

POSITRON emission tomography (PET) was used to identify brain regions associated with two component processes of episodic retrieval; those related to thinking back in subjective time (retrieval mode) and those related to actual recovery of stored information (ecphory). Healthy young subjects recognized words that had been encoded with respect to meaning or the speaker's voice. Regardless of how the information had been encoded, recognition was associated with increased activation in regions in right prefrontal cortex, left anterior cingulate, and cerebellum. These activations reflect retrieval mode. Recognition following meaning encoding was specifically associated with increased activation in left temporal cortex, and recognition following voice encoding involved regions in right orbital frontal and parahippocampal cortex. These activations reflect ecphory of differentially encoded information.

Key words: Human; Episodic memory; Retrieval mode; Ecphory; Encoding operations; PET; Brain

Functional brain maps of retrieval mode and recovery of episodic information

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Introduction

A current theory of episodic memory retrieval postulates a distinction between retrieval mode and ecphory.¹ The former term refers to processes related to thinking back in subjective time; the latter to the actual recovery of stored information. Ecphory probably engages brain regions involved in information storage.² In the case of episodic information, these regions may overlap those involved in the perception and initial encoding of the events to be remembered.³ By this view, different brain regions should be related to ecphory, depending on what is retrieved.⁴ Similarly, even if the information to be remembered is held constant, different brain regions may be related to ecphory depending on the particular nature of the encoding operations. In contrast, brain regions related to retrieval mode should be the same regardless of what is retrieved and how the information was encoded. In the present study, we measured regional cerebral blood flow (rCBF) with positron emission tomography (PET) to map the brain regions associated with retrieval mode independently of ecphory, and those associated with ecphory of differentially encoded information.

Materials and Methods

Eleven right-handed healthy volunteers (six females, five males; age range 24–31 years) participated in the study. The study was approved by the Human Subjects Use Committee of Baycrest Centre and written informed consent was obtained from the subjects. Subjects were screened to ensure that none suffered from major medical, neurological or psychiatric disorder. Subjects encoded the material, single common words, approximately 10 min before PET scanning commenced. There were two encoding lists, each comprising a different set of 80 concrete nouns. The words were presented by an audio recorder at the rate of 1.5 s per word. In each list, half of the words were read by a female voice, the other by a male voice; about half of the words referred to living things, the other half to non-living. In the first encoding condition, subjects categorized each presented word in terms of the gender of the speaker's voice (voice encoding). In the second, they made living/non-living judgements about the presented words (meaning encoding). They responded by pressing the appropriate computer mouse button.

PET scans were obtained with a GEMS-Scandi-

tronix PC2048-15B head scanner using bolus injections of 30 mCi [^{15}O]H $_2$ O and 60 s acquisition scans. All subjects underwent eight PET scans representing four experimental conditions (two scans per condition). Three of these were recognition conditions, in which subjects were instructed to indicate whether or not they recognized visually presented words from any of the two encoding tasks. One recognition condition included words from the meaning encoding task, another had words from the voice encoding task, and the third had words never specifically encoded (new). A fourth (baseline) condition involved silent word reading of non-studied words. In all conditions, single words were presented every 3 s in the centre of a computer screen, and they remained on the screen for 2 s. In the recognition scans, subjects pressed with their right hand the left button of a computer mouse if they recognized a word and the right if they did not. In the reading condition, subjects pressed any of two mouse buttons after reading a word. A reading scan started and ended the session and the recognition scans were given in between in a counterbalanced order such that the average study-test delay was the same across conditions. Each cognitive task was begun 30 s before the injection and lasted 30 s after the data acquisition had ended. During the 60 s scan window, all test items were of the specified type (meaning, voice, new). Before and after, a mixture of studied and nonstudied words were presented in the recognition conditions and nonstudied words were presented in the reading condition.

The logic of the task design was as follows. First, although the degree of ecphory was expected to vary between the recognition conditions (high in the meaning condition, low in the voice condition, and none in the new condition), brain regions associated with retrieval mode were expected to be more active in terms of rCBF in all three recognition conditions compared with the reading condition since all of the recognition conditions, but not the reading condition, involved thinking back in time and space. Second, brain regions related to ecphory were identified by comparing the meaning and voice recognition conditions with the new condition. These comparisons cancel out activations associated with retrieval mode; any activations that remain should signify recovery of previously encoded information. To identify brain regions specifically involved in recovery depending on the encoding operations, the meaning and voice conditions were also compared directly.

The data were analysed using statistical parametric mapping (using software from the Wellcome Dept. of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks Inc. Sherborn, MA, USA). Following realignment of all images to the subjects' first scan, they were transformed into a standard space.⁵ As a final pre-processing step the images were

smoothed using a 15 mm FWHM isotropic Gaussian kernel. To test hypotheses about regionally specific condition effects the estimates were compared using linear contrasts.^{6,7} The resulting set of voxel values for each contrast constitute a statistical parametric map of the *t* statistic SPM(*t*). The SPM(*t*) were transformed to the unit normal distribution (SPM(*z*)) and thresholded at 3.09 [$p = 0.001$ uncorrected]. The location of the activations was confirmed using the SPM PET template.

Results

The hit rate of meaning words (0.58) was significantly higher than that of voice words (0.30, $t(10) = 5.34$, $p < 0.01$), and the latter was higher than the false alarm rate of the new words (0.17, $t(10) = 2.93$, $p < 0.05$). Regions showing significantly higher activation in all recognition conditions than in the reading condition were the right prefrontal cortex, left anterior cingulate, vermis of cerebellum, and the left ventral occipital cortex (Table 1). The spatial extent of the activations is illustrated in Figure 1.

In the voice-new subtraction, regional cerebral blood flow (rCBF) differences were largely confined to the right hemisphere (Table 2). Activated regions were found in the parahippocampal gyrus, middle temporal gyrus, retrosplenial, and orbital frontal cortex. Additional activations occurred in the calcarine sulcus and the left medial frontal cortex. In the voice-meaning subtraction, significant increases were observed in the right parahippocampal gyrus (x, y, z coordinates = 28, -36, -12)⁵ and right orbital frontal cortex ($x, y, z = 16, 26, -12$). In the meaning-new subtraction, activations were observed in left caudate/insula and left middle temporal gyrus (Table 2). In the meaning-voice subtraction, there was a tendency to a significant increase in the left superior temporal gyrus ($x, y, z = -56, -48, 20$; $Z = 3.00$).

Discussion

Recognition of studied as well as non-studied words was related to increased activation in regions in right prefrontal cortex, left anterior cingulate, cerebellum and occipital cortex. These regions have been found to be implicated in episodic retrieval in several previous PET studies, in which different episodic tests and different baseline tasks have been used,⁸⁻¹² suggesting that the present findings reflect increased involvement of these regions during recognition rather than decreased activity in the baseline condition. Recent PET findings^{13,14} indicate that the involvement of the right prefrontal cortex in episodic retrieval is related to retrieval attempt rather than to retrieval success. The present results supported this view, and together these studies

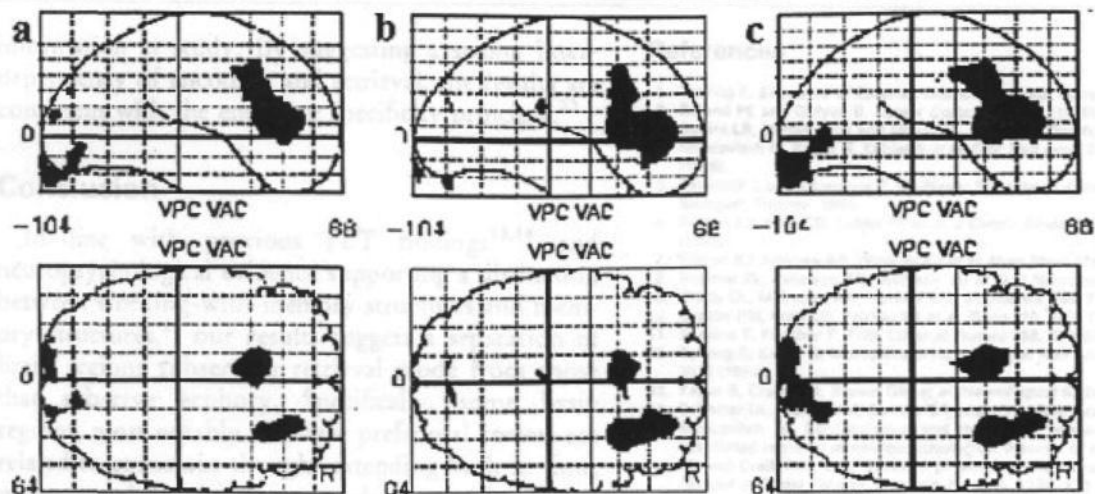


FIG. 1. Brain maps of retrieval mode. Sagittal (upper) and transverse (lower) projections of brain regions were significantly more activated in the recognition conditions than in the reading condition. (a) Meaning-Read, (b) Voice-Read, (c) New-Read.

Table 1. Activations related to retrieval mode

Brain area (Brodmann number)	Meaning-Read	Voice-Read	New-Read
	x, y, z	x, y, z	x, y, z
Right prefrontal cortex (45)	28, 30, 8	28, 30, 8	28, 24, 8
Left anterior cingulate (24/32)	-16, 20, 28	-10, 18, 28	-10, 18, 28
Left ventral occipital cortex (18)	-18, -100, -16	-14, -102, -16	-14, -102, -16
Vermis of cerebellum	-8, -96, -24	8, -78, -28	4, -92, -20

Each voxel is reported as its x (right/left), y (anterior/posterior), and z (superior/inferior) coordinates in mm.⁵ The reported voxels represent peaks in brain regions showing significant differences in activation between conditions ($p < 0.001$, one-tailed; Z-scores = 3.54-6.47).

Table 2. Activations related to ecphory

Brain area (Brodmann number)	x	y	z
Voice-New			
Left medial frontal cortex (10/47)	-20	46	-4
Right parahippocampal cortex (36)	28	-30	-12
Right middle temporal gyrus (21)	62	-42	-4
Calcarine sulcus (17)	-2	-96	0
Right orbitofrontal cortex (11)	14	26	-20
Right retrosplenial cortex (23)	10	-44	4
Semantic-New			
Left caudate/insula	-22	26	4
Left middle temporal gyrus (39)	-50	-64	24

Coordinates reported as in Table 1 (Z-scores = 3.09-3.93).

suggest that the consistent activation of the right prefrontal cortex in neuroimaging studies of episodic retrieval signifies retrieval mode. This suggestion is consistent with neuropsychological theories of the role of the frontal lobes in memory functioning.¹⁵ It remains to be determined whether the activation of the other regions is related to the thinking back in time, or to other general aspects of episodic retrieval such as strategic processing, attentional demands, and response selection.¹⁶⁻¹⁸ Nevertheless, with the exception of the occipital activation which may be specific to visual tests, we suggest that these regions can be thought of as constituting components of a general episodic retrieval network.¹⁹ By contrast, recovery of

stored information, ecphory, seems to engage specific brain circuits. Despite the fact that the materials to be remembered, the retrieval cues and the test procedures were the same, recovery following meaning and voice encoding was associated with different brain regions. Note that these regions were not identified when voice and meaning were compared with the baseline condition. Examination of task means suggested that this was not a threshold effect; rather it appears that each retrieval condition was associated with a unique pattern of rCBF that was only revealed when voice and meaning were compared with new.

A previous PET study found that semantic encoding is associated with increased activation in the left frontal cortex,²⁰ whereas single word processing has been shown to involve left temporal brain regions.²¹ These data suggest that the left temporal activation, associated with ecphory of meaning words in our study, may be related to the type of processing performed during encoding. Recovery of voice words was found to be associated with increased activation in regions in the right orbital frontal and parahippocampal cortices. Previous PET studies have shown that pitch processing and memory for pitch is related to frontal and temporal regions in the right hemisphere.²² Based on these results, it seems plausible that our findings are related to the processing of voice

