



Top-down and bottom-up attention-to-memory: Mapping functional connectivity in two distinct networks that underlie cued and uncued recognition memory

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ABSTRACT

The objective of this study was to examine the functional connectivity of brain regions active during cued and uncued recognition memory to test the idea that distinct networks would underlie these memory processes, as predicted by the attention-to-memory (AtoM) hypothesis. The AtoM hypothesis suggests that dorsal parietal cortex (DPC) allocates effortful top-down attention to memory retrieval during cued retrieval, whereas ventral parietal cortex (VPC) mediates spontaneous bottom-up capture of attention by memory during uncued retrieval. To identify networks associated with these two processes, we conducted a functional connectivity analysis of a left DPC and a left VPC region, both identified by a previous analysis of task-related activations. We hypothesized that the two parietal regions would be functionally connected with distinct neural networks, reflecting their engagement in the differential mnemonic processes. We found two spatially dissociated networks that overlapped only in the precuneus. During cued trials, DPC was functionally connected with dorsal attention areas, including the superior parietal lobules, right precuneus, and premotor cortex, as well as relevant memory areas, such as the left hippocampus and the middle frontal gyri. During uncued trials, VPC was functionally connected with ventral attention areas, including the supramarginal gyrus, cuneus, and right fusiform gyrus, as well as the parahippocampal gyrus. In addition, activity in the DPC network was associated with faster response times for cued retrieval. This is the first study to show a dissociation of the functional connectivity of posterior parietal regions during episodic memory retrieval, characterized by a top-down AtoM network involving DPC and a bottom-up AtoM network involving VPC.

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Introduction

Recent functional neuroimaging (fMRI) studies (for reviews see Cabeza et al., 2008; Ciaramelli et al., 2008; Vilberg and Rugg, 2008; Wagner et al., 2005) have shown that posterior parietal cortex (PPC), especially in the left hemisphere, is among the brain regions that most consistently show retrieval success effects, i.e., higher activity for correctly recognized items than for correctly rejected items (but see Cabeza et al., 2012, for exception to rejections). Because PPC had not been conventionally associated with memory, these findings were surprising, but suggested that PPC, nevertheless, may have an important role in episodic memory retrieval. In this paper, we

follow up on these initial observations by conducting a functional connectivity analysis to determine the inter-related network of structures associated with top-down and bottom-up attentional processes in the parietal cortex during memory retrieval.

It is well known that PPC supports attentional processes (e.g., Posner and Petersen, 1990). Dorsal parietal cortex (DPC) mediates top-down attention, which enables selection of stimuli based on internal goals, whereas ventral parietal cortex (VPC) mediates bottom-up attention, which enables detection of relevant stimuli (Corbetta and Shulman, 2002; Marois et al., 2000). One example of this dissociation is that DPC was maximally engaged during the cue period, when participants searched for a target, whereas VPC was exclusively engaged during target detection (Corbetta et al., 2000). This work has led some to suggest that PPC might provide “attentional support” to memory retrieval as well (Cabeza, 2008; Ciaramelli et al., 2008; Wagner et al., 2005). One proposal is the attention-to-memory (AtoM) hypothesis (Cabeza et al., 2008; Ciaramelli et al., 2008), according to which DPC and VPC play differential roles during episodic memory retrieval, reflecting their functional diversity in the attentional domain. DPC would mediate

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the allocation of attentional resources to memory retrieval, which would be needed when the retrieval conditions demand reliance upon controlled operations, such as memory search and monitoring (top-down AtoM). VPC, on the other hand, would be associated with the bottom-up capture of attention by retrieved memories, which would be maximal when memory contents are retrieved spontaneously and with high confidence (bottom-up AtoM).

Empirical support for the AtoM hypothesis has been provided by functional neuroimaging studies of recognition memory in which left DPC (intraparietal sulcus) is consistently active when the need for top-down AtoM is supposedly maximal, e.g., for difficult memory decisions and for memories retrieved with low confidence (Ciaramelli et al., 2008; Vilberg and Rugg, 2008). Other support comes from work showing that left VPC (supramarginal gyrus and angular gyrus) is consistently active when the attentional capture by memory contents is supposedly maximal, i.e. for vividly recollected memories, and for memories retrieved with high confidence (Ciaramelli et al., 2008; Vilberg and Rugg, 2008). Consistent with this finding is the neuropsychological evidence that patients with lesions affecting mainly VPC have problems detecting memory contents spontaneously, but can access them if probed appropriately (Berryhill et al., 2007; Ciaramelli et al., 2010a,b), and may show reduced levels of recollection (Davidson et al., 2008; Drowos et al., 2010; see also Simons et al., 2010).

In a recent fMRI study, Ciaramelli and colleagues have shown a dissociation between top-down and bottom-up AtoM in PPC within the same paradigm (Ciaramelli et al., 2010a,b). In a recognition memory paradigm, participants studied word pairs and later classified single words as studied or new while being scanned. To-be-recognized words could be “cued” by an old word, a new word, or a meaningless stimulus (*No-cue* condition). Most old-word cues preceded the word with which they were paired at study (*Intact* condition), facilitating recognition. Appearance of an old-word cue, therefore, encouraged participants to search for its original associate in order to anticipate the upcoming memory target, requiring top-down AtoM. On the other hand, when there was no cue, recognition of the memory target crucially depended on *detection* of bottom-up signals originating from the memory probe, engaging bottom-up AtoM. The results showed that the left intraparietal sulcus of DPC was engaged when participants searched for/anticipated memory targets upon presentation of relevant memory cues, and predicted the ensuing behavioral advantage (Ciaramelli et al., 2010a,b), consistent with a role in top-down AtoM (see also Kuhl et al., 2007; Wheeler et al., 2006). In contrast, the left angular gyrus of VPC predicted efficacy and speed of target detection in non-cued trials, consistent with a role in bottom-up AtoM (Ciaramelli et al., 2010a,b). In an accompanying lesion study, Ciaramelli et al. (2010a,b) found that damage to DPC and VPC impaired performance differentially on the top-down and bottom-up aspects of the task, respectively. Importantly, Cabeza and colleagues have shown that DPC and VPC regions involved in top-down and bottom-up AtoM may overlap with regions mediating top-down and bottom-up attention to environmental stimuli (Cabeza et al., 2011).

Although the results of the aforementioned studies reflect regional activations of brain areas that are involved in top-down and bottom-up AtoM, they do not provide direct evidence as to whether distinct brain networks are engaged during AtoM. Highly complex cognitive processes, such as attention or episodic memory retrieval, would presumably not be localized to discrete brain regions, such as DPC and VPC, but rather would be mediated by the interaction among a number of functionally related neural areas. Recent studies, indeed, have shown that DPC and VPC are embedded in two independent, yet interacting, groups of brain regions that constitute two fundamental attention systems: the dorsal frontoparietal system, supporting top-down attention, and the ventral frontoparietal system, supporting bottom-up attention (Corbetta and Shulman, 2002; Corbetta et al., 2008). Regions within the dorsal and ventral frontoparietal systems are connected functionally during attention tasks (Corbetta and Shulman, 2002), as well as at

rest (Fox et al., 2006). Many researchers have argued that it is the activity of distributed neural networks and the interactions among anatomically connected brain regions that directly yield cognitive functions (e.g., Bressler and Menon, 2010; Friston, 1997; McIntosh, 1998, 2000). Thus, what is important in determining the neural underpinning of a cognitive function is to understand covarying activity within a network, i.e., the correlations between activity in a brain area thought to be important for the function, and activity of other brain areas with which it is connected.

Because measurements of mean neural activity changes across tasks in a specific brain area, or areas, provide no direct evidence of relevant interregional functional interactions that occur (e.g., Grady et al., 1998; McIntosh et al., 1994), a common approach to quantifying such interactions is to assess the degree of functional connectivity among brain regions. Functional connectivity is the degree to which activity in a specific region correlates or covaries with activity in other areas across the whole brain, and is one way to define a network (Friston, 1994; Friston et al., 1993; Horwitz et al., 1984). To statistically study complex neural interactions between different brain structures, the analytical methods must provide a means to quantifying the relation between brain regions, rather than focusing on mean activity differences. Multivariate approaches, such as the partial least squares (PLS) approach to image analysis, enable investigation of functional connectivity of neural regions by calculating the covariance between the activity within selected seed voxels and all other brain voxels across the experimental conditions (McIntosh & Gonzalez-Lima, 1994; McIntosh et al., 1996). We used this approach to address three goals: (i) to expand on the previous findings of task-related regional activations (Ciaramelli et al., 2010a,b) by examining the functional connectivity of left DPC and left VPC during cued and uncued recognition memory retrieval to identify the neural networks that mediate top-down and bottom-up AtoM; (ii) to determine whether these two networks were distinct from one another by assessing their spatial overlap (i.e., whether they have any brain regions in common); and (iii) to investigate how regions mediating top-down or bottom-up AtoM interact with the MTL to support cued and uncued recognition memory performance. To map the networks, we used seed voxel PLS analysis (Della-Maggiore et al., 2000; McIntosh, 1999; McIntosh et al., 1997; Schreurs et al., 1997), in which we determined whole-brain patterns of activity that correlated with DPC and VPC, two seed regions localized in the previous study (Ciaramelli et al., 2010a,b). Delineating the neural networks associated with cued (top-down) and uncued (bottom-up) recognition memory would allow us to verify whether the systems mediating top-down and bottom-up attention to external and internal contents extend from PPC regions to dorsal and ventral frontal regions, respectively; to verify the degree to which top-down and bottom-up AtoM systems overlap; and to reveal how these systems interact with the MTL to support different paths to remembering.

Methods

Participants

Fourteen right-handed, healthy young participants (mean age = 26 years; age range = 20–33 years, 10 females) took part in the study. All participants were native English speakers. They signed an informed consent that was approved by the ethics committee of the Rotman Research Institute at Baycrest.

Stimuli

Four hundred and eighty words (mean frequency = 36.6, SD = 34.9), between 4 and 8 letters long, were selected from the Kucera and Francis (1967) pool and randomly assigned to the experimental runs. In each run, 70% of the words formed the study pairs, whereas

the remaining 30% of the words served as distracters or non-studied cues in the test phase.

Procedure

The experiment consisted of 8 runs, each divided into a study phase and a cued-recognition phase. During the study phase, participants viewed 21 word pairs for 3 s and were instructed to form a sentence that included both words of each pair. The cued-recognition memory phase followed immediately after the study phase. First, a cue stimulus was presented for 1900 ms. The cue stimulus could be a studied word, a new word, or a meaningless stimulus (i.e., @@@@). After a 100-ms delay, a target word appeared for 500 ms. The target word could be a studied word or a new word. Participants were instructed to maintain attention in the middle of the screen, where the cue stimulus appeared, wait for the appearance of the target word, and then decide, as quickly and as accurately as possible, whether the target word was old or new. It was emphasized to subjects that they had to respond to the episodic status of the target word only, although consideration of the cue stimulus could be beneficial to performance. Subjects responded by pressing one of two keys, located on an MRI-compatible response pad, with their right (dominant) hand, according to whether they judged the target word to be old or new. An inter-trial-interval (ITI) ranging from 0–4 s was interspersed across test trials to “jitter” the onset times of trials and allow for event-related fMRI analyses.

The nature of the cue and the target determined 7 types of trial. A detailed description of all experimental conditions is reported elsewhere (see Ciaramelli et al., 2010a,b). In the current study, we focused on 3 experimental conditions. In the *Intact* condition (6 trials per run), the cue was a previously studied word, and the target was a word previously paired with the cue word. In the *No-Old* condition (6 trials per run), the cue was a meaningless stimulus (@@@@) and the target was a previously studied word. In the *No-New* condition (3 trials per run), the cue was a meaningless stimulus (@@@@) and the target was a new word (Fig. 1).

We expected that, in the *Intact* condition, upon presentation of a studied word as the cue, participants would search for its original associate in order to anticipate the upcoming target. Retrieving that cue word A was studied with word B, indeed, would make it relatively easy to decide that B is a studied word, in case it is presented as the target stimulus. In contrast, no search activity should be triggered by meaningless cues. Thus, whereas comparing the neural networks implicated in the *No-Old* condition and in the *No-New* condition would reveal the basic system supporting bottom-up recognition memory when no cue is provided, comparing the neural networks implicated in the *Intact* condition and the *No-Old* condition would reveal the system specifically recruited during cued (top-down) recognition memory.

fMRI data acquisition

Anatomical and functional images were acquired at Baycrest Hospital using a 3 T Siemens Magnetom Trio scanner with a matrix 12-channel head coil. Anatomical images were acquired using a T1-weighted 3D MP-RAGE sequence (160 oblique axial slices, TR = 2 s, TE = 2.63 s, FOV = 25.6 cm, voxel size = 1 mm³, acquisition matrix = 256 × 256). Brain activation was assessed using the blood oxygenation level-dependent (BOLD) effect (Ogawa et al., 1990) with optimal contrast. Functional images were obtained using a whole head T2*-weighted echo-planar image (EPI) sequence (28 oblique axial slices with interleaved acquisition, TR = 2 s, TE = 30 ms, flip angle = 70°, FOV = 20 cm, voxel size = 3.1 × 3.1 × 5 mm, acquisition matrix = 64 × 64). Physiological data (heart and respiration rates) were acquired during the scanning session.

fMRI data preprocessing

Only fMRI data collected at retrieval were analyzed for the purpose of the current study. The initial five time points from each image volume were removed from analyses to allow for the brain magnetization to stabilize. Images were reconstructed and motion-corrected utilizing the Analysis of Functional Neuroimages (AFNI; Cox, 1996). The peak range of head motion did not exceed 1 mm across all participants. The time-series data were further corrected for cardiac and respiratory parameters. To enable group comparisons, each brain scan was spatially normalized, i.e., scaled and warped to match a standard template (the Montreal Neurological Institute [MNI] spiral template) utilizing Statistical Parametric Mapping (SPM5) software. The warping of the brain surface was achieved via a linear transformation with sinc interpolation (i.e., a signal resampling method designed to minimize aliasing in the signal). Lastly, the images were smoothed with a 6 mm Gaussian filter, which, acting as a low pass filter, makes the data less noisy by reducing the images' high-frequency components. The voxel size, after preprocessing, was 2 × 2 × 2 mm.

Seed voxel PLS analysis

Based on the findings of regional activations underlying top-down and bottom-up AtoM (Ciaramelli et al., 2010a,b), we conducted a seed voxel analysis (Schreurs et al., 1997) in which two seed voxels (i.e., the left DPC [−36 −56 48] and the left VPC [−44 −66 28]) were selected to examine task-related functional connectivity (i.e., the degree of nonzero correlation between brain regions). The seed activity was contrasted across task conditions and participants by partial least squares (PLS) analysis, delineating a pattern of functional connectivity between the seed voxels and the rest of the brain. Seed PLS is a multivariate statistical method utilized in the investigation of the relation of activity in a selected brain region or regions (i.e., a seed voxel) and activity in the rest of the brain across the task conditions (Della-Maggiore et al., 2000; McIntosh, 1999; McIntosh et al., 1997; Schreurs et al., 1997). In other words, seed PLS analysis examines functional connectivity across experimental conditions or during rest (Grigg and Grady, 2010a,b). The selection of the seed voxel(s) can be either data-driven (i.e., determined by previous analyses of the data) or hypothesis-driven (i.e., determined by theoretical assumptions), or both. In our study, the selection of the seed voxels was data-driven (see Ciaramelli et al., 2010a,b). To delineate the top-down attention-to-memory network, we correlated activity in the left DPC with activity in the rest of the brain in the *Intact* and *No Old* conditions. To delineate the bottom-up attention-to-memory network, we correlated activity in the left VPC and the rest of the brain in the *No Old* and *No New* conditions. We included in the analyses only those trials for which participants made a correct response.

The analytical procedure for seed PLS was threefold: firstly, the BOLD values from the two seeds were extracted (i.e., from the peak voxels identified in the previous study) for each memory event of interest, across 8 timepoints from the onset of the trial. The activity for each seed was averaged across the peak and adjacent timepoints, and then this average measure of seed activity was correlated with activity in all other brain voxels, across the participants, within each condition. Secondly, these correlations were combined into a matrix and decomposed with singular value decomposition (SVD), resulting in a set of latent variables (LVs; i.e., mutually orthogonal variables). Each LV consists of a singular image (i.e., “brain LV,” or the pattern of brain regions that covary in activity with the seed voxel), a singular profile (i.e., “seed LV,” or the pattern of covariance of the seed voxel and the rest of the brain across the experimental conditions), and a singular value (i.e., the amount of covariance accounted for by each LV). Finally, the significance for each LV was determined by a permutation test (McIntosh et al., 1996), which involves a random reordering of the data matrix and calculation of a

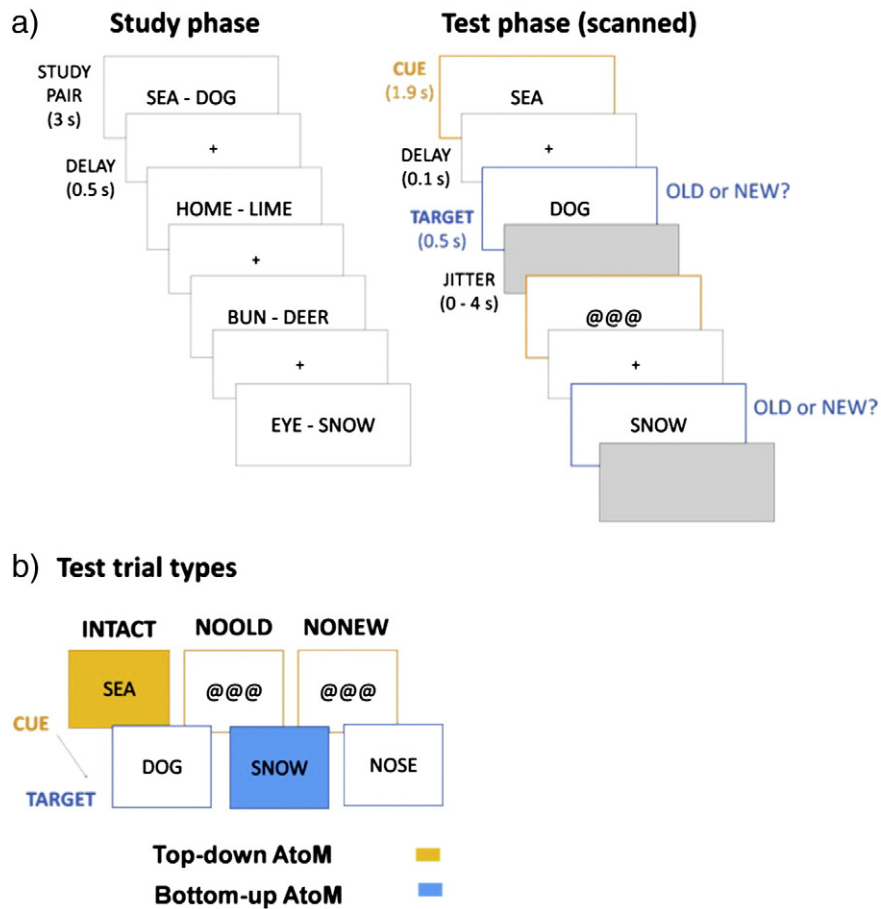


Fig. 1. Task layout. A) During the study phase, participants studied word pairs. During the test phase (in the scanner), participants underwent a cued-recognition task. B) 3 types of test trials. *Intact*: the cue was a previously studied word and the target was a word previously paired with the cue word; *No Old*: the cue was a meaningless stimulus and the target was a previously studied word; *No New*: the cue was a meaningless stimulus and the target was a new word.

new set of LVs for each reordering. The singular value of each newly permuted LV is compared to the singular value of the original LV, yielding a probability of the number of occurrences that the permuted values exceed the original value. Five hundred permutations were conducted. For each TR, a “brain score” was calculated for each participant, providing an index of how strongly that participant shows the particular pattern of brain activity identified for that TR. The brain scores can be used to examine differences in brain activity across conditions, because greater activity in brain areas with positive (or negative) weights on a latent variable will yield positive (or negative) mean scores for a given condition. We calculated the correlation between the brain scores from each significant LV and the seed BOLD values to assess the relation between the whole-brain pattern and activity in the two reference regions. The reliability of the weights (or saliences) for the brain voxels was assessed by a bootstrap estimation of the standard errors (Efron and Tibshirani, 1985), randomly resampling participants, with replacement, and computing the standard error of the saliences after 100 bootstrap samples. Peak voxels with a salience/SE ratio > 3.3 were considered to be reliable, as this approximates $p < 0.001$ (Sampson et al., 1989).

Behavioral PLS analysis and assessment of network overlap

In addition to the functional connectivity analysis, we assessed (i) whether activity in the delineated functional networks was correlated with behavioral performance in the tasks, and (ii) whether parts

of the two networks spatially overlapped (i.e., brain regions that show functional connectivity with both the left DPC and left VPC).

To assess the relation of behavioral performance on the task and activity in the functional networks, we conducted behavioral PLS analysis in which we correlated a) activity in the left DPC and the rest of the brain with reaction times of the participants in the *Intact* and *No Old* conditions, and b) activity in the left VPC and the rest of the brain with reaction times of the participants in the *No Old* and *No New* conditions.

To assess the spatial overlap of the two networks, for each time point, we created a conjunction map by multiplying the thresholded voxel BSR maps of the two connectivity analyses. In this way we could identify any brain areas that were robustly correlated both with DPC and VPC.

Results

Functional connections with left DPC

The statistically significant latent variable yielded by this seed PLS analysis accounted for 63% of covariance in the data ($p < 0.001$), delineating a group of brain regions whose activity correlated with the left DPC during cued recognition decisions, but not during uncued decisions (see Fig. 2). The left DPC was functionally connected with the superior parietal lobules, right precuneus, premotor cortex, dorsolateral and dorsomedial frontal gyri, middle temporal gyri, inferior frontal gyri,

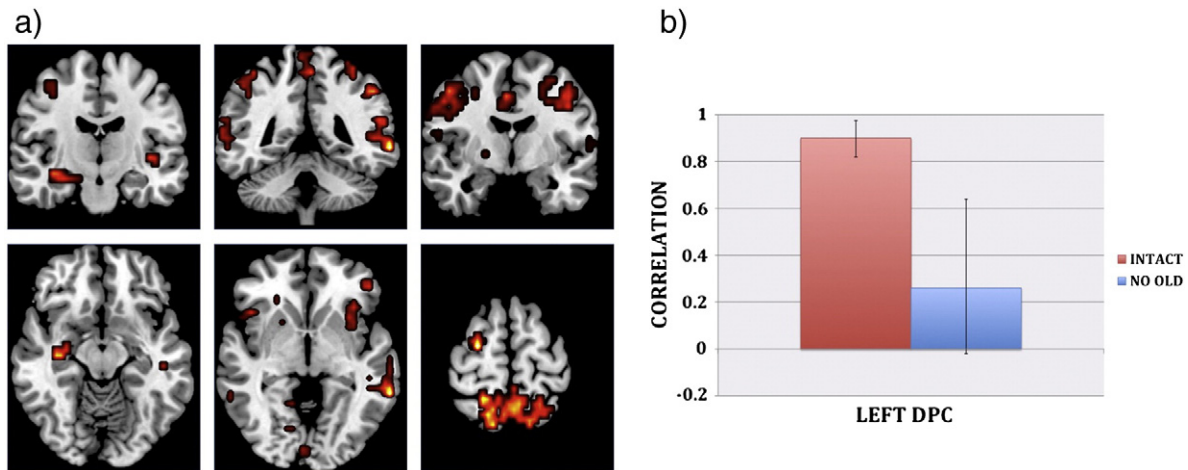


Fig. 2. Seed PLS results: functional connections with left DPC. (a) A pattern of correlated activity at 6–8 s after the trial onset. (b) Correlations between activity in left DPC and scores representing activity in the regions seen in (a) during *Intact* and *No Old* conditions. Error bars are 95% confidence intervals for the correlations calculated from the bootstrap procedure.

left lateral occipital gyrus, the pulvinar nucleus of the left thalamus, and the left hippocampus (see Table 1 for a summary).

Functional connections with left VPC

The statistically significant latent variable yielded by this seed PLS analysis accounted for 57% of covariance in the data ($p < 0.001$), delineating a group of brain regions whose activity was positively correlated with the left VPC during direct (uncued) recognition memory decisions, but not during presentation of new words (see Fig. 3). Activity in the left VPC positively correlated with the inferior parietal lobules (specifically the supramarginal gyri), bilateral precuneus, bilateral insula, a number of frontal, temporal, and occipital areas, as well as the dorsomedial nucleus of the right thalamus. During the No-New trials, the left VPC was not correlated with this functional network, but rather with the right middle occipital gyrus and left posterior cingulate gyrus (see Table 2 for a summary). In addition, activity in these two regions was negatively correlated with activity in the VPC network seen during uncued recognition.

Behavioral PLS analysis

Activation in the top-down functional network correlated negatively with reaction times in the *Intact* and *No Old* conditions ($p < 0.001$),

accounting for 49% of covariance in the data (see Fig. 4). This finding indicates stronger activation of the top-down network in response to faster recognition performance, suggesting that increased activity in this network may be due to anticipation or goal-directed attention. Only in the *Intact* condition was activity in this network positively correlated with activity in DPC, which emphasizes the interaction of this posterior parietal area with the top-down network during cue-related activity. Finally, we did not find a significant correlation between activity in the bottom-up network and performance in the *No New* or *No Old* conditions.

Spatial overlap between networks

To address whether there are any spatial commonalities between the two functional networks, we created, for each TR, a conjunction map of their spatial overlap. These conjunction maps showed a general lack of spatial overlap of the networks across most TRs, with regions functionally related to DPC lying generally more dorsally than regions functionally related to VPC (see Figs. 2 and 3). The only exception to the general segregation of the two networks was in the right precuneus (Brodmann area 7) whose sustained activity was evident in both functional networks (see Fig. 5).

Discussion

The purpose of this study was to examine the functional connectivity of the left DPC and VPC, two posterior parietal areas that play an important role in attention (Corbetta et al., 2000, 2002; Kincade et al., 2005) and episodic memory retrieval (Cabeza, 2008; Ciaramelli et al., 2008; Wagner et al., 2005) under retrieval conditions that are more weighted towards top-down AtoM (cued recognition) or bottom-up AtoM (uncued recognition). Our findings provide further evidence supporting the AtoM hypothesis, and extend current knowledge in two ways. Firstly, we showed evidence for a functional dissociation of two brain networks that support top-down and bottom-up AtoM during cued and uncued episodic memory retrieval. There was a large-scale network functionally connected with the left VPC that was engaged during recognition memory when no cue was provided (i.e., bottom-up AtoM), and a network of brain regions functionally connected with the left DPC during cued retrieval (i.e., top-down AtoM). The two networks were, for the most part, spatially independent, overlapping only in the posterior precuneus. The second novel finding from this study is that activity only in the DPC network, not in the VPC network, was associated with response speed, in that faster reaction

Table 1
Functional connections with L DPC.

| Region | Hem | BA | MNI coordinates | | | Ratio |
|--------------------------|-----|-------|-----------------|-----|-----|-------|
| | | | x | y | z | |
| Superior parietal lobule | R | 7 | 32 | -72 | 48 | 18.13 |
| | L | | -36 | -60 | 52 | 18.14 |
| Precuneus | R | 7 | 20 | -68 | 36 | 38.36 |
| Premotor cortex | R | 6 | 44 | -8 | 48 | 11.14 |
| | L | | -48 | -4 | 48 | 13.73 |
| Inferior frontal gyrus | R | 47 | 36 | 24 | -4 | 7.55 |
| | L | | -44 | 20 | -4 | 8.31 |
| Dorsomedial PFC | L | 8 | -4 | 20 | 44 | 13.11 |
| Dorsolateral PFC | R | 9/46 | 44 | 28 | 28 | 13.67 |
| Lateral occipital gyrus | L | 18/19 | -40 | -76 | -4 | 9.41 |
| Hippocampus | L | | -36 | -16 | -12 | 7.41 |
| Middle temporal gyrus | R | 21 | 64 | -44 | -4 | 18.52 |
| | L | | -60 | -52 | 0 | 8.36 |
| Thalamus (pulvinar) | L | | -20 | -28 | 4 | 16.48 |

Abbreviations: Hem = hemisphere; BA = Brodmann's Area; R = right; L = left; Ratio = salience/SE ratio from the bootstrap analysis; x coordinate = right/left; y coordinate = anterior/posterior; z coordinate = superior/inferior; PFC = prefrontal cortex.

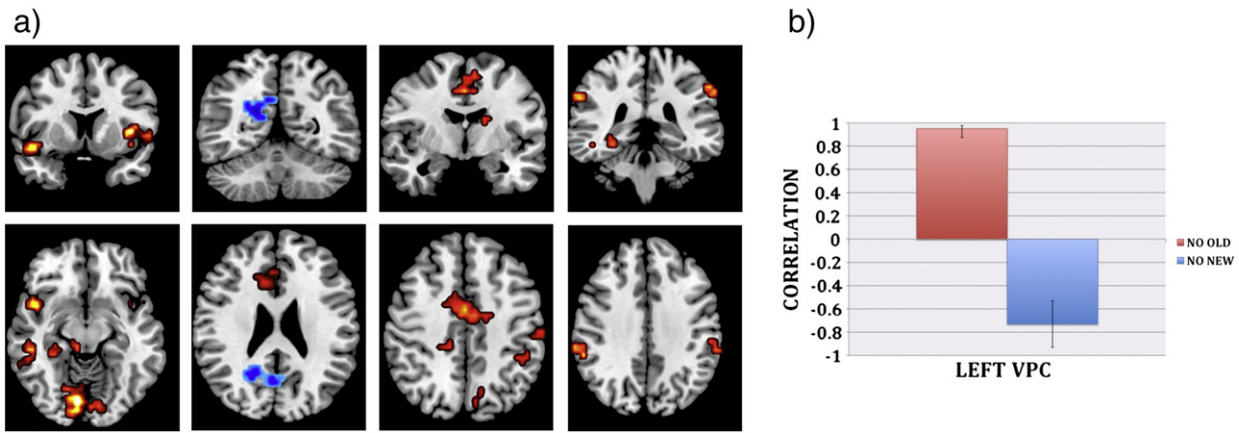


Fig. 3. Seed PLS results: functional connections with left VPC. (a) A pattern of correlated activity at 6–8 s after the trial onset. (b) Correlations between activity in left VPC and scores representing activity in the regions seen in (a) during *No Old* and *No New* conditions. Error bars are 95% confidence intervals for the correlations calculated from the bootstrap procedure.

times for cued recognition memory decisions were associated with greater activity in this functional network.

Bottom-up AtoM network

Several regions in the VPC, including the left angular gyrus and the supramarginal gyrus bilaterally were engaged when recognizing memory contents in the absence of cues. VPC is consistently involved in recognition memory studies, showing more activity for studied stimuli that are correctly recognized compared to new stimuli that are correctly rejected (see for reviews, Ciaramelli et al., 2008; Kim et al., 2009; Spaniol et al., 2009). According to the AtoM hypothesis, VPC mediates bottom-up attention to salient memory contents retrieved by the MTL (Cabeza et al., 2008; Ciaramelli et al., 2008). We found that during uncued recognition memory decisions, VPC was functionally connected with the left parahippocampal gyrus, a region that plays a prominent role in single-item recognition (Yonelinas et al., 2005). This finding is consistent with the AtoM hypothesis that, upon retrieval of memory contents via the MTL, VPC promotes a switch in

attention toward the incoming memory, just as this region mediates stimulus-driven reorienting of attention to external percepts. In line with this hypothesis, a recent study found that overlapping VPC regions mediated detection of memories and percepts (Cabeza et al., 2011). In addition to the parahippocampal gyrus and VPC, the uncued recognition memory network involved the right inferior frontal gyrus (BA 45). The inferior frontal gyrus is a crucial node of the ventral frontoparietal attentional system (Corbetta and Shulman, 2002), and is consistently recruited, along with VPC, during detection of low-frequency events, independently of modality and response demands, and in association with stimulus-driven reorienting of attention (Corbetta and Shulman, 2002). The fact that this region was functionally connected with VPC and parahippocampal gyrus during detection of memory contents reinforces the AtoM hypothesis that similar attentional mechanisms may mediate detection of external and internal (memory) information.

Moreover, VPC was functionally connected with the insula, sensorimotor regions in both hemispheres, right posterior fusiform gyrus, and left anterior cingulate gyrus, all of which have been identified in numerous studies as participating in the ventral frontoparietal attention network (Corbetta et al., 2000, 2002; Kincade et al., 2005). Additional nodes of the bottom-up AtoM network were the cuneus and dorsal medial nucleus of the thalamus. The cuneus is an important region of the ventral visual stream, enabling basic visual processing, as well as visual and spatial attention (Goldstone, 1995; Vanni et al., 2001). The dorsal medial nucleus of the thalamus receives direct input from the parahippocampal gyrus, conveying the information further via reciprocal connections with supplementary motor, parietal, and prefrontal cortices (Tanaka, 1976; Vogt and Pandaya, 1987). These connections and the known effects of injury to this brain region suggest its critical role in attention and active memory retrieval (Li et al., 2004; Taber et al., 2004). The functional connections with all of these regions and the VPC suggests that there is substantial overlap between the ventral network involved in bottom-up attention to stimuli in the environment and the bottom-up AtoM network that mediates attention to retrieved memories, supporting the idea that similar mechanisms are involved.

In addition to the positive correlations between the ventral frontoparietal regions and VPC, the connectivity analysis also identified a right middle occipital region and one in left posterior cingulate cortex (PCC), whose activity negatively correlated with the left VPC during uncued memory decisions. This specific region of the middle occipital gyrus corresponds to the dorsal V3 area of the dorsal visual pathway, implicated in spatial visual performance, motion, and visual control of saccadic movement (Goodale and Milner, 1992; Lyon and Kaas, 2002). The posterior cingulate has been pinpointed as a critical node of the default network (Shulman et al., 1997), but also is

Table 2
Functional connections with L VPC.

| Region | Hem | BA | MNI coordinates | | | Ratio |
|------------------------------|-----|----|-----------------|-----|-----|--------|
| | | | x | y | z | |
| <i>Positive correlations</i> | | | | | | |
| Inferior parietal lobule/SMG | R | 40 | 60 | −36 | 44 | 5.44 |
| | L | | −56 | −40 | 36 | 6.66 |
| Precuneus | R | 7 | 24 | −68 | 52 | 8.26 |
| | L | | −12 | −76 | 40 | 9.44 |
| Insula | R | 13 | 40 | 8 | 4 | 9.43 |
| | L | | −40 | 12 | −4 | 11.10 |
| Supplementary motor area | R | 6 | 4 | −8 | 52 | 9.37 |
| Inferior frontal gyrus | R | 45 | 48 | 16 | 16 | 7.13 |
| Precentral gyrus | L | 4 | −36 | −28 | 64 | 10.95 |
| Postcentral gyrus | R | 3 | 64 | −16 | 32 | 8.79 |
| | L | | −64 | −20 | 16 | 8.63 |
| Anterior cingulate gyrus | L | 24 | −8 | −4 | 44 | 10.06 |
| Fusiform gyrus | R | 37 | 52 | −52 | −16 | 5.47 |
| Cuneus | R | 18 | 20 | −96 | 12 | 9.19 |
| | L | | −20 | −92 | 8 | 5.18 |
| Thalamus (dorsomedial) | R | | 12 | −20 | 8 | 7.63 |
| Parahippocampal gyrus | L | 36 | −28 | −28 | −16 | 7.99 |
| <i>Negative correlations</i> | | | | | | |
| Posterior cingulate gyrus | L | 31 | −4 | −60 | 28 | −9.36 |
| Middle occipital gyrus | R | 19 | 40 | −68 | 4 | −12.79 |

Abbreviations: Hem = hemisphere; BA = Brodmann's Area; R = right; L = left; Ratio = salience/SE ratio from the bootstrap analysis; x coordinate = right/left; y coordinate = anterior/posterior; z coordinate = superior/inferior; SMG = supramarginal gyrus.

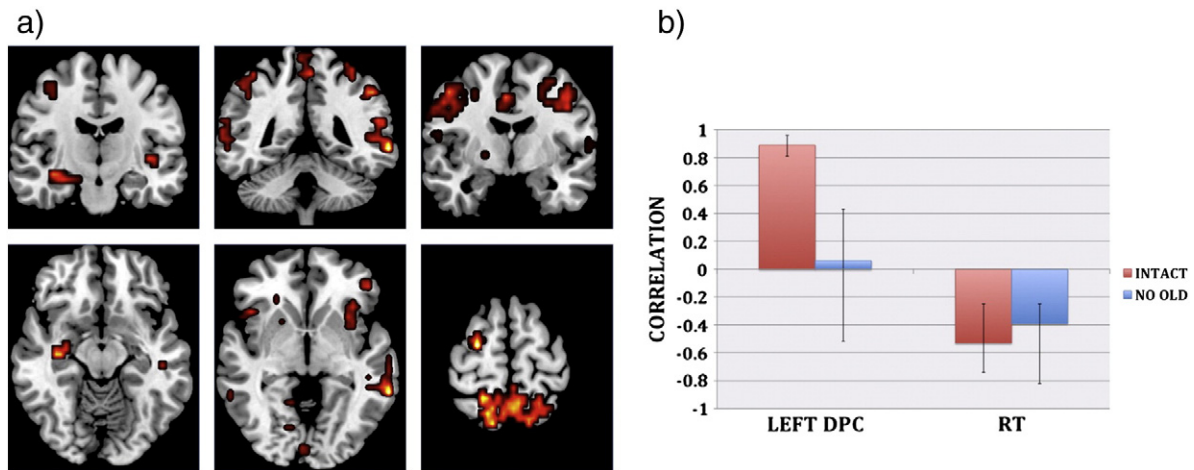


Fig. 4. Seed/behavior PLS results: (a) A pattern of correlated activity at 6–8 s after the trial onset. (b) Correlations between activity in left DPC, scores representing activity in the regions seen in (a), and reaction times during *Intact* and *No Old* conditions. Error bars are 95% confidence intervals for the correlations calculated from the bootstrap procedure.

involved in episodic memory retrieval (Cabeza and Nyberg, 2000), and cued spatial orientation (Small et al., 2003). Based on the converging functional evidence and PCC's afferent connections with the hippocampus (Maddock, 1999), it is believed that the primary role of PCC is top-down evaluation of sensory events, spatial orientation, and memory (Vogt et al., 2005). Both the right middle occipital gyrus and left PCC therefore may subserve top-down, cued processes, which would explain why their activity correlated negatively with the left VPC and the bottom-up AtoM network.

Top-down AtoM Network

When recognition memories are cued, the neural network mediating recognition decisions changes markedly, recruiting mostly dorsal brain regions. We have previously shown that cued recognition decisions engage the left intraparietal sulcus of DPC (Ciarumelli et al., 2010a,b). According to the AtoM hypothesis, DPC is implicated in the top-down allocation of attention to strategic memory operations, such as memory search. In our task, upon presentation of a studied

word as a cue, participants presumably started searching for the word that was associated with it at study. Recognition memory decisions were indeed more accurate and faster if subjects could anticipate the memory probe based on mnemonic expectations (*Intact* condition). Here we show an entire network of brain regions functionally connected with DPC during cued memory retrieval whose activity predicted efficient use of cues for recognition.

Several DPC regions, including the left intraparietal sulcus, bilateral superior parietal lobe, and precuneus were engaged while searching for and/or anticipating memory contents based on associative cues. Additionally, the DPC was functionally connected with the left hippocampus during cued recognition. The left hippocampus is active during retrieval of declarative memories that are recollected and during relational memory tasks (Burianova and Grady, 2007; Cabeza et al., 2004; Davachi and Wagner, 2002; Eldridge et al., 2000; Prince et al., 2005) and there is evidence that it is more involved in associative than item memory retrieval (Giovanello et al., 2004). The functional connection that we found between the DPC and left hippocampus during cued recognition memory supports the hypothesis that the left DPC initiates a search for the original associate of cue words, biasing activity in the hippocampus in accordance with retrieval goals (see also Cabeza et al., 2011).

Other brain regions functionally connected with DPC included the pulvinar nucleus of the thalamus, bilateral middle temporal gyrus, right dorsolateral and left dorsomedial prefrontal cortices. The pulvinar mediates visual attention processes (Grieve et al., 2000; Shipp, 2004; Smith et al., 2009) and is considered the gateway structure that funnels top-down biases from the posterior parietal regions to the visual cortex (Petersen et al., 1987; Shipp, 2004). The middle temporal gyri subserve memory retrieval of semantic representations (e.g., Martin and Chao, 2001) and are directly connected to the inferior frontal gyri via the temporo-frontal pathway, which is important in retrieval, monitoring, and manipulation of semantic representations (Levine et al., 1999), processes essential to associative memory recognition. Numerous studies have demonstrated the fundamental role of the right dorsolateral prefrontal cortex in remembering associations between items, organizing memory strategies, and controlling memory retrieval (Blumenfeld and Ranganath, 2006; Kirchoff et al., 2000; Murray and Ranganath, 2007). Moreover, the dorsomedial prefrontal cortex mediates introspective processes (Andrews-Hanna et al., 2010; Gusnard et al., 2001; Lane et al., 1997) and attention to internally cued activity (Gusnard et al., 2001).

The fact that the dorsal prefrontal cortex was recruited along with DPC for cued recognition memory decisions suggests that a dorsal frontoparietal neural network mediates top-down AtoM, just as a

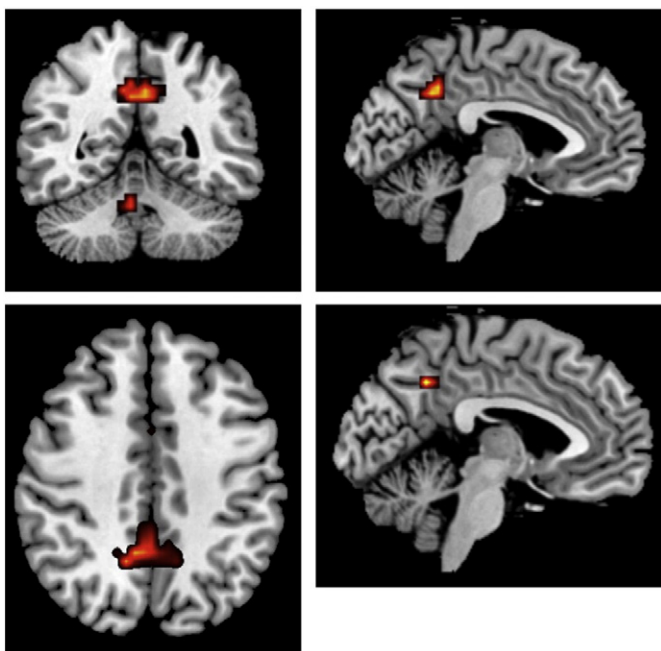


Fig. 5. Network overlay. Spatial overlap of the two functional networks at the precuneus.

dorsal frontoparietal network mediates top-down attention to external stimuli. We note, however, that the dorsal prefrontal regions involved in AtoM do not fully overlap with prefrontal regions classically involved in top-down attention to percepts, which include the frontal eye fields (Corbetta and Shulman, 2002). This evidence may suggest that although the dorsal prefrontal cortex subserves a general top-down control function, different subregions may be involved in different cognitive domains, processing specific types of information (e.g., top-down control of attention vs. top-down control of memory; see Cabeza, 2008; Miller and Cohen, 2001; Shimamura, 2000; Vincent et al., 2008).

Finally, in addition to dorsal PFC, cued recognition memory also engaged the inferior frontal gyrus bilaterally (BA 47). This region is not commonly activated while processing cues in tasks requiring spatial attention (Corbetta and Shulman, 2002). We attribute this finding to the specific nature of our task, which relied on associative memory. In the memory domain, activity in ventrolateral PFC has been linked with selection of task-relevant memories among distractors (Badre and Wagner, 2007). This process was arguably necessary in our task to guide memory search to the retrieval of the original associates of relevant cues (Kuhl et al., 2007), but less crucial in perceptual-attentional tasks where cue–target relations are not ambiguous.

Importantly, our findings show that the two networks implicated during non-cued and cued recognition memory are, for the most part, spatially independent. Thus, a change in the requirements of a recognition memory task, making recognition memory relatively more weighted towards bottom-up AtoM or top-down AtoM determines *qualitative* differences in the neural networks mediating recognition memory. These results provide further evidence supporting the AtoM hypothesis, showing a functional dissociation in the posterior parietal cortex during episodic memory retrieval. The two neural networks overlapped only in the right (posterior) precuneus. The posterior precuneus is pervasively implicated in episodic memory retrieval, and activity in this brain region is strongly associated with successful retrieval of remembered episodes and imagery (Cavanna and Trimble, 2006). These processes, at the very core of episodic memory, are arguably shared between our two memory conditions.

Finally, the analysis of how behavioral performance on the memory tasks relates to activity in the two delineated networks yielded novel findings. On the one hand, activity in VPC and the bottom-up AtoM network did not correlate with reaction times, suggesting that bottom-up attention capture may be relatively automatic and response times to the target may depend on this automatic response rather than the degree of activity in the bottom-up AtoM network. On the other hand, activity in DPC and the top-down AtoM network correlated significantly with reaction times, i.e., the network was engaged more during faster responses, suggesting that goal-directed attention begins *prior* to target presentation and that the degree of attention, reflected in the top-down AtoM network, would influence response times.

Beyond revealing a whole-brain network of inter-related regions supporting cued and uncued memory decisions, the present functional connectivity analysis extends findings from the previous regional activation analysis (Ciaramelli et al., 2010a,b), showing multiple nodes for top-down and bottom-up AtoM *within* PPC. First of all, whereas the previous study had evinced only left lateralized activations, the present findings reveal bilateral activations in both DPC and VPC. In addition to the left intraparietal sulcus, top-down AtoM was associated with activity in the right superior parietal lobe, consistent with evidence that patients with both right and left DPC lesions may show reduced top-down AtoM (Ciaramelli et al., 2010a,b). Moreover, in addition to the left angular gyrus, bottom-up AtoM was associated with activity in the supramarginal gyrus bilaterally. These findings deserve attention, considering that one important critique of the AtoM model is that activations associated with episodic memory retrieval do not completely coincide with those on orienting of attention. Indeed, the former are more frequently lateralized to the left, the latter to the right. Moreover,

different subregions of PPC appear mainly involved in one process or the other: Episodic memory retrieval is more frequently associated with activity in the angular gyrus, whereas activations during attention (re)orienting tend to be localized in anterior VPC regions, including the supramarginal gyrus (Hutchinson et al., 2009; see also Sestieri et al., 2010). The present findings provide support for the AtoM model, showing that brain networks for episodic memory retrieval and orienting of attention do in fact have strong commonalities. However, we concur with other authors that fully understanding the role of PPC during episodic retrieval will require elucidating the contribution of different subregions. One view posits that the angular gyrus is critical for episodic retrieval, while putatively attention-to-memory functions are ascribed to the supramarginal gyrus (Hutchinson et al., 2009; Uncapher, 2011; Uncapher et al., 2010). For example, the angular gyrus may act as an output buffer (Vilberg and Rugg, 2008), or a convergence/integration zone (Shimamura, 2011) for recovered mnemonic features. The AtoM model would posit instead that different VPC subregions may mediate different cognitive components of orienting attention to memory, or alternatively, process information in different domains all of which are related to an overarching common function (see Cabeza et al., 2012). In our previous study (Ciaramelli et al., 2010a,b), patients with left, but not right, VPC lesions showed bottom-up AtoM deficits. Notably, left-lesioned patients had lesions centered on the angular gyrus, whereas right-lesioned patients had more anterior lesions around the supramarginal gyrus, which does not allow one to determine whether left VPC in general, or the angular gyrus in particular, is crucial for mediating the capture of attention by memory contents. Further neuropsychological studies, therefore, are needed to articulate the functional relationship between left and right, anterior and posterior PPC during episodic retrieval.

To conclude, we have shown two largely independent neural networks for cued and uncued recognition memory decisions, extending the regional activation findings reported by Ciaramelli et al. (2010a,b). Consistent with the AtoM model, non-cued recognition memory mainly recruited a network associated with bottom-up AtoM, including VPC, ventral PFC, and parahippocampal gyrus, whereas cued recognition memory recruited a network associated with top-down AtoM, with nodes in DPC, dorsal PFC, and hippocampus. These findings extend our previous study in a very significant way, as it is not the case that functional connectivity simply recapitulates task-related differences. Indeed, earlier work has shown that functional connectivity of a given region may be similar across tasks despite marked differences in mean activity levels of this region across tasks (e.g., Grigg and Grady, 2010a), so it is not a given that functional connectivity patterns will differ across tasks in the same way that mean activity does. The fact that we find both task-related differences in DPC vs. VPC (Ciaramelli et al., 2010a,b) and that these regions are part of networks that also show differences in functional connectivity across tasks lend stronger support to the AtoM hypothesis than either result alone.

References

- Andrews-Hanna, J.R., Reidler, J.S., Sepulcre, J., Poulin, R., Buckner, R.L., 2010. Functional-anatomic fractionation of the brain's default network. *Neuron* 65, 550–562.
- Badre, D., Wagner, A.D., 2007. Left ventrolateral prefrontal cortex and the cognitive control of memory. *Neuropsychologia* 45, 2883–2901.
- Berryhill, M.E., Phuong, L., Picasso, L., Cabeza, R., Olson, I.R., 2007. Parietal lobe and episodic memory: bilateral damage causes impaired free recall of autobiographical memory. *J. Neurosci.* 26, 14415–14423.
- Blumenfeld, R.S., Ranganath, C., 2006. Dorsolateral prefrontal cortex promotes long-term memory formation through its role in working memory organization. *J. Neurosci.* 26, 916–925.
- Bressler, S.L., Menon, V., 2010. Large-scale brain networks in cognition: emerging methods and principles. *Trends Cogn. Neurosci.* 14, 277–290.
- Burianova, H., Grady, C.L., 2007. Common and unique activations in autobiographical, episodic, and semantic retrieval. *J. Cogn. Neurosci.* 19, 1520–1534.
- Cabeza, R., 2008. Role of parietal regions in episodic memory retrieval: the dual attentional processes hypothesis. *Neuropsychologia* 46, 1813–1827.
- Cabeza, R., Nyberg, L., 2000. Imaging cognition II: an empirical review of 275 PET and fMRI studies. *J. Cogn. Neurosci.* 12, 1–47.

- Cabeza, R., Prince, S.E., Daselaar, S.M., Greenberg, D.L., Budde, M., Dolcos, F., LaBar, K.S., Rubin, D.C., 2004. Brain activity during episodic retrieval of autobiographical and laboratory events: an fMRI study using a novel photo paradigm. *J. Cogn. Neurosci.* 16, 1583–1594.
- Cabeza, R., Ciaramelli, E., Olson, I., Moscovitch, M., 2008. The parietal cortex and episodic memory: an attentional account. *Nat. Rev. Neurosci.* 9, 613–625.
- Cabeza, R., Mazuz, Y., Stokes, J., Kragel, J., Woldorff, M., Ciaramelli, E., Olson, I., Moscovitch, M., 2011. Overlapping parietal activity in memory and perception: evidence for the attention to memory (AtoM) model. *J. Cogn. Neurosci.* 23, 3209–3217.
- Cabeza, R., Ciaramelli, E., Moscovitch, M., 2012. Cognitive contributions of the ventral parietal cortex: an integrative theoretical account. *Trends in Cognitive Sciences* 16, 338–352.
- Cavanna, A.E., Trimble, M.R., 2006. The precuneus: a review of its functional anatomy and behavioural correlates. *Brain* 129, 564–583.
- Ciaramelli, E., Grady, C.L., Moscovitch, M., 2008. Top-down and bottom-up attention to memory: a hypothesis (AtoM) on the role of the posterior parietal cortex in memory retrieval. *Neuropsychologia* 46, 1828–1851.
- Ciaramelli, E., Grady, C.L., Levine, B., Ween, J., Moscovitch, M., 2010a. Top-down and bottom-up attention to memory are dissociated in posterior parietal cortex: neuroimaging and neuropsychological evidence. *J. Neurosci.* 30, 4943–4956.
- Ciaramelli, E., Rosenbaum, R.S., Solcz, S., Levine, B., Moscovitch, M., 2010b. Mental space travel: damage to posterior parietal cortex prevents egocentric navigation and reexperiencing of remote spatial memories. *J. Exp. Psychol. Learn. Mem. Cogn.* 36, 619–634.
- Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. *Nat. Rev. Neurosci.* 3, 201–215.
- Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P., Shulman, G.L., 2000. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nature Neuroscience* 3, 292–297.
- Corbetta, M., Kincade, M.J., Shulman, G.L., 2002. Two neural systems for visual orienting and the pathophysiology of unilateral spatial neglect. In: Karnath, H., Milner, D., Vallar, G. (Eds.), *The Cognitive and Neural Bases of Spatial Neglect*. Oxford University Press.
- Corbetta, M., Patel, G., Shulman, G., 2008. The reorienting system of the human brain: from environment to theory of mind. *Neuron* 58, 306–324.
- Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput. Biomed. Res.* 29, 162–173.
- Davachi, L., Wagner, A.D., 2002. Hippocampal contributions to episodic encoding: insights from relational and item-based learning. *J. Neurophysiol.* 88, 982–990.
- Davidson, P.S.R., Anaki, D., Ciaramelli, E., Cohn, M., Kim, A.S.N., Murphy, K.J., Troyer, A.K., Moscovitch, M., Levine, B., 2008. Does lateral parietal cortex support episodic memory? Evidence from focal lesion patients. *Neuropsychologia* 46, 1743–1755.
- Della-Maggiore, V., Sekuler, A.B., Grady, C.L., Bennett, P.J., Sekuler, R., McIntosh, A.R., 2000. Corticolimbic interactions associated with performance on a short-term memory task are modified by age. *J. Neurosci.* 20, 8410–8416.
- Drowos, D.B., Berryhill, M., André, J.M., Olson, I.R., 2010. True memory, false memory, and subjective recollection deficits after focal parietal lobe lesions. *Neuropsychology* 24, 465–475.
- Efron, B., Tibshirani, R., 1985. The bootstrap method for assessing statistical accuracy. *Behaviormetrika* 17, 1–35.
- Eldridge, L.L., Knowlton, B.J., Furmanski, C.S., Bookheimer, S.Y., Engel, S.A., 2000. Remembering episodes: a selective role for the hippocampus during retrieval. *Nat. Neurosci.* 3, 1149–1152.
- Fox, M.D., Corbetta, M., Snyder, A.Z., Vincent, J.L., Raichle, M.E., 2006. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. *Proc. Natl. Acad. Sci. U. S. A.* 103, 10046–10051.
- Friston, K.J., 1994. Functional and effective connectivity: a synthesis. *Hum. Brain Mapp.* 2, 56–78.
- Friston, K.J., 1997. Imaging cognitive anatomy. *Trends Cogn. Sci.* 1, 21–27.
- Friston, K.J., Frith, C.D., Liddle, P.F., Frackowiak, R.S.J., 1993. Functional connectivity: the principal component analysis of large (PET) data sets. *J. Cereb. Blood Flow Metab.* 13, 5–14.
- Giovanello, K.S., Schnyer, D.M., Verfaellie, M., 2004. A critical role for the anterior hippocampus in relational memory: evidence from an fMRI study comparing associative and item recognition. *Hippocampus* 14, 5–8.
- Goldstone, R.L., 1995. Effects of categorization on color perception. *Psychol. Sci.* 6, 298–304.
- Goodale, M.A., Milner, A.D., 1992. Separate visual pathways for perception and action. *Trends Neurosci.* 15, 20–25.
- Grady, C.L., McIntosh, A.R., Bookstein, F., Horowitz, B., Rapoport, S.I., Haxby, J.V., 1998. Age-related changes in regional cerebral blood flow during working memory for faces. *Neuroimage* 8, 409–425.
- Grieve, K.L., Acuna, C., Cudeiro, J., 2000. The primate pulvinar nuclei: vision and action. *Trends Neurosci.* 23, 35–39.
- Grigg, O., Grady, C.L., 2010a. The default network and processing of personally relevant information: converging evidence from task-related modulations and functional connectivity. *Neuropsychologia* 48, 3815–3823.
- Grigg, O., Grady, C.L., 2010b. Task-related effects on the temporal and spatial dynamics of resting-state functional connectivity in the default network. *PLoS One* 5 (e13311–e13311).
- Gusnard, D.A., Akbudak, E., Shulman, G.L., Raichle, M.E., 2001. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc. Natl. Acad. Sci. U. S. A.* 7, 4259–4264.
- Horwitz, B., Duara, R., Rapoport, S.I., 1984. Interrelations of glucose metabolic rates between brain regions: application to healthy males in a state of reduced sensory input. *J. Cereb. Blood Flow Metab.* 4, 484–499.
- Hutchinson, J.B., Uncapher, M.R., Wagner, A.D., 2009. Posterior parietal cortex and episodic retrieval: convergent and divergent effects of attention and memory. *Learn. Mem.* 16, 343–356.
- Kim, A.S.N., Vallesi, A., Picton, T.W., Tulving, E., 2009. Cognitive association formation in episodic memory: evidence from event-related potentials. *Neuropsychologia* 47, 3162–3173.
- Kincade, J.M., Abrams, R.A., Astafiev, S.V., Shulman, G.L., Corbetta, M., 2005. An event-related functional magnetic resonance imaging study of voluntary and stimulus-driven orienting of attention. *J. Neurosci.* 25, 593–604.
- Kirchhoff, B.A., Wagner, A.D., Maril, A., Stern, C.E., 2000. Prefrontal-temporal circuitry for episodic encoding and subsequent memory. *J. Neurosci.* 20, 6173–6180.
- Kucera, H., Francis, W.N., 1967. *Computational Analysis of Present-day American English*. Brown University Press, Providence.
- Kuhl, B.A., Dudukovic, N.M., Kahn, I., Wagner, A.D., 2007. Decreased demands on cognitive control reveal the neural processing benefits of forgetting. *Nat. Neurosci.* 10, 908–914.
- Lane, R.D., Reiman, E.M., Ahern, G.L., Schwartz, G.E., Davidson, R.J., 1997. Neuroanatomical correlates of happiness, sadness, and disgust. *Am. J. Psychiatry* 154, 926–933.
- Levine, B., Freedman, M., Dawson, D., Black, S., Stuss, D.T., 1999. Ventral frontal contribution to self-regulation: convergence of episodic memory and inhibition. *Neurocase* 5, 263–275.
- Li, X.B., Inoue, T., Nakagawa, S., Koyama, T., 2004. Effect of mediodorsal thalamic nucleus lesion on contextual fear conditioning in rats. *Brain Res.* 1008, 261–272.
- Lyon, D.C., Kaas, J.H., 2002. Evidence for a modified V3 with dorsal and ventral halves in macaque monkeys. *Neuron* 33, 453–461.
- Maddock, R.J., 1999. The retrosplenial cortex and emotion: new insights from functional neuroimaging of the human brain. *Trends Neurosci.* 22, 310–316.
- Marois, R., Leung, H.C., Gore, J.C., 2000. A stimulus-driven approach to object identity and location processing in the human brain. *Neuron* 25, 717–728.
- Martin, A., Chao, L.L., 2001. Semantic memory and the brain: structure and processes. *Curr. Opin. Neurobiol.* 11, 194–201.
- McIntosh, A.R., 1998. Understanding neural interactions in learning and memory using functional neuroimaging. *Ann. N. Y. Acad. Sci.* 855, 556–571.
- McIntosh, A.R., 1999. Mapping cognition to the brain through neural interactions. *Memory* 7, 523–548.
- McIntosh, A.R., 2000. Towards a network theory of cognition. *Neural Netw.* 13, 861–870.
- McIntosh, A.R., Gonzalez-Lima, F., 1994. Structural equation modeling and its application to network analysis in functional brain imaging. *Hum. Brain Mapp.* 2, 2–22.
- McIntosh, A.R., Grady, C.L., Ungerleider, L.G., Haxby, J.V., Rapoport, S.I., Horowitz, B., 1994. Network analysis of cortical visual pathways mapped with PET. *J. Neurosci.* 14, 655–666.
- McIntosh, A.R., Grady, C.L., Haxby, J.V., Ungerleider, L.G., Horowitz, B., 1996. Changes in limbic and prefrontal functional interactions in a working memory task for faces. *Cereb. Cortex* 6, 571–584.
- McIntosh, A.R., Nyberg, L., Bookstein, F.L., Tulving, E., 1997. Differential functional connectivity of prefrontal and medial temporal cortices during episodic memory retrieval. *Hum. Brain Mapp.* 5, 323–327.
- Miller, E.K., Cohen, J.D., 2001. An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* 24, 167–202.
- Murray, L.J., Ranganath, C., 2007. The dorsolateral prefrontal cortex contributes to successful relational memory encoding. *J. Neurosci.* 27, 5515–5522.
- OGawa, S., Lee, T.M., Kay, A.R., Tank, D.W., 1990. Brain magnetic-resonance-imaging with contrast dependent on blood oxygenation. *Proc. Natl. Acad. Sci. U. S. A.* 87, 9868–9872.
- Petersen, S.E., Robinson, D.L., Morris, J.D., 1987. Contributions of the pulvinar to visual spatial attention. *Neuropsychology* 25, 97–105.
- Posner, M.I., Petersen, S.E., 1990. The attention system of the human brain. *Annu. Rev. Neurosci.* 13, 25–42.
- Prince, S.E., Daselaar, S.M., Cabeza, R., 2005. Neural correlates of relational memory: successful encoding and retrieval of semantic and perceptual associations. *J. Neurosci.* 25, 1203–1210.
- Sampson, P.D., Streissguth, A.P., Barr, H.M., Bookstein, F.L., 1989. Neurobehavioral effects of prenatal alcohol: II. Partial least squares analysis. *Neurotoxicol. Teratol.* 11, 477–491.
- Schreurs, B., McIntosh, A.R., Bahron, M., Herscovitch, P., Sunderland, T., Molchan, S., 1997. Lateralization and behavioural correlation of changes in regional cerebral blood flow with classical conditioning of the human eyeblink response. *J. Neurophysiol.* 77, 2153–2163.
- Sestieri, C., Shulman, G.L., Corbetta, M., 2010. Attention to memory and the environment: functional specialization and dynamic competition in human posterior parietal cortex. *J. Neurosci.* 23, 8445–8456.
- Shimamura, A.P., 2000. The role of the prefrontal cortex in dynamic filtering. *Psychobiology* 28, 207–218.
- Shimamura, A.P., 2011. Episodic retrieval and the cortical binding of relational activity. *Cogn. Affect. Behav. Neurosci.* 11, 277–291.
- Shipp, S., 2004. The brain circuitry of attention. *Trends Cogn. Sci.* 8, 223–230.
- Shulman, G.L., Fiez, J.A., Corbetta, M., Buckner, R.L., Miezin, F.M., 1997. Common blood flow changes across visual tasks: II. Decreases in cerebral cortex. *J. Cogn. Neurosci.* 9, 648–663.
- Simons, J.S., Peers, P.V., Mazuz, Y.S., Berryhill, M.E., Olson, I.R., 2010. Dissociation between memory accuracy and memory confidence following bilateral parietal lesions. *Cereb. Cortex* 20, 479–485.
- Small, D.M., Gitelman, D.R., Gregory, M.D., Nobre, A.C., Parrish, T.B., Mesulam, M.M., 2003. The posterior cingulate and medial prefrontal cortex mediate the anticipatory allocation of spatial attention. *NeuroImage* 18, 633–641.
- Smith, A.T., Cotton, P.L., Bruno, A., Moutsiana, C., 2009. Dissociating vision and visual attention in the human pulvinar. *J. Neurophysiol.* 101, 917–925.
- Spaniol, J., Davidson, P.S.R., Kim, A.S.N., Han, H., Moscovitch, M., Grady, C.L., 2009. Event-related fMRI studies of episodic encoding and retrieval: meta-analyses using activation likelihood estimation. *Neuropsychologia* 47, 1765–1779.

- Taber, K.H., Wen, C., Khan, A., Hurley, R.A., 2004. The limbic thalamus. *J. Neuropsychiatry Clin. Neurosci.* 16, 127–132.
- Tanaka, D., 1976. Thalamic projections of the dorsomedial prefrontal cortex in the rhesus monkey (*Macaca mulatta*). *Brain Res.* 110, 21–38.
- Uncapher, M.R., 2011. Functional heterogeneity in posterior parietal cortex: a multi-pronged story. Fifth International Conference on Memory. University of York, York, United Kingdom. July, 2011.
- Uncapher, M.R., Hutchinson, J.B., Wagner, A.D., 2010. A roadmap to brain mapping: toward a functional map of human parietal cortex. *Neuron* 67, 5–8.
- Vanni, S., Tanskanen, T., Seppä, M., Uutela, K., Hari, R., 2001. Coinciding early activation of the human primary visual cortex and anteromedial cuneus. *Proc. Natl. Acad. Sci.* 98, 2776–2780.
- Vilberg, K., Rugg, M., 2008. Memory retrieval and the parietal cortex: a review of evidence from a dual-process perspective. *Neuropsychologia* 46, 1787–1799.
- Vincent, J.L., Kahn, I., Snyder, A.Z., Raichle, M.E., Buckner, R.L., 2008. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *J. Neurophysiol.* 100, 3328–3342.
- Vogt, B., Pandaya, D.N., 1987. Cingulate cortex of the rhesus monkey. II. Cortical afferents. *J. Comput. Neurol.* 262, 271–289.
- Vogt, B.A., Vogt, L., Laureys, S., 2005. Cytology and functionally correlated circuits of human posterior cingulate areas. *NeuroImage* 29, 452–466.
- Wagner, A.D., Shannon, B.J., Kahn, I., Buckner, R.L., 2005. Parietal lobe contributions to episodic memory retrieval. *Trends Cogn. Sci.* 9, 445–453.
- Wheeler, M.E., Shulman, G.L., Buckner, R.L., Miezin, F.M., Velanova, K., Petersen, S.E., 2006. Evidence for separate perceptual reactivation and search processes during remembering. *Cereb. Cortex* 16, 949–959.
- Yonelinas, A.P., Otten, L.J., Shaw, K.N., Rugg, M.D., 2005. Separating the brain regions involved in recollection and familiarity in recognition memory. *J. Neurosci.* 25, 3002–3008.