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A parieto-medial temporal pathway for the strategic control over working memory biases in human visual attention

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Abstract

The contents of working memory (WM) can both aid and disrupt the goal-directed allocation of visual attention. WM benefits attention when its contents overlap with goal-relevant stimulus features, but WM leads attention astray when its contents match features of currently irrelevant stimuli. Recent behavioral data have documented that WM biases of attention may be subject to strategic cognitive control processes, whereby subjects are able to either amplify or attenuate the influence of WM contents on attention. However, the neural mechanisms supporting cognitive control over WM biases on attention are presently unknown. Here, we characterize these mechanisms by combining human functional magnetic resonance imaging (fMRI) with a task that independently manipulated the relationship between WM cues and attention targets during visual search (with WM contents matching either search targets or distracters), as well as the predictability of this relationship (100% vs. 50% predictability) to assess participants' ability to strategically enhance or inhibit WM biases on attention when WM contents reliably matched targets or distracter stimuli, respectively. We show that cues signaling predictable (>unpredictable) WM-attention relations reliably enhanced search performance, and that this strategic modulation of the interplay between WM contents and visual attention was mediated by a neuroanatomical network involving the posterior parietal cortex, the posterior cingulate, and medial temporal lobe structures, with responses in the hippocampus proper correlating with behavioral measures of strategic control of WM biases. Thus, we delineate a novel parieto-medial temporal pathway implementing cognitive control over WM biases on attention in order to optimize goal-directed selection.

Introduction

One important function of working memory (WM) is for its contents to guide the deployment of attention based on goals and intentions. Nevertheless attention can be *involuntarily* biased by WM-matching stimuli, even when these are irrelevant to performance, suggesting an obligatory coupling between WM and attention (Soto et al., 2008; Olivers et al., 2011). Recent studies suggest that these involuntary WM biases may nevertheless be subject to strategic control (Han and Kim, 2009; Carlisle and Woodman, 2011; Kiyonaga et al., 2012). That is, WM's hold over attention can be partly enhanced or inhibited based on goals. However, the neural mechanisms underlying strategic control over WM biases of attention are currently unknown.

The present functional magnetic resonance imaging (fMRI) study was designed to elucidate these mechanisms. We assessed the neural substrates of strategic control over WM biases, namely (i) the intentional use of a WM cue for directing attention towards a matching target and (ii) the controlled inhibition of an irrelevant WM cue to avoid attentional capture by matching distracters. To this end, we modified a well-established experimental protocol for assessing the involuntary coupling between WM and attention (Soto et al., 2008). The canonical finding is that visual search for a target object is impaired by the presence of a distracter item in the search array that matches the contents of WM (Soto et al., 2005) even when observers know that the contents of WM are always detrimental to search. Here we compared behavioral performance and neural responses when WM cues were either always invalid or always valid with a condition where valid and invalid cue trials were equally likely and therefore observers had little incentive to control the WM bias on attention; when WM cues were either always invalid or always valid, however, subjects could optimize search by intentionally enhancing or inhibiting the WM bias.

First, we isolated *anticipatory* components for enhancement/inhibition of WM biases, by comparing their neural signature during cue-only trials (where the WM cues were not followed by search displays, see Materials and Methods). Second, we investigated the consequences of these control operations on the search process itself. Prior evidence implicates the posterior parietal cortex (PPC) in developing attentional sets for relevant target features (Toth and Assad, 2002; Egner et al., 2008; Schenkluhn et al., 2008), indicating a prime candidate for selectively enhancing the influence of WM content on attention when this is known to be valid. By contrast, the neural substrate for inhibiting the influence of irrelevant WM contents on attention has to our knowledge not been previously investigated. Here we show that bilateral PPC is involved in anticipatory cognitive control over relevant and irrelevant WM signals for selection. Moreover, we delineate a parieto-medial temporal network supporting cognitive control over WM biases based on foreknowledge about WM validity and we reveal the presence of the hippocampus proper in this process. This work extends existing accounts of attentional control that predominantly focus on fronto-parietal networks only (Corbetta and Shulman, 2002).

Materials and Methods

Participants

Twenty-one healthy observers (8 females; age range 22-34 years) who provided written informed consent and took part in the study in return of £20. The study was approved by the West London Research Ethics Committee.

Experimental protocol

The task was programmed and controlled using E-prime (Version 2.0; Psychology Software Tools, Pittsburgh, USA). Each trial began with a fixation display for 500 msec. that was followed by a memory cue for 250 ms (see Figure 1A). The WM cue was a colored circle drawn in one of five different colors selected at random (see below). Extinction of the cue was followed by a delay period of 2 seconds. The search display then appeared for 100 ms, and was composed of three colored circles at the corners of an imaginary triangle. Each circle contained a line; two of the lines were vertical while the target line was tilted 16° either to the left or right. The participants' task was to indicate the orientation of the tilted line via button press during a time window of 1000 ms. Target location and orientation were randomly selected on a trial-by-trial basis. The memory and search circles were randomly selected from one of four colors (red, blue, green or yellow). Each circle was a color singleton in the search display. WM cues could be "valid" or "invalid", depending on whether the memory cue surrounded the search target or a search distracter, respectively. Valid and invalid conditions were blocked leading to blocks where the cue was (i) always valid (valid blocks), (ii) always invalid (invalid blocks), or (iii) equally likely to be valid or invalid (50/50 blocks).

As in previous studies using this protocol (Soto et al., 2007) we ensured that participants held the cues in memory throughout the trials by using memory 'catch' trials

(18.5%) where a memory probe was presented for 2 seconds instead of the visual search display. The probe consisted of a colored circle and participants had to perform a match/mismatch response, indicating whether or not the probe was the same color as the memory cue. In order to estimate BOLD responses associated with the processing of the WM cue alone (i.e. cue delay period activity), we also included 22.2% of 'cue-only' trials per block where the memory cue was not followed by a search display (Ollinger et al., 2001). Here the cue was followed by the usual 2 seconds delay plus the inter-trial time interval (ITI). Participants were given appropriate training instructions outside the scanner and also received a 10 s instruction display at the beginning of each scanning block to inform them about the nature of cue predictability. Participants received clear instructions on the presence of cue-only trials and memory 'catch' trials. The ITI was jittered between 2.5 - 4.5 seconds, with a pseudo-exponential distribution (48% of ITIs were 2.5s, 22.2% of ITIs were 3s, 11.1% wer 3.5 s, 7.4% were 4 s and 7.4% were 4.5 s), in order to facilitate the independent estimation of BOLD responses across trials (Ollinger et al., 2001).

The task was divided into three runs. Each run was composed of 4 blocks of 27 trials each, including 5 memory-catch trials and 6 'cue only' trials. The remaining 16 trials per block were either 100% valid or invalid on high predictable valid and invalid blocks, or half (8) valid and half invalid in low predictable 50/50 blocks. The order of blocks within a run was selected randomly.

Participants completed several practice sessions outside the scanner, initially with a visual search display duration of 500 ms, followed by a search display duration of 100ms until performance was above 90% correct. They were told to avoid eye movements during the search and we used the very brief search display time (100ms) to further discourage eye movements.

Image acquisition/scanning parameters

MRI scanning was conducted using a Siemens Magnetom Verio 3T MRI scanner and a 32-channel head coil. Following a brief localizer scan to determine the orientation of the subject's head within the field, 176 T1 weighted anatomical sagittal images were acquired with an FOV of 220 x 220mm, TR of 1900 ms, TE of 2.48 ms and slice thickness of 1mm, leading to a voxel resolution of 1x1x1 mm. Three functional runs of 2* weighted echo planar imaging were conducted to obtain 38 contiguous sagittal slices covering the whole brain. Each run contained 367 volumes that were acquired with an

FOV of 222x222mm, TR of 2200 ms, TE of 30 ms and slice thickness of 3 mm. The resulting voxel resolution was 2.4x2.4x3.0 mm.

Imaging data analysis

fMRI data processing was carried out using FEAT (fMRI Expert Analysis Tool) Version 5.98, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). The first 6 volumes of the EPI scan were removed from each scanning session to account for T1 equilibrium effects, leaving 361 scans per run. The following pre-statistics processing was applied: non-brain removal using BET (Smith, 2002); motion correction using MCFLIRT (Jenkinson et al., 2002); 150 seconds high-pass temporal filtering and spatial smoothing using a Gaussian kernel of FWHM 6.0mm; Time-series statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction (Woolrich et al., 2001) for each individual run. The different trial types were modeled from the onset of the memory cue and each event had 2.35 seconds duration (including cue exposure, cue-search delay and search exposure time) as boxcar functions convolved with the hemodynamic response function. Explanatory variables (EVs) included the onset times for valid and invalid trials separately for the 100% and 50% probability of validity (4 EVs), and the onset times of cue only trials in the context of 100% valid, 100% invalid and 50/50 blocks (3 EVs). Additional regressors of no interest included memory catch trials, errors and the motion realignment parameters. The temporal derivative of the haemodynamic response function was also added to the model for each EV in order to account for latency differences between slice acquisitions. Subsequently, we carried out cross-run individual analyses using fixed-effects to derive Z statistic images for all conditions and thereafter performed group-level analyses using FLAME (FMRIB's Local Analysis of Mixed Effects) stage 1+2 as implemented in FEAT. We report maps of BOLD responses thresholded using clusters determined by a voxelwise Z threshold of 2.3 and a corrected cluster significance threshold of p=0.05, unless otherwise noted. Each individual's EPI scans were registered to high-resolution structural images using FLIRT and were then co-registered and transformed to standard (Montreal Neurological Institute) space. The location of the activations was based on the Juelich histological atlas within FSL.

Results

Behavioral results

Due to a technical problem, behavioral responses in 2 out of the 21 participants were not recorded. Data from the remaining participants were entered in the analyses. Memory performance on catch trials was very high (invalid blocks = 93%; 50/50 blocks = 95.7%; valid blocks = 95%) and did not differ across blocks (F(2, 36)=1.44, p>.25). These data confirm that participants encoded and maintained the WM cues as instructed. Median reaction times (RTs) of trials with correct responses in the search task were entered into a 2 (trial type: valid, invalid) × 2 (predictability: high [100% valid/invalid], low [50/50 valid/invalid]) ANOVA. In line with previous studies, we observed a main effect of trial type (F(1,18)=81.65, p<0.0001) with faster performance on valid relative to invalid trials There was also a main effect of predictability (F(1,18)=14.25, p<0.001), with faster performance when participants expected the WM cue to be either valid or invalid throughout the block relative to the low predictability condition. This pattern of results is depicted in Figure 1B. Trial and block type factors did not interact (F<1, p>0.94).

The search accuracy results replicated the general pattern of the RT data. There was a main effect of trial type (F(2,18)=16.09, p<0.001), with better performance on valid than on invalid trials, and there was a non-significant trend for higher search accuracy on valid/invalid relative to 50/50 blocks (F(2,18)=2.57, p>.126) and no interaction between factors (F<1, p>0.33).

In sum, the behavioral results demonstrate that (i) participants encoded and maintained the cue stimuli in WM; (ii) valid, target-matching WM cues enhanced search performance relative to invalid, distracter-matching cues; and (iii) the degree to which WM cues affected search performance was partly under the subjects' control, as search RTs were faster when the validity of the WM cue was known *a priori*. Specifically, subjects managed to exploit the predictability of the WM-attention relationship, by enhancing the influence of the WM cue on the search process in 100% valid blocks and inhibiting that influence in 100% invalid blocks, relative to unpredictable (50/50) blocks.

fMRI results

Our main goal was to delineate the neural regions associated with cognitive control over WM biases. Prior to exploring these effects of predictability, however, we first investigated whether the effects of WM-validity *per se* would replicate previous findings. Main effects of trial validity of the WM cue during search were found in fronto-parietal regions, with increased BOLD response on invalid relative to valid trials. Specifically, invalid as compared to valid trials were associated with activity in a large, bilateral cluster in posterior parietal cortex (BA7) (MNI: -16, -60, 44, 971 voxels in the right hemisphere; MNI: 16, -76, 54, 4139 voxels in the right hemisphere) comprising superior regions and also more inferior ventral regions around the angular gyrus in the vicinity of the temporoparietal junction. We also observed a cluster of activation in the right inferior frontal gyrus (BA48) (MNI 50, -2, 14, 817 voxels). These results broadly replicate previous research (Corbetta and Shulman, 2002) and the involvement of these fronto-parietal regions may reflect their well-documented role in attentional capture (here driven by WM-matching distracters) and the re-orienting of attention towards the sought-after target (Corbetta and Shulman, 2002). As part of the same cluster we found activations in the right thalamus, including the pulvinar (MNI: -22, -28, 10) and the lateral thalamus (MNI: 14, -18, 14), which have previously been implicated in WM biases of attention (Soto et al., 2007; Grecucci et al., 2010; Soto et al., 2011b), the filtering of distracters during search (Strumpf et al., 2012) and goal-based inhibition of irrelevant WM-matching contents (Rotshtein et al., 2011). Finally, we also found a cluster in the parahippocampal gyrus (MNI: -12, -4, -26; 936 voxels) that showed enhanced bilateral responses during valid relative to invalid trials (Valid > Invalid contrast, collapsed across 100% and 50/50 conditions). In sum, these data replicated previous studies in highlighting frontoparietal and thalamic involvement in attention and WM biasing. We next turn to the main goal of the present study, namely, characterizing the neural substrates of subjects' strategic control over the degree to which WM cues affected the allocation of visual attention

<u>Source regions of cognitive control over WM biases on attentional selection</u>: In order to isolate the source of control signals associated with observer's foreknowledge about WM validity for search behavior, we analyzed activity associated with cue-only trials (not followed by search displays) in the different blocks (Ollinger et al., 2001). Specifically, by contrasting cue-related activity in 100% valid and invalid blocks with that obtained in 50/50 blocks, we could delineate control signals associated with enhancing or inhibiting the influence of WM on attention, respectively.

Figure 2 shows the signal change in the different high predictability conditions relative to the 50/50 baseline. There was an increase in left PPC activity when the WM-cue conveyed valid information regarding the search target relative to when it predicted a distracter (Figure 2A), while the right PPC was found to be more active when the WM content predicted a distracter relative to when it predicted the search target (Figure 2B). Specifically, cue-related activity associated with 100% valid blocks (relative to 50/50 conditions) was associated with increased activity in a cluster around the left intraparietal sulcus and angular gyrus (BA40) (MNI: -36 -48 38, 1455 voxels), as well as a cluster in visual cortex around the lingual gyrus (BA18) (MNI-14 -84 -12, 1302 voxels) (Figure 2). By contrast, cue-related activity associated with 100% invalid blocks (relative to 50/50 conditions) was observed around the right intraparietal sulcus (BA39) (MNI: 40 -48 30, 1538 voxels) extending into the right superior parietal lobe (Figure 2). We also found a right PPC cluster (BA7) (MNI: 22 -52 54, 1132 voxels) that was generally more active in the predictable conditions (either valid or invalid) relative to the 50/50. The activity peak of this cluster overlapped with the regions activated in either of the contrasts between 100% valid and 100% invalid conditions and depicted in Figure 2 relative to the 50/50 baseline; this right PPC cluster also extended more medially into the precuneus cortex (MNI 0 -56 40).

These results indicate the presence of preparatory signals in the PPC based on foreknowledge of WM-validity for either enhancing or inhibiting the coupling between WM content and attention.

We performed further exploratory analyses by extracting the contrast of parameter estimates of the BOLD response for the above conditions using 3 mm spheres around the cluster-peak of the predictable > unpredictable condition contrasts for both left and right PPC. A 2 x 2 ANOVA with PPC (left, right) and cue predictability context (target, distracter) showed an interaction between those factors F(1,20)=8.21, p<0.01). No main effects were observed (lowest p = 0.255). Post-hoc t tests showed that engagement of the PPC during ‘cue only’ trials when the WM content predicted the search target was stronger in the left than in the right PPC (t(20)=2.83, p=0.01) and that the right PPC was more active when the WM content predicted a distracter relative when it predicted the search target (t(20)=2.2, p=0.04). These results raise the intriguing possibility of a lateralization in the PPC according to whether subjects enhanced or suppressed the influence of the WM cue on attention. We note however that this pattern of results was not borne out by a whole-brain (corrected) level of analyses that revealed no differential PPC activations between 100% valid vs. 100% invalid contrasts.

Regions of cognitive control over WM biases on attentional selection during search: We next assessed the effects of cognitive control resulting from foreknowledge of WM cue validity on search-related neural activity, by analyzing trials that included a search display. (Note that we already reported the orthogonal main effect analysis of the cue validity factor above). A contrast assessing the main effect of predictability, comparing search trials with WM-validity foreknowledge, namely the 100% valid and the 100% invalid blocks, with the unpredictable 50/50 valid and invalid conditions, revealed that generally knowing that the cue was associated with the sought after target or with a distracter activated a network involving the anterior and posterior right hippocampus (BA30) (MNI: 22, -22, -16, 921 voxels) extending into right orbitofrontal cortex. Figure 3A depicts the pattern of results. Another cluster covered the retrosplenial cortex (BAs 26 and 30), posterior cingulate (BA23) (MNI: 2, -42, 24; 713 voxels), and the visual cortex around the lingual gyrus (BA17) (MNI: 16, -56, 12, 921 voxels). Thus, responses in these regions appear to reflect the consequences of attentional control signals stemming from WM foreknowledge, enhancing activity under conditions that maximally predict whether the WM content will be associated with a target or a distracter. Intriguingly, this result points to a role of the hippocampus in controlling the effect of WM representations on attentional selection. To garner additional evidence for this possibility, we further assessed whether the relative activation of the hippocampus in the above contrast was correlated with individual variation in the size of the behavioral effect of validity foreknowledge on search performance [(RT Valid 100% - RT Valid 50/50) + (RT Invalid 100% - RT Invalid 50/50)/2]. Signal change was extracted from a 3 mm sphere centered at the peak of our medial temporal lobe cluster (MNI: 18 -10 -16). The pearson correlation coefficient between BOLD and behaviour was significant (r=0.55, p<0.14; Figure 3B). We replicated this result using an anatomical 3 mm ROI centered on of the hippocampus proper (MNI: 28 -26 -12) according to the Harvard-Oxford anatomical probabilistic atlas part of FSL (r= 0.66, p<0.002, two tailed), thus indicating that the modulation of hippocampal activity by foreknowledge about WM cue validity was of functional relevance to behavior.

In addition to this main effect of cognitive control by WM-validity foreknowledge, we also tested whether the neural substrates of this cognitive control effect as a function of the particular validity status of the WM-cue in the search task, by assessing the predictability by validity interaction effect. In other words, we tested for regions that were selectively involved in inhibiting (in invalid cases) or enhancing (in valid cases) the effects of WM cue during search) as a function of WM-foreknowlege. The results revealed that WM-validity responses in visual cortex (BA18) (MNI: -22, -100, -14; 1553 voxels) and superior temporal cortex (BA21) (MNI: -64, -18, -14; 1266 voxels) were selectively modulated by foreknowledge of valid WM-predictability (Figure 3B). There were no regions above threshold that showed increased in-validity effects during search at the highest level of predictability.

In sum, these results document the involvement of the PPC in generating preparatory signals linked to foreknowledge about WM validity prior to the onset of the search displays. An additional network of regions involving the medial temporal lobe, including the hippocampus proper, and regions of the posterior cingulate/retrosplenial cortex was associated with the cognitive control of WM biases during search itself.

Discussion

We assessed the neural substrates associated with the strategic use of WM contents for directing visual attention towards a matching target versus the controlled inhibition of an irrelevant WM cue likely to reappear as a distracter in search. Behavioral performance revealed that search was faster on valid relative to invalid WM cue trials. Critically, knowing about the validity status of WM content optimized search efficiency on both valid and invalid trials. Observers appeared to inhibit the WM content from guiding attention on predictable trials with invalid cueing. Conversely, the deployment of attention to the WM-matching item was enhanced when participants expected it to reliably coincide with the sought target. This pattern of results suggests that WM biases can be controlled in a top-down manner by foreknowledge about the validity of the WM content (Han and Kim, 2009; Carlisle and Woodman, 2011). We also note that recent behavioral evidence using the same paradigm as employed here showed that predictable invalid blocks still can lead to slower performance relative to a neutral baseline block without memory matching items (Kiyonaga et al., 2012), suggesting that cognitive control can attenuate but not fully overcome the WM bias. Taken together, these results are in line with evidence for co-existence of automatic and strategic components in the guidance of attention by memory representations (Han and Kim, 2009; Carlisle and Woodman, 2011).

Turning now to the imaging data, we found evidence that cognitive control over WM biases involves mechanisms that operate during the memory delay maintenance period (in anticipation of search) and also during the search period itself. A first critical finding is that the PPC is involved in generating preparatory control signals during the cue-delay period stemming from WM-validity foreknowledge prior to the onset of the search relative to the 50/50 baseline condition where the forthcoming validity status of the WM content for search behavior could not be predicted. The preparatory control signals originating in the PPC exhibited some evidence for hemispheric lateralization, whereby when WM contents were known to be valid, activity predominated in the left PPC, whereas WM contents known to be invalid for search were associated with activity in the right PPC. This evidence of lateralisation in the PPC signal is interesting because extant data suggest that engagement of dorsal fronto-parietal networks in attentional control is bilateral (Shulman et al., 2010). Lateralisation of dorsal PPC function has however been observed in bottom-up saliency-based selection tasks depending on whether the salient item needs to be selected or ignored (Mevorach et al., 2006). However, our evidence for PPC lateralization in the control of WM biases is only preliminary and further work is needed to address this interesting possibility in more depth.

Prior research on spatial attention (Grent-'t-Jong and Woldorff, 2007; Bressler et al., 2008; Sylvester et al., 2009) has delineated how preparatory neural activity for expected relevant target locations in the scene is implemented through an interplay between frontal cortex, PPC and visual regions. The PPC is also involved in the integration of *relevant* feature- and space-based cues to optimize the deployment of attention in visual search (Egner et al., 2008). The current findings expand on the role of the PPC in attentional control because, to our knowledge, this is the first evidence of PPC involvement in preparatory control of *irrelevant* WM biases, that is, in the apparent suppression of WM influences on attention. In addition to computing target biasing signals (Shulman et al., 2002) our evidence suggests that the PPC may also play a role in generating a ‘template for rejection’ (Woodman and Luck, 2007), which may help to prevent attentional capture by irrelevant information held in memory. Previous evidence for a role of the PPC in inhibitory processing comes from visual marking studies in which the pre-exposure to irrelevant item locations is immediately followed by a set of new items containing the critical search target. Search performance benefits from pre-exposure to the distracters relative to when all sets of items appear at once. Regions of the superior parietal cortex (BA7) have been linked with the parsing of the pre-exposed irrelevant locations (Pollmann et al., 2003; Olivers et al., 2005).

We note that parietal regions were not consistently activated in previous studies assessing biases of attention by the contents of WM (Soto et al., 2007; Grecucci et al., 2010; Soto et al., 2011a; Soto et al., 2011c; Soto et al., 2011b); however these previous studies used non-predictive WM cues that may not have maximized the engagement of cognitive control processes. Notably, superior dorsolateral prefrontal regions did not appear to be associated with the control of WM biases in the current study, as could have been anticipated from well-established evidence for a dorsal fronto-parietal engagement in top-down attentional control (Corbetta and Shulman, 2002). Instead, our data indicate that cognitive control of WM biases may recruit a different pathway involving the PPC, the posterior cingulate and medial temporal regions (see below).

The role of temporal structures in WM-guidance is associated with both WM-validity effects and also with their strategic cognitive control. First, regions around the anterior parahippocampal gyrus displayed enhanced activity when WM contents overlapped with the sought-after target relative to when they were invalid for search. These results are likely to reflect the bias of attention in search through WM. This is concordant with single-unit work from Chelazzi and colleagues (Chelazzi et al., 1993; Chelazzi et al., 1998) which has shown enhanced neuronal responses in anterior medial temporal cortices around the rhinal sulci for remembered items that had to be selected for a response. Similar evidence from single unit studies has been reported in perihirnal cortex (Lehky and Tanaka, 2007). Activity in the parahippocampal gyrus has also been observed in functional MRI studies in humans assessing WM biases of visual attention (Soto et al., 2007; Grecucci et al., 2010).

A second type of response in the medial-temporal lobe was associated with the strategic control over WM biases. Notably, the magnitude of the hippocampal response here predicted the efficiency of attentional selection based on foreknowledge of whether the WM content was invalid or valid for search. Responses in the right anterior and posterior hippocampus proper extended into the right orbitofrontal cortex, the posterior cingulate and retrosplenial cortex and the precuneus.

Anatomical studies in primates indicate the existence of a parieto-middle temporal pathway, stemming from regions in the inferior PPC– that project to hippocampal and parahippocampal regions either directly or via the posterior cingulate and retrosplenial cortices (Kravitz et al.; Vann et al., 2009). A similar network is present in humans (Margulies et al., 2009). The functional role of this circuitry has been mainly associated with spatial processing (i.e. navigation) and memory (Aguirre and D'Esposito, 1999; Gron et al., 2000; Buckner et al., 2008). Interestingly, all of the regions comprising this parieto-medial temporal pathway in the present study were linked to the guidance of visual of selection by memory representations.

There is fast-growing evidence of hippocampal involvement in WM processing, specifically in maintenance operations (Ranganath and D'Esposito, 2001; Axmacher et al., 2007; Hartley et al., 2007; Axmacher et al., 2010; Poch et al., 2011); but see also an alternative view (Jeneson and Squire, 2012). In the current study, the hippocampal responses did not merely reflect the maintenance of the memory cues but the behavioral 'validity' and the task-set associated with the cues being maintained. It appears difficult to argue that hippocampal engagement in our WM-guided attentional task could reflect contributions from long-term memory (Jeneson and Squire, 2012) considering that a single item had to be maintained for a 2 second delay and WM-validity foreknowledge was blocked. Thus, the data presented here suggest that the hippocampus, like surrounding regions of the medial temporal lobe complex (i.e. perihirnal cortex), may have an important role in visual processing functions (Lee et al., 2005; Devlin and Price, 2007), under conditions that do not depend on long-tem memory, and are more akin to attentional selection guided in a top-down manner by the contents of WM. Recent research on the role of long-term memory in attentional biasing has shown hippocampal involvement when the spatial locus of the target of attention is precued from long-term memory representations of the visual scene (Summerfield et al., 2006; Stokes et al., 2012). Taken together this evidence suggests that the hippocampus may play a role in attentional selection guided both by long-term and short-term memory representations.

Recent research suggests that WM may be compartimentalised according to the relevance of the information for selection, such that irrelevant memory items for current selection goals may be relegated to an accessory memory state and maintained outside of the focus of internal attention (Oberauer, 2002; Olivers et al., 2011), thus reducing their interference with the selection of goal-relevant targets. A role of the hippocampus in inhibiting information held in memory at will has also been put forward (Anderson et al., 2004). We here suggest that the hippocampus forms part of a parieto-medial temporal pathway that may support the ‘switching’ of the state of memory representations for the control of goal-directed attention.

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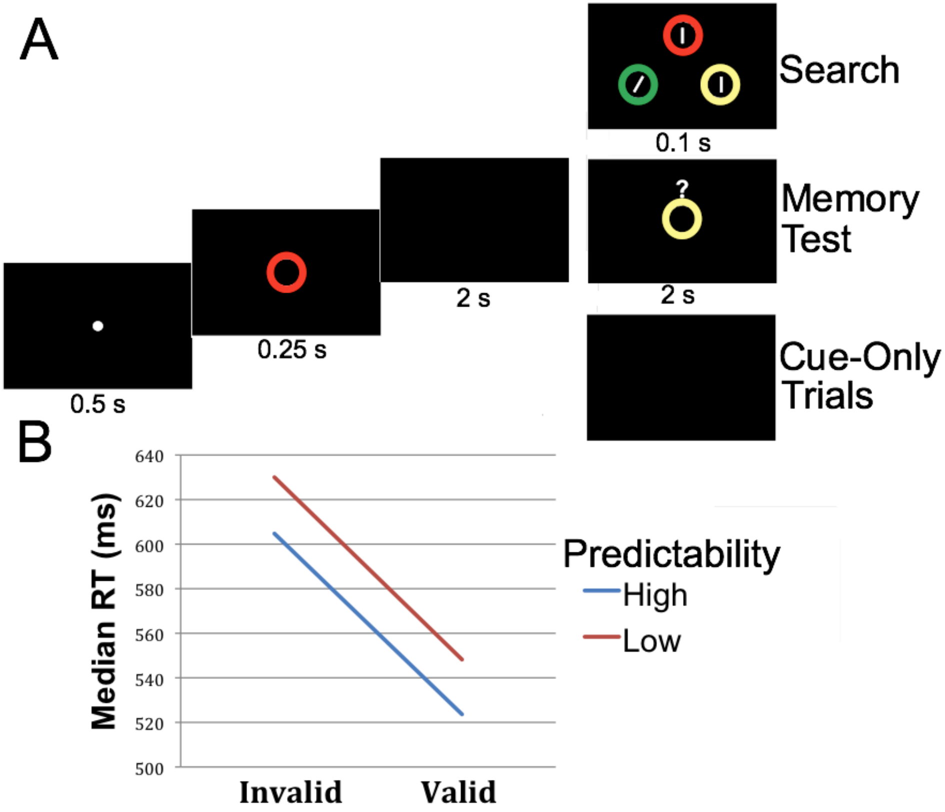
Figure Legends

Figure 1. Experimental protocol and behavioral results. ***A***, Illustration of the timing and sequence of events within an example trial. Each trial consisted of a fixation period, followed by a memory cue, followed by a cue-to-probe interval, followed by either a visual search display (on standard search trials), a memory probe (on memory catch trials), or no display (on cue-only trials). Trials were separated by a jittered inter-trial interval (not shown, see text for details). In the example trial displayed here, the WM cue would be considered an invalid cue for the visual search, because the WM cue surrounds a search distracter (the search target is the tilted bar). ***B***, Median search response time (± mean standard error) is plotted as a function of WM cue validity and whether the cue validity was predictable.

Figure 2. Neural substrates of anticipatory control over WM-attention interaction. ***A***, Activated voxel clusters in a whole-brain analysis ($P<0.05$, corrected) of cue-only trials, showing areas that are more active when observers have foreknowledge that the WM cue is a valid (shown in green) or invalid (shown in red) predictor of the search target than when they have no such foreknowledge. ***B***, Signal change (%) is plotted for the peak active cluster (MNI -36 -48 38) of the left PPC, for cue-related activity in 100% valid blocks and 100% invalid blocks (effects are displayed relative to the 50/50 unpredictable baseline). ***C***, Signal change (%) is plotted for the peak active cluster (MNI 40 -48 3) of the right PPC, for cue-related activity in 100% valid blocks and 100% invalid blocks (effects are displayed relative to the 50/50 unpredictable baseline).

Figure 3. Neural effects of control over WM-attention interaction during visual search. ***A*** Activated voxel clusters in a whole-brain analysis ($P<0.05$, corrected) of cue plus search periods, showing areas that are more active when cues predictably coincided with targets or distracters than when cue-target relations were unpredictable (100% valid/invalid > 50% valid/invalid blocks). ***B***, Correlation between hippocampal response enhancement by predictable cues (see panel A) and behavioral search efficiency due to foreknowledge of WM validity (see text for details). ***C***, Voxel clusters that were selectively more activated during search in the reliably valid cue condition than in the predictably invalid cue condition.

Figure 1


A
Search
0.1 s
Memory Test
2 s
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0.5 s
0.25 s
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Median RT (ms)
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High
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Figure 2

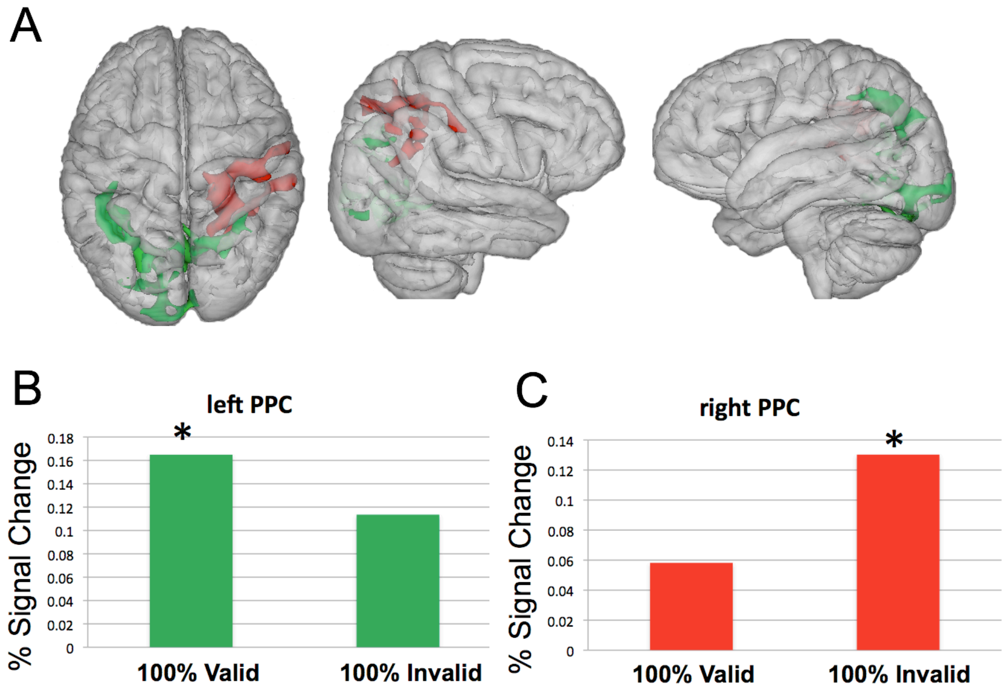
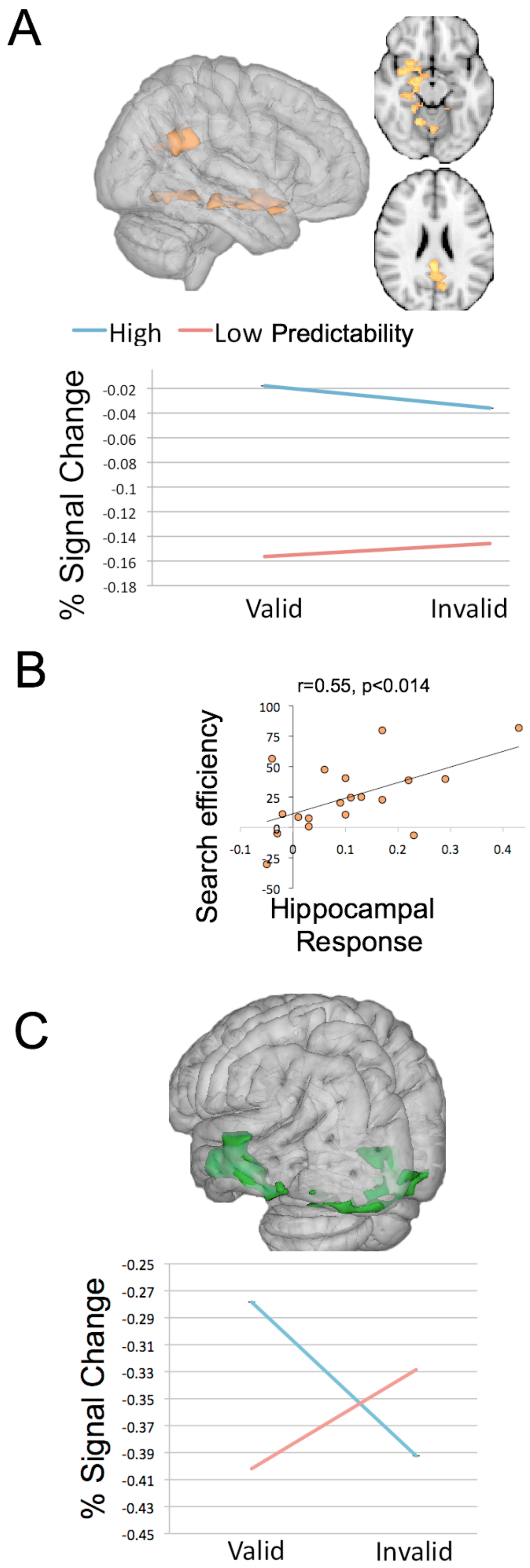


Figure 3


A
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Low Predictability
% Signal Change
-0.02
-0.04
-0.06
-0.08
-0.1
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Valid
Invalid
B
r=0.55, p<0.014
100
75
50
25
0
-25
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Search efficiency
Hippocampal Response
C
-0.25
-0.27
-0.29
-0.31
-0.33
-0.35
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-0.39
-0.41
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-0.45
% Signal Change
Valid
Invalid