

Interactive report

Brain imaging of human memory systems: between-systems similarities and within-system differences

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Abstract

There is much evidence for the existence of multiple memory systems. However, it has been argued that tasks assumed to reflect different memory systems share basic processing components and are mediated by overlapping neural systems. Here we used multivariate analysis of PET-data to analyze similarities and differences in brain activity for multiple tests of working memory, semantic memory, and episodic memory. The results from two experiments revealed between-systems differences, but also between-systems similarities and within-system differences. Specifically, support was obtained for a task-general working-memory network that may underlie active maintenance. Premotor and parietal regions were salient components of this network. A common network was also identified for two episodic tasks, cued recall and recognition, but not for a test of autobiographical memory. This network involved regions in right inferior and polar frontal cortex, and lateral and medial parietal cortex. Several of these regions were also engaged during the working-memory tasks, indicating shared processing for episodic and working memory. Fact retrieval and synonym generation were associated with increased activity in left inferior frontal and middle temporal regions and right cerebellum. This network was also associated with the autobiographical task, but not with living/non-living classification, and may reflect elaborate retrieval of semantic information. Implications of the present results for the classification of memory tasks with respect to systems and/or processes are discussed. © 2002 Elsevier Science B.V. All rights reserved.

Theme: Neural basis of behavior

Topic: Learning and memory: systems and functions

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1. Introduction

Despite intense debate and numerous empirical studies there is still no consensus on the architecture of memory [14]. At present, the dominating view is that memory can be divided into a number of independent but interacting systems [13,15,40,45]. By this view, measures of different systems have in common certain cognitive and neural properties, and these properties differ from those associ-

ated with measures of other systems. Support for the memory-systems view comes from demonstrations of dissociations between measures of different systems [24,25,37]. Functional neuroimaging studies lend further support to this view, indicating that measures of separate systems are associated with different patterns of brain activity [26,32,35,38].

Notwithstanding differences, it has been argued that measures of distinct systems may share basic processes and neural correlates [34,36]. In fact, for some constellations of measures, similarities may be more pronounced than differences. The results from recent within- [2,9] and between-study [7,11] comparisons of neural activity associated with measures of different memory systems provide

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support for the existence of between-systems similarities. However, studies of similarities between multiple systems are lacking, and it should be critical to include multiple measures of the same system in such studies. This is because there is evidence from dissociation studies and brain imaging studies for differences between measures that are assumed to reflect the same underlying system [6,8,18].

Here we present results from two large-scale PET experiments designed to examine similarities and differences between working memory, episodic long-term memory and semantic long-term memory. All of these systems can be classified as declarative memory systems, and similarities at the cognitive and neural levels have been noted for episodic and working memory [1,2,9] as well as for episodic and semantic memory [22,34,41]. Thus, theoretical as well as empirical analyses indicated that there should exist similarities among these particular systems. For other systems it is less obvious that similarities should exist, such as between episodic memory and procedural memory [25], and an interesting task for future research will be to extend the present approach to analysis of systems and tasks assumed to be more distinct.

To examine differences and similarities between and within systems, we used a multivariate statistical approach: task partial least-squares (PLS) [21]. Task PLS identifies spatial patterns of brain activity that represent the optimal association between brain images and a block of contrast vectors coding for the experimental design. The results are expressed as latent variables (LVs), where each LV relates a specific grouping of experimental conditions to a specific pattern of brain activity. By using task PLS we were able to explore whether the groupings of conditions were in keeping with traditional system-based divisions or whether they indicated alternative divisions. That is, rather than a priori specifying how the various conditions should be grouped, we used functional brain imaging data as a guide to the classification of memory measures.

In the first experiment, the memory tasks were selected such that one task per system either emphasized categorization or generation processes (Fig. 1a). Previous analyses have indicated that these processes are correlated with distinct neural responses [7]. Of primary interest was whether support would be provided for a grouping of experimental conditions that related to type of system (working, episodic, semantic memory), type of process (categorization, generation), or some mixture between the two. A second experiment tested the generality of the findings from the first experiment by including additional measures for each system (Fig. 1b). Across the two experiments, three different measures were used per system. By including multiple measures of each system, we were able to examine whether any observation of between-systems similarities was task-general or whether within-system differences existed.

a	MEMORY	TASK	
	SYSTEM	Categorization	Generation
	Working	2-back	random number
	Episodic	recognition	cued recall
	Semantic	living / non-living	fact retrieval

b	MEMORY	TASK	
	SYSTEM		
	Working	1-back	
	Episodic	cued recall, autobiographical memory	
	Semantic	fact retrieval, synonym generation	

Fig. 1. Experimental tasks in experiments 1 (a) and 2 (b). Both experiments included tests of working memory and long-term (non-working) episodic and semantic memory. The tasks in experiment 1 were selected to emphasize categorization or generation processes. Both experiments additionally included reading baseline tasks. All tasks were performed and scanned twice.

2. Materials and methods

2.1. Participants

A total of 29 right-handed [28] healthy male subjects participated in the two studies (experiment 1: $n=15$, age = 28 ± 7 years; experiment 2: $n=14$, age = 24 ± 4 years). Due to a missing scan for one subject in experiment 2, the PLS-analyses were based on 13 subjects (all 14 were included in the SPM-analyses). The subjects were pre-screened and none of the subjects used any medication, had a history of drug abuse (including nicotine), head trauma, neurological or psychiatric illness, or a family history of neurological or psychiatric illness. All had university level education. The local Ethics and Radiation Safety committees at the Karolinska Hospital approved the study. All the subjects gave written informed consent.

2.2. Procedure

The procedure for stimulus presentation and responding was the same for all tasks in both experiments: single items were presented on a computer screen placed above the subjects' heads and they responded by saying one word per stimulus. Thus, the perceptual (visual) as well as the motor demands were held constant across experimental conditions. Therefore, findings of similarities or differ-

ences between experimental conditions should be more likely to reflect cognitive processes than similarities/differences in perceptual-motor demands. The presentation time was 3 s and the ISI was 2 s. A total of 18 stimuli were presented during each experimental run, 12 of which were presented during the scan interval. The experimental tasks were given in a counterbalanced order with the restriction that all seven conditions were performed before the replications were presented. An experimenter recorded subjects' responses. Accuracy was uniformly high (>90%).

The task specific instructions in experiment 1 were as follows. *Cued recall*: A study list consisting of category-instance pairs (AUTHOR–STRINDBERG) was presented 5 min before scanning/testing. Subjects were instructed to memorize the pairs so that they could remember the instance when the category was presented. At test, subjects were presented with the cue words in a different order than at study. For each category cue, they responded by saying the target or 'no' in cases they could not recall the target (mean proportion of no-responses in the two experiments was 30%). *Recognition*: A study list consisting of single words was presented 5 min before scanning/testing. Subjects were instructed to memorize the words for a later test. At test, subjects were presented with nine targets (in a different order than at study) and nine distracters. They were asked to say 'yes' when they recognized a word from the study list and 'no' when they thought a non-studied word was presented. *2-Back*: 5 min before scanning/testing subjects were instructed that a sequence of words was to be presented and that their task was to decide for each word whether it was the same as the one presented two items earlier in the list. They were instructed to say 'yes' when they thought a specific word was the same as two items back and 'no' if they thought it had not appeared two items back (some items were repeated at a different lag). A short practice list was given before testing started. *Random-number generation*: 5 min before scanning/testing subjects were instructed that each time a '?' appeared on the screen their task was to randomly generate a number between 1 and 10. They were told not to mention the same number twice in succession and to use all numbers between 1 and 10 before starting over again. *Living/non-living classification*: 5 min before scanning/testing subjects were instructed that a list of words was to be presented and that their task was to decide if the words referred to living or non-living things. For each word they responded by saying 'living' or 'non-living'. *Fact retrieval*: 5 min before scanning/testing subjects were instructed that they were going to be shown a series of cue words. For example, if 'AUTHOR' was presented they were supposed to think of a person and respond by saying the family name. If they could not think of any factual information for a specific cue word they said 'no' (mean proportion of no-responses in the two experiments was

4%). *Reading*: Subjects were told that a series of words was going to be presented and that their task was to read each word aloud. They were explicitly told that these words were not part of any test and that they did not have to memorize them.

The task specific instructions in experiment 2 were as follows. *Cued recall*: Same procedure as in experiment 1. *Autobiographical cued word retrieval task*: 5 min before scanning/testing subjects were instructed that they were going to be shown a series of cue words. They were instructed to use the cues to remember personal events that could be related to each cue word. For example, if 'VACATION' was presented they were supposed to think of a personal event associated with vacation. They responded by saying one word that described their memory (e.g. 'GREECE'). They were instructed to try to remember each event in detail. If they could not come up with a personal memory in response to a specific cue word they said 'no' (mean proportion of no-responses was 18%). A short practice list was given before testing started. *1-Back*: the same procedure was used as for the 2-back task in experiment 1, with the exception that subjects now decided whether presented words were identical to the immediately preceding item in the list. A short practice list was given before testing started. *Fact retrieval*: Same procedure as in experiment 1. *Synonym generation*: 5 min before scanning/testing subjects were instructed that they were going to be shown a series of words. For each word they were instructed to generate a different word with similar meaning (e.g. VACATION–HOLIDAY) or with a strong semantic association to the cue word (e.g. CAR–VOLVO). If they could not generate a word in response to a specific cue they said 'no' (mean proportion of no-responses was 17%). A short practice list was given before testing started. *Reading*: Same procedure as in experiment 1. One reading condition included different words (as in experiment 1), whereas the same word was repeatedly presented in the other condition.

2.3. Data acquisition

In both experiments, each subject underwent 14 measurements of regional cerebral blood flow (rCBF) with a 3D ECAT EXACT HR PET scanner [46] and bolus injections of $H_2^{15}O$. The PET scanner was used in 3D-sampling mode producing 60-s tracer uptake images. The different tasks were started at the time of tracer injection and the scanning was automatically initiated when the activity level in the brain exceeded a predetermined level above background. Scatter correction was done and a 2D-transmission scan was used for attenuation correction.

2.4. Data analysis

Using SPM99 (<http://www.fil.ion.ucl.ac.uk/>), the PET-

Table 1
Activation peaks in experiment 1

Region (BA)	X	Y	Z
<i>LV1: working memory</i>			
Right inferior parietal cortex (40)	52	-42	44
Left inferior parietal cortex (40)	-54	-50	44
Medial parietal cortex/precuneus (7)	2	-68	52
Right middle frontal gyrus (9/46)	36	38	24
Right superior frontal gyrus/premotor cortex (6)	30	0	64
Right inferior temporal gyrus (37)	60	-50	-12
Left middle frontal gyrus (9/46)	-50	28	28
<i>LV2: fact retrieval</i>			
Left inferior frontal cortex (45)	-44	22	20
Left inferior/middle frontal cortex (9/44)	-42	14	32
Left medial frontal cortex (8)	-10	16	52
Left middle temporal gyrus (21)	-58	-44	-12
Left primary visual cortex (17)	-8	-92	0
Right cerebellum	44	-68	-28
Brain stem	4	-22	-4
Left inferior parietal cortex (40)	-42	-56	48
<i>LV3: episodic memory</i>			
Right inferior frontal cortex/insula (47)	36	18	0
Right fronto-polar cortex (10)	26	66	0
Right temporo-polar cortex (38)	54	16	-16
Left superior temporal gyrus (21)	-56	-44	8
Mid-cingulum/retrosplenial cortex (23/31)	-2	-36	28
Cuneus (7/19)	-8	-76	36
Right inferior parietal cortex (40)	52	-54	56
Left inferior parietal cortex (40)	-36	-58	40
Left occipital cortex (18)	-32	-92	12
Right occipital cortex (18/19)	28	-86	8

Size of all regions >100 voxels; threshold $Z > 3.09$. BA, Brodmann area. X, Y, Z are Talairach coordinates [42].

images were realigned, spatially normalized and transformed into a common approximate Talairach stereotactic space [42] as defined by the SPM99 PET template, 3D-Gaussian filtered (14 mm FWHM), and proportionally scaled to account for global confounders. SPM99 was used for specific linear contrasts between conditions (all P -values relating to significant activations were corrected for multiple non-independent comparisons). For the multivariate analyses, task PLS was used as previously described [21]. The significance of LVs was assessed by permutation tests [12,17]. Within each LV, reported regions

were significant at $P < 0.01$ (see Tables 1 and 2 for size of regions).

3. Results

3.1. Experiment 1

3.1.1. PLS-groupings of experimental conditions

The first three LVs from the PLS-analysis were significant ($P < 0.001$) and will be presented here. The first LV separated the two working-memory tasks from all other conditions (Fig. 2a). Working memory was associated with increased activity in the dorsal and mid-dorsal frontal regions and in the lateral and medial parietal cortex (Fig. 2b, Table 1). Note that for this effect as well as for those that will be presented later, the separation was expressed for both replications of each task. Such independent replication within subjects lends support to the reliability of the effects. The second LV separated fact retrieval from the other conditions (Fig. 2c). The separation was maximal against the non-memory reading task, but it was also clear against the memory tasks, including the other semantic task (living/non-living classification). Fact retrieval was associated with increased activity in the left inferior frontal cortex, the anterior cingulate, the left inferior temporal cortex, as well as the cerebellum (Fig. 2d, Table 1). The third LV separated the two episodic tasks, recognition and cued recall, from the other conditions (Fig. 2e). The episodic tasks were associated with increased activity in the right fronto-polar cortex, the right inferior frontal cortex, bilateral occipito-temporal cortex, and bilaterally in the lateral and medial parietal cortices (Fig. 2f, Table 1). For this LV, there was a tendency for one of the working-memory tasks, 2-back, to cluster with the episodic tasks (Fig. 2e). This prompted additional analyses of episodic memory and working memory by linear contrasts with SPM99.

3.1.2. Specific comparisons of the episodic and working-memory tasks

To further explore similarities between episodic and working memory, the episodic tasks and the 2-back task

Table 2
Common regional activations for tests of episodic memory and working memory in experiment 1

Memory task	Region			
	Cuneus/precuneus	Left inferior parietal cortex	Right inferior parietal cortex	Right fronto-polar cortex
Cued recall and recognition	-10, -72, 36; 6, -70, 48	-36, -54, 52	48, -52, 52	28, 62, -4; 46, 42, 20
2-Back task	-10, -72, 48; 12, -70, 52	-36, -52, 44	50, -42, 46	30, 62, -6; 42, 38, 24
Random-number generation	-6, -72, 52; 10, -68, 50	-38, -50, 44	50, -40, 46	30, 50, -16; 42, 38, 24

X, Y, Z are approximate Talairach coordinates [42]; the memory tasks were contrasted with the reading and semantic tasks.

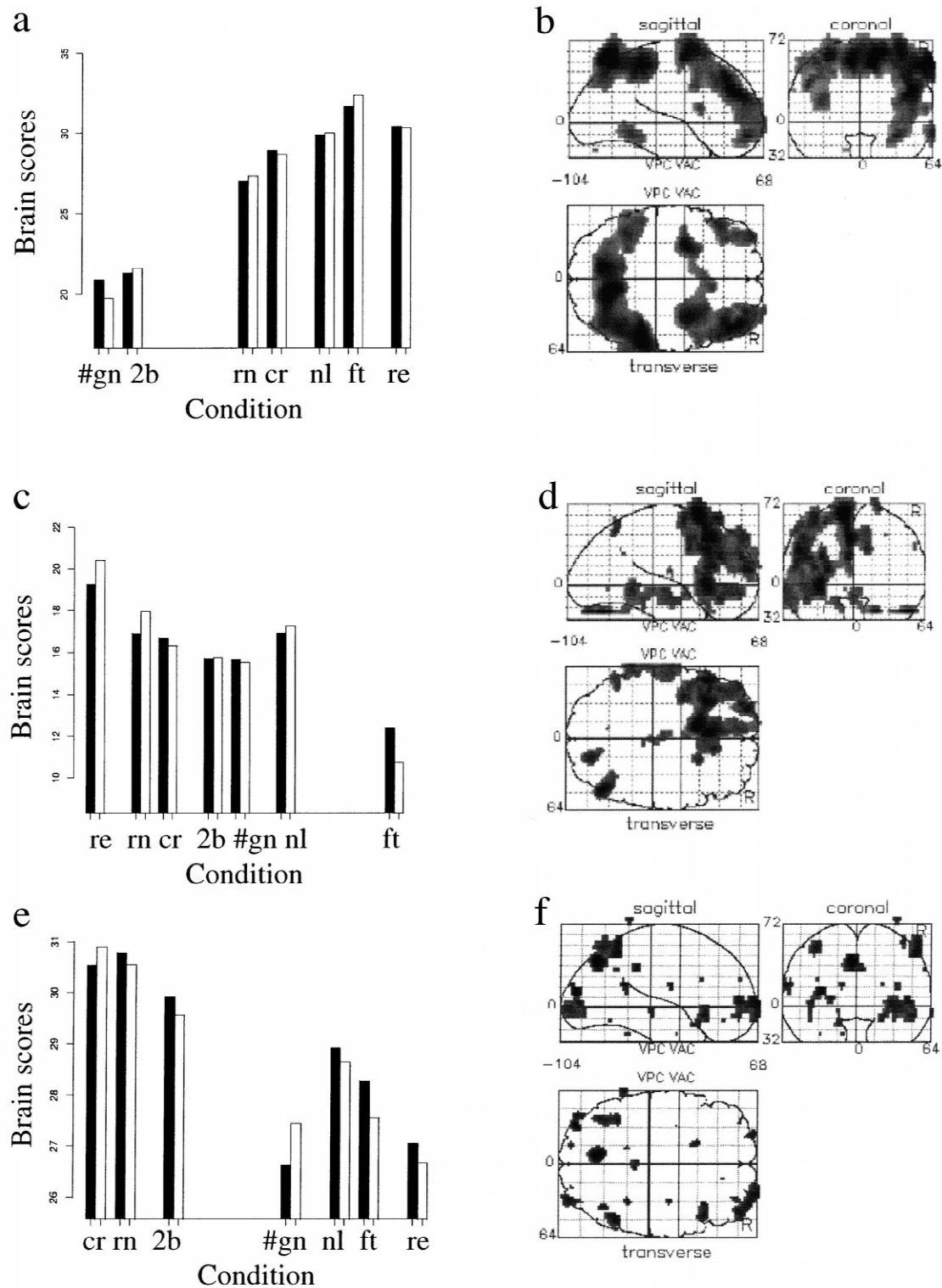


Fig. 2. PLS-groupings of experimental conditions in experiment 1. (a) Separation of the working-memory tasks from the other conditions. (b) Brain regions showing relative increased activity during the working-memory tasks. (c) Separation of the fact retrieval task from the other conditions. (d) Brain regions showing relative increased activity during the fact retrieval task. (e) Separation of the episodic tasks from the other conditions. (f) Brain regions showing relative increased activity during the episodic tasks. Brain scores on the y-axis in a, c and e are analogous to factor scores in factor analysis. Black bars represent the first scan of each condition; white bars represent replication scans. Conditions are grouped on the x-axis to highlight their separation. The salience threshold for projection was 0.2 in (b) and 0.15 in (d) and (f). See Table 1 for local maxima. 2b, 2-back; cr, cued recall; ft, fact retrieval; #gn, random-number generation; nl, living/non-living; re, read; rn, recognition.

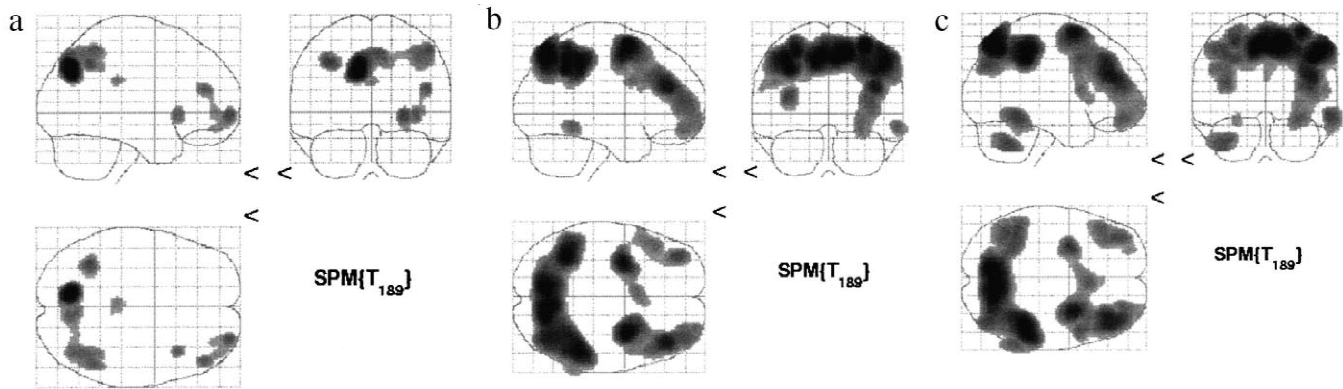


Fig. 3. Brain activity associated with episodic memory and working memory in experiment 1. (a) Brain regions showing relative increased activity during episodic memory (cued recall and recognition). (b) Brain regions showing relative increased activity during the 2-back test. (c) Brain regions showing relative increased activity during random-number generation. In all contrasts, fact retrieval, living/non-living classification and reading served as the reference condition. Display threshold in (a)–(c): $P < 0.05$ (corrected for multiple comparisons); size of all regions > 20 voxels.

were contrasted with the reading and semantic tasks. In keeping with the PLS-analysis, several overlapping activations were observed (corrected $P < 0.05$; Fig. 3a,b, Table 2). These included cuneus/precuneus, the left and right inferior parietal cortex, and the right fronto-polar cortex. When the other working-memory task, random-number generation, was contrasted with the same baseline, a similar activation pattern was observed (Fig. 3c, Table 2). These results agree with previous findings of similarities in frontal and parietal activity for episodic and working memory [9]. A direct contrast between the 2-back and random-number generation tasks suggested that one basis for the separation between the working-memory tasks in LV3 of the PLS-analysis was that the 2-back task more strongly activated several posterior visual regions (corrected $P < 0.05$). These regions included bilateral occipital cortex ($x, y, z = -18, -94, -8; 34, -82, -14$) and left lateral and medial temporal cortex ($x, y, z = -62, -48, 8; -40, -36, -20$). This difference may reflect a greater role for visual memory/visual processing in the 2-back task, and in the episodic tasks (cf. LV3), than in the random-number task.

3.2. Experiment 2

Experiment 1 was designed to examine whether support would be provided for a grouping of experimental conditions that related to type of memory system (working, episodic, semantic) or type of process (categorization, generation). No LV was identified that related to the distinction between categorization or generation processes across tasks (Fig. 1). One interpretation of this is that such processes do not operate in an uniform fashion across tasks (e.g. generation of factual information does not engage the same neural system as generation of random numbers). Instead, the results of experiment 1 were more in keeping with a grouping according to system. Strong support was provided for a task-general working-memory network

(LV1). In experiment 2, working memory was measured with a 1-back task. Previous investigations indicate that a similar network is operating for 1-back and 2-back tests of working memory, with degree of activity being modulated by memory load [3]. Experiment 1 also revealed similarities between the two episodic measures, cued recall and recognition (LV3). In experiment 2, cued recall was again used as a measure of episodic memory and a test of autobiographical memory (cued word retrieval task) was additionally included. In the cued word retrieval task, subjects were presented cue words (e.g. vacation) and were instructed to generate personal memories based on these cues. A previous study revealed differences between cued recall and the cued word retrieval task [8], despite the fact that they both are considered tests of episodic memory. This indicated that within-system differences might exist for episodic memory. A third main finding in experiment 1 was that fact retrieval separated from the other tasks (LV2). Fact retrieval was again used in experiment 2, and a test of word knowledge (synonym generation) was additionally included. Of primary interest was whether the inclusion of two elaborate semantic tasks [4] would have the effect that a common semantic network was revealed.

3.2.1. PLS-groupings of experimental conditions

The first four LVs from the PLS-analysis were significant ($P < 0.001$). Three of these will be presented here (LV3 showed a tendency to cluster synonym generation with fact retrieval but this effect did not hold across replications). LV1 separated the long-term memory tasks from the working memory and baseline tasks (Fig. 4a). The long-term memory tasks were associated with increased activity in the left inferior, medial, and superior frontal cortices, the right inferior frontal cortex, and the left middle temporal cortex (Fig. 4b, Table 3). Cerebellar activation was observed bilaterally, although there was a clear tendency for this activation to be right lateralized (Fig. 4b). LV2 separated cued recall from all other

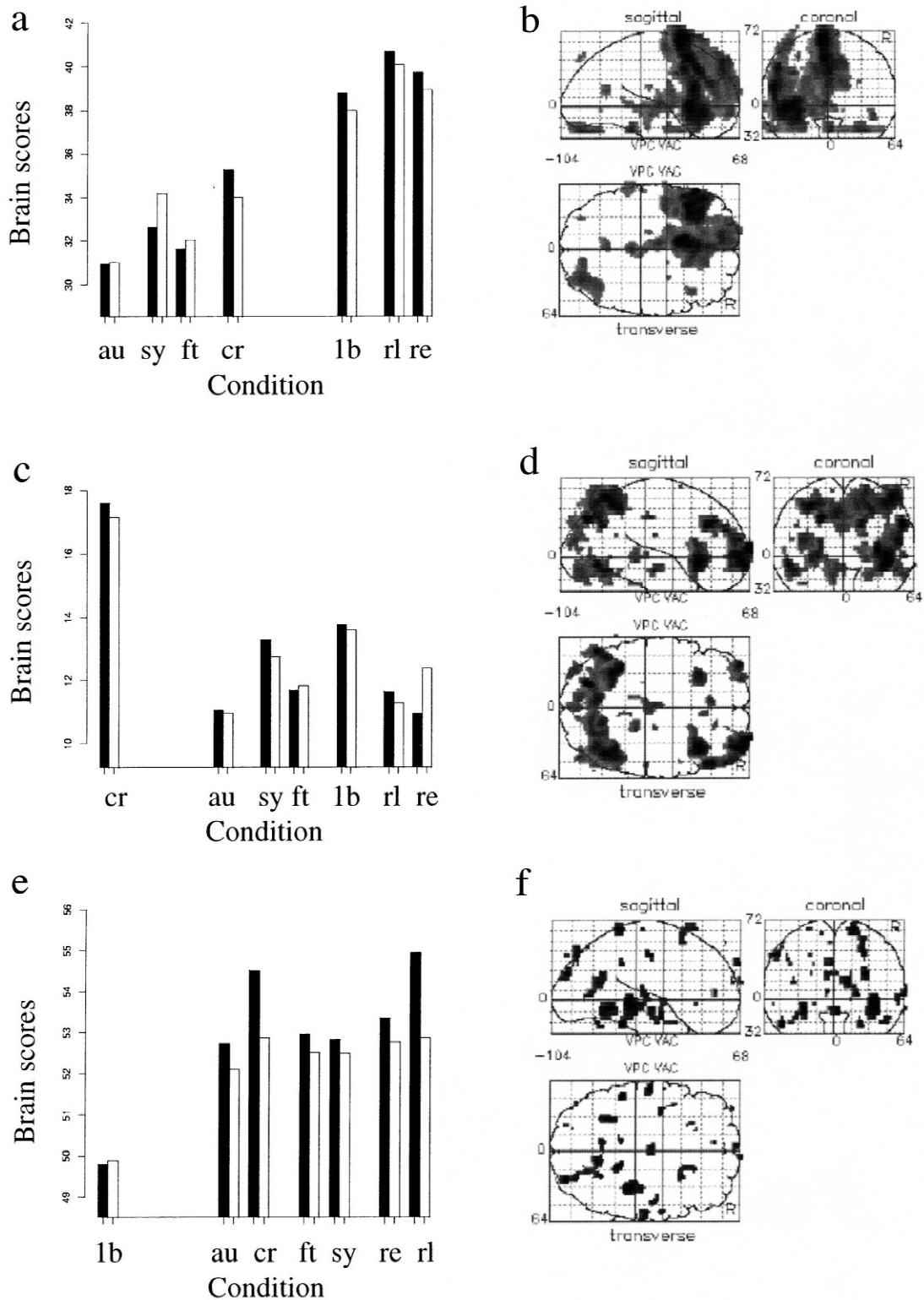


Fig. 4. PLS-groupings of experimental conditions in experiment 2. (a) Separation of the long-term memory tasks from the other conditions. (b) Brain regions showing relative increased activity during the long-term memory tasks. (c) Separation of the cued recall task from the other conditions. (d) Brain regions showing relative increased activity during the 1-back task. (e) Separation of the 1-back task from the other conditions. (f) Brain regions showing relative increased activity during the 1-back task. See Table 2 for local maxima. 1b, 1-back; au, autobiographical cued word retrieval task; rl, read same word repeatedly; sy, synonym generation. Other abbreviations and conventions are the same as in Fig. 2.

Table 3
Activation peaks in experiment 2

Region (BA)	X	Y	Z
<i>LV1: long-term memory</i>			
Left inferior frontal cortex (44/45)	-48	18	16
Left medial frontal cortex (6)	0	14	44
Left superior frontal cortex (6)	-6	16	64
Right inferior frontal cortex (47)	36	14	-8
Left middle temporal gyrus (21)	-56	-40	-4
Right cerebellum	34	-82	-28
Left cerebellum	-42	-66	-24
<i>LV2: cued recall</i>			
Right fronto-polar cortex (10)	32	52	-8
Right middle frontal cortex (9/46)	50	30	28
Left middle frontal cortex (10/46)	-42	52	20
Left inferior parietal cortex (40)	-34	-70	44
Right inferior parietal cortex (40)	36	-62	40
Right occipito-temporal cortex (19)	46	-80	0
Right inferior frontal cortex/insula (47)	38	18	-8
Left inferior frontal cortex/insula (47)	-26	26	-4
Right medial temporal cortex (35/36)	18	-36	-8
Posterior cingulate gyrus/retrosplenium (29/30)	0	-46	12
Mid-cingulate cortex (23)	-6	-24	28
Anterior cingulate cortex (32)	-4	32	24
<i>LV4: working memory</i>			
Right medial temporal cortex (35)	18	-30	-12
Left inferior parietal cortex (40)	-36	-48	44
Left inferior parietal cortex (39/40) ^a	-58	-56	24
Right inferior frontal cortex/insula ^a	34	14	8
Right superior frontal gyrus/premotor cortex (6) ^a	30	-2	68

Threshold $Z > 3.09$. BA, Brodmann area. X, Y, Z are Talairach coordinates [42].

^a Size $<100 > 60$, otherwise size of all regions >100 voxels.

conditions, including the cued word retrieval task (Fig. 4c). Cued recall was associated with increased activity in several fronto-parietal regions, including the right fronto-

polar cortex, bilateral inferior frontal cortex (right>left), and bilateral lateral and medial parietal cortex (Fig. 4d, Table 3). Increased activity was also observed in right medial temporal cortex. LV4, finally, revealed a separation between the 1-back working-memory task and all other conditions (Fig. 4e). The 1-back task involved increased activity in the right medial temporal cortex, and in the dorsal frontal and parietal cortices (Fig. 4f, Table 3).

3.2.2. Specific comparisons of the episodic tasks

In LV1, the separation of long-term memory from working memory and reading was the least pronounced for cued recall, and there was a tendency to a separation between cued recall and autobiographical memory. Moreover, LV2 revealed a separation between cued recall and all other conditions, including the cued word retrieval task. Collectively, these results suggested differences between cued recall and the other long-term memory tasks, and most critically a within-system difference between cued recall and the autobiographical cued word retrieval task. Specific linear contrasts with SPM99 provided further support for this impression. A contrast between cued recall and the cued word retrieval task showed that cued recall was associated with relatively higher activity (corrected $P < 0.05$) in the right fronto-polar cortex, the right inferior frontal/insular cortex, left occipito-temporal cortex, the left precuneus, and bilateral parietal cortex (Fig. 5a, Table 4). The cued word retrieval task was associated with relatively higher activity in right cerebellum, the left inferior frontal gyrus, the medial frontal cortex, and the left middle temporal cortex (Fig. 5b, Table 4). The latter set of regions was similar to the network identified by LV1 of the PLS-analysis. Thus, the SPM-analyses provided additional evidence for differences between cued recall and the autobiographical cued word retrieval task, and for simi-

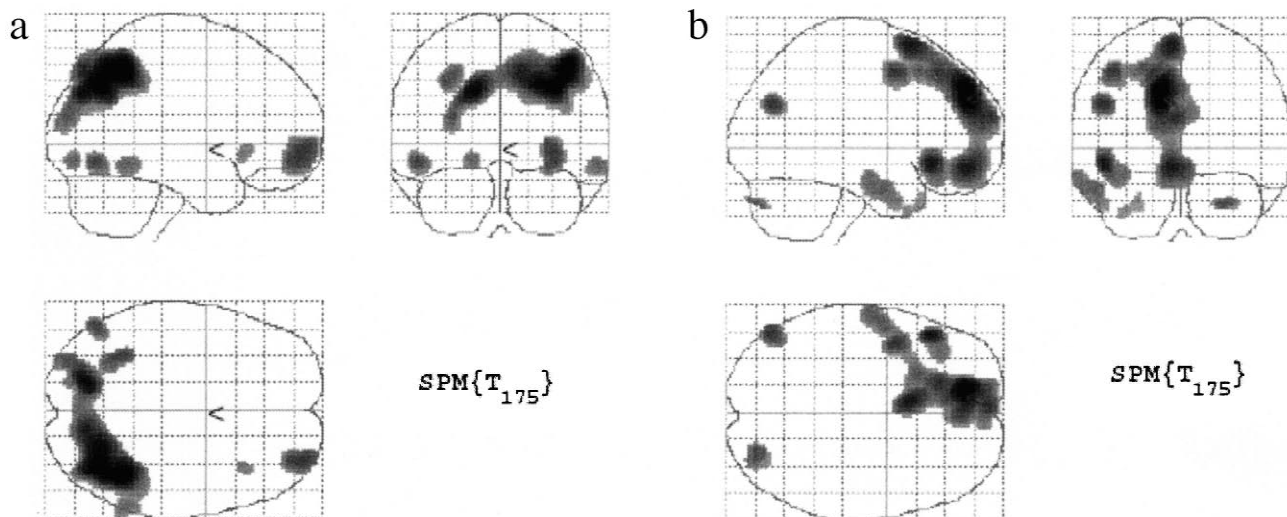


Fig. 5. Results from direct contrast between episodic tasks in experiment 2. (a) Brain regions showing relative increased activity during cued recall. (b) Brain regions showing relative increased activity during the autobiographic cued word retrieval task. Display threshold in (a) and (b): $P < 0.05$ (corrected for multiple comparisons).

Table 4
Direct comparison of episodic tests in experiment 2

Region	X	Y	Z
<i>Cued recall</i>			
Right fronto-polar cortex	34	58	-8
Right inferior frontal/insular cortex	36	24	-4
Left occipito-temporal cortex	-52	-70	-10
Left precuneus	-16	-74	34
Right parietal cortex	42	-52	48
Left parietal cortex	-32	-54	40
<i>Autobiographical cued word retrieval task</i>			
Right cerebellum	26	-82	-34
Left inferior frontal gyrus	-48	26	-10
Medial frontal cortex	-12	48	34
	-6	50	-12
	6	14	64
Left middle temporal cortex	-48	-72	28

X, Y, Z are approximate Talairach coordinates [42].

larities between the cued word retrieval task and the semantic tasks.

3.2.3. Comparison of working-memory networks in studies 1 and 2

A working-memory network was identified in both study 1 (LV1) and study 2 (LV4). Bilateral parietal and right dorsal frontal (premotor) regions were salient network components in both studies (Tables 1 and 3). To more formally assess this overlap in activations between studies 1 and 2, a conjunction analysis was used [31]. This analysis revealed regions that were differentially activated ($P < 0.05$ corrected) when the 2-back and random-number

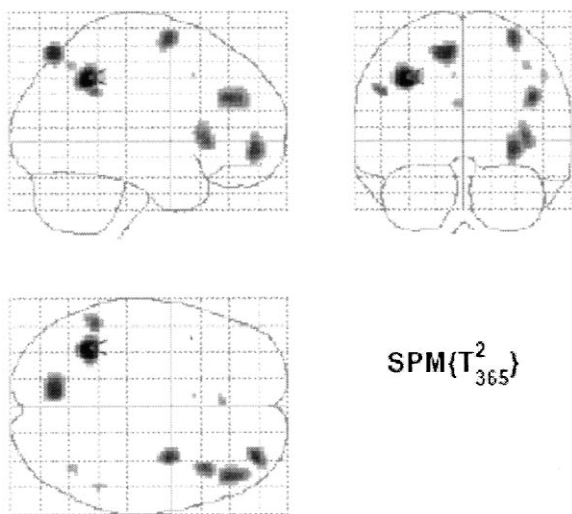


Fig. 6. Overlapping activity during working-memory tasks in experiments 1 and 2. The reading task served as baseline. Increased activity was observed in the right inferior frontal/insular cortex ($x, y, z = 38, 20, 4$), the right middle frontal cortex ($x, y, z = 44, 36, 28$), the right fronto-polar cortex ($x, y, z = 32, 52, -4$), right premotor cortex ($x, y, z = 32, -2, 66$), the precuneus ($x, y, z = -10, -72, 56$), and left parietal cortex ($x, y, z = -36, -52, 40$; $-52, -48, 32$). Display threshold: $P < 0.05$ (corrected for multiple comparisons).

generation tasks were contrasted with the reading baseline in study 1, and when the 1-back task was contrasted with the same baseline (reading of different words) in study 2. In agreement with the within-experiment analyses, increased activity was observed in several frontal and parietal regions (Fig. 6).

4. Discussion

The first experiment identified three networks of brain regions whose activity correlated with the working-memory tasks, fact retrieval, and the episodic tasks. A network for working memory was also identified in experiment two, as was a network for episodic memory. Here, the episodic network was specific for cued recall and did not correlate with the autobiographical cued word retrieval task. Instead, PLS- and SPM-analyses converged in showing that the cued word retrieval task activated a network of brain regions in common with fact retrieval and synonym generation.

The finding of a working-memory network is in keeping with a systems perspective. The identification of a common set of activations for three different tasks (1-back, 2-back, random-number generation) suggests that the network is task-general. This is not to say that there were no differences between the working-memory tasks. Dorsolateral prefrontal activation (area 9/46) was not salient for the 1-back task (Fig. 4f), but more so for 2-back and random-number generation (Fig. 2b). Consistent with this apparent graded response, increased dorsolateral prefrontal activation has been associated with increased executive demands [39] and increased demands for manipulation of the information held in working memory [29]. Further differences were revealed in the direct contrast between the working-memory tasks in experiment 1. Nevertheless, a common set of working memory related activations was observed across experiments (Figs. 2b, 4f, 6). In line with previous observations [7,39], the common activations included bilateral parietal (left > right) and dorsal frontal (premotor) regions. These regions have been associated with *active maintenance/rehearsal* of information [39]. Thus, active maintenance of verbal information may account for the common activations associated with the working-memory tasks.

The identification of a network for episodic memory is also in keeping with a memory-systems perspective. This effect was observed for cued recall and recognition in experiment one and for cued recall in experiment two. In line with this finding, a previous PET study of cued recall and recognition found substantial overlap between activation patterns for these tasks, although some differences were also noted [6]. In both our experiments, the episodic tasks were associated with increased activity in right inferior frontal cortex, right fronto-polar cortex, and lateral and medial parietal cortex (Figs. 2f, 4d, 5a). These regions

have consistently been associated with episodic-memory retrieval in previous studies [7,19,20,27,47]. Interestingly, right fronto-polar cortex and the lateral and medial parietal cortices were also activated during working-memory tasks (Fig. 3, Table 2). This commonality indicates a shared processing component for at least some episodic and working-memory tasks. Moreover, fronto-parietal activation was recently associated with a test of prospective memory [5]. It remains to be determined whether fronto-parietal activation in these tasks reflects shared cognitive processes, but it is interesting to note that all these tests involve *explicit retrieval* [43] in that they require that a current stimulus is matched against stored or maintained information. By this view, fronto-parietal activation during episodic retrieval can be seen as reflecting more strategic processes that are not related to actual recovery of information, which is in keeping with a *retrieval mode* interpretation [27]. Other component processes of episodic retrieval, not revealed by the current PLS-analyses, are related to actual recovery of information and engage additional regions, such as the hippocampus [7].

The within-system difference between cued recall and the autobiographic cued word retrieval task in experiment two is noteworthy since autobiographical memory often is seen as the hallmark of episodic memory. A possible explanation of the present and related [8] findings is that questions about past personal experiences can be answered in a non-episodic (semantic) manner. The task of the subjects was to come up with personal memories in response to cue words (e.g. vacation). The retrieval time was limited to 5 s. According to some studies [8], retrieval times in the cue word procedure approximate 5 s, but other studies indicate that it is two to three times longer [33]. Thus, given the limited time for retrieval, it seems likely that many responses were quite general or semantic in nature (e.g. a subject says ‘France’ because he *knows* he has been to France on vacation—not because he actually *remembers* specific information from that event). Moreover, it has been argued that autobiographical memory is not restricted to past personal *events*, but also includes *personal semantic information* (information that is repeatedly experienced) [10]. Indeed, informal comments by some of the subjects held that it was difficult to come up with ‘living/intensive’ memories. Taken together, these considerations indicate that the cued word retrieval task elicited general semantic memory retrieval. An interesting question for future studies is whether the neural signature of autobiographical memory is more similar to that for cued recall and recognition if the specific autobiographical test emphasizes retrieval of specific details and if more time is allowed for retrieval.

The observation of a common network for the cued word retrieval task, fact retrieval and synonym generation provides support that the autobiographical test taxed semantic rather than episodic retrieval. Salient components of this network included left inferior frontal and middle

temporal regions and also right cerebellum (Figs. 2d, 4b). These regions were not strongly activated during the living/non-living task, as indicated by the within-system difference between fact retrieval and living/non-living classification in experiment 1 (Fig. 2c). This difference is in keeping with several previous studies showing that semantic tasks that emphasize generation processes are more strongly associated with left posterior frontal activation than tasks that emphasize classification [7]. Thus, the observed network may underlie more elaborate retrieval of semantic information [4].

Taken together, our findings may be interpreted as reflecting networks for working memory, episodic/explicit memory, and elaborate semantic memory. As such, the present data provide support for a memory-systems account. The fact that this support was generated by task PLS, rather than a priori defined contrasts, is noteworthy. At the same time, our observations of within-system differences as well as between-systems similarities highlight certain issues concerning the classification of tasks and the relation between systems and processes. In the context of a systems view it has been noted that memory systems operate in terms of processes—some shared with other systems, some unique [36,44]. On the assumption that our findings reflect both systems and processes they are consistent with this view, although it remains to be specified what constitutes a system and what constitutes a process. Another theoretical account seems to unite systems and processes by proposing that memory systems are neural networks that mediate specific mnemonic processes [16]. By this view, memory systems are both more numerous and specific than what is typically held. A third theoretical account, the *components of processing framework* [23,34], holds that some component processes are shared by many tasks whereas others may be unique for specific classes of measures, or not even shared by related measures. It is unclear how processing components differ from memory systems [30], especially when systems are defined in the more specific sense, and the present results may be taken to reflect specific systems as well as processing components. Clearly, further work is necessary to resolve this issue. The type of approach presented here, combined task analysis and multivariate analysis of brain-imaging data associated with multiple tasks, represents one way of addressing the overall functional organization of human memory.

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