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High temporal resolution imaging of spatial working memory

Jared X. Van Snellenberg [a,*], Jennifer Whitman [b], John J. McDonald [b], Mario Liotti [b]

[a] Columbia University, 1190 Amsterdam Avenue, Mail Code 5501, New York, NY 10027, New York, NY USA
[b] Simon Fraser University, Burnaby, BC Canada

Abstract. A substantial literature examining the neural correlates of working memory using functional magnetic resonance imaging (fMRI) has revealed the involvement of a predominantly fronto–parietal network in the maintenance and manipulation of information in working memory. However, the temporal dynamics of activity in this system cannot be revealed by fMRI at the sub-second level. We employed magnetoencephalography ($n=12$) to investigate the temporal dynamics of spatial working memory in a well-studied task, the *n*-back. Dynamic imaging of coherent sources (beamforming) was employed to determine the sources of effects evident in temporal spectral evolution analyses. Results indicated the involvement of brain regions traditionally identified in fMRI, predominantly in the beta frequency range 500–1500 ms post-stimulus. © 2007 Elsevier B.V. All rights reserved.

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1. Introduction

Functional neuroimaging investigations of human working memory (WM) have revealed the involvement of a network of brain regions in the active maintenance and manipulation of information over short delays [1,2]. However, functional Magnetic Resonance Imaging (fMRI) and Positron Emission Tomography (PET) have relatively poor temporal resolution, and investigations using electroencephalography (EEG) and magnetoencephalography (MEG) have generally been limited in the spatial localization of observed effects (e.g. [3–10]). In order to better describe the temporal dynamics of activity in the network of brain regions that subserve

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[*] Corresponding author. Tel.: +1 212 854 7858; fax: +1 212 854 3609.
E-mail address: jared@psych.columbia.edu (J.X. Van Snellenberg).

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WM in humans, the present study employed MEG to study the neural correlates of a well-studied WM task, the *n*-back.

2. Methods

2.1. Subjects

Thirteen individuals gave written informed consent to participate in the study. One was excluded because of excessive head motion during recording, leaving twelve subjects (5 female) with a mean age of 28 years (S.D. = 5.3).

2.2. Task and stimuli

Stimuli were disks appearing in one of eight evenly distributed locations equidistant from fixation. In both the 0-back and the 2-back conditions, participants completed 8 blocks of ten trials, and the order of blocks was randomized. For each 0-back block, subjects were required to indicate each time a stimulus appeared at a previously signaled location. In the 2-back condition, subjects were required to indicate whenever the presented stimulus matched the stimulus presented two trials previously. Stimuli were presented for 150 ms, followed by a delay of 5850 ms.

2.3. Data collection and signal preprocessing

Data were collected from a 151-channel OMEGA (CTF Systems) axial gradiometer system at the Down Syndrome Research Foundation (Burnaby, BC, Canada). Recordings were high-pass filtered at 0.1 Hz and digitized at 600 Hz. Trials were averaged in 6500 ms epochs, with a 500 ms baseline time-locked to each stimulus presentation. Trials contaminated by ocular artifacts were corrected in Brain Electrical Source Analysis (BESA) software. Trials that were not adequately corrected or which were responded to incorrectly were excluded from the analysis.

2.4. Source analysis

First, we carried out temporal spectral evolution (TSE) analyses in BESA at a wide range of frequencies (1–80 Hz) in the 2-back minus 0-back difference waveforms at each sensor channel, and identified time-frequency ranges with significant spectral power effects across subjects in a large number of channels. Source analysis using dynamic imaging of coherent sources (DICS) [11] implemented in BESA was carried out in the identified time-frequency ranges (alpha, 10.5–14 Hz, 400–1800 ms; beta, 14–30 Hz, 500–1500 ms; theta, 6–8 Hz, 500–3500 ms; delta, 1–3 Hz, 500–1000 ms). The beamformer data were then exported to Fieldtrip (F. C. Donders Centre), wherein voxel-wise *t*-tests were carried out and thresholded at $p < 0.0001$ (uncorrected), and the source space was normalized and interpolated to the MNI template. Clusters smaller than 10 voxels were ignored. Also, to avoid reporting contiguous clusters as a single brain region, local maxima (>20 mm between maxima) were calculated, and those including grey matter are reported. Clusters were labeled with an automated

Table 1
Regions significantly active ($p<0.0001$, $k>10$) in DICS analysis

Location	Coordinates (Talairach)				
	x	y	z	k	t-score
Beta (14–30 Hz; 500–1500 ms)					
Left superior frontal gyrus (BA 6)	−22	4	62	2928	−9.01
Right superior/middle frontal gyrus (BA 6)	18	8	62	1447	−7.65
Left postcentral/precentral gyrus	−56	−18	40	1915	−8.94
Anterior cingulate/insula	8	0	6	1647	−9.61
Left cingulate gyrus	−22	−32	32	4567	−7.82
Left superior parietal lobule (BA 7)	−24	−68	56	311	−8.33
Left supramarginal gyrus	−44	−50	30	803	−7.23
Left superior/middle temporal gyrus	−44	−60	14	2159	−7.89
Right parahippocampal gyrus	20	−30	−10	962	−7.05
Left parahippocampal gyrus	−26	−26	4	434	−7.21
Left middle occipital gyrus (BA 18/19)	−28	−86	10	1329	−8.59
Left middle occipital gyrus (BA 18)	−44	−72	−6	1629	−9.38
Left cuneus (BA 18)	−16	−80	22	832	−7.26
Cerebellar tonsil	20	−52	−32	9777	−8.70
Culmen	−14	−52	−4	9334	−9.56
Declive	26	−58	−2	3475	−7.53
Alpha (10.5–14 Hz; 400–1800 ms)					
Inferior parietal lobule BA (40)	−44	−64	44	131	−6.55
Declive	4	−72	−10	768	−6.4

Note. Voxels are 2 mm isotropic. BA=Brodmann's Area; DICS=Dynamic Imaging of Coherent Sources; k=extent (number of voxels).

algorithm based on the Talairach Daemon [12] according to the brain regions in which the most voxels in the cluster fell.

3. Results

There were no above threshold voxels in the theta (max $|t_{11}|=4.08$) or delta (max $|t_{11}|=1.59$) time-frequency ranges, while both the alpha and beta analyses indicated significant activations, which are reported in Table 1.

4. Discussion

The results of the DICS analysis reveal activity in a network of brain regions (bilateral premotor areas, anterior cingulate, separate regions in posterior and inferior parietal cortices, extrastriate cortex, and the cerebellum) also found to be active in recent meta-analyses of fMRI and PET studies of WM [13,14], and furthermore reveals that—with the exception of the inferior parietal lobule, which was active in high alpha frequencies—the activity of these regions occurs in beta frequencies, between 500–1500 ms following a to-be-remembered stimulus. The temporal range over which these activations occur makes sense in light of the differential cognitive demands of the 0-back and 2-back, in that manipulation of the contents of WM can be expected to occur early in the delay between stimuli, while simple maintenance of items in WM would occur later in the delay once manipulation of items has been completed.

Two aspects of our results differ substantively from hemodynamic imaging studies. First, we observed activity bilaterally in the parahippocampal gyrus, which is not generally reported in fMRI studies [13,14]. However, this is not the first MEG study to detect MTL activity in spatial WM [5], raising the possibility that MEG is sensitive to activity in the MTL during spatial WM, which for some reason is not detected by fMRI. Second, we did not observe any effects in dorsolateral prefrontal cortex (BA 46/9), which probably indicates that these regions are active in time-frequency ranges that were not evident in our TSE analyses. Alternatively, the orientation of the relevant sources may simply produce minimal signal detectable by MEG.

In conclusion, our results indicate that the majority of the regions identified as being involved in WM by fMRI are also identified by MEG, and are predominantly beta oscillations early in the delay period.

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