Supplemental Material

Method

Participants

Participants were screened and excluded if they had a history of neurological or psychiatric disorders, history of illicit drug use, English was not their first language, they were left handed, visual impairments that could not be corrected with glasses or contacts, history of cardiac abnormalities, concussion in the preceding year, diabetes, kidney disorders, or any condition that prevented them being safely scanned. A total of 55 participants passed through screening and was originally recruited to participate in the study. A between-groups design was utilized given the length of the experimental session for each PM condition, and difficulty in recruiting participants for a return scanning session to perform the other PM condition.

Technical issues resulting in a loss of data led to the exclusion of 3 participants from the Focal condition and 1 participant from the Nonfocal condition. Additionally, 2 Focal participants were excluded due to excessive movement during functional scanning, and 1 Nonfocal participant withdrew from the study after the onset of a headache. Moreover, participants were excluded for chance-level performance in the ongoing task (i.e., 50% accuracy), indicating a failure to understand or comply with task instructions (one subject in the NonFocal group). Two additional NonFocal participants were excluded due to a very low number of PM-Hits (2 and 1), which was non-sufficient for accurate modeling of the BOLD response for neuroimaging analysis.

Demographic information on the remaining sample of 45 participants is provided in Table S1.

Stimulus Materials

Each category word appeared in Tahoma bold font (e.g., **STATE**) and the member word appeared in Courier New font (e.g., missouri) to help distinguish trial components. There were a total of 54 category words that were repeated 4-15 times (mean=13.6) throughout the experiment. For each category word there were 3 category member words. One category member word was paired with the category word 4 times, another paired 2 times, and the third was paired once. Each category member was also presented with one or more category words (randomly determined) to create an equal number of "category no" and "category yes" trials for each particular coordinate. Accordingly, the particular category members were presented an unequal number of times (some 8 times, some 4 times, some twice) in an attempt to decrease the salience of the focal PM target word (presented 20 times), as well as to keep some words novel (i.e., those only presented once for category yes and category no trials). The order of category decision items was randomized except that no category word or category member was repeated on consecutive trials. Furthermore, there was never more than 4 "category yes" or "category no" trials in a row.

fMRI acquisition

Functional MRI data were acquired on a Siemens 3T Trim TRIO scanner at Washington University in St. Louis School of Medicine. Ten functional BOLD runs were collected (TR=2500 ms, TE=25 ms, flip=90°, 384x384 acquisition matrix, 192 volumes, 34 slices, voxel size=4 x 4 x 4 mm). We also collected a T1 structural image using a sagittal MP-RAGE 3D sequence (TR=2400 ms, TE=3.16 ms, flip=8°, 256x256 acquisition matrix, 176 slices, voxel size=1 x 1 x 1 mm) and a T2 image in

the same space as the functional scans (TR=3200 ms, TE=455 ms, flip=120°, 256x256 acquisition matrix, 176 slices, voxel size=1 x 1 x 1 mm).

fMRI Data Analysis

All fMRI analyses were conducted using Statistical Parametric Mapping software (SPM8, Wellcome Department of Cognitive Neurology, London). Image preprocessing included slice-time correction, motion correction through realignment to the first image, coregistration of the subjects' mean image to their own structural T1 image, spatial normalization into the standard stereotaxic atlas space of the Montreal Neurological Institute (MNI space) and $2mm^3$ resized voxels, and spatial smoothing using a 8mm FWHM Gaussian filter. Additional high pass filtering (128Hz cutoff) was included to account for scanner drifts.

A general linear model (GLM) approach (Friston, et al. 1995) was used to estimate parameter values for sustained and transient (event-related) effects (Laurienti, Burdette, & Maldjian, 2003). Event-related model regressors were created by convolving neural input functions for the different event types with the assumed canonical hemodynamic response function as implemented in SPM8. Event-related regressors were created for PM trials, Ongoing trials of the semantic classification task during the PM block (Ong-PM) and during the Control block (Ong-CTL); all error trials were modeled separately with a single regressor. The event of interest for transient effects was time-locked to the onset of the category member/target word. Sustained effects were estimated by including regressors for PM condition (PM-Sus) and Control condition (CTL-Sus) task blocks by convolving a boxcar function with the standard hemodynamic response function. Fixation periods between trials and task blocks were not directly modeled and so were treated as an implicit estimate of baseline activation (termed "Fixation Baseline" below).

After computing the GLM for each subject, random effects group level analyses were conducted to identify sustained and transient activation. For *sustained effects*, a strong a-priori hypothesis was that a canonical network of brain regions engaged in cognitive control and WM ('canonical cognitive control network', CCN) would show sustained activations specifically related to the PM task as compared to the control condition. To test this a-priori hypothesis, a region of interest (ROI) analysis was conducted in a mask comprised of 10-mm radius spherical regions centered on coordinates identified in meta-analyses of working memory and cognitive control tasks (Owen, McMillan, Laird, & Bullmore, 2005; Wager & Smith, 2003), which predominantly includes regions located in dorsal medial and lateral prefrontal and parietal cortex, This same ROI mask has been successfully used for similar purposes in other studies (Beck, Locke, Savine, Jimura, & Braver, 2010; Chiew & Braver, 2011) see Figure S1). The second a-priori ROI was the lateral anterior prefrontal cortex (aPFC) that was previously shown to be consistently engaged by PM tasks (Burgess, Gonen-Yaacovi, & Volle, 2011), as well as episodic memory retrieval, working memory and multitasking (Gilbert et al., 2006). An aPFC mask was defined by placing a 8mm radius sphere around the mean coordinates (x = +/- 34 y = 56, z = 9) reported in Gilbert et al. (2006).

The group level statistical analysis for sustained effects inside the a-priori ROIs involved a conjunction of multiple contrasts as previously used in an earlier study on PM related activations (Reynolds, West, & Braver, 2009), where each thresholded contrast constitutes a mask, and voxels are identified via the intersection of all masks (Friston, Penny, & Glaser, 2005; Price & Friston, 1997; Reynolds, et al., 2009). The threshold for each contrast was set to $p < 0.01$. Applying a relatively liberal threshold for each contrast but combining multiple contrasts in a conjunction

helps to balance the trade-off between power and false-positive protection (with the overall alpha rate for a set of conjunctions resulting in $p < 0.0001$). In order for a voxel to be accepted as sensitive to the effect of interest, it was required to meet the criterion in all tests (described below). For additional false positive protection, Monte Carlo simulations were run on the individual ROIs (CCN, aPFC) using AFNI's AlphaSim (http://afni.nimh.nih.gov/afni/doc/manual/AlphaSim) for identifying the minimum number of contiguous voxels for additional cluster size correction of at least $p < 0.05$. Only activation clusters with that extent of voxels or greater were considered significant.

To identify *sustained activation* specifically related to the NonFocal or Focal PM task in the pre-defined ROIs, a voxel had to meet the following criteria: (i) Significantly increased sustained response in the NonFocal / Focal PM task relative to the CTL task (PM-Sus – CTL-Sus) and (ii) Significant interaction effects showing stronger increase of sustained responses during the PM task relative to the control condition in the NonFocal compared to the Focal condition (Nonfocal [PM-Sus – CTL-Sus] – Focal [PM-Sus – CTL-Sus]) or in Focal compared to NonFocal (Focal [PM-Sus – CTL-Sus] – NonFocal [PM-Sus – CTL-Sus]). Since there were no regions identified for the Focal contrast, an additional whole-brain exploratory analysis was also conducted, using a more liberal threshold ($p < .05$ uncorrected, for each contrast, using AlphaSim to determine cluster size correction). Even with this more liberal threshold, across the whole brain there were no Focal sustained regions that met criteria for identification.

Another analysis identified *transient activations* occurring on PM trials. Since we expected broader effects for PM-related transient activation, but also had less strong a priori predictions regarding the anatomical locations of such effects, these

analyses were conducted in a whole-brain exploratory fashion. Transient activations on PM trials were identified through the contrast of PM – [Ong-PM & Ong-CTL]. This was followed by a direct comparison of activity in the two conditions (Focal/NonFocal) to identify activity patterns that were both common and unique to each condition. Therefore, a second whole brain analysis for each transient interaction contrast, i.e. NonFocal [PM – (Ong-PM & Ong-CTL)] – Focal [PM – (Ong-PM & Ong-CTL)] and Focal [PM – (Ong-PM & Ong-CTL)] – NonFocal [PM – (Ong-PM & Ong-CTL)] was conducted. Additionally, an overlap (conjunction) analysis identified regions composed of overlapping voxels across the two conditions. All of the transient analyses were conducting using a statistical threshold of $p < .05$ with whole-brain FWE correction.

The ROIs identified from both the sustained and transient analyses were further interrogated to determine the specific pattern of activity across conditions. To enable such analyses, beta estimates were extracted for the identified regions using the MarsBar plug-in for SPM (http://marsbar.sourceforge.net/). In these ROI-based analyses involving aPFC (including the PPI analyses described below), two participants were excluded due to some voxels in the region exhibiting excessive susceptibility artifact, which prevented reliable extraction of the ROI estimates. It is important to note that this exclusion only affected plotting of beta estimates rather than the analyses themselves.

Psychophysiological Interaction Analysis

A psychophysiological interaction (PPI) analysis was also conducted to examine the relationship between aPFC activity and other brain regions on PM trials, as a function of task condition (Focal, NonFocal). PPI is a functional connectivity method that examines the interaction between the activity in specified brain regions

and psychological manipulations (Friston et al., 1997; Gitelman, Penny, Ashburner, & Friston, 2003; McLaren, Ries, Xu, & Johnson, 2012). In the present study, we expected that aPFC might exhibit dissociable patterns of functional connectivity across the two conditions, with stronger interactions observed in the NonFocal condition to regions associated with top-down episodic retrieval, while in the Focal condition, we expected to observe stronger connectivity with regions involved in bottom-up retrieval and/or target detection.

We focused on the aPFC as a seed region for the PPI analysis based on theorizing regarding its critical functional role in PM tasks, and also the observed selective pattern of sustained activity in NonFocal PM, but equivalent transient activity on PM trials across the two conditions. The seed region was selected by extracting voxels of left aPFC that showed significant PM-trial related activation in both the Focal and NonFocal PM conditions. The PPI analysis was implemented with the gPPI toolbox for SPM (McLaren, et al., 2012). This toolbox is an extension of the standard PPI implementation, which enables more comprehensive modeling of all sustained and transient task events (rather than just a binary contrast of two conditions), in order to test for connectivity changes related to specific task events after other events have been appropriately modeled. Our particular interest was in connectivity changes selectively related to PM events. The gPPI analysis identifies target regions for which variability in trial-by-trial activation on PM events can be explained in terms of variability in the seed region on those events. It uses an extension of the GLM approach in which three predictor variables are used: 1) the BOLD activation effect due to correct PM events (psychological variable; coded with an indicator variable that isolates these events); 2) the time-series of the seed region across all events (physiological variable); and 3) the trial-by-trial variability in the

time-series of the seed region selectively on PM events (the psychophysiological variable).

Using the same logic as standard GLM activation analyses, the gPPI analysis is conducted in two stages:1) a fixed-effects analysis to estimate gPPI beta values for each participant; 2) a random-effects to test for a specific contrast across conditions or groups. In the current analysis, the random-effects analysis tested for significant increases in connectivity that were selectively present for either Focal or NonFocal PM trials. Thus, for a region to show significant increase of connectivity with left aPFC occurring on correct Focal PM trials, each voxel had to show significant PPI effects for (i) Focal (PM – Fixation Baseline) and (ii) Focal [PM – Fixation Baseline] - NonFocal [PM – Fixation Baseline]; for a region to show significant increase of connectivity on correct NonFocal PM trial, each voxel had to show significant PPI effects for (i) NonFocal (PM – Fixation Baseline) and (ii) NonFocal [PM – Fixation Baseline] - Focal [PM – Fixation Baseline]. Each contrast was set at a threshold of $p < 0.01$, resulting in an overall alpha rate of $p < 0.0001$ and a cluster extent of 26 voxels (whole brain cluster size correction for $p < 0.05$ at an initial threshold of $p < 0.0001$ using MonteCarlo simulations with AlphaSim).

Analyses on Performance-Matched Subsample

Participants

In order to control for possible effects of task difficulty on results, a performance-matched sub-sample was created. Exclusion criteria were also chosen so as to result in the inclusion of the same number of participants in each condition. Therefore, the subjects in the Focal condition showing the best performance were excluded. Top performance was considered having 100% accuracy on PM trials, but also performance on Ongoing trials in the PM task to be no less than 1 SD below the

mean accuracy rate for the sample. This resulted in the exclusion of four Focal subjects. For the NonFocal condition, participants with the worst performance on PM trials were excluded. Specifically, this resulted in exclusion of 9 participants with 70% or less accuracy on PM trials (less than two standard deviations below the mean of the NonFocal sample). Moreover, two subjects (one from each condition) that had been excluded for PPI analysis of the whole sample due to strong susceptibility artifacts in aPFC were additionally removed from the sub-sample. This resulted in a performance-matched sub-sample of 15 subjects in each condition.

Behavioral Performance.

A comparison of the two conditions demonstrated that performance matching across the two subsamples was successful. Accuracy on PM trials did not differ across the two conditions ($t(28) = 0.44$, p = n.s). Moreover, a 2x2 repeated-measures ANOVA (Condition [Focal/NonFocal] x Block [PM/CTL]), yielded no difference in overall task performance accuracy (main effect Condition : $F(1, 28) = 2.17$, p =n.s., ηp^2=.072) or on accuracy cost (Condition x Block interaction: $F(1, 28) = 0.73$, p = n.s., ηp^2 =.025).

Likewise, although significant monitoring costs in RT were still present in each condition (Focal, $t(14) = 4.22$, $p = .001$, and NonFocal, $t(14) = 7.99$, $p < .001$), there was no longer any statistically reliable difference in monitoring cost (Condition x Block interaction: $F(1, 28) = 3.71$, $p = 0.064$, ηp^2 =.117), or overall RT between the two conditions (main effect of Condition: $F(1, 28) = 0.95$, p=n.s., ηp^2 =.033). These results are summarized in Table S1.

Neuroimaging Effects

In order to show that the observed sustained and transient effects and also PPI connectivity changes could not be attributable to differences in task difficulty among

the conditions, imaging analysis were re-performed for the performance-matched sub-groups. All regions showing significant effects in the whole sample analysis were defined as ROIs for sub-sample analysis. From those ROIs, beta estimates of sustained and transient regressors were extracted from the sub-sample and analyzed with multifactorial ANOVAs.

A 2x2x10 ANOVA with the factors ROI (10 regions showing sustained effects in the whole sample, including the left aPFC and CCN-regions), Condition (Focal, Nonfocal), and Block (PM, CTL) tested for sustained effects. The same pattern of Nonfocal PM specific sustained effects was observed in the sub-sample, with stronger sustained activation during the PM compared to the CTL block for the Nonfocal group (significant interaction of Condition x Block: $F(1,28) = 7.82$, $p < 0.01$, $\eta p^2 = .218$) and no significant difference between regions (ROI x Condition x Block interaction: $F(7,20) = .61$, p = n.s., $\eta p^2 = .021$). An additional post-hoc t-test confirmed that the 2-way interaction was driven by stronger sustained activation increases in the Nonfocal compared to the Focal group during the PM block relative to the CTL block ($t(28) = -2.80$, $p < 0.01$).

References

Beck, S. M., Locke, H. S., Savine, A. C., Jimura, K., & Braver, T. S. (2010). Primary and secondary rewards differentially modulate neural activity dynamics during working memory. *PloS one, 5*(2), e9251.

Burgess, P. W., Gonen-Yaacovi, G., & Volle, E. (2011). Functional neuroimaging studies of prospective memory: what have we learnt so far? *Neuropsychologia, 49*(8), 2246-2257.

Chiew, K. S., & Braver, T. S. (2011). Neural circuitry of emotional and cognitive conflict revealed through facial expressions. *PloS one, 6*(3), e17635.

Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., & Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage, 6*(3), 218-229.

Friston, K. J., Penny, W. D., & Glaser, D. E. (2005). Conjunction revisited. *Neuroimage, 25*(3), 661-667.

Gilbert, S. J., Spengler, S., Simons, J. S., Steele, J. D., Lawrie, S. M., Frith, C. D., et al. (2006). Functional specialization within rostral prefrontal cortex (area 10): a meta-analysis. *Journal of Cognitive Neuroscience, 18*(6), 932-948.

Gitelman, D. R., Penny, W. D., Ashburner, J., & Friston, K. J. (2003). Modeling regional and psychophysiologic interactions in fMRI: the importance of hemodynamic deconvolution. *Neuroimage, 19*(1), 200-207.

Laurienti, P. J., Burdette, J. H., & Maldjian, J. A. (2003). Separating neural processes using mixed event-related and epoch-based fMRI paradigms. *J Neurosci Methods, 131*(1-2), 41-50.

McLaren, D. G., Ries, M. L., Xu, G., & Johnson, S. C. (2012). A generalized form of context-dependent psychophysiological interactions (gPPI): a comparison to standard approaches. *Neuroimage, 61*(4), 1277-1286.

Oishi, K., Faria, A., van Zijl, P., & Mori, S. (2011). *MRI Atlas of Human White Matter*. Amsterdam: Elsevier.

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: a meta-analysis of normative functional neuroimaging studies. *Hum Brain Mapp, 25*(1), 46-59.

Price, C. J., & Friston, K. J. (1997). Cognitive conjunction: a new approach to brain activation experiments. *Neuroimage, 5*(4 Pt 1), 261-270.

Reynolds, J. R., West, R., & Braver, T. (2009). Distinct Neural Circuits Support Transient and Sustained Processes in Prospective Memory and Working Memory. *Cerebral Cortex, 19*(5), 1208-1221.

Wager, T. D., & Smith, E. E. (2003). Neuroimaging studies of working memory: a meta-analysis. *Cogn Affect Behav Neurosci, 3*(4), 255-274.

	Focal (all)	Nonfocal (all)	Focal (sub-sample)	NonFocal (sub-sample)
Demographics				
n (females)	20 (14)	25 (16)	15 (12)	15 (8)
Age	23.8 (5.0)	24.0 (5.0)	23.3 (5.1)	24.5 (5.8)
Reaction Time				
PM	760.40 (83.28)	813.08 (68.25)	770.66 (89.63)	812.10 (74.35)
CTL	720.60 (78.99)	741.72 (64.04)	723.19 (80.44)	736.29 (70.66)
Cost	39.79 (42.92)**	71.35 (43.23)**^^	47.46 (43.59)**	75.81 (36.76)**
Accuracy				
PM Target	.89 (.11)	.74 (.18)^^	.86(.11)	.84 (.07)
Ong-PM	.92 (.04)	.88 (.05)	.91 (.04)	.90 (.59)
Ong-CTL	.92 (.04)	.91 (.04)	.92 (03)	.91 (.04)
Cost	-.007 (.03)	-.027 (.05)*	.00 (.04)	-.02 (.04)

Table S1: Demographic and behavioral performance in Focal and Nonfocal conditions.
One-sample t-test significance: *p<.05, ** p<.001, significant difference of the NonFocal group compared to Focal group: ^p<.05, ^^p<.01; Standard deviation are reported in brackets if not otherwise stated.

Regions exhibiting increased sustained activity in NonFocal PM, as well as NonFocal PM > Focal PM

L/R	Region	size	BA	x	y	z	Z value
R	Middle Frontal Gyrus (dorsolateral PFC)	36	46	42	44	26	3.04
L	Middle Frontal Gyrus (dorsolateral PFC)	43	46	-38	44	26	3.11
R	Anterior Cingulate Cortex /pre-SMA	209	32	8	18	40	2.90
R	Precentral Gyrus / IFJ	355	47	42	-6	24	4.03
L	Precentral Gyrus / IFJ*	164	44	-54	10	32	2.82
R	Precentral Gyrus/Middle Frontal Gyrus (FEF)	108	6	38	-6	50	2.98
L	Middle Frontal Gyrus (FEF)*	157	6	-32	0	56	3.17
R	Superior Parietal Lobule	318	7	24	-64	46	2.92
L	Superior Parietal Lobule	68	7	-28	-58	54	2.75

Table S2. Regions showing selective sustained activations during NonFocal PM and transient activations for Focal and NonFocal PM trials. Sustained activations statistics are reported for the Nonfocal interaction contrast (Nonfocal (Sus-PM – Sus-CTL) > Focal (Sus-PM – Sus-CTL)). Anatomical locations are provided in MNI coordinates, with regions labeled according to the MRI Atlas of Human White Matter (Oishi, Faria, van Zijl, & Mori, 2011).

Regions exhibiting increased transient activity on correct PM trials, in both Focal and NonFocal conditions

			Focal PM					***Nonfocal PM***				
L/R	**Region**	**size**	**BA**	**x**	**y**	**z**	**Z value**	**BA**	**x**	**y**	**z**	**Z value**
L	Anterior Cingulate Gyrus	130	**32**	-2	36	26	5.30	**24**	0	36	22	5.23
R	Anterior Insula	75	**47**	34	20	-12	5.22	**47**	32	20	-10	5.58
L	Anterior Insula	366	**47**	-30	18	-10	5.88	**47**	-28	20	-6	6.22
L	Precentral Gyrus/ IFJ*	37	**44**	-56	10	28	5.27	**44**	-52	10	26	5.01
R	Middle Frontal Gyrus (FEF)	60	**6**	30	4	50	5.35	**8**	26	4	56	5.13
L	Middle Frontal Gyrus (FEF)*	176	**6**	-26	4	56	5.63	**6**	-22	2	52	5.09
R	Parietal Lobule (Ventral Parietal Cortex)	89	**40**	56	-40	34	5.69	**40**	50	-34	46	4.85
L	Parietal Lobe (Ventral Parietal Cortex)	268	**40**	-46	-38	40	6.46	**40**	-50	-36	40	5.10
R	Basal Ganglia (Globus Pallidus)	48	**-**	16	4	-2	5.43	*****	8	-8	-2	5.43
L	Thalamus/Midbrain	273	**-**	-6	-12	-6	5.55	*****	-2	-12	0	5.68

Table S3. Transient activations from the whole brain analysis. Overlapping regions identified from PM contrast (PM > (Ong-PM + Ong-CTL)) in both Focal and Nonfocal conditions. Statistics reported separately for each condition. FEF: frontal eye field, IFJ: inferior frontal junction, PFC: prefrontal cortex, SMA: supplementary motor area. *: Regions showing overlap of transient and Nonfocal sustained activity. Anatomical locations are provided in MNI coordinates, with regions labeled according to the MRI Atlas of Human White Matter (Oishi, et al., 2011).

Figure S1. ROI mask of canonical cognitive control network (CCN). Created by drawing 10mm radius spheres around coordinates identified by previous meta analysis on cognitive control and working memory (Owen, et al., 2005; Wager & Smith, 2003).