



Brain regions involved in prospective memory as determined by positron emission tomography

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Abstract

Prospective memory (PM) refers to the functions that enables a person to carry out an intended act after a delay. Despite the ubiquity of this behaviour, little is known about the supporting brain structures and the roles that they play. In this study, eight healthy participants performed four different PM tasks, each under three conditions: a baseline, and two conditions involving an intention. In the first of the intention conditions, subjects were asked to make a novel response to a certain class of stimuli whilst performing an attention-demanding task. However, the expected stimuli never actually occurred. In the second intention condition subjects were expecting to see these stimuli as before, and they did occur on $\approx 20\%$ of trials. Relative to the baseline condition, increases in regional cerebral blood flow (rCBF) as estimated by oxygen-15 positron emission tomography technique across all four tasks were seen in the frontal pole (Brodmann's area 10) bilaterally, right lateral prefrontal and inferior parietal regions plus the precuneus when subjects were expecting a PM stimulus regardless of whether it actually occurred. Further activation was seen in the thalamus when the PM stimuli occurred and was acted upon, with a corresponding rCBF decrease in right lateral prefrontal cortex. It is argued that the first set of region play a role in the maintenance of an intention, with the second set involved additionally in its realisation. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Prospective memory (PM), or the “realisation of delayed intentions” ([26], p. 1) is an ability which is at the heart of competent behaviour in everyday life. Without PM functions one could not carry out an intended future action without continuous verbal rehearsal of the intention until the appropriate time (or context) occurred. In this way PM functions serve to bind together complex goal-directed behavioural sequences and enable a person to carry out their plans and wishes in a meaningful order and at the appropriate time. Neurological patients who have lost this ability demonstrate the importance of PM to everyday life competency. Despite high IQ and no problems with language, perception or retrospective memory, they are

nevertheless severely impaired in everyday life (see Ref. [13] for review).

Tasks or situations that stress PM can easily be characterised. First, they involve a delay interval (or “retention interval” ([26], p. 2)) between forming an intention and carrying it out. For some [2], this interval may only be a matter of seconds, but most investigators [1,8,17,20,24,25,27,37,45,46,49,51,53,63,72] consider that the retention interval is typically much longer, ranging from a minute or more to several hours.

A second characteristic, which is agreed by most commentators, is that situations tapping PM abilities involve both an ongoing¹ and a PM task. The demands

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¹ There are many terms in the prospective memory literature for the task in which the participant is engaged until the retrieval context occurs. In an attempt to avoid terminological confusion, the delegates at the First International Conference on Prospective Memory (University of Hertfordshire, UK, July 2000) carried a vote for researchers in this area to use the term “ongoing task”. It was preferred principally because of its theoretically neutral character.

of the ongoing task are often unrelated to the PM intention or retrieval context. However, the ongoing task must be such that it prevents a simple verbal (or sub-vocal) rehearsal strategy [24,52]. Indeed, it is this characteristic more than any other which distinguishes a typical PM task from a vigilance one (see [24,52] for discussion on this point). As regards the retrieval context (i.e. the situation, event or time where the intended action should be performed), the currently most discussed forms are either event-based intentions (i.e. “when x occurs then do y ”) or time-based ones (i.e. “at time x , do y ”; see [25]).

A third feature of PM is that the delayed action is self-initiated [19]. This demand implies that ongoing task performance should not halt or change at the point where the intention should be carried out, and that the retrieval cue or context should not interfere with performance of the ongoing task [12].

Many everyday situations conform to these criteria. Consider for instance the circumstance where one wishes to remember to send an important letter at lunchtime tomorrow. Clearly one would not normally indulge in verbal rehearsal of the intention until the retrieval context (i.e. lunchtime tomorrow) occurred. Instead, one’s attention would be given over (even if only momentarily) to many events in the intervening period. Thus the first two criteria are met: that there should be a retention interval, and that verbal rehearsal cannot be maintained continuously during the whole of that interval. (In this situation the intervening events between forming the intention to send the letter and lunchtime tomorrow would count as the “ongoing task”.) The third criterion – that of self-initiated retrieval – would also be met in this naturalistic example, supposing that one did not use a reminder such as an alarm as an aid.

1.1. Candidate brain regions involved in prospective memory

There is a current consensus amongst investigators that at least some of the processes which are critical to realising delayed intentions are supported by brain structures located in the frontal lobes and related structures [3,4,16,17,67], although there are currently only a few studies that suggest a finer level of discrimination. One of these is the study of Burgess et al. [14]. They reviewed the lesion loci of five neurological cases, whose everyday life impairments included failure to create and carry out intentions, taken from the case studies of Eslinger and Damasio [28], Shallice and Burgess [66] and Goldstein et al. [36] using the Damasio and Damasio [23] method of CT scan analysis. Burgess et al. [14] found that all the cases had sustained damage to at least one of the following frontal areas: left frontal pole and surrounding regions (Damasio and Damasio

region LF04, which encompasses parts of Brodmann’s areas (BAs) 8–10), left anterior cingulate (Damasio and Damasio region LF01) and right dorsolateral prefrontal cortex (RDLPFC; Damasio and Damasio region RF07). Burgess et al. [14] also report these regions, in addition to the left posterior cingulate and forceps major region, as implicated in performance of a multi-tasking test requiring PM in 60 neurological patients with circumscribed cerebral lesions. They contend that the anterior and posterior cingulates are involved in the basic retrospective memory components of PM, with RDLPFC involved in planning and creation of intentions [35], and BA 10 critical to maintenance of intentions.

Interestingly, these findings find some support in a positron emission tomography (PET) study by Okuda et al. [55,73]. In this study subjects were taught a set of 10 nouns (“targets”) before the scanning began. There were two scanning phases: “experimental” and “control”. During the experimental scanning phase participants were required to repeat verbally a series of 10 sets of five nouns that were presented to them auditorily. Occasionally, one of the stimuli they heard was a target word that they had learnt before scanning, and subjects were instructed to tap with their left hand when they heard these. The control scanning phase consisted merely of the word string repetition task alone. The subjects repeated both tasks in random order. Okuda et al. [55] found regional cerebral blood flow (rCBF) increases in the experimental (i.e. the PM) condition, compared with the control task in the following regions: Left hemisphere: anterior cingulate gyrus (BA 24), superior frontal gyrus (BA 10), and parahippocampal gyrus (BA 28); Right hemisphere: inferior and middle frontal gyri (BA 8, 9 and 47). In addition there was involvement of the frontal lobe medially (BA 8) (Talairach and Tournoux [69] co-ordinates 0, 40, 41).

These two studies, despite using different methods, show a number of areas of agreement, and together provide some hypotheses both regarding the regions of the brain involved in PM, and the roles that they play. Thus both studies suggest involvement of the anterior cingulate gyrus plus BA 8–10, especially on the left, plus some involvement more dorsolaterally in the right frontal lobe. However, there is less agreement between them as to the roles these regions play in the realisation of a delayed intention. Thus Okuda et al. [55] suggest that the right middle frontal activation reflects the extra load upon memory in a PM task, with the left BA 10 and right BA 47 regions “related to the process of holding intention of future behaviour” (p. 130) while the left parahippocampal activation reflects the novelty detection requirements of the task. However, in the Burgess et al. lesion study [14], the suggested role of the right frontal lobe is in the creation of intentions (as a function of planning), with an area which includes left

hemisphere region BA 10 involved in the prospective components of RDI such as the maintenance or triggering of an intention. More promisingly, both sets of investigations agree that parts of BA 8 (especially on the left) may also be involved in these prospective components.

One problem in equating results from these studies, however, is that the experimental tasks they used were quite different from each other, and many of the points of disagreement may reflect these differences. An even more critical difficulty for both studies, however, is in their ability to distinguish between the regions involved in the maintenance of an intention, and those involved in its triggering or execution. The present study therefore has two basic aims. The first is to confirm the involvement in PM of the regions just discussed, using tasks that on theoretical grounds should make similar cognitive demands. In particular, the investigation uses a cognitive conjunction design [62]. This is an important characteristic since use of a PM task which, a priori, makes demands upon just one cognitive domain, such as language or visual perception (as in the Okuda et al. study [55]) may reveal only task-specific activations which are likely to be of less theoretical interest [34,62]. The second aim of the present investigation is to attempt to achieve a resolution regarding the roles that the processes supported by these different regions play in PM. In particular, the design used here contrasts the brain regions involved in the maintenance of an intention with those involved in its execution.

2. Methods

2.1. Experimental design

Four tasks which all involved the realisation of a delayed intention were administered to each participant, with the exact form of the retrieval context and the nature of the ongoing task differing from task to task. The logic of such a design is that when the patterns of activation across tasks are considered, only the activations that are common to them (and are therefore of theoretical interest) are likely to reach significance [62].

Each task was administered under four conditions: a training condition which was given before each scan, plus three conditions during which rCBF data acquisition occurred: (1) a baseline condition where no PM stimuli occurred and where there was no expectation that they would; (2) an “expectation” condition, where the participant was told that PM stimuli might occur, but where none actually did; and (3) an “execution” condition, where participants were told that PM stimuli might occur, and they did. In this way, the hope was to be able to contrast the activities specifically associated

with maintaining an intention, with those involved in the manifestation or realisation of it.

In the training conditions the stimuli were arranged in such a way that correct responding would involve a sequence of left–right (i.e. forefinger–middle finger) key presses in strict alternation (i.e. LRLRLR...). One hundred trials were given. The aim of this training stage was to establish a response pattern, prior to scanning the other three conditions. This is necessary for two reasons: First, it is axiomatic that responding to a delayed intention involves making a novel response in the retrieval context, and pre-training should minimise any potential difference in patterns of activation between the experimental conditions which might be associated merely with making a novel response. Second, the training condition should minimise learning effects over the course of the 12 conditions.

In each of the scanned conditions (baseline, expectation, execution), 120 stimuli were presented. The “execution” condition contained PM stimuli pseudorandomly distributed throughout the trials, amounting to 20% of them. No PM stimuli appeared within the first seven trials of a set. The eight participants all received each of the four tasks under each of the three conditions (baseline, PM expectation, and PM execution) requiring 12 scans for each. To avoid potential order effects, the presentation order of the tasks differed across the participants, with each of the tasks appearing twice in each possible position in the sequence: e.g. two of the eight subjects received task one first of all, two received it after one other task; two received it after two of the other tasks, and so forth. The order of the conditions (baseline, expectation, and execution), however, was the same for all participants across these tasks. The baseline for each task was always given first, but the order of the expectation and execution conditions alternated to prevent subjects being able to work out which condition would be which, thereby maintaining the “expectation” aspect of the expectation condition. To summarise, the overall condition order for all subjects was: First task: B, Exe, Exp; Second task: B, Exp, Exe; Third task: B, Exe, Exp; Fourth task: B, Exp, Exe, where B – baseline, Exp – expectation and Exe – execution, and where the identity of the first, second, etc. tasks was determined as above.

2.2. Experimental procedure

The four individual tasks used with each subject are summarised in Fig. 1. In all tasks, stimuli were subject-paced: the onset of the next stimulus was cued by a response by the subject, and stimuli remained visible until that response. There was an 80 ms blank white screen interval between presentations. In task one, the display changed from trial to trial in two respects: one

of the two arrows was always black, and the position of this black one varied pseudorandomly, and the colours of two colour bars placed at equal distances above and below a fixation point changed from trial to trial. Each horizontal bar could be coloured red, blue, yellow or green. Participants were positioned with the forefinger, middle finger and third finger of their right hand resting on the three horizontally arranged keys of a keypad. They were asked to press with their forefinger if the arrow was on the left of a fixation point, and with their middle finger if it was on the right. They were told to respond with their third finger instead if on any trial the two colour bars above and below the fixation point were the same colour.

In task two, subjects were shown a series of nouns that were either four or six letters long, shown one at a time in a pseudorandom order. The sets of four and six letter words were matched for frequency. Twenty per cent of the entire stimulus set were animal words (e.g. “spider”) which were also matched for frequency between length categories and within length exemplars. Subjects pressed with their forefinger if the word was four letters long and with their middle finger for six letter words. They were told to press with their third finger instead if the word was an animal.

For task three, participants were shown a series of sets of two numbers, which were never the same. The key presses were determined by whether the larger number was on the left or the right of a central fixation point (appearing pseudorandomly), and a press with the third finger was required if both numbers were even numbers.

In task four, subjects were presented on each trial with a rectangle divided into quadrants. Two shapes were always present, each in a different quadrant. One of these shapes was always a circle. The other whilst never being a circle, otherwise changed pseudorandomly from trial to trial as did the positions of both shapes. The participants’ attention was drawn to the vertical dividing line which separated the two quadrants on the left of the rectangle from those on the right, and told to press with the forefinger if the shape which was not a circle appeared on the left, with the middle finger if it appeared on the right, and with the third finger if both shapes ever occupied the bottom two quadrants. In all tasks, the trials requiring a third finger response were the PM trials.

2.3. Participants

The experimental subjects were eight male undergraduates from University College London aged between 20 and 46 (mean age = 26.3, S.D. = 9.2). All claimed to be right-handed. All subjects were physically fit and none was taking medication. Written informed consent was obtained prior to the study. The study was approved by the local hospital ethics committee and the Administration of Radiation Safety Advisory Committee (UK).

2.4. Instructions to participants

Written versions of the instructions outlined above were read to the participants immediately before each experimental block was given, and they were asked to repeat the instructions. If mistakes were made, the entire instructions were read again, and repetition was again required. No subject was unable to repeat the instructions perfectly after the second presentation. Subjects then demonstrated their understanding of the ongoing task by completing 10 trials; practice of intention execution was not given since this would interfere with the novelty of the PM stimulus (for a discussion of the importance of this characteristic see [11]).

In the case of the expectation and execution conditions of each experiment, participants were told that the stimulus set might include the PM stimuli (they were explicitly told in the training and baseline conditions that it would not), and that they would be rewarded with 20 pence for each one that they responded to correctly. They were also told that the experimenters had been recording their reaction times (RTs) in the baseline conditions, and that if their speed of responding to the ongoing task dropped below a certain point (no further details were given) relative to the baseline condition, they would forfeit this extra money. Thus, they were told, they had to perform the basic task (i.e. pressing left and right) just as well as they had done

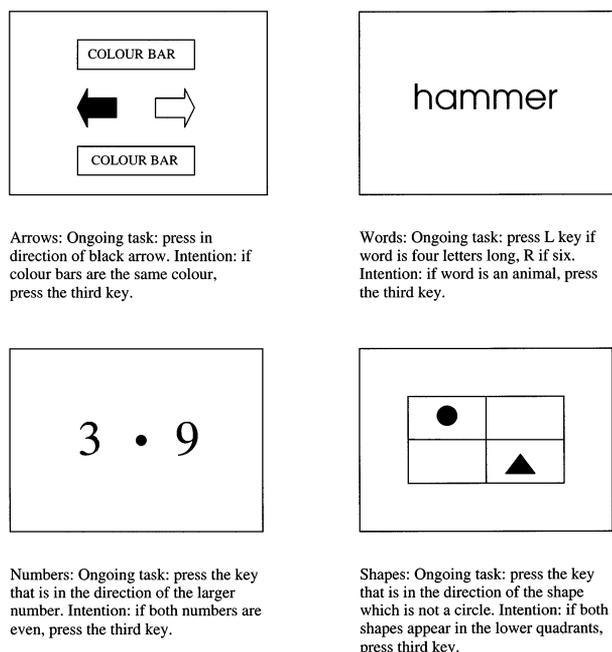


Fig. 1. Description of the four experimental tasks.

previously. This procedure was intended to prevent participants from ignoring the ongoing task and watching for the PM stimuli, and also to increase the personal significance of the PM stimuli, since in real life an intention to do something in the future is always associated with a reason for carrying out the action. The exact length of the retention interval (i.e. delay between receiving the instructions and presentation of the first PM stimulus) differed according to the subject's individual physiology (since the length of time taken for sufficient tracer to reach the brain to allow data acquisition differs between individuals, and in the execution condition the first PM target was not presented until this point was reached) but ranged between 1 and 3 min. During this interval participants listened to music they had chosen, which was switched off ≈ 15 s before the first (ongoing) stimulus occurred.

2.5. Data acquisition

All subjects underwent both PET and MRI scanning on the same day. A Siemens VISION (Siemens, Erlangen) operating at 2.0T was used to acquire axial T1 weighted structural images for anatomical coregistration. PET scans were performed with an ECAT EXACT HR + scanning system (CTI Siemens, Knoxville, TN) PET in high sensitivity 3-D mode with septa retracted. A venous cannula to administer the tracer was inserted in the antecubital fossa vein. Approximately 350 Mbq of $H_2^{15}O$ in 3 ml of normal saline were loaded into intravenous tubing and flushed into subjects over 20 s at a rate of 10 ml/min by an automatic pump. After a delay of ≈ 35 s, a rise in counts could be detected in the head that peaked 30–40 s later (depending on individual circulation time). The data were acquired in one 90 s frame, beginning 5 s before the rising phase of the head curve. Images were reconstructed by filtered back projection (Hanning filter, cut off frequency 0.5 cycles per pixel) into 63 image planes (separation 2.4 mm) and into a 128×128 -pixel image matrix (pixel size 2.1 mm). Twelve scans were collected over 96 min with an 8-min interval between scans during which the training conditions and task instructions were given.

2.6. Statistical analysis

Functional imaging analysis used the technique of Statistical Parametric Mapping implemented in SPM97 (Wellcome Department of Cognitive Neurology, London, UK, <http://www.fil.ion.ucl.ac.uk/spm>). For each subject, the set of 12 PET scans was automatically realigned and then stereotactically normalised [33] into the space of Talairach and Tournoux [69]. The scans were then smoothed using a Gaussian kernel of 12 mm full-width half-maximum.

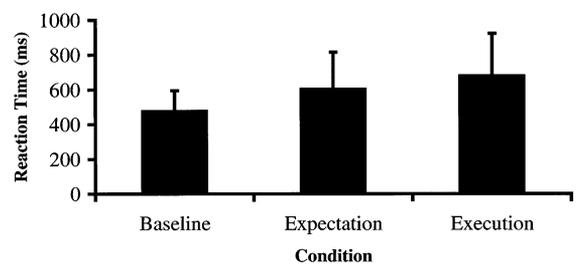


Fig. 2. Mean RTs (S.D.) across tasks by condition (data for execution condition is from non-PM trials only).

The analysis of functional imaging data entails the creation of statistical parametric maps that represent a statistical assessment of condition-specific effect hypothesised by the experimenter [32]. The effects of global changes in blood flow were modelled as a confound using a subject-specific ANCOVA [31]. Areas of significant change in brain activity were specified by appropriately weighted linear contrasts of the condition specific effects and determined using the t -statistic on a voxel by voxel basis. We created the relevant SPM [t] for each comparison of conditions, which was then transformed into an SPM [Z] and thresholded at a Z -score of 3.09 ($P < 0.001$ uncorrected). Clusters of activated voxels were characterised in terms of their peak height and spatial extent conjointly.

3. Results

3.1. Behavioural data

Performance on the experimental tasks from the first 30 s of the PET data acquisition period only were analysed since these would be most relevant to the anatomical data. Repeated measures ANOVA of the participants' mean RTs showed main effects of task (i.e. the four experiments shown in Fig. 1), $F = 10.4$, d.f. = 21, 3, $P < 0.001$ and condition (i.e. baseline, expectation, execution; $F = 7.99$, d.f. = 14, 2, $P = 0.005$) but no task by condition interaction ($F = 1.47$, d.f. = 42, 6, $P = 0.21$). Post-hoc comparisons showed that the participants' RTs were significantly slower in both the expectation and execution conditions relative to baseline (Tukey $Q = 3.82$, $P < 0.05$ and $Q = 6.05$, $P < 0.01$, respectively), but that there was no significant difference between expectation and execution RTs (see Fig. 2; data is for non-PM stimuli in the execution condition). The mean RTs across tasks to the PM stimuli alone in the execution condition were slightly longer than to the non-PM stimuli in the same condition, but the difference did not approach significance (PM stimuli, mean (S.D.): 719.8 (268.4); non-PM stimuli: 678.1 (243.1), $P = 0.12$ paired t -test).

Errors to non-PM stimuli across the four tasks were rare. The mean percentage of errors made by each subject for the ongoing tasks in each condition were 2%, 2%, and 1% for the baseline, expectation and execution conditions, respectively. In the expectation and execution conditions, the mean percentages of false positives (i.e. mistaking a non-PM stimulus for a PM one) were 0.2% and 0.3%, respectively. False negatives in the execution condition (i.e. failing to respond correctly to a PM stimulus) were more common, with a mean percentage per subject across the four tasks of 13.9% (S.D. 6.8; range 4.3–25.0%).

3.2. Imaging data

Contrasts between conditions were conducted across the four different tasks, using a random effects model. The first two of these concerned the regions of change in rCBF, relative to the baseline condition, when participants were expecting to see a PM stimulus (this of course occurred in both expectation and execution conditions). The results are summarised in Table 1. Significant rCBF increases were seen in the frontal pole (BA 10) bilaterally, and also in the right lateral prefrontal cortex, inferior parietal cortex (Fig. 3) and the precuneus. These increases were accompanied by significant rCBF decreases in the insula of the left hemisphere.

The second two contrasts concerned regions of rCBF changes when the participants executed their intentions, relative to when they were merely expecting a PM

stimulus. These results are shown in Table 2. Significant activation increases were found in the thalamus (Fig. 3), accompanied by decreases in the RDLPFC.

4. Discussion

The results from two sets of contrasts are of especial interest in this study. The first is the contrast between the baseline and the two conditions where a PM stimulus was expected. The intended phenomenological correlate of this condition is the maintenance of an intention. Relative to the baseline condition, the results suggested increased rCBF associated with this function in the following regions: the frontal pole (especially BA 10) bilaterally; right lateral prefrontal cortex, the right parietal lobe, and the precuneus bilaterally. Decreases in blood flow were also seen in the left insula.

The second of the contrasts aimed to identify the brain regions involved in the realisation of an intention, rather than just the maintenance of it, by contrasting the expectation and execution conditions. The logic of the contrast of course assumes that the brain regions involved in the expectation conditions are also involved in the execution ones, and asks which regions may be involved in the realisation of a delayed intention that are not also involved in its maintenance. The results here were relatively straightforward, with just one region showing an increase (the thalamus) and one showing a decrease (RDLPFC).

Table 1
SPM results and Talairach and Tournoux [69] co-ordinates for regions of significant change when participants are expecting a PM stimulus^a: regions of greater activation, relative to baseline, when the participants were expecting to see a PM stimulus ((execution+expectation)–baseline) (Panel 1) and regions of decreased activation when the participants were expecting to see a PM stimulus, relative to baseline (baseline–(execution+expectation)) (Panel 2)

Region	Structure	BA	x	y	z	Z
<i>Panel 1</i>						
R frontal pole	IFGO _r	10	40	50	0	4.36
	MFG	10/46	44	56	4	4.12
RLPFC	Fop	45/46	42	22	24	4.03
L frontal pole	MFG	10	–30	62	–6	4.53
	MFG	10	–30	68	2	4.29
R parietal	IPL	39/19	50	–70	38	4.34
	IPS	40/7	44	–60	48	3.69
Precuneus	Pcu	7	12	–66	54	4.41
	Pcu	7	6	–66	48	4.40
	Pcu	7	–8	–72	38	4.29
<i>Panel 2</i>						
L Fronto-temporal	PrG	38/47	–58	2	–10	4.57
	IG	Insula	–46	0	10	4.43

^a L, left; R, right; BA, Brodmann's area; Fop, Frontal operculum; IFGO_r, Inferior frontal orbital gyrus; IG, Insula gyrus; IPL, Inferior parietal lobule; IPS, Inferior parietal sulcus; MFG, Middle frontal gyrus; Pcu, Precuneus; PrG, Precentral gyrus; RDLPFC, Right dorsolateral prefrontal cortex.

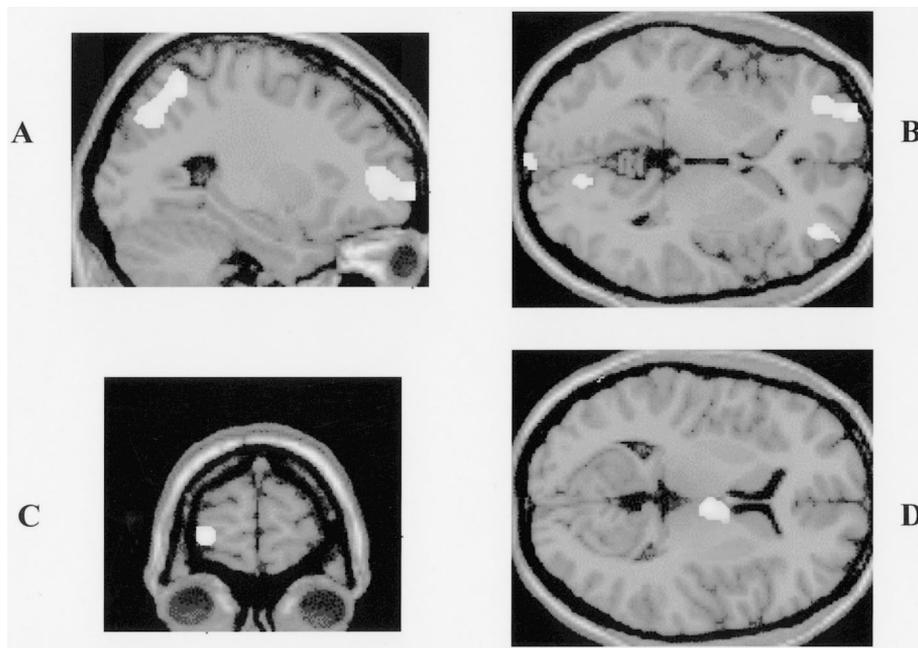


Fig. 3. Selected significant activation foci: plates A, B and C show the right parietal, bilateral orbitofrontal, right lateral prefrontal and regions associated with intention maintenance, and plate D shows the thalamic region associated with intention execution.

At the broadest level of analysis, the results from this study show accord in some regards with both the PET study of Okuda et al. [55] and the human lesion study of Burgess et al. [14]. These studies have also suggested involvement of BA 10 and the right frontal lobe in PM functions. To be more specific, the left BA 10 region implicated in the Okuda et al. [55] study (Talairach and Tournoux co-ordinates $-11, 66, 14$) is not dissimilar to one of those in this study ($-30, 68, 2$), and whilst these co-ordinates may appear to refer to different structures (the superior frontal gyrus and middle frontal gyrus, respectively), it is likely that the difference between them is actually within the resolution parameters of the method and cross-study variation. A case of this sort can also be made for the right lateral frontal region of activation found in this study ($42, 22, 24$), which corresponds closely to a region implicated by Okuda et al. [55] ($35, 26, 38$). Interestingly, the involvement of both left BA 10 and the right lateral region is confirmed in the human lesion study of Burgess et al. [14]. Thus these results show promising cross-method concordance.

The matter of the roles that these regions – and the others implicated in this study – play in PM is, however, more complicated. Consider the regions implicated in the two conditions where the participants were anticipating a target (PM) stimulus (Table 1). The first of these was bilateral activation of BA 10, principally at the level of the middle frontal gyrus. Although as already noted, these regions have been previously implicated in PM functions, they have also been found to be active in other paradigms [29,39,44,60,70]. Blaxton et

al. [7] for instance, found bilateral middle frontal gyrus activations during tasks requiring either the production of semantic associates to novel word cues or recall of the second of a previously studied word pair given the first (Talairach and Tournoux co-ordinates $-32, 50, 12$ and $34, 46, 12$; $-30, 58, 4$ and $34, 42, 20$, respectively). Moreover, in a different study, Blaxton et al. [7] has shown similar bilateral sites of activation ($-24, 58, 0$ and $32, 54, 0$) in an eyeblink conditioning paradigm and Rugg et al. [65] also found the same region ($-32, 52, 0$ and $40, 50, 8$) to be involved in a word recognition paradigm. This last study is of particular interest since Rugg et al. [65] found that peak rCBF increases in these areas were associated with increasing target density in the memory tasks, and concluded from this that these regions support processes that operate selectively

Table 2

SPM results and Talairach and Tournoux [69] co-ordinates for regions of significant change when participants execute their intentions: regions of greater activation when the intentions were executed, relative to the expectation condition where no PM stimuli occurred (execution–expectation) (Panel 1) and Regions of decreased activation when the intentions were executed, relative to the expectation condition where no PM stimulus occurred (expectation–execution) (Panel 2)

Region	Structure	BA	x	y	z	Z
<i>Panel 1</i>						
R thalamus	–	–	6	–12	6	5.41
<i>Panel 2</i>						
RLPFC	MFG	45/46	44	30	16	4.38

on the products of memory retrieval. However, the results of the present study run contrary to this view, since we found bilateral frontopolar activations regardless of whether retrieval occurred. A similar finding of rCBF changes in the absence of retrieval (in the right frontal lobe) was reported by Kapur et al. [44]. The current study therefore, together with the results from the diverse paradigms outlined above, perhaps suggests a relationship with the adoption of a state of watchfulness, which is more akin to the interpretation presented by Nyberg et al. [54] and is similar to the Kapur et al. [44] “retrieval mode” explanation, as least as far as the right frontal lobe is concerned [59]. An interpretation of this kind is lent support by lesion study findings of pathological “absent-mindedness” in patients with damage to these regions (see [13] for review). An explanation at another level would be to argue that the rCBF differences between the ongoing task and the intention conditions reflect the more complex instructions that have to be remembered in the latter. In fact this is axiomatic of situations involving the realisation of a delayed intention. However, it is unlikely to be a good explanation of the right frontal lobe rCBF changes since there was a significant decrease in this region despite no change in the task instructions (i.e. between expectation and execution conditions).

Considering in more detail the right lateral prefrontal activation during the conditions where a PM target was expected (Talairach and Tournoux co-ordinates 42, 22, 24), a similar region has been found to be activated in the selective responding paradigm of Coull et al. [18] (co-ordinates 46, 34, 20). In this study, participants were shown single letters at a rate of one every two seconds, and were required to press a response button whenever a pre-designated target letter appeared. This region was also implicated in Blaxton et al.’s [6] semantic cued recall task, where subjects were asked to recall target items (e.g. “eagle”) given a studied cue word (e.g. “sky”) where the test consisted of half studied and half non-studied items (Blaxton et al.’s [6] co-ordinates 40, 22, 24). Both studies clearly require responding to specified targets, however, the present study helps in further interpretation. We found that right lateral frontal regions showed greater activation in the condition where no targets appeared (“expectation” condition) than when targets were being seen and responded to (“execution” condition). Thus it would seem that the involvement of this region is not with target recognition itself or with post-detection retrieval processes, but with some form of anticipatory processing. This suggestion is supported by the behavioural data, where the significant increases in RTs occurred between the baseline and the two conditions where a PM stimulus was expected and not between the expectation and execution conditions. The three most obvious candidate operations for this anticipatory processing might be

checking the current stimulus against the stored representation of the target; maintenance of the stored representation itself (e.g. working memory); or perhaps some more abstract cognitive operation such as the constraint of search possibilities or strategy adoption (e.g. deciding whether to solve the ongoing problem before checking the stimulus as a PM target or vice versa). However, it is not possible on the present evidence to decide between these alternatives, although perhaps helpful in this respect are the findings from human lesion studies that damage to this region can lead to planning deficits [14,35]. Thus the preliminary adoption of the theoretically neutral term “anticipatory processing” [48] for the functions of this region seems appropriate.

Theories regarding the functions of the next region implicated in this study – the inferior right parietal lobe – are more developed. In most cases [18,56,58], it is assumed to play an important role in sustained attention or vigilance, particularly when the stimuli have a strong visuospatial component: an account of this type might explain the absence of a right inferior parietal activation pattern in the Okuda et al. [55] study (Okuda et al. presented their stimuli auditorily).

Similarly, activations in the precuneus are relatively common in the literature, usually in the context of memory experiments [10,29,40,60,68,70]. The most commonly expressed opinion is that the precuneus plays a role in visual imagery (see Ref. [30] for review). The finding that the precuneus was no more active in the condition where targets occurred than when they were expected but did not occur certainly rules out its role in post-retrieval memory processes [71]; instead a synthesis with the visual imagery hypothesis might be achieved by suggesting a role of the precuneus either in the imagining of the target stimuli, perhaps in a working memory (i.e. rehearsal) context [15], or in maintenance of the prospective response.

Consider next the activation patterns in the area of the insula and precentral gyrus. This was the only region that showed significantly higher activation in the baseline condition relative to those where a PM stimulus was expected. It seems likely therefore that its role is related to the cognitive operations that are being carried out more frequently and/or with greater intensity in the baseline condition. As the lower RTs in the baseline condition indicates (Fig. 2), the participants performed a greater number of the ongoing task items in the baseline condition; thus it seems likely that the insula activation pattern reflects the basic semantic retrieval demands (e.g. at the level of categorisation or classification) of the tasks [22].

Lastly, there are the patterns of activation that were different between the expectation and execution conditions, in other words where an intention is realised rather than just maintained. There was greater activa-

tion in the thalamus (more on the right than left) accompanied by decreased activation in the RDLPFC. Considering first the role of the thalamus, there are three current interlinked characterisations of thalamic cognitive functions that seem especially relevant. The first suggests a general role in attention [9,41], or more specifically in mediating the interaction of attention and arousal [61]. The second stresses the role of the thalamus in episodic retrieval [71], especially in item recognition [43] rather than free recall. The third implicates this region in the monitoring of self-generated actions [5]. These views are clearly not mutually exclusive, and all are potential candidate explanations for the current finding where recognition of the retrieval (PM) cue is likely to be accompanied by increased arousal (because of its significance), retrieval of the intention, and execution of a novel self-generated response. An alternative possibility is that performance of the intended action is likely to require inhibition of the prepotent response tendency. However, this is not a function most commonly associated with the thalamus, and we assume in any case that this must occur after the PM target has been recognised as such, and probably before retrieval of the intended action. Both of these latter functions are more congruent with previous explanations of thalamic rCBF changes in cognition. Overall, therefore, one might conclude that the present evidence suggests a role for the thalamus the recognition of the PM target, or in retrieval of the intended response to it.

In this way, the current findings speak to our current understanding of the relationship between prospective and retrospective memory at a theoretical level. A current debate in the literature [21] centres on whether PM can be considered to be anything more than a special application of retrospective memory. Roediger [64] summarises one side of the debate as follows: "... if retrospective memory ... is the study of lists of events from subjects' pasts, is the study of PM any more than the study of "lists of things to do" in the future?" (p. 151). Essentially this view sees little occurring by way of anticipatory processing between the setting up (or encoding) of the intentions and subsequent recognition of the appropriate retrieval context.

The contrasting view has a long history going back to Lewin [47] and Zeigarnik's [74] notions of "goal tension" and has recent incarnations in the work of Mäntylä and Sgaramella [50] and Goschke and Kuhl [38]. On this account, the representation of intentions is not equivalent to the representation of other sorts of memories, either in form or in level of activation. The results of the present experiment suggest that the intervening period between encoding and the occurrence of the retrieval context is not "cognitively silent" as the first view suggests. In fact, the expectation of a PM stimulus appears to be accompanied by a rich network of cortical activations, which are not equivalent to

those associated with the recognition of (and response to) the retrieval context. There is no reason to assume that this state of anticipation or readiness occurs in situations which do not require self-generated action and where the retrieval context is directly signalled to the participant, as is the case in most retrospective memory paradigms. In this way the current study supports a view more akin to that of Hunt and Smith [42] who regard the difference between PM and traditional retrospective memory paradigms as lying with the degree of "intentionality" involved.

This argument, however, raises an interesting issue. In many prototypical everyday situations that involve the realisation of a delayed intention (e.g. remembering to send a letter tomorrow lunchtime) the retention interval is of sufficient duration that one can be almost certain that over that period less time is spent in thinking about one's intention than in thinking about other matters. However, it is less certain that this is the case for many experimental paradigms in the literature, including the ones used here. In this way, the rCBF changes accompanying the expectation of a target stimulus or "retrieval context" [26] are unlikely to remain static in degree over longer retention intervals. It is more likely that they accompany periods of intention rumination or awareness of a potential retrieval context. The rCBF changes (if any) that accompany other periods during the retention interval are less adequately addressed by the present study, and remain to be discovered. However, whatever the cause of the rCBF changes seen in this study when PM targets were expected but not encountered, it is unlikely that they merely reflect subvocal intention rehearsal or the operation of a phonological short-term memory system since functional imaging studies of these functions consistently report rCBF changes remote from the sites implicated here [2,39,57].

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