Cerebral Cortex April 2007;17:778–786
doi:10.1093/cercor/bhk035
Advance Access publication May 17, 2006

A Common Prefrontal–Parietal Network for Mnemonic and Mathematical Recoding Strategies within Working Memory

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Previous studies have indicated that the lateral prefrontal cortex (LPFC) is closely involved in strategic recoding, even when such processes lessen task demands. For example, 2 studies presented, in the spatial and verbal domains, sequences of stimuli for participants to retain during a short interval and then retrieve. Stimuli were either randomly arranged or structured (forming symmetries and regular shapes for the spatial task and mathematical patterns for the verbal task). Although participants performed the structured tasks better by reorganizing or "chunking" them into more efficient forms, LPFC activity was greater for the structured compared with the random sequences. However, although these results demonstrate that LPFC is involved in strategic recoding, regardless of the type of modality, it remains to be seen whether such a result generalizes to different types of strategic recoding processes. To test this, we presented digit sequence trials that separately emphasized mnemonic or mathematical recoding strategies. While participants were able to gain a performance benefit from either type of recoding strategy, increased LPFC activity was observed for both mathematical and mnemonic recoding trials, compared with either unstructured sequences or control conditions matched for mathematical or mnemonic processes. However, mathematically structured trials activated the LPFC significantly more than mnemonic recoding trials. In addition, lateral posterior parietal cortex was consistently coactivated with LPFC for strategic recoding trials, both in the current experiments and in previous related studies. We conclude that a prefrontal–parietal network is involved in strategic recoding in working memory, regardless of the type of recoding process.

Keywords: chunking, digit span, neuroimaging, parietal cortex, prefrontal cortex, working memory

Introduction

Considerable data suggest that the lateral prefrontal cortex (LPFC) is involved in strategic control (Petrides and Milner 1982; Shallice and Burgess 1991; Owen and others 1996; Bor and others 2001, 2003, 2004; Savage and others 2001; Manly and others 2003; Kondo and others 2005). For instance, patients with prefrontal damage often fail to implement prespecified strategies (Shallice and Burgess 1991) or notice obvious tactics that improve performance (Owen and others 1996). In addition, normal volunteers activate the LPFC when applying strategies in both working memory (WM) and long-term memory (LTM) domains (Savage and others 2001; Bor and others 2003, 2004; Kondo and others 2005).

Neuroimaging studies have also implicated the LPFC in task difficulty (Duncan and Owen 2000). Using a meta-analysis, Duncan and Owen (2000) demonstrated that in a wide variety of cognitive domains more demanding tasks were associated with increases in activity in a network of regions, including the dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC), as well as the anterior cingulate. However, whereas this is undoubtedly a common empirical finding, an increasing number of studies involving strategic processing have shown the opposite result: applying effective strategies has been reported both to lessen task demands and increase LPFC activity (Prabhakaran and others 2000; Savage and others 2001; Bor and others 2003, 2004; Manly and others 2003). For example, in a previous study, we presented either geometrically structured or unstructured novel sequences of spatial locations for participants to encode in WM (Bor and others 2003). Structured sequence trials were recalled significantly better, with concomitant activation increases in LPFC. Further behavioral testing indicated that the performance increases for the structured trials were due to participants strategically recoding or "chunking" (Miller 1956; Ericcson and others 1980) these sequences into a more efficient form based on the symmetries and regular shapes inherent in them. Chunking involves reorganizing the material into familiar or regular structures and can sometimes improve WM performance substantially (Ericcson and others 1980). In many domains, including language acquisition and chess (Bryan and Harter 1899; Chase and Simon 1973; Gobet and others 2001), chunking has been proposed as the major basis for increasing expertise.

This spatial chunking result has recently been replicated in the auditory–verbal domain (Bor and others 2004). In that study, participants were required to encode novel sequences of either mathematically structured (e.g., 24689753) or random digit sequences into WM. Again, performance improvement for the structured sequences was linked to raised activity in the LPFC.

Whereas these 2 studies suggest that one critical role of the LPFC is in strategically exploiting data redundancy in order to optimize performance, 3 important issues remain unresolved. First, it is unclear whether the structures were recoded based on their mathematical or mnemonic content. For instance, the sequence 24689753 might have been converted into the algorithm: start at 2 and then add 2 three times, then start at 9 and subtract 2 three times. Alternatively, patterns of single-digit even and odd numbers might have been recognized from well-established LTM representations (for instance, 2468 being recalled as part of a chant). Second, although the studies were well controlled for WM content, it is possible that LPFC activity was being driven by either episodic memory retrieval or mental arithmetic, rather than by strategic processing. Third, the lateral parietal cortex was activated in addition to the LPFC for all structured versus unstructured contrasts in our previous studies. Therefore, we sought to establish whether this involvement generalizes to other types of strategic recoding,

rather than, for example, playing a specific role in mental arithmetic.

In order to test these questions, we carried out 2 experiments using novel digit sequence tasks that emphasized either purely mnemonic or purely mathematical recoding processes. For the purely mnemonic trials, 4-digit sections of novel 8-digit sequences were identical to unstructured chunks that had been overlearned prior to functional magnetic resonance imaging (fMRI) scanning. Participants could therefore recode these sections in order to lessen WM demands and improve performance. For the purely mathematical trials, structured relations between items in novel sequences were not reliant on heavily established mnemonic information (such as multiplication tables). Nor did sequences include digit chunks learned for the mnemonic trials above. Instead, novel mathematical rules could be recognized to improve performance. In the first experiment, both mathematical and mnemonic recoding tasks were used, as well as random trials that included neither mathematical structure nor mnemonic content. In addition, a mnemonic control was used that required retrieval of the same memory chunks but no recoding. One surprising result of this experiment was that the mathematical recoding trials activated the LPFC to a greater extent than the mnemonic recoding trials. To ascertain whether this was due to mental arithmetic processes, known to activate the same regions, or recoding processes, a second experiment was carried out including the mathematical recoding task and a mental arithmetic control. This control matched the mathematical recoding task for mental arithmetic but did not require any recoding process.

Whereas the LPFC has been activated in our previous studies across a range of modalities, we predicted that this result would extend to a range of strategic recoding processes. Therefore, in both the mnemonic and mathematical recoding trials, we predicted activation increases in LPFC. In addition, given that lateral parietal activity was observed in all previous contrast-involved strategic recoding, we predicted that this region would be coactivated with LPFC in the current experiments.

Materials and Methods

FMRI Experiment 1: Mnemonic and Mathematical Chunking

Participants

Eighteen right-handed participants (11 females, aged 18–31 years) were scanned for approximately 40 min of echo planar imaging (EPI) and 30 min of structural scans. All participants gave informed written consent for participation in the study after its nature and possible consequences had been explained to them. The study was approved by the Local Research Ethics Committee.

Task Details

During the week prior to fMRI scanning, participants carried out a behavioral task over the course of 4 h, spread over 3 or 4 sessions. Participants were told to imagine that they were a new receptionist in a company and had to memorize the 4-digit phone extension number of 20 key members of staff (10 males). Stimulus lists were presented and tested in groups of 5 of the same gender until proficiency was reached, then combined into a complete single-gender group of 10 until proficiency was reached again before finally combined into all 20 stimuli. Initially, a face photograph was presented for 8 s above a name, which was above a 4-digit number, repeated once within a group of 5, to elicit encoding. The 4-digit numbers were chosen to ensure that they had no mathematical structure linking the single digits (e.g., 2638). During subsequent testing, the criterion to reach the next stage was 20 correct answers in a row. For the first stage, a face and a name were presented above 2 sets of 4-digit numbers, so that the participant had to choose the correct set by keyboard response. For the second stage, the face and name were presented above a single 4-digit number with a single non-initial digit missing, which the participant would input via the keyboard. Once the criterion had been reached for this, 2 adjacent numbers would be missing and then the last 3 numbers, and finally all numbers would have to be recalled and entered. Once this criterion had been reached, participants would only be shown either the face or name and would have to input all 4 numbers correctly. Participants would not be allowed to participate in the fMRI study unless at least 50 correct answers in a row were posted for the full set of stimuli on this final stage. In this way, participants had overlearned 20 sets of mathematically unstructured 4-digit numbers prior to fMRI scanning.

During fMRI scanning, 3 span conditions and 1 memory control condition were visually presented. In total, subjects carried out 24 trials for each condition. A 1 s cue was shown to indicate the current trial type, followed by a 0.5 s delay. For the 3 span conditions, 4 sets of double-digit numbers were presented in turn in the center of the screen (500 ms stimulus onset and 250 ms stimulus offset for each number). Subjects were encouraged to encode all items as double digits in the format presented. Double digits were used, as opposed to a previous related study (Bor and others 2004) that used single digits, in order to avoid any possibility of recoding via multiplication tables or other memory device in the mathematical span condition (see below). There followed a delay that exponentially varied between 1.5 and 7 s (mean 2.89 s). Following this, 3 asterisks presented in the center of the screen for 750 ms cued the subject to make a response. The random span condition (RandS) (see Fig. 1*A*) involved no mathematical structure and bore no relation to the numbers learned during the prior behavioral study. All mathematical span condition (MathS) trials (see Fig. 1*B*) included a novel mathematical structure, which could take the form of addition or subtraction (e.g., 18 30 42 54, thus increasing each time by 12), doubling or halving (e.g., 07 14 28 56), or symmetry (e.g., 81 18 72 27). Most MathS trials involved addition or subtraction. Doubling/halving- and symmetry-based trials were included in order to widen the subject's search for possible strategies. In addition, the inclusion of doubling/halving- and symmetry-based trials prevented the subject from employing the strategy of encoding only the first 2 double digits and inferring the whole sequence from this, which would be an effective strategy if only addition and subtraction trials were used. Subjects were informed about, and given examples of, the possible structures during practice immediately before scanning. Care was taken to ensure no resemblance between MathS trials and the 4-digit numbers learned from the behavioral study. For the memory span condition (MemS) (see Fig. 1*C*), although no trials included any mathematical structure, the first 2 double-digit stimuli in each trial corresponded to 1 extension number out of the set of 20 from the prior behavioral study, whereas the last 2 double digits corresponded to another. Subjects were told that the mathematical pattern in MathS trials and mnemonic information in MemS trials may help them carry out the task but were not explicitly told to use such information. For the memory control condition (MemCon) (see Fig. 1*D*), subjects were serially presented in the center of the screen with 2 names from the prior behavioral study (1 s stimulus onset and 0.5 s stimulus offset for each name) and were required to respond with the 2 corresponding phone extension numbers. The 4 trial types were presented in a pseudorandom interleaved fashion.

For all the 4 conditions, subjects were required to respond verbally with 4 double-digit numbers, spoken always as double digits (e.g., "twenty-one" for 21 and "zero-seven" for 07). Subjects were given a 5 s window in which to respond.

Subject responses were recorded using a digital audio tape recorder. In order to remove scanner noise so that responses were audible, a post hoc noise cancellation tool was used outside the scanner (Cusack and others 2005).

FMRI Data Acquisition and Analyses

Subjects were scanned on a 3-T Bruker scanner. Functional images were collected using 21 slices covering the whole brain (slice thickness = 4 mm, interslice distance = 1 mm, in-plane resolution = 3.91 × 3.91 mm) with an EPI sequence (time repetition = 1.1 s, time echo = 27.5 ms, flip angle = 65.5 degrees). Six hundred and twenty-five scans were acquired

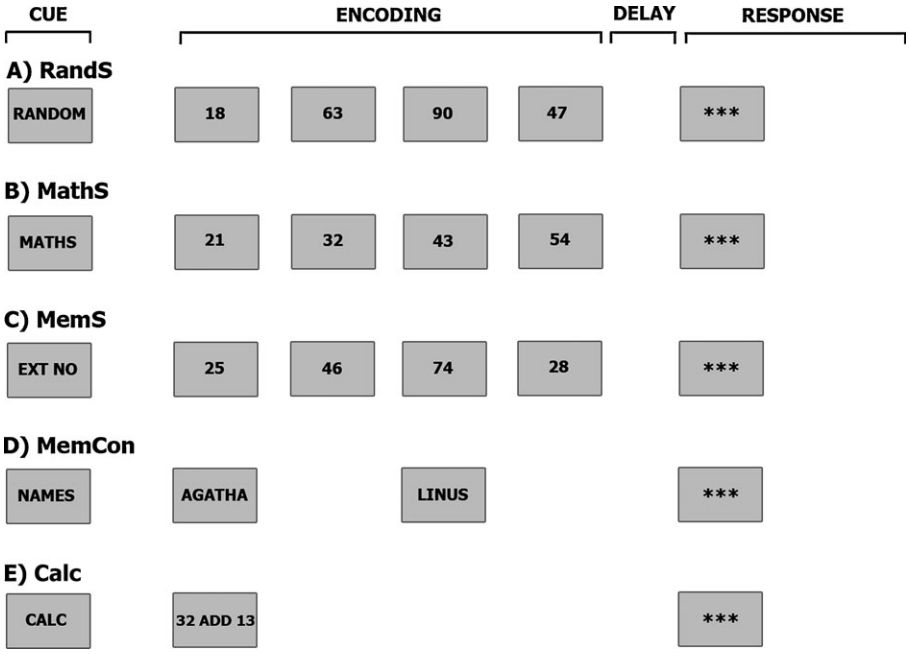

Figure 1. Conditions used in fMRI experiments 1 and 2. For all conditions, a 1 s cue preceded an encoding stage (approximately 3 s). Following stimulus presentation, a variable delay (approximately 4 s) ended in the presentation of 3 asterisks, which signified the start of the verbal response stage (5 s). (*A–D*) were presented to participants in experiment 1, whereas (*B*) and (*E*) were presented in experiment 2. (*A*) Random span condition (RandS) participants were visually presented with a pseudorandom sequence of 4 double digits to encode over a short delay and then repeat back. (*B*) Mathematical span condition (MathS) as (*A*), except that there was a mathematical pattern that linked the 4 double digits together (e.g., increasing by 11 each time, as in this case). (*C*) Memory span condition (MemS) as (*A*), except that the first 2 double digits corresponded to one 4-digit number overlearned in a previous behavioral study, whereas the second pair of double digits corresponded to another. (*D*) Memory control condition (MemCon) participants were presented with 2 names from a prior behavioral study and had to retrieve the 2 linked 4-digit numbers. (*E*) Mental arithmetic condition (Calc) participants were provided with a single instruction and were required to generate 4 double-digit numbers from the instruction (e.g., the current case would require a response of "32 45 58 71").

per run, including 10 dummy scans. Three functional runs were acquired. Spoiled gradient recalled (SPGR) structural scans were also collected for each subject. In addition, field maps were acquired in order to correct distortions in the functional images during analysis (Cusack and Papadakis 2002).

All fMRI data were processed and analyzed using SPM2 software (http://www.fil.ion.ucl.ac.uk/spm). Prior to analysis, all images were corrected for slice timing and then realigned with respect to the first image. Distortions in the EPIs were corrected using the field maps and a custom toolbox (Cusack and others 2003) (see also http://www.mrc-cbu.cam.ac.uk/Imaging/Common/fm_background.shtml). All images were then normalized using affine and smoothly nonlinear transformations to a template in Montreal Neurological Institute (MNI) space. Finally, all normalized images were spatially smoothed with a 10-mm full width half maximum Gaussian kernel.

For the analysis, each trial was split into 4 events: cue, encoding, delay, and retrieval. Due to potential subject movement from verbal responses at the retrieval stage, this event was not included in any contrast. Consequently, trial-based contrasts were taken only to include encoding and delay events. Encoding- or delay-specific activations were not examined as durations of these events were too brief to be adequately disambiguated from one another.

Single-subject statistical contrasts were set up by using the general linear model to fit each voxel with a combination of functions derived by convolving the standard hemodynamic response with the time series of the events, removing low-frequency noise with a high-pass filter, and correcting for temporal autocorrelation with an auto regressive (AR) (1) process. Group data were analyzed with a random effects analysis. All reported peaks were from the group analysis and had to pass a whole-brain false detection rate (FDR) (Benjamini and Hochberg 1995; Genovese and others 2002) threshold of $P < 0.05$. The FDR approach controls for the expected proportion of false positives among supra-threshold voxels. An FDR threshold is determined from the observed P value distribution and hence is adaptive to the amount of signal within a given contrast (Genovese and others 2002). In addition, all significant peaks were required to be at least 20 voxels in volume.

All reported coordinates underwent a transformation from normalized MNI space to Talairach space (www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml), in order to ascertain more precisely the site of activation relative to the atlas of Talairach and Tournoux (1988).

An additional region of interest (ROI) analysis was carried out to directly test differential activation between the trial types in specific frontal and parietal regions commonly associated with task demand: mid-DLPFC, mid-VLPFC, anterior cingulate cortex (ACC) (Duncan and Owen 2000), and inferior parietal sulcus (IPS) (Duncan 2006). The DLPFC ROI centers were –40 28 19 (left) and 35 31 22 (right), the VLPFC ROI centers were –41 20 0 (left) and 37 20 3 (right), the ACC center was 0 26 31, and the IPS centers were –37 –53 40 (left) and 37 –53 40 (right). The ROI in each case was defined as a 10-mm radius sphere surrounding the coordinates given above. The frontal ROIs are identical to those used in our previous span chunking studies (Bor and others 2003, 2004). In order to analyze the ROIs, the MarsBaR software suite was used (http://marsbar.sourceforge.net/). For each ROI, a t-test was carried out to compare the mean voxel value during the structured versus the unstructured trials, as based on the whole-brain group analysis.

Results

Behavioral data. For all conditions, each trial was marked out of 8. A single digit in a trial was marked correct if it matched the number and temporal position during presentation. A repeated measures analysis of variance showed that there were significant differences among the conditions ($F_{3,51} = 19.14$, $P < 0.001$). Further analysis revealed that RandS trial accuracy (78.2%) was significantly lower than MathS accuracy (86.9%) ($t = 3.91$, df = 17, $P = 0.001$), MathS accuracy was significantly lower than MemS accuracy (92.1%) ($t = 3.29$, df = 17, $P = 0.004$), and MemS accuracy exhibited a trend toward lower performance compared with MemCon accuracy (96.2%) ($t = 2.06$, df = 17, $P = 0.055$, 2 tailed). In line with this, most subjects reported that

RandS was the most difficult, followed by MathS, and then MemS, with MemCon being the easiest.

Functional imaging data. When the chunking span (MathS and MemS) conditions were compared with RandS (see Table 1 and Fig. 2*A*,*B*), extensive lateral prefrontal and parietal activations were observed in a similar network for both contrasts. Specifically, the MathS minus RandS contrast yielded bilateral increases in large portions of LPFC and lateral parietal cortex. In addition, bilateral increases were observed laterally in the inferior temporal gyrus (Brodmann area [BA] 37). No significant activations were observed for the opposite contrast (RandS – MathS). MemS exhibited significant increases compared with RandS bilaterally in lateral parietal cortex but only in the left LPFC. No lateral temporal cortex activations were observed, although significant activations were seen in medial parietal regions and the hippocampus. For the opposite contrast (RandS – MemS), only one activation was observed, in superior temporal gyrus (BA 22).

When MemS was compared with its own control (MemCon) (Table 2 and Fig. 2*C*), a similar prefrontal–parietal network (PPN) was activated. Specifically, activation increases were observed in left LPFC and bilaterally in lateral parietal cortex. For the opposite contrast (MemCon – MemS), no significant activations were observed.

When the chunking span trials were compared directly (Table 3 and Fig. 3), MathS exhibited significant increases in activation bilaterally in

Table 1
Experiment 1: Peak increases in activation for chunking span conditions versus RandS

Brain regions and BAs	Coordinates			Cluster volume (voxels)	*t*-Score
	x	*y*	*z*		
MathS – RandS					
R lateral frontal					
46	48	42	15	366	6.77
46	48	28	26		4.75
44	48	13	21		6.39
8	27	20	40	131	6.06
L lateral frontal					
47	−42	40	−7	234	4.43
45	−50	35	7		4.16
9	−50	19	29		5.14
6	−30	17	43	257	7.43
R lateral parietal					
7	42	−38	46	256	4.51
7	30	−59	47		4.57
7	42	−68	34		4.28
L lateral parietal					
40	−48	−44	49	447	8.3
7	−33	−59	44		4.94
7	−30	−71	45		4.91
R lateral temporal					
37	53	−50	−5	63	5.1
L lateral temporal					
37	−50	−59	−5	51	6.39
Subcortical					
Brain stem	0	−32	−3	32	4.02
RandS – MathS					
No significant activations					
MemS – RandS					
L lateral frontal					
8	−21	37	37	247	4.68
8	−30	26	46		5.87
8	−42	14	41		4.2
R lateral parietal					
7/40	36	−59	44	67	4.26
L lateral parietal					
40	−42	−62	45	435	8.63
Medial parietal					
31	0	−33	29	1075	7.66
31/7	6	−65	36		8.97
7	−6	−68	45		8.94
Subcortical					
Hippocampus	−30	−30	−11	37	6.51
RandS – MemS					
L lateral temporal					
22	−53	−43	21	65	7.26

Note: All reported peaks passed a whole-brain FDR (Benjamini and Hochberg 1995; Genovese and others 2002) threshold of $P < 0.05$ and were required to be at least 20 voxels in volume. Coordinates underwent a transformation from normalized MNI space to Talairach (Talairach and Tournoux 1988). Activation peaks without volume details belong to the cluster of the last reported volume. L, left; R, right.

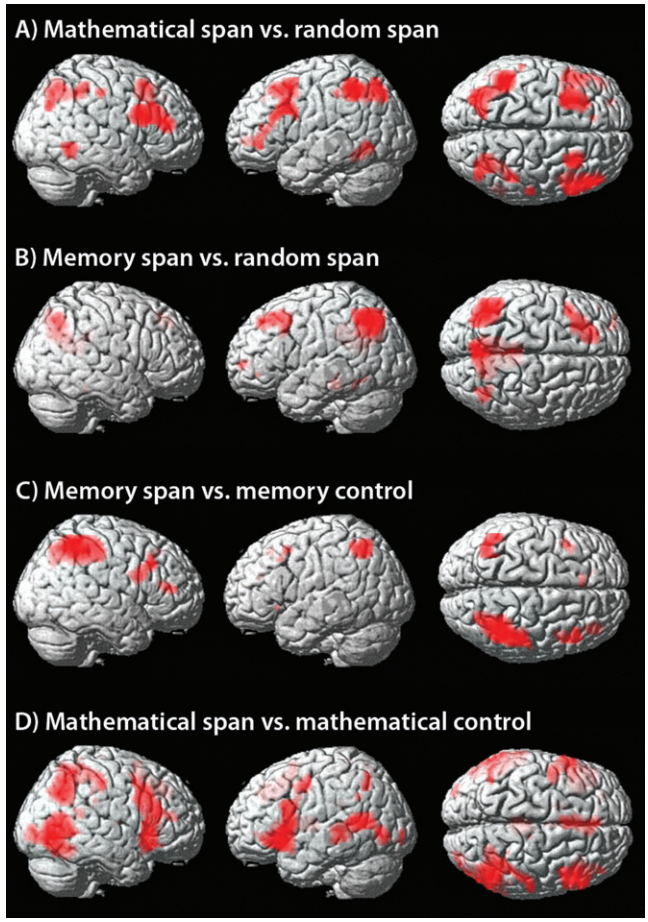

Figure 2. Regions of increased activation for strategic recoding trials compared with controls. (A) Mathematical span (MathS) versus random span (RandS). (B) Memory based span (MemS) versus RandS. (C) MemS versus memory control (MemCon). (D) MathS versus mathematical control (Calc). Activations are those exceeding a whole-brain FDR threshold of $P < 0.05$, and a cluster size of 20, rendered onto the canonical T_1-weighted brain image of SPM2. Left panels are right hemisphere view, middle panels are left hemisphere view, and right panels are from the top.

Table 2
Experiment 1: Peak increases in activation for MemS versus MemCon

Brain regions and BAs	Coordinates			Cluster volume (voxels)	*t*-Score
	x	*y*	*z*		
MemS – MemCon					
R lateral frontal					
45	39	35	9	41	5.68
45/46	45	22	29	122	4.81
9/44	48	10	22		5.73
R lateral parietal					
40	48	−27	40	708	5.43
40	45	−41	46		7.37
7	39	−50	49		7.39
L lateral parietal					
40	−48	−53	47	147	4.58
7	−33	−59	50		4.5
MemCon – MemS					
No significant activations					

Note: For details, see Table 1.

Table 3
Experiment 1: Peak increases in activation for MathS versus MemS

Brain regions and BAs	Coordinates			Cluster volume (voxels)	*t*-Score
	x	y	z		
MathS − MemS					
R lateral frontal					
46	48	42	15	1237	6.21
8/6	33	17	46		9.71
44	50	13	21		5.97
L lateral frontal					
46	−48	38	9	552	5.87
6	−27	11	44		5.67
44	−45	7	22		7.57
Medial frontal					
11	18	20	−9	54	4.42
R lateral parietal					
1	53	−24	48	356	8.48
40/7	39	−36	40		5.32
40	45	−38	52		5.93
7	24	−56	55	58	4.16
7/19	39	−71	34	35	5.22
L lateral parietal					
40	−45	−41	49	128	6.75
R lateral temporal					
37	50	−50	−13	71	6.87
L lateral temporal					
37	−50	−59	−5	38	5.59
Subcortical					
Caudate nucleus	−15	15	2	68	5.05
Caudate nucleus	12	6	2	54	3.45
MemS − MathS					
Medial parietal					
23/31	−3	−51	30	678	7.01
23/31	15	−51	36		5.72
7	9	−59	36		5.63

For details, see Table 1.

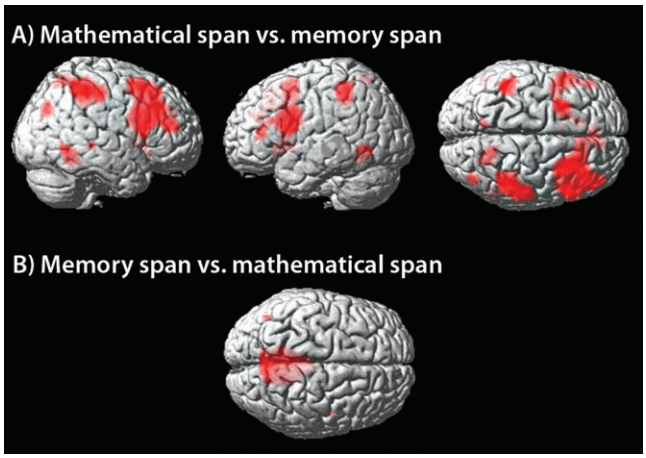

Figure 3. Regions of increased activation for direct comparison of mathematical and memory-based span conditions. (*A*) MathS versus MemS. (*B*) MemS versus MathS. Activations are those exceeding a whole-brain FDR threshold of $P < 0.05$, and a cluster size of 20, rendered onto the canonical T_1-weighted brain image of SPM2. Left panel is right hemisphere view, middle panel is left hemisphere view, and right panel is from the top. Only the top view was shown for (*B*) as no activity was present on the lateral surface of either hemisphere.

lateral frontal and parietal areas, as well as ventral medial prefrontal cortex, bilateral lateral temporal cortex, the right somatosensory cortex, and bilaterally in the caudate nucleus. In contrast, the MemS minus MathS comparison yielded only significant activations in medial parietal regions.

For the ROI analysis, MemS exhibited significantly greater activation bilaterally in DLPFC, IPS, and left VLPFC when compared with MemCon (L DLPFC: $t = 2.22$, $P = 0.020$; R DLPFC: $t = 2.76$, $P = 0.007$; L VLPFC: $t = 2.25$, $P = 0.019$; L IPS: $t = 3.04$, $P = 0.003$; R IPS: $t = 5.01$, $P < 0.001$). There was significantly greater activation in the DLPFC and IPS ROI bilaterally for MathS compared with RandS (L DLPFC: $t = 2.45$, $P = 0.012$; R DLPFC: $t = 2.30$, $P = 0.017$; L IPS: $t = 3.98$, $P < 0.001$; R IPS: $t = 3.27$, $P = 0.002$). MemS compared with RandS yielded significant activations bilaterally in IPS (L: $t = 4.79$, $P < 0.001$; R: $t = 1.98$, $P = 0.032$) but no significant activations in any of the frontal ROIs, presumably due to the shift superiorly in the lateral prefrontal activations for this contrast in comparison with the MemS minus MemCon contrast or the activity associated with MathS. When the 2 chunking span conditions were compared directly, MathS showed significant increases bilaterally in the DLPFC ROIs (L DLPFC: $t = 2.29$, $P = 0.017$; R DLPFC: $t = 4.34$, $P < 0.001$) as well as in the ACC ROI ($t = 2.15$, $P = 0.023$) and right IPS ($t = 2.22$, $P = 0.020$), whereas no significant increases were observed for MemS.

FMRI Experiment 2: Mathematical Chunking and Mental Arithmetic

One unexpected result of experiment 1 was that MathS activated the LPFC to a greater extent than MemS. To ascertain whether this was due to mental arithmetic processes, known to activate similar areas (Prabhakaran and others 2001; Simon and others 2004), or recoding processes, we carried out a second fMRI experiment. For this, we compared MathS with a mental arithmetic control, which matched MathS for mental arithmetic processes but did not require any recoding process.

Methods

Participants. Fourteen right-handed participants (8 females, aged 18–31 years) were scanned for approximately 40 min of EPI and 30 min of structural scans. All subjects gave informed written consent for participation in the study after its nature and possible consequences had been explained to them. The study was approved by the Local Research Ethics Committee.

Task details. Two tasks were presented in the fMRI scanner: MathS of the previous experiment and a mental arithmetic condition (Calc) (see Fig. 1*E*). For Calc trials, subjects were presented with a double-digit number followed by a command and a second number (for instance, "32 ADD 13"). Possible commands were "ADD," "SUBTRACT," "DOUBLE," and "HALF." Subjects were required to perform the command operation on the left-hand number 3 times, in order to generate 4 double-digit numbers (including the left-hand number). For instance, if the instruction was 32 ADD 13, then the response would be "32 45 58 71." The instruction was on screen for 3250 ms, before a delay period of between 4 and 8 s. This delay period was extended compared with experiment 1 in order to allow sufficient time in Calc trials for the subjects to carry out the mental arithmetic task. For both conditions, the response stage was the same as in the previous experiment.

The 2 trial types were presented in a pseudorandom interleaved fashion. In total, there were 44 trials of each condition.

FMRI data acquisition and analyses. All acquisition and analysis parameters were the same as experiment 1, except that 680 scans were collected for each of the 3 runs.

Results

Behavioral data. For both conditions, each trial was marked out of 8. A single digit in a trial was marked correct if it matched the number and temporal position during presentation. Although performance in the 2 tasks cannot be related directly, MathS accuracy was 80.9%, whereas Calc accuracy was 91.7%.

Functional imaging data. When MathS was compared with Calc (Table 4 and Fig. 2*D*), significant increases were observed for MathS bilaterally in the LPFC and lateral parietal cortex, as well as in anterior and posterior cingulate. Additional regions of activation were the bilateral lateral temporal cortex, right somatosensory cortex, left

Table 4

Experiment 2: Peak increases in activation for MathS versus Calc

Brain regions and BAs	Coordinates			Cluster volume (voxels)	*t*-Score
	x	y	z		
MathS − Calc					
R lateral frontal					
47	36	20	−6	828	5.09
47	53	17	−1		4.77
9	50	16	35		5.09
L lateral frontal					
47	−50	20	−11	746	10.84
44	−59	12	5		6.24
6	−48	−1	41		5.02
Medial frontal					
32/8	3	31	34	240	4.26
32	−3	19	38		4.31
6	−3	11	52		5.02
24	0	4	27	20	3.77
R lateral parietal					
1	59	−21	43	566	5.1
40	50	−54	36		6.68
40	45	−56	47		8.75
L lateral parietal					
7	−42	−56	55	34	4.16
40	−53	−56	44		3.57
Medial parietal					
23	0	−31	26	118	5.59
R lateral temporal					
37	45	−53	−10	607	7.76
37/19	45	−64	−7		8.17
37	50	−67	1		10.83
L lateral temporal					
21	−50	−49	8	388	7.89
37	−62	−58	14		5.53
L occipital					
19	−48	−73	4		4.98
18	−30	−93	2	20	4.63
Subcortical					
Putamen	−18	6	8	123	4.79
Thalamus	−12	−11	6		5.85
Calc − MathS					
R medial parietal					
7	9	−64	58	1017	7.64
L occipital					
18	−21	−73	−4		7.5
17	−9	−90	2		7.7
R occipital					
18	15	−79	−4	25	4.75

For details, see Table 1.

occipital cortex, putamen, and thalamus. In contrast, regional increases in activation for Calc were largely restricted to striate and extrastriate cortices.

For the ROI analysis, all ROIs showed significantly greater activation for the MathS minus Calc contrast, except the left IPS, which approached significance (L DLPFC: $t = 1.96$, $P = 0.036$; R DLPFC: $t = 2.40$, $P = 0.016$; L VLPFC: $t = 5.04$, $P < 0.001$; R VLPFC: $t = 3.36$ $P = 0.003$; ACC: $t = 3.18$, $P = 0.004$; L IPS: $t = 1.36$, $P = 0.098$; R IPS: $t = 4.28$, $P < 0.001$).

Discussion

For both the mathematical and memory-based sequence trials, performance was improved compared with random sequence trials, indicating that strategic recoding was used in both conditions. The fMRI data confirmed that either type of strategic recoding relies on the recruitment of the LPFC. Thus, when MathS or MemS was compared either with the RandS to control for WM content or with Calc or MemCon, respectively, to control for mental arithmetic or mnemonic processing, the LPFC was significantly activated.

While our previous studies have together shown the involvement of the LPFC in strategic recoding, regardless of modality (Bor and others 2001, 2003, 2004), the current experiments extend this by demonstrating a link between LPFC and chunking, independent of the type of recoding process that is used to generate the chunks. If the information is recoded in order to optimize performance, either based on its inherent mathematical or logical redundancy or due to its connection with well-established memories, then the LPFC will be activated. LPFC involvement in such cases appears stronger than more basic WM processes, mental arithmetic, or episodic memory retrieval, despite such processes robustly activating the LPFC themselves (Owen and others 1998, 1999; Cabeza and Nyberg 2000; Lee and others 2000; Fletcher and Henson 2001; Pochon and others 2001; Prabhakaran and others 2001; Wager and Smith 2003; Simon and others 2004). In fact, it is possible that strategic processes account for some of the prefrontal activation foci reported in such studies, although the results obtained may not generally have been interpreted in terms of strategy use.

It is interesting to note that our data and those of others (Ericcson and others 1980; Bor and others 2003, 2004) suggest that WM is a more complex function than is often proposed by standard models, such as that of Baddeley and Hitch (Baddeley 1992). Under certain situations, in both verbal and spatial domains, WM can be modulated by chunking so that performance is significantly improved. This is true not only for high-level WM chunks (Bor and others 2003, 2004) but also for more basic recoding processes, such as feature binding (Mitchell and others 2000; Prabhakaran and others 2000) and relational complexity in a paired associates task (Phillips and Niki 2002). It is interesting to note that in each case, the LPFC was associated with both chunking and performance improvement. Whereas Baddeley has recently attempted to revise his model to include an extra module that carries out binding processes (Baddeley 2000), other studies suggest further complications. For instance, Vogel and others (Vogel and Machizawa 2004; Vogel and others 2005) have shown via electroencephalographic recordings that WM capacity can be impaired by inappropriately storing irrelevant items in WM. Therefore, strategic recoding and selective attentional components may need to be included in any future WM models.

One common debate in the literature concerns the level of dissociation between the VLPFC and DLPFC. Whereas some authors suggest that there is virtually no functional division between these regions (Duncan and Owen 2000), others propose a clear dissociation, such that the VLPFC supports basic WM processes, such as encoding and retrieval, whereas the DLPFC is involved in the monitoring or manipulation of the contents of WM (Petrides 1994; Owen and others 1999; Postle and others 1999). The majority of our comparisons between chunking conditions and their controls or with RandS yielded bilateral DLPFC activation, with little sign of VLPFC activity (even in the ROI analysis). However, there were contrasts (such as MemS vs. MemCon or MathS vs. Calc) that activated large portions of the LPFC, including both DLPFC and VLPFC regions. It is possible that this pattern of results indicates that the DLPFC has a relatively distinct role from the VLPFC and subserves more complex processing, such as chunking. The additional VLPFC activations, largely in comparison with nonspan controls, might be explained by imperfect matching of basic WM content between conditions. However, given that such conclusions

rest on null results, it is important to point out that our data are still consistent with the suggestion that large sections of the LPFC are functionally homogeneous.

In our previous studies (Bor and others 2001, 2003, 2004), posterior lateral parietal cortex was consistently coactivated with LPFC during strategic recoding processes. Both of our current experiments demonstrated the same result. Indeed, in the current set of contrasts, lateral parietal cortex was perhaps a more reliable activator than LPFC in relation to chunking processes. Although this prefrontal parietal network (PPN) has now commonly been linked with strategic recoding processes, it is important to emphasize that the LPFC is coactivated with the lateral parietal cortex in many circumstances involving executive tasks (Cabeza and Nyberg 2000; Duncan 2006). Recent neuropsychological data lend support to the notion that these regions form an executive network (Peers and others 2005). Peers and others (2005) collected a set of behavioral measures on patients with frontal or parietal lesions. They found no evidence of regional selectivity either for attentional spatial bias or for top–down control measures. Instead, lesion volume either in the frontal or in the parietal lobes correlated with impairment on either of these 2 processes. Based on this neuropsychological study and many neuroimaging studies that have reported PPN activation, it is an open question whether lateral parietal cortex and LPFC are a single integrated system for executive processing or play complimentary, separable roles in tasks that rely on these processes.

One crucial question arising from the current experiments is the degree of similarity between the networks for mnemonic and mathematical recoding processes. Whereas both strategic processes activated the lateral parietal cortex and LPFC, only MemS additionally activated the medial parietal cortex, encompassing the posterior cingulate. This region was quite distinct from the lateral parietal cortex activity associated with recoding strategies, referred to as part of the PPN above. Previous studies have suggested that this medial parietal region is involved in LTM retrieval (Cabeza and Nyberg 2000; Konishi and others 2000), and the results of the current study are entirely consistent with such a suggestion. Thus, MemS was related to increased activation in the posterior cingulate when compared with all non-LTM conditions (RandS and MathS) but not when compared with a condition matched for LTM retrieval processes (MemCon). MathS showed no activation in this region, consistent with the suggestion that recoding strategies for these trials included no or little LTM retrieval component. At the same time, no increases in activation were observed for the posterior cingulate in our 2 related studies (Bor and others 2003, 2004). One explanation for this could be that in both of those earlier studies, the recoding strategies adopted by the subjects were far more closely aligned with MathS than with MemS. In other words, it seems likely that both studies involved strategies that largely relied on the mathematical redundancies inherent in structured stimuli, rather than on mnemonic information.

A second difference between the 2 strategic recoding conditions was the raised activity in the basal ganglia for MathS alone. For instance, when the 2 recoding conditions were compared directly, MathS trials showed significantly more activity in the caudate nucleus bilaterally. It is possible that this is due to MathS involving additional strategic processing as the caudate nucleus has previously been implicated in strategies and planning (Owen and others 1996). However, the caudate nucleus has also been linked to calculation processes (Simon and others 2004). Therefore, although it is unclear which specific process was associated with basal ganglia activation, this regional activity clearly implies that additional logical rule–based processing was occurring for MathS.

A third major difference between the 2 types of chunking processes was the more dorsal LPFC activation for MemS (compared with RandS) than for MathS (also compared with RandS). This MemS activation pattern was also dissimilar to the structured conditions of our previous studies, where DLPFC was significantly activated (Bor and others 2003, 2004). It is important to note that this pattern of activation only occurred when MemS was compared with RandS. When instead it was contrasted with its own mnemonic control, robust lateral prefrontal activation was observed, including in VLPFC and DLPFC (as shown by the ROI analysis). However, this partial activation of PPN may reflect the fact that mnemonic-based chunking both involves less processing requirements and is less associated with PPN than MathS. Evidence to support this comes from the direct comparison of MemS with MathS. Whereas MathS demonstrated robust activation of the PPN, including the DLPFC, MemS only showed activation in an LTM retrieval region, the posterior cingulate. Therefore, mathematical recoding strategies appear to show a closer connection with PPN than mnemonic strategies. The possibility that mental arithmetic processes themselves are driving this difference is unlikely given that in the second experiment the PPN was still activated for MathS compared with a mental arithmetic–based control, despite the latter condition including at least as much mental arithmetic. One important difference between MathS and MemS is that whereas enhanced performance on MemS relies on utilizing pre-existing chunks, MathS performance improvement relies on laying down new chunks. A second major difference is that only in the MathS stimuli are there regularities, in the form of mathematical or logical relationships between the numbers. In contrast, the stimuli in MemS would be the same as the random, unstructured span condition if it were not for the fact that chunks within the stimuli had been overlearned beforehand. The recognition of these inherent regularities, in a task context, may be a particularly crucial process for 2 reasons. First, the discovery of "rules" that capture the data will normally be far more efficient than separately remembering each item. In this experiment, converting the mathematical sequences into an algorithmic form caused performance improvement as WM capacity was used more efficiently. In other more complex tasks (for instance chess), such rule discovery may lead to far more effective strategies (Chase and Simon 1973). Second, because such rule spotting has the potential to reduce processing, for instance by reducing the WM load, or by reducing the number of steps required to complete a task, the recognition of regularities also promises significant metabolic savings when the task is repeated. It is possible that either novelty or structure or both of these differences explains why mathematical recoding strategies activated the PPN far more robustly than mnemonic recoding strategies.

Although some studies of LPFC are confounded by difficulty, which commonly activates this network (Duncan and Owen 2000), it is important to emphasize that neither in our previous related studies (Bor and others 2001, 2003, 2004) nor in our current study is this factor relevant. In our 2 previous studies, an easier version of the task activated PPN to a significantly greater extent than a more difficult version (Bor and others 2003,

2004). In addition, in experiment 1 of the current study, a PPN was activated both for an easy versus a difficult comparison (MathS – RandS) and a difficult versus an easy comparison (MathS – MemS), confirming that task difficulty per se does not correlate with activity in this network. All contrasts were also examined only on the correct trials, with very similar results, providing further evidence against the relevance of difficulty as a factor here.

A better general perspective may be to interpret PPN activity as reflecting the number of cognitive processes involved, rather than the effort. For instance, RandS merely required subjects to encode and retain a sequence of items. However, mathematical span trials, which increased PPN activity, presumably involved a search for candidate algorithms based on potential mathematical rules, the conversion of sequences into successful algorithmic chunks, as well as the retention of the recoded information in WM. Whereas there are increasing examples in the literature of dissociations between difficulty (as indexed by greater subjective effort or reduced performance) and PPN activity, we know of no examples where PPN activity is reduced when the number of cognitive processes increases.

Although the precise role of the PPN remains a mystery, it is clear that this network is involved in general high-level cognitive tasks, particularly when the goals are novel or complex (Dehaene and others 1998; Miller and Cohen 2001). The current results have shown that one crucial aspect of this set of processes is to carry out recoding strategies on any available data in order to improve performance and lower processing demands.

Notes

We thank the radiographers at the Wolfson Brain Imaging Centre for their assistance in the conduct of the study and Dr Rhodri Cusack and Dr Rik Henson for technical assistance. This work was supported by the Medical Research Council of the United Kingdom. *Conflict of Interest*: None declared.

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