learning – the studies covered in the initial review by Tulving et al. included incidental learning – and the left frontal asymmetric activation pattern was found to hold true for these intentional encoding tasks. Moreover, all the encoding studies in the initial review used verbal materials, and an important extension of the follow-up studies was the inclusion of a study using non-verbal stimuli (faces). This study, in common with most of the other studies, was associated with left frontal activation, and it was concluded that ‘because these studies, with a single exception (…), used verbal materials, it is not entirely clear whether the pattern would hold for other kinds of materials, but the fact that Grady and Haxby, and their colleagues, obtained left-frontal encoding activation with faces suggests that the pattern may turn out to be more general’ (Ref. 4, p. 148). This interpretation has now been challenged by recent MRI findings reported by Kelley et al.\(^1\)

In two experiments, Kelley et al.\(^1\) used functional MRI to study episodic memory encoding. In Experiment 1, the brain-activation pattern associated with encoding of (i) visual words, (ii) nameable line-drawn objects, and (iii) unfamiliar faces was compared with encoding of (i) visual words, (ii) nameable line-drawn objects, and (iii) non-verbal materials it is especially challenging to try to explain why this study, but not a previous one involving similar materials,\(^5\) found right- but not left-sided frontal activation.

It is quite possible, as alluded to by Kelley et al., that one key factor is the type of encoding strategy. In the Kelley et al. study, the stimuli were presented at a fast rate, which presumably made it difficult for the subjects to make use of elaborate (verbally mediated)
Significant frontal activation peaks from studies involving intentional encoding of verbal and non-verbal information. The peaks from the first experiment by Kelley et al. are indicated by arrows.

In the context of specific localization of activations, it can further be noted that (bilateral) activation of the posterior frontal region has been suggested that the dorsal frontal posterior region observed by Kelley et al. has been associated with semantic processing and intentional learning respectively. The study by Kelley et al. adds important information to these previous studies by pointing to the relevance of materials and strategies in the hemispheric specificity of encoding-related processing. More investigations are needed to determine whether elaboration of nonverbal information will consistently activate left frontal regions as has repeatedly been demonstrated for verbal materials. The results shown in Figs. 1, and if found, what such activations signify.

To sum up: (1) Are the Kelley et al. findings important? Yes. They are very clear, and clearly important. (2) Do they invalidate HERA? No. It is logically impossible for the finding of a single experiment to invalidate a large pattern consisting of many findings. (3) Is the right-frontal activation to faces an ‘exception’ to HERA? Yes. It is definitely an exception to HERA. (4) Are the results consistent across experiments? Yes. They are consistent across experiments.

In the follow-up review of HERA, we noted that there was considerable variability in more precise localization of memory function within the frontal regions and that ‘future research will reveal a much richer and more complex picture than HERA in its present form suggests’ (Ref. 4, p. 145). Subsequent work has already begun, aimed at the elucidation of the specific contributions of distinct frontal regions to retrieval operations. Similarly, as noted above, studies of encoding processes have pointed to dissociations between the involvement of left frontal regions, and recently different left frontal regions have been associated with semantic processing and intentional learning respectively. The study by Kelley et al. adds important information to these previous studies by pointing to the relevance of materials and strategies in the hemispheric specificity of encoding-related processing. More investigations are needed to determine whether elaboration of nonverbal information will consistently activate left prefrontal cortex as has repeatedly been demonstrated for verbal materials (Fig. 1), and if found, what such activations signify.

Fig. 1 Frontal cortical activation peaks from multiple neuroimaging studies of episodic memory encoding. Significant foci from activation peaks from studies involving intentional encoding of verbal and non-verbal information. The peaks from the first experiment by Kelley et al. are indicated by arrows.