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Neural Correlates of Successful and Unsuccessful Verbal Memory Encoding

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Recent neuroimaging studies suggest that episodic memory encoding involves a network of neocortical structures which may act interdependently with medial temporal lobe (mTL) structures to promote the formation of durable memories, and that activation in certain structures is modulated according to task performance. Functional magnetic resonance imaging (fMRI) was used to determine the neural structures recruited during a verbal episodic encoding task and to examine the relationship between activation during encoding and subsequent recognition memory performance across subjects. Our results show performance-correlated activation during encoding both in neocortical and medial temporal structures. Neocortical activations associated with later successful and unsuccessful recognition memory were found to differ not only in magnitude, but also in hemispheric laterality. These performance-related hemispheric effects, which have not been previously reported, may correspond to between-subject differences in encoding strategy. © 2002 Elsevier Science (USA)

Key Words: functional imaging; episodic memory; encoding; hemispheric effects.

INTRODUCTION

Episodic memory encoding is the process by which the experience of an event is transformed into a memory trace that is available for conscious recollection (Tulving et al., 1994). Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have reported activation associated with verbal episodic encoding in a widely distributed network of brain regions that includes the prefrontal, temporal, parietal, occipital, and cerebellar cortices as well as the hippocampal formation (Tulving, Habib, Nyberg, Lepage, & McIntosh, 1999; Wagner et al., 1998), yet it is unclear to what extent activation in these regions predicts whether experienced events will be remembered. The majority of functional imaging studies of memory have sought to identify the neural structures that subserve particular memory processes. Recently, however, functional imaging has also been used to investigate how activation in these structures varies according to the success of a subject's task performance.

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There is considerable disagreement among the initial fMRI studies that have examined the relationship between activation during verbal episodic encoding and subsequent memory performance. (For a complete review including PET and ERP literature on subsequent memory effects, see Wagner et al., 1999.) Using a blocked-trial word list learning paradigm, Fernandez et al. (1998) found positive within-subject correlations between the number of successfully recalled words and the intensity of activation during encoding in the bilateral posterior hippocampus, but not in surrounding mesial temporal lobe (mTL) structures that have also been implicated in declarative memory encoding (Fernandez et al., 1998). In a subsequent experiment, Fernandez et al. (1999) found a correlation between word recall and sustained activation during encoding in the bilateral entorhinal cortex, but not the hippocampus (Fernandez et al., 1999). Wagner et al. (1998) used an event-related paradigm that allowed direct comparison of encoding trials resulting in successful and unsuccessful word recognition, which showed that the left prefrontal cortex, parahippocampus, and fusiform gyrus were more active during encoding of words later remembered than words later forgotten (Wagner et al., 1998). The finding of performance-correlated prefrontal activation differs from that of the 1999 Fernandez et al. study, which showed prefrontal activation during word encoding that did not correlate significantly with subsequent word recall. Also, in the study by Wagner et al. hippocampal activation was not found to correlate with success of encoding, in contrast with Fernandez et al. (1998). A more recent study by Kirchhoff et al. (2000) found no verbal subsequent memory effects that were significant at the voxel level in either the prefrontal cortex or MTL, although both regions were activated during word encoding (Kirchhoff, Wagner, Maril, & Stern, 2000). Some of these discrepancies may be attributable to variations in experimental design. For example, the studies by Fernandez et al. used blocked trials and required intentional encoding of word lists, whereas the studies by Wagner et al. and Kirchhoff et al. used event-related designs and induced incidental encoding of single words. Nevertheless, it is clear that further experimentation is needed to elucidate the relationship between functional activation during verbal encoding and subsequent memory performance.

In the present study, fMRI was used to examine neural activity during intentional encoding of verbal stimuli. Subjects viewed blocks of four-word declarative sentences alternating with matched blocks of nonverbal control strings and were instructed to remember the sentences for a postscan recognition memory test. The goal of the experiment was to determine the relationship between encoding success and functional activation across subjects and to compare the locations of brain regions in which activation was performance-invariant with those in which activation was modulated by task performance. Two successive analyses were performed. Cognitive subtraction was used to identify brain structures recruited during sentence encoding, and correlational analysis was used to reveal how activation during encoding varied according to subjects' performance on the postscan recognition test, which served as an index of encoding success.

MATERIALS AND METHODS

Subjects

Eleven healthy, normal volunteers (five men and six women) between the ages of 18 and 30 years were recruited from the University of Pennsylvania community and paid $20 for their participation. All subjects were students or trainees at the University, were native speakers of English, and were right-handed by self-report. Informed consent was obtained from each subject prior to participation in the study, which was approved by the University of Pennsylvania Institutional Review Board.