Regional Brain Activity During Updating in Working Memory

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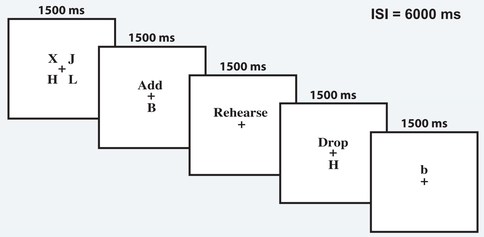
1. Introduction

- Neuroimaging studies using a variety of working memory tasks have succeeded in parsing out several distinct processes involved in the overall function of WM, including encoding, retrieval, maintenance, rehearsal, and updating.
- Tasks used thus far have generally not allowed for the separation of updating processes, such as adding and dropping items, from rehearsal processes.
- Here, we present preliminary fMRI data from a novel task allowing for the separation of these processes: adding, dropping, and rehearsing item representations held in WM.
- This updating task also allows for a clearer distinction of these processes from other aspects of WM by presenting items to be added or removed directly and thereby minimizing use of additional cognitive control processes recruited in more complex WM tasks.

2. fMRI Design

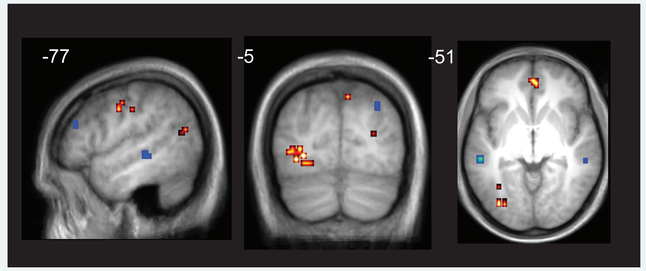
- Whole-brain fMRI data was acquired on 9 subjects with a 3T Phillips scanner at the Columbia University MRI center at the Neurological Institute of New York. Functional data were acquired with an EPI BOLD sequence using a TR of 2000 ms, TE of 20 ms, flip angle of 77°, field of view of 192 mm, 45 slices, and 3 mm isotropic voxels. High resolution structural scans were acquired using an MPRAGE sequence with a field of view of 256 mm, 165 slices, and 1 mm isotropic voxels. All preprocessing and analysis was carried out using SPM8, except where noted.
- All participants were checked to ensure motion no greater than 2.5 mm and rotation no greater than 2.5°.
- Following slice-timing correction, data were realigned using INRIalign. T1 and EPI images were manually reoriented to match the MNI template, and were then coregistered to each other before normalization parameters were estimated using the SPM8 segmentation algorithm. Images were then smoothed (8mm FWHM) and a mask was defined from the intersection of the gray matter segmentation and a skull-stripped mean EPI image.
- First-level models for each subject were analyzed using a canonical-HRF model with temporal and dispersion derivatives. Following model estimation, the estimated response at each voxel for regressors of interest was computed and the peak amplitude of the response was used to compute percent signal change values for all second-level analyses. A separate regressor was used for variability in the number of items to be remembered (i.e. WM load). Mean-centered motion parameters, their derivatives, and squared motion parameters and their derivatives, and spikes in the fMRI timeseries data were modelled as nuisance regressors.
- Second level models were estimated using robust regression (Wager et al., 2005).

3. Updating Working Memory Task



Each trial begins with a presentation of 3-5 target letters that the participant has been instructed to remember. This initial presentation is followed by three events. Each event presents either a new letter to add to the target set, a letter to drop from the target set, or instruction to rehearse. A probe letter is then presented and the subject must respond with a button press to indicate whether or not the probe is part of the updated target set. There are 2-7 letters in the target set at time of probe, depending on event types, which are randomized using a genetic algorithm (Wager 2002) to optimize power to detect add-rehearse and drop-rehearse contrast.

4. Imaging Results: Add - Drop



p ≤ 0.25, FDR corrected

Regions with differential BOLD activation

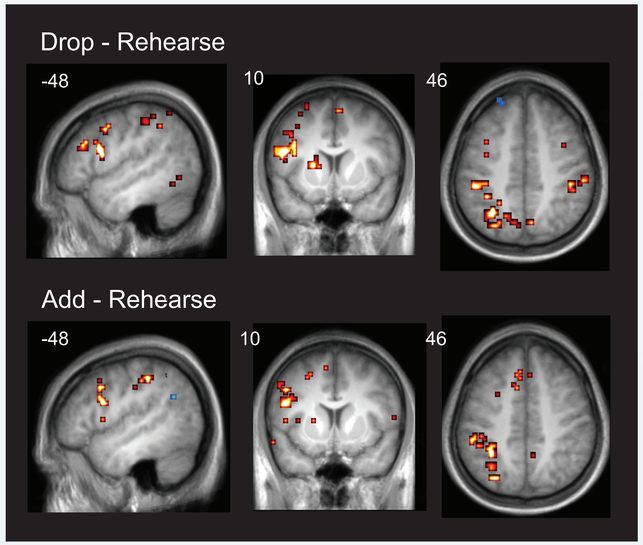
Positive results

Region	Coordinates (MNI) x	y	z	voxels	t_{max}
Right medial frontal gyrus (BA 10)	3	48	-8	8	11.06
Left precentral gyrus (BA 4)	-48	-9	37	3	9.8
Left cingulate gyrus (BA 21)	-18	-33	40	3	7.1
Left posterior cingulate (BA 23)	0	-45	28	4	7.75
Left inferior occipital gyrus (BA 19)	-33	-78	-5	12	18.21
Left middle occipital gyrus (BA 18)	-24	-84	-11	6	9.44

Negative Results

Region	Coordinates (MNI) x	y	z	voxels	t_{max}
Left inferior frontal gyrus (BA 9)	-54	27	22	4	-10.06
Left middle temporal gyrus	-51	-33	-8	5	-8.79
Left cerebellar tonsil	-15	-48	-47	3	-9.13

5. Imaging Results: Updating - Rehearsal



p ≤ 0.05, FDR corrected

Regions with differential BOLD activation

Add - Rehearse

p ≤ 0.05

Positive results

Region	Coordinates (MNI) x	y	z	voxels	t_{max}
Right inferior frontal gyrus (BA 47)	45	24	-2	3	15.06
Left inferior frontal gyrus (BA 9)	-45	6	22	14	18.11
Left superior frontal gyrus (BA 8)	-6	18	49	3	11.63
Left cingulate gyrus (BA 32)	-6	24	43	3	8.04
Left precentral gyrus (BA 6)	-48	9	34	9	10.54
Left inferior parietal lobule (BA 40)	-33	-45	40	27	16.08
Left inferior parietal lobule (BA 40)	-45	-36	43	7	11.33
Left superior parietal lobule (BA 40)	-30	-60	46	6	11.53
Left precuneus (BA31)	-24	-69	28	14	17.17
Left precuneus (BA 19, 7)	-30	-72	40	7	13.92

Negative results

Region	x	y	z	voxels	t_{max}
Right lingual gyrus (BA 18)	18	-81	-8	6	-9.65

Drop - Rehearse

p ≤ 0.05

Positive Results

Region	Coordinates (MNI) x	y	z	voxels	t_{max}
Right middle frontal gyrus (BA 10)	39	45	19	3	9.86
Left inferior frontal gyrus (BA 44, 9)	-48	9	19	40	20.58
Left middle frontal gyrus (BA 46)	-45	24	22	9	12.73
Right superior frontal gyrus (BA 47)	30	60	-11	3	11.91
Left inferior frontal gyrus (BA 47)	-33	30	-5	3	9.55
Right inferior frontal gyrus (BA 47)	42	21	-2	4	11.09
Left middle frontal gyrus (BA 6)	-27	-3	55	11	10.16
Right superior frontal gyrus (BA 6)	9	12	58	6	8.78
Left precentral gyrus (BA 6)	-42	3	37	14	25.27
Left caudate body	-15	6	10	23	12.45
Left inferior parietal lobule (BA 40)	-30	-48	40	9	13.71
Left inferior parietal lobule (BA 40)	-42	-33	43	10	14.17
Right inferior parietal lobule (BA 40)	33	-42	37	3	12.81
Right inferior parietal lobule (BA 40)	45	-36	43	8	7.83
Right inferior parietal lobule (BA 40)	54	-33	46	10	8.68
Right superior occipital gyrus (BA 39)	36	-69	34	14	11.55
Right precuneus (BA 7)	6	-69	46	5	10.23
Left precuneus (BA 7)	-9	-69	49	19	11.17
Left superior parietal lobule (BA 7, 19)	-27	-63	46	32	16.55
Left precuneus (BA 19)	-27	-69	34	8	8.67
Left cerebellar tonsil	-27	-54	-35	4	9.15

Negative results

Region	x	y	z	voxels	t_{max}
Left superior frontal gyrus (BA 8)	-6	-63	25	3	-7.12
Left superior frontal gyrus (BA 8)	-18	42	40	4	-11.99
Left anterior cingulate (BA 24)	-3	36	7	3	-7.86
Right insula (BA 13)	54	-33	13	7	-9.14
Right insula (BA 13)	39	-24	19	12	-8.26
Right posterior cingulate (BA 29)	12	-48	16	4	-13.61
Left posterior cingulate (BA 30)	0	-45	22	8	-12.24
Right lingual gyrus (BA 18)	18	-81	-11	12	-13.24

6. Conclusions

- Adding and removing items from WM activates mainly left dorso- and ventro-lateral prefrontal cortex (DLPFC and VLPFC), as well as premotor cortex, posterior parietal cortex, and inferior parietal lobule, which is consistent with the role of these regions as critical for WM, though activation of prefrontal regions is more specific to inferior frontal gyrus than with other WM tasks.
- Activation of left inferior frontal regions (VLPFC, inferior frontal gyrus) likely reflects selection of item to be dropped from WM load.
- During rehearsal, there is increased activation in the right extrastriate cortex of the occipital lobe (Brodmann area 18), which is most likely attributable to the focus of attention on items already encoded.
- Adding items also showed differential activation in left inferior and middle occipital gyrus, indicating an increased engagement of visual processing for items to be remembered.

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