

Brief Communication

Parahippocampal Reactivation Signal at Retrieval after Interruption of Rehearsal

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Verbal information is maintained on-line within working memory by rehearsal. However, we still can recall the verbal information when rehearsal is interrupted. Here we show that this is achieved by reactivation of maintained information. We used event-related functional magnetic resonance imaging to identify brain activation at encoding, during memory delay, and at retrieval, within the same trial of a verbal working memory task. On half of the trials, retrieval was tested after arithmetic distraction to interrupt rehearsal of the remembered verbal items. We found that the parahippocampal cortex (PHC) was highly active at retrieval on trials with distraction compared with trials without distraction. The PHC did not show sustained activation during the memory delay. By contrast, the dorsolateral prefrontal cortex (DLPF), left superior temporal region (ST), and Bro-

ca's area showed sustained activation during the memory delay, suggesting their role in maintenance of verbal items. After arithmetic distraction, the DLPF and ST were engaged in arithmetic processing. Thus, these areas could not maintain the verbal items during the distraction. At retrieval of verbal items after the distraction, the DLPF, ST and Broca's area were also active. The activity was taken to reflect reactivated representation of the verbal items. The primary role of the PHC in retrieval may be to trigger the reactivation of these cortical areas that had maintained the remembered items, thereby reactivating the information that is no longer maintained on-line.

Key words: verbal working memory; rehearsal; retrieval; reactivation; parahippocampal cortex; prefrontal cortex

In working memory, information of the remembered item is maintained on-line during the memory delay (Goldman-Rakic, 1987). For verbal items, rehearsal is the key mechanism for this on-line maintenance. At retrieval, the relevant information is selected from the on-line item representation, possibly by the prefrontal cortex (Rowe et al., 2000). However, when rehearsal is interrupted by a distractor task that requires concurrent articulation, the verbal information can no longer be maintained on-line (Baddeley, 1986). This raises the question as to how information is retrieved after distraction.

In long-term memory, the stored item information is thought to be "reactivated" at retrieval (Squire and Zola-Morgan, 1991; Nyberg et al., 1996). It has been shown that the neurons in the neocortical areas that had been active at the initial processing of the information became active again at retrieval, that is, the neurons are "reactivated" (Naya et al., 1996; Nyberg et al., 2000; Wheeler et al., 2000). This reactivation of neurons may be achieved by backward spreading of activation from the medial temporal lobe structures (Naya et al., 2001) or top-down signals from the prefrontal cortex (Tomita et al., 1999).

In the present study, we investigated whether a similar reactivation process is involved in retrieval from memory over a short duration when rehearsal is interrupted by a distractor. The main questions are (1) whether the neocortical areas are reactivated at retrieval after distraction and (2) whether the prefrontal cortex

and medial temporal lobe play specific roles in reactivation. We have analyzed the temporal profile of brain activation during a trial of a verbal working memory task with arithmetic distraction and compared it with activation during the same task without distraction.

MATERIALS AND METHODS

Subjects. Twelve normal, right-handed volunteers (five men, seven women, aged 22–35 years) participated in the study. Written informed consent was obtained from all subjects. The study was approved by the joint ethics committee of the Institute of Neurology and University College London Hospital (London, UK).

Behavioral procedures. Subjects had to remember a sequence of five consonant letters (Fig. 1). A memory delay of variable length (8–16 sec, varied in steps of 2 sec) followed, during which subjects rehearsed the letters. Subsequently subjects had to perform an arithmetic task, serial addition of five numbers, for 6 sec. Subjects were then tested on their memory for the remembered letter sequence.

We tested four conditions in a factorial design with two levels for memory (memory and no memory) and distractor (distractor and no distractor) (Fig. 1). The memory task ("Mem") presented five different letters that were randomly chosen from consonants other than "X". The no memory ("NoMem") task used a sequence of five Xs. In NoMem task as well as in Mem task, subjects had to give a "yes" or "no" response to the memory probe (Fig. 1). Thus, on the memory probe test, a judgment on the probe and a button press were required in both Mem and NoMem tasks, but recall of a five-letter sequence was required only in Mem task. Each of Mem and NoMem tasks was embedded with either a distractor or no distractor task. The distractor task ("Dist") used five numbers randomly chosen from 3 to 9, whereas the no distractor task ("NoDist") used five 0s. The Dist task prevented subjects from rehearsing the remembered letter sequence, whereas the NoDist task permitted them to continue the rehearsal because a 0 was inevitably followed by 0, and the sum would be 0. Thus, there were four conditions, Mem–Dist, Mem–NoDist, NoMem–Dist, and NoMem–NoDist.

After practice of the behavioral paradigm for 20 min, imaging was

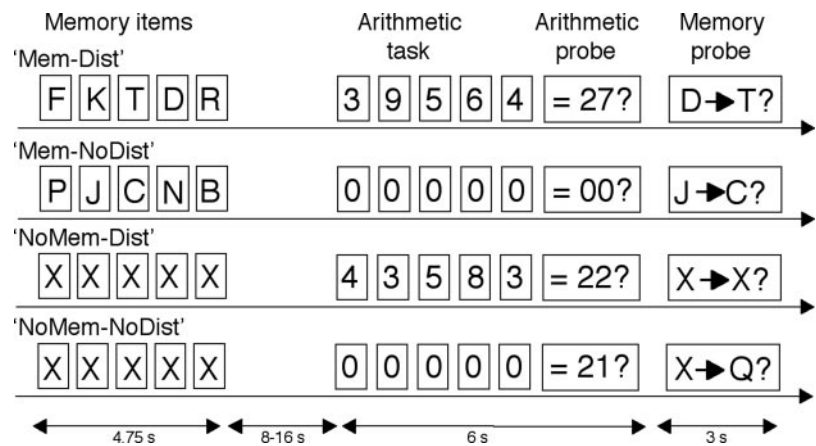
Received April 9, 2002; revised May 22, 2002; accepted May 24, 2002.

This work was supported by the Wellcome Trust. K.S. was supported by the Human Frontier Science Program.

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Figure 1. Behavioral paradigm. A sequence of five consonant letters was presented on a screen, each for 750 msec separated by 250 msec interval. Subjects rehearsed the letters during an unfilled delay period ranging from 8 to 16 sec. Subsequently, five numbers were presented, each for 600 msec separated by 200 msec interval. Subjects had to add the numbers cumulatively. Then, after 200 msec, an arithmetic probe was presented for 800 msec, which the subjects had to confirm or disagree with by pressing a yes or no button. Then, after 1 sec, a memory probe followed, in which two letters were presented. The subjects judged whether the order of the two letters was the same as or different from the remembered sequence and responded by pressing the yes or no button. The four trial types (*Mem-Dist*, *Mem-NoDist*, *NoMem-Dist*, and *NoMem-NoDist*) were intermixed pseudorandomly and presented 15 trials each.



started. The four conditions were intermixed pseudorandomly, and fifteen trials of each condition were presented in a pseudorandom order with intertrial intervals of variable length, 8–16 sec, varied in steps of 2 sec.

Imaging procedures. Imaging was performed using a 2-T Siemens Vision scanner. The functional images sensitive to blood-oxygen level dependent (BOLD) contrasts were acquired by T2*-weighted echoplanar imaging [repetition time (TR) 4.5 sec; echo time (TE) 40 msec; 525 sequential whole brain volume acquisitions; 48 axial slices; slice thickness, 2 mm; slice gap, 1 mm; 64 × 64 in-plane resolution with field of view (FOV) of 192 mm]. The onset of each task trial relative to the preceding image acquisition was jittered in steps of 0.3 sec within 1 TR (4.5 sec). High-resolution structural T1-weighted MPRAGE images (TR 9.5 sec, TE 4 msec, inversion time 600 msec, voxel size 1 × 1 × 1.5 mm, 108 axial slices) were also acquired on all subjects.

fMRI data analysis. Image processing and analysis was performed using SPM99 (<http://www.fil.ion.ucl.ac.uk>). The first five volumes of images were discarded to allow for T1 equilibration. The remaining 520 image volumes were realigned spatially to the first image, and the time-series for voxels within each slice was realigned temporally to acquisition of the middle slice. The resulting volumes were normalized to a standard echoplanar imaging template based on the Montreal Neurological Institute reference brain. The data were spatially smoothed with a Gaussian kernel of full-width half-maximum at 10 mm.

Statistical parametric maps of *t* statistics were calculated for condition-specific effects within a general linear model. The model included separate covariates for transient activation in response to the presentation of each memory item, arithmetic item, arithmetic probe, and memory probe, each separately for the four conditions. We also modeled sustained activation during the memory delay as an epoch with its onset time-locked to the start of the memory delay and with its duration matched to the length of the memory delay. All events and epochs were convolved with a canonical hemodynamic response function. The data were high-pass filtered with a frequency cutoff at 90 sec.

We performed a random-effects analysis. Images of parameter estimates for the contrast of interest were created for each subject (first-level analysis), and were then entered into a second-level analysis using one-sample *t* test across the 12 subjects, thresholded at $p < 0.05$ corrected ($t > 8.95$). For the medial temporal lobe, hypothesis-driven testing was performed on a restricted region of interest including the hippocampus, parahippocampal, entorhinal, and perirhinal cortices ($t > 3.83$). This was determined based on the mean structural images averaged across the 12 subjects.

All the 12 subjects made at least 10 correct responses among the 15 trials in *Mem-Dist*. To equate the weighting of each subject contributing to the second-level analysis, we have randomly chosen 10 correct trials in *Mem-Dist* for each subject. Other correct trials and error trials were modeled separately.

Identification of activation foci. First, we identified areas that show significant phasic activation in response to the presentation of a letter sequence (encoding). We compared phasic BOLD responses between the two *Mem* conditions and the two *NoMem* conditions (main effect of memory). Because subjects did not know whether the trial would be *Dist* or *NoDist*, activation on *Mem-Dist* and *Mem-NoDist* should be the same and so should activation on *NoMem-Dist* and *NoMem-NoDist*. We next identified areas that showed sustained activation during the

memory delay (maintenance) by testing the main effect of memory on sustained BOLD response. Finally, we identified areas that showed phasic activation in response to the memory probe (retrieval) by testing the main effect of memory. Additionally, using those retrieval-related areas thus identified as an inclusive mask, we tested the main effect of distraction, thus identifying areas that were more active on *Mem-Dist* than on *Mem-NoDist*.

Time course of activation. We next examined the temporal profiles of activation. We extracted the adjusted BOLD signal data from the peak of activation foci identified as above. The time course of the signals was realigned at the onset and offset of the memory delay and was resampled in 2 sec time bins. Then, the signals within each bin were averaged across the trials for the 12 subjects (120 correct trials for *Mem-Dist* and 180 trials for each of the other conditions). To investigate at which time point the activation differed between the conditions, we compared the signals for each bin using ANOVA. When there were significant differences across the four conditions, Tukey's honestly significant difference test was used as a *post hoc* test.

RESULTS

Behavioral data

On the memory probe, subjects made more errors on memory trials with distractor than the other conditions: 21% (*Mem-Dist*), 3% (*Mem-NoDist*), 0% (*NoMem-Dist*), and 0% (*NoMem-NoDist*). On the reaction times to the memory probe, there were significant main effects of and an interaction between memory and distractor ($p < 0.001$). The reaction times were longer on memory trials with distractor; 2352 msec, 1809 msec, 1098 msec, and 1062 msec for *Mem-Dist*, *Mem-NoDist*, *NoMem-Dist*, and *NoMem-NoDist*, respectively.

On the arithmetic probe, subjects made only a few errors (<3% in all the four conditions). The reaction times to the arithmetic probe did not differ significantly between memory and no memory trials ($p > 0.1$: 1079 vs 1096 msec for *Mem-Dist* and *NoMem-Dist*, 910 vs 912 msec for *Mem-NoDist* and *NoMem-NoDist*). There was no significant interaction between the memory and distractor factors on the arithmetic probe ($p > 0.1$). The numbers for the arithmetic task were presented quickly, 600 msec for each number separated by a 200 msec interval, so that any attempt to rehearse letter sequences during the arithmetic task would have severely impaired performance on the arithmetic, which was not observed in the present experiment.

Imaging data

After stimulus presentation (encoding), areas including the left parahippocampal cortex (PHC) were more active on memory trials (*Mem*) than on no memory trials (*NoMem*) (Table 1). During the memory delay, areas including the dorsolateral prefrontal cortex (DLPF), posterior part of the left superior tempo-

Table 1. Coordinates and *t* values at the peak activation

Region	Side	Encoding	Maintenance	Retrieval
PHC	L	(-16, -28, -14) 4.91		(-20, -30, -10) 4.39
	R			(20, -28, -12) 4.26
DLPF (BA46)	L		(-40, 36, 16) 11.26	(-36, 32, 12) 9.79
	R		(38, 46, 18) 10.24	(32, 40, 28) 9.85
ST (BA22)	L		(-56, -50, 22) 11.21	(-58, -48, 18) 10.68
Broca (BA44)	L		(-48, 20, 6) 10.42	(-50, 24, 2) 9.22
FG	L	(-36, -42, -24) 11.39		
	R	(40, -54, -24) 12.08		
IOG (BA19)	L	(-46, -70, -12) 11.67		
	R	(46, -68, -8) 10.16		
PM (BA6)	L		(-54, -4, 46) 12.11	(-50, 0, 38) 11.95
	R		(54, 0, 44) 12.26	
PreSMA (BA6)	L		(-4, 8, 58) 11.63	
IPS	L		(-44, -36, 40) 11.82	
	R		(38, -40, 44) 9.98	
CblI	L		(-24, -62, -26) 11.67	
	R		(24, -64, -26) 12.23	
ACC (BA32)	R			(10, 20, 42) 10.77

BA, Brodmann's area; PHC, parahippocampal cortex; DLPF, dorsolateral prefrontal cortex; ST, superior temporal region; Broca, Broca's area; FG, fusiform gyrus; IOG, inferior occipital gyrus; PM, premotor cortex; PreSMA, presupplementary motor area; IPS, intraparietal sulcus; CblI, cerebellum; ACC, anterior cingulate cortex.

ral region (ST), and Broca's area showed sustained activation on Mem trials as compared with NoMem trials (Table 1). There was no significant activation during the memory delay in the medial temporal lobe, even at a lower threshold of $p < 0.05$ uncorrected. At retrieval, areas including the PHC, DLPF, ST, and Broca's area were more active on Mem trials than on NoMem trials (Table 1). Of these areas, only the PHC and anterior cingulate cortex showed significantly higher activation on trials with distraction (Mem-Dist) than on trials without distraction (Mem-NoDist). In Broca's area there was a difference at a low significant level ($p < 0.001$ uncorrected).

After presentation of the memory items, the PHC showed a phasic increase of BOLD response on both Mem-Dist and Mem-NoDist trials compared with NoMem trials (Fig. 2). The response peaked at 4 sec after the onset of the memory delay, that is, 8.75 sec after the presentation of the first letter. Taking into account the delay of BOLD responses, this activity was taken to be related to the encoding of a letter sequence. A phasic BOLD response was also observed after the offset of the memory delay on Mem-Dist and Mem-NoDist trials, but the response on the Mem-Dist was significantly larger than that on Mem-NoDist between 14 and 18 sec after the offset of the memory delay ($p < 0.05$). The peak of the PHC response on Mem-Dist trials was seen at 14 sec after the offset of the memory delay, that is, 8 sec after the presentation of the memory probe, suggesting that the response was related to the retrieval of a letter sequence after distractors. The BOLD response in the PHC did not differ between NoMem-Dist and NoMem-NoDist trials; the presence or absence of the arithmetic distractor task, which was presented between 0 and 6 sec after the offset of memory delay, did not affect the PHC activation. The PHC did not show sustained activation between the two phasic responses. From 12 sec after the onset of memory delay to 8 sec after the offset of memory delay, the BOLD signal in the two Mem conditions did not differ significantly from that in the two NoMem conditions ($p > 0.1$).

In contrast, the DLPF showed sustained increase of the BOLD response in the two Mem conditions compared with NoMem

conditions (Fig. 2). The DLPF activity in the two Mem conditions was significantly larger than that in the NoMem-NoDist condition from 6 sec after the onset of the memory delay to 18 sec after the offset of the memory delay ($p < 0.05$). Importantly, the activity was sustained throughout the memory delay, whatever the length of the memory delay (8–16 sec). On NoMem-Dist trials compared with NoMem-NoDist trials, the BOLD signals in the DLPF showed a phasic increase after the offset of memory delay with its peak at 10 sec after the offset of the memory delay. Because the arithmetic task was presented between 0 and 6 sec after the offset of the memory delay, this activity was taken to be related to the arithmetic processing. However, during this time period, the BOLD signals in the DLPF did not differ significantly between Mem-Dist (when the subjects were performing arithmetic) and Mem-NoDist trials (when they were maintaining the items) ($p > 0.1$).

The ST and Broca's area also showed sustained activity during the memory delay (Fig. 2); their activity on the Mem trials was significantly larger than that on the NoMem trials from 2 sec after the onset of memory delay to 18 sec after the offset of memory delay ($p < 0.01$). The time course of BOLD signals in the ST was similar to that in the DLPF; on NoMem-Dist trials there was a phasic increase after the offset of memory delay (arithmetic processing), and between Mem-Dist and Mem-NoDist trials there was no significant difference.

In contrast, Broca's area differed from the DLPF and ST with respect to the response to the arithmetic distractor (Fig. 2). Its BOLD response did not increase on NoMem-Dist as compared with NoMem-NoDist after the arithmetic. The response was significantly smaller on Mem-Dist than that on Mem-NoDist at time 8–12 sec after the offset of memory delay, which corresponds to the period of arithmetic distraction. However, a more superior and posterior portion of the Broca's area (coordinate: -48, 20, 10) was active during the arithmetic distraction. On NoMem-Dist this area showed a phasic increase of activation with its peak at 10 sec after the offset of the memory delay. On Mem-Dist, this

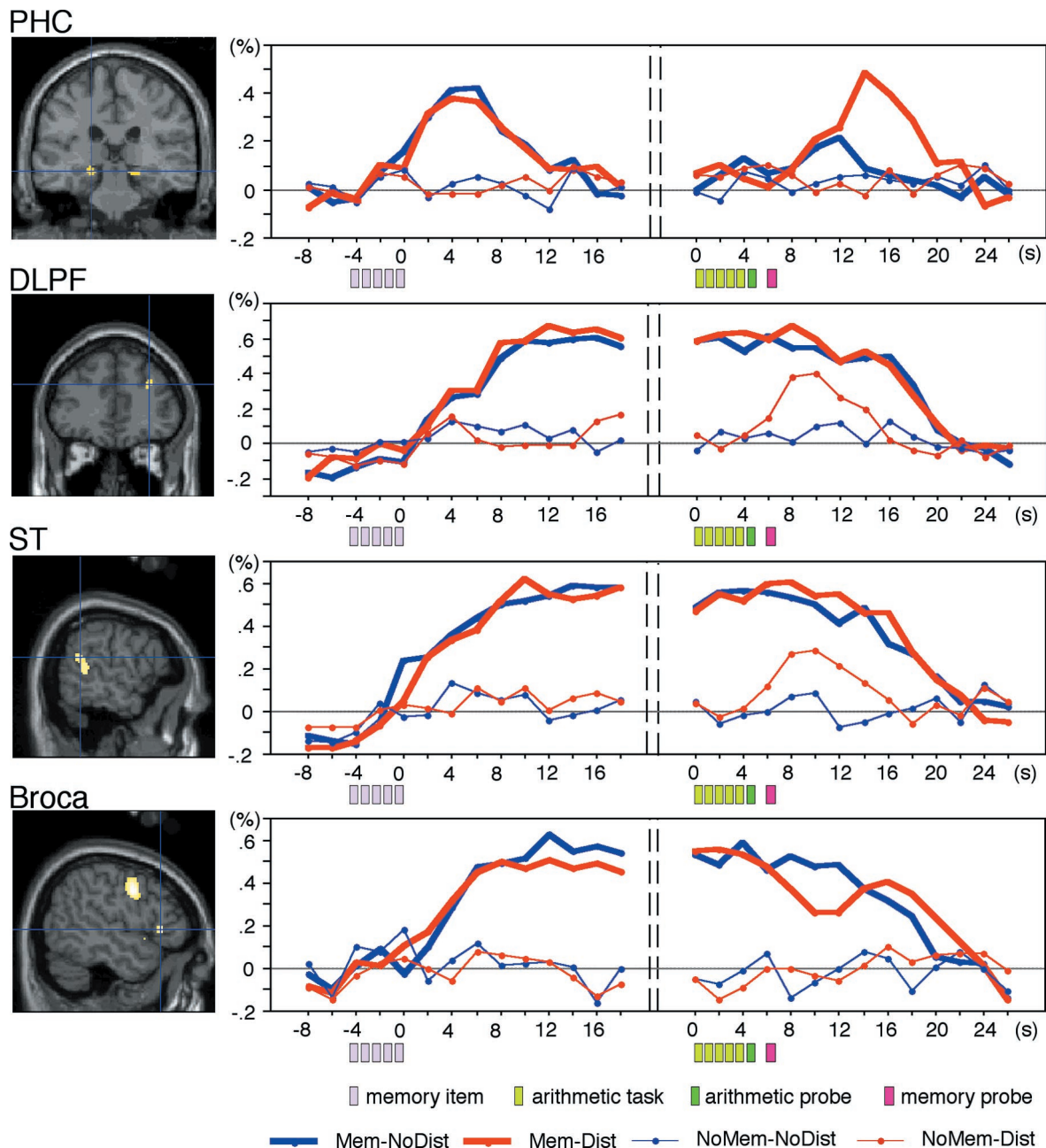


Figure 2. Areas showing significant activation at retrieval (left) and their time course of activation aligned at the onset (center) and offset (right) of the memory delay. From top to bottom, activities in the PHC, DLPF, ST, and Broca's area are shown. The timing of task events are shown below each panel. The four conditions are shown separately.

area showed significant activation during the memory delay, during the arithmetic distraction, and also at retrieval.

DISCUSSION

The present study showed that the PHC was active at verbal retrieval specifically when the rehearsal was interrupted by arithmetic distraction. We argue that this activation reflects a reactivation signal.

Parahippocampal activation at retrieval after distraction

Mental arithmetic has been shown to use the subvocal rehearsal component of working memory (Logie et al., 1994), and hence is effective in suppressing rehearsal of verbal items (Baddeley,

1986). In the present study, subjects were allowed to rehearse the verbal items for 8–16 sec, and then were interrupted by the arithmetic task. On memory trials with the distracting arithmetic task (Mem-Dist), all subjects reported that they were unable to rehearse the letter sequence during the arithmetic. At retrieval, subjects had to recall the remembered five-letter sequence. This required recovery or “reactivation” of the off-line information. By contrast, on memory trials without distraction (Mem-NoDist), subjects were able to continue the rehearsal during the nondistracting arithmetic task and maintained the verbal information on-line. Thus, there was no need to reactivate the information at retrieval because it was still active in working memory. The present study has shown that the PHC is especially activated at

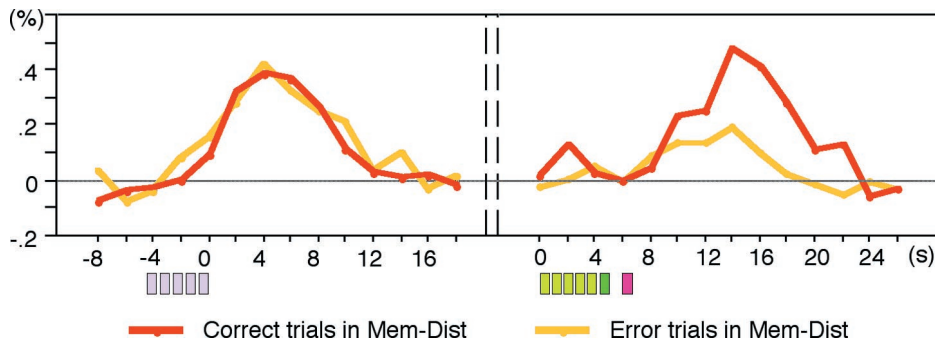


Figure 3. Differential time course of parahippocampal activation between correct and error trials.

retrieval when the memory item is no longer maintained on-line as compared to when the item is maintained on-line. The finding suggests that the PHC plays a role in reactivating the off-line information at retrieval. The activity in the PHC cannot be attributable to performing mental arithmetic because the PHC was no more active in NoMem–Dist than in NoMem–NoDist.

An important question is whether the parahippocampal reactivation processes are essential for retrieval of the off-line information. To answer the question, we have compared all the correct and error trials across subjects (142 vs 38 trials) (Fig. 3). We were only able to perform the fixed-effects analysis because of variation in the number of error trials across subjects. We found that the PHC activity was significantly smaller on error trials than on correct trials ($p < 0.05$ corrected for small volume correction). This effect was observed only at retrieval. At encoding and during maintenance, the PHC activity did not differ significantly between correct and error trials. Although the finding should be confirmed with a random-effects analysis on a larger set of data, it suggests that the parahippocampal activity at retrieval is critical for correct retrieval after distraction.

The idea that the medial temporal lobe plays a role in reactivation of long-term memory has been suggested previously (Squire and Zola-Morgan, 1991; Nyberg et al., 1996, 2000). Our study shows that only 6 sec of distraction is sufficient to elicit the reactivation process in the PHC and that the process is not needed when the memory is held on-line. The finding may explain why patients with medial temporal lobe lesions can remember items as long as they rehearse the items, but they fail totally as soon as they are distracted (Scoville and Milner, 1957). Recently Ranganath and D'Esposito (2001) have also shown that the PHC was active at retrieval in a working memory task for faces, in which a memory delay of 7 sec was used. The activity was observed even when there was no distractor. The present study also showed significant activation at retrieval without distraction, but demonstrated in addition that the activation was much enhanced when retrieval was preceded by a distractor task. It may also be significant that we tested memory for familiar letters, whereas Ranganath and D'Esposito (2001) tested memory for novel faces (Stern et al., 2001).

The PHC was not active during on-line maintenance of the verbal items. Although we cannot exclude the possibility of insufficient sensitivity, the finding is consistent with Ranganath and D'Esposito (2001). Thus, the activity in the PHC may not reflect the representation of verbal items per se.

Neocortical activation at retrieval

The item representations may be maintained in the DLPF, ST, and Broca's area, which showed sustained activation during the memory delay. During the arithmetic distraction on Mem–Dist

trials, these areas could no longer hold the remembered verbal information because they were either engaged in arithmetic processing or were less active during the arithmetic. However, the DLPF, ST and Broca's area were active at retrieval, well after the arithmetic distraction. Thus these neocortical areas became re-engaged in the memory processing. Because these areas maintained the item representations, their activity at retrieval on Mem–Dist trials may reflect reactivated item representations. On Mem–NoDist trials, on the other hand, their activity during the nondistracting arithmetic task may reflect the on-line maintenance continuous from the preceding memory delay period. Thus, at retrieval on Mem–NoDist trials, the activity in the DLPF, ST, and Broca's area may reflect the item representations that had been already active. Unlike the activity in the PHC, the activity in DLPF and ST at retrieval did not differ between Mem–Dist and Mem–NoDist. These neocortical areas may be involved in retrieval irrespective of whether the information is retrieved from on-line working memory or from off-line stored memory. At a low threshold, activity in Broca's area at retrieval was higher in Mem–Dist than in Mem–NoDist. At retrieval after interruption of rehearsal (Mem–Dist), subjects had to restart the rehearsal of the remembered verbal items, whereas in Mem–NoDist subjects simply continued the rehearsal. Initiation of rehearsal has been shown to result in an increase of activation in Broca's area (Chein and Fiez, 2001).

Mechanisms of reactivation

Reactivation of item representation in the DLPF, ST, and Broca's area may require interactions with the medial temporal regions that include the parahippocampal cortex (Lavenex and Amaral, 2000). One possibility is that the PHC triggers the reactivation of information stored in the ST and Broca's area. Although the present study could not determine the causality of the activation, the idea would be supported by backward spreading of item-specific activity from the medial temporal lobe to the neocortical memory store (Naya et al., 2001).

Our results suggest that the role of the DLPF may not be specific to reactivation processes. Prefrontal cortex has been shown to play critical roles in recall of off-line information (Shimamura, 1995; Buckner and Koutstaal, 1998; Tomita et al., 1999). We have shown, in addition, that the prefrontal cortex is also active at retrieval of on-line information. The area specifically involved in recall of off-line information may be located more anteriorly (Brodmann's area 10) than that identified in the present study (area 46) (Buckner and Koutstaal, 1998). The DLPF may also play different roles from the ST and Broca's area. In another study, we tested the same memory paradigm for letters except that an immediate memory task for five numbers (low interference) or five letters (high interference) was used as a

distractor (Sakai and Passingham, 2002). At retrieval of a letter sequence, the DLPF was significantly highly active when letters were used as distractors than when numbers were used as distractors. The activity in the PHC, ST, and Broca's area did not differ significantly between the two conditions. The finding suggests that the DLPF may play roles in counteracting the interference effects. This may be achieved by top-down selection signals from the DLPF to the posterior cortical areas (Tomita et al., 1999). Sustained activation in the DLPF during the memory delay may also reflect the repeated selection of items in memory to counteract the future distraction (Sakai et al., 2002).

REFERENCES

- Baddeley AD (1986) Working memory. New York: Oxford UP.
- Buckner RL, Koutstaal W (1998) Functional neuroimaging studies of encoding, priming, and explicit memory retrieval. *Proc Natl Acad Sci USA* 95:891–898.
- Chein JM, Fiez JA (2001) Dissociation of verbal working memory system components using a delayed serial recall task. *Cereb Cortex* 11:1003–1014.
- Goldman-Rakic P (1987) Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In: *Handbook of physiology, The nervous system, Higher functions of the brain, Section 1, Vol V, Part 1* (Plum F, ed), pp 374–417. Bethesda, MD: American Physiological Society.
- Lavenex P, Amaral DG (2000) Hippocampal-neocortical interaction: a hierarchy of associativity. *Hippocampus* 10:420–430.
- Logie RH, Gilhooly KJ, Wynn V (1994) Counting on working memory in arithmetic problem solving. *Mem Cognit* 22:395–410.
- Naya Y, Sakai K, Miyashita Y (1996) Activity of primate inferotemporal neurons related to a sought target in pair-association task. *Proc Natl Acad Sci USA* 93:2664–2669.
- Naya Y, Yoshida M, Miyashita Y (2001) Backward spreading of memory-retrieval signal in the primate temporal cortex. *Science* 291:661–664.
- Nyberg L, McIntosh AR, Houle S, Nilsson L-G, Tulving E (1996) Activation of medial temporal structures during episodic memory retrieval. *Nature* 380:715–717.
- Nyberg L, Habib R, McIntosh AR, Tulving E (2000) Reactivation of encoding-related brain activity during memory retrieval. *Proc Natl Acad Sci USA* 97:11120–11124.
- Ranganath C, D'Esposito M (2001) Medial temporal lobe activity associated with active maintenance of novel information. *Neuron* 31:865–873.
- Rowe JB, Toni I, Joseph O, Frackowiak RSJ, Passingham RE (2000) The prefrontal cortex: response selection or maintenance within working memory? *Science* 288:1656–1660.
- Sakai K, Passingham RE (2002) Prefrontal selection and parahippocampal reactivation at memory retrieval. *NeuroImage* 16:S10368.
- Sakai K, Rowe JB, Passingham RE (2002) Active maintenance in prefrontal area 46 creates distractor-resistant memory. *Nat Neurosci* 5:479–484.
- Scoville WB, Milner B (1957) Loss of recent memory after bilateral hippocampal lesions. *J Neurol Neurosurg Psychiatr* 20:11–21.
- Shimamura AP (1995) Memory and the prefrontal cortex. *Ann NY Acad Sci* 769:151–159.
- Squire LR, Zola-Morgan S (1991) The medial temporal lobe memory system. *Science* 253:1380–1386.
- Stern CE, Sherman SJ, Kirchoff BA, Hasselmo ME (2001) Medial temporal and prefrontal contributions to working memory tasks with novel and familiar stimuli. *Hippocampus* 11:337–346.
- Tomita H, Ohbayashi M, Nakahara K, Hasegawa I, Miyashita Y (1999) Top-down signal from prefrontal cortex in executive control of memory retrieval. *Nature* 401:699–703.
- Wheeler ME, Petersen SE, Buckner RL (2000) Memory's echo: vivid remembering reactivates sensory-specific cortex. *Proc Natl Acad Sci USA* 97:11125–11129.