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Distinguishing between lateralized and nonlateralized brain activity associated with visual short-term memory: fMRI, MEG, and EEG evidence from the same observers

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ABSTRACT

Previous functional neuroimaging studies have shown that maintenance of centrally presented objects in visual short-term memory (VSTM) leads to *bilateral* increases of BOLD activations in IPS/IOS cortex, while prior electrophysiological work suggests that maintaining stimuli encoded from a single hemifield leads to a sustained posterior *contralateral* negativity (SPCN) in electrophysiology and magnetoencephalography. These two findings have never been investigated using the same physiological measures. We recorded the BOLD response using fMRI, magnetoencephalography (MEG), and electrophysiology (EEG), while subjects encoded visual stimuli from a single hemifield of a balanced display. The EEG showed an SPCN. However, no SPCN-like activation was observed in the BOLD signals. The BOLD response in parietal cortex remained bilateral, even after unilateral encoding of the stimuli, but MEG showed both bilateral and contralateral activations, each likely reflecting a sub portion of the neuronal populations participating in the maintenance of information in VSTM. Contrary to the assumption that BOLD, EEG, and MEG responses – that were each linked to the maintenance of information in VSTM – are markers of the same neuronal processes, our findings suggest that each technique reveals a somewhat distinct but overlapping neural signature of the mechanisms supporting visual short-term memory.

Introduction

While behaving in a constantly changing environment, the visual system must maintain, in a readily available form, a portion of what was seen; a process supported by visual short-term memory (VSTM). Recently, important insights about the neural representation of VSTM were obtained following the identification of several new physiological markers of VSTM. Researchers have argued that the maintenance of information in VSTM is likely supported by the intra-parietal and intra-occipital cortex (IPS/IOS), because activity in these cerebral regions is strongly correlated with the amount of information held in memory (Todd and Marois, 2004). Conversely, lateralized visual stimuli, to be encoded and maintained for a brief period of time (e.g., 1 or 2 s), lead to sustained neural activity over the posterior regions of the cerebral cortex, contralateral to the stimuli to be encoded (Klaver et al., 1999). An increase of the amplitude of this memory-related ERP component (labeled SPCN, for Sustained Posterior Contralateral Negativity) as the number of items remembered increased was found (Brisson et al., 2008), and was subsequently used in several investigations of VSTM (Brisson and Jolicoeur, 2007; Jolicoeur et al., 2008; Robitaille and Jolicoeur, 2006; Robitaille et al., 2007).

These two physiological markers of VSTM (the BOLD response, and the SPCN) have several features in common. The topographical distribution of the SPCN (Brisson and Jolicoeur, 2007, 2008; Jolicoeur et al., 2008; McCollough et al., 2007; Perron et al., 2009; Robitaille and Jolicoeur, 2006; Robitaille et al., 2007) is very similar to that of the N2pc, for which parietal sources were identified(Hopf et al., 2000). The amplitudes of the electrophysiological and hemodynamic markers increase monotonically with the number of items presented, but reach a maximum at the subject's maximal VSTM capacity (e.g., calculated using Cowan's k formula (Cowan, 2001; Pashler, 1988)), creating a plateau for higher number of items. Moreover, both markers were linked to individual differences in VSTM capacity (Todd and Marois, 2005; Vogel and Machizawa, 2004). The most prominent difference between the SPCN and the BOLD activation in IPS/IOS is the encoding field manipulation used to isolate the SPCN. Indeed, the SPCN, as other ERP

Abbreviations: ER-SAM, event-related SAM; fMRI, functionnal magnetic resonnance imaging; IPS/IOS, intra-parietal/intra-occipital cortex; MEG, magnetoencephalography; MEM, maximum entropy of the mean; MNE, minimum-norm estimates; SAM, synthetic aperture magnetometry; SPCM, sustained posterior contralateral magnetic field; SPCN, sustained posterior contralateral negativity; VSTM, visual short-term memory.

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components like the N2pc and the LRP, is based on a "contralateral–ipsilateral" difference to isolate the lateralized portion of the brain response, where the ipsilateral side of the brain is used as a control "condition," or as a control activation (Gratton, 1998) for the contralateral activation. This manipulation is intended to remove the effect of any activity that is not lateralized according to the stimulus presentation side (or response-button side, for LRP). Studies of VSTM using fMRI so far have used bilateral stimulus presentations and found bilateral activation in IPS/IOS.

The goal of the present study was to observe, directly, the relationship between the BOLD activation in IPS/IOS, the electrophysiological (SPCN) component, and the magnetoencephalographical (SPCM) marker of the maintenance of information in VSTM. We tested the same subjects both with fMRI and MEG – with EEG recorded simultaneously with MEG – in very similar experiments designed to allow comparisons across brain imaging modalities. To allow the use of a regression analysis on the number of items accurately held in memory (Todd and Marois, 2005), we presented 1, 2, 4, or 6 visual objects. We used bilateral stimulus presentations, with an arrow indicating which stimuli (on the left or right side of fixation) had to be encoded (Grimault et al., 2009; Robitaille et al., 2009; Vogel and Machizawa, 2004). This allowed us to compute both load-related activity (by collapsing trials with left-encoding and right-encoding) and an SPNC-like activation (using the "contralateral minus ipsilateral" measure) with the data from all imaging modalities. We recently coined the term SPCM, a magnetic equivalent of the SPCN (labeled SPCM for Sustained Posterior Contralateral Magnetic field) (Robitaille et al., 2009). Sensors showing the SPCM were located on two separate clusters of sensors, over parietal cortex. A critical finding of that study was that for different sensor clusters (different from the SPCM), we found an increase in magnetic field amplitude with the increase in the number of items held in memory that was independent from the encoding hemifield (i.e., no interaction between hemifield and the increase in activation as a function of memory load). This led us to conclude that a more complex network of neural generators was active during the retention period than what was isolated as the SPCM. However, this previous study only used two loads, preventing the use of a parametric analysis based on estimated memory capacity across loads (e.g., regression using Cowan's k (Todd and Marois, 2004)). Furthermore, anatomical MRIs were available for only 5 participants, which limited the possibility of source localization. These limitations were overcome here because an anatomical MRI was acquired for every subject and we used a broader range of memory loads.

The specific hypothesis we will test is that both physiological markers (BOLD activation in IPS/IOS and the SPCN/M) reflect the same underlying neural processes. In others words, the generators of the SPCN/M would be the left and right IPS/IOS; each of them would increase in activation level more for stimuli encoded from the contralateral side of space, relative to activation for stimuli encoded from the ipsilateral side. When stimuli are encoded from both sides of the screen simultaneously, the result would be a bilateral activation, as found in fMRI and suggested by the results of Klaver et al. (1999). We consider that this is commonly assumed, as both papers (Todd and Marois, 2004; Vogel and Machizawa, 2004) are often cited as though the SPCN/M and BOLD responses are different manifestations of the same underlying brain functions.

Methods

Subject

13 subjects were recorded in this experiment. One subject was excluded for a failure to maintain fixation during the task. The twelve remaining subjects (7 females) were between 19 and 31 years old (average 23.3), reported having no neurological problem and were able to easily discriminate the colors used in the memory task. For the first six subjects we counterbalanced the order of MEG and fMRI sequences. However, the three subjects who performed the fMRI first showed strong artifact in their MEG signal. To avoid further contamination of the MEG signal (of magnitude around 3e-14 Tesla) following the ~75 min exposure to the 3 Tesla magnetic field of the MRI, the remaining subjects did the MEG experiment first. An ICA artifact removal procedure (see below) successfully cleaned the MEG signals of the three subjects tested first with fMRI, so their results could be included in the analyses.

MEG and EEG

MEG and EEG procedures

Stimuli were presented on a back-projected translucent screen, located 75 cm in front of the subject. The area containing all the possible stimuli subtended 14° (width) by 7° (height) of visual angle centered within the display. Each trial started with the presentation, for 200 ms, of two arrowheads directly above and below the fixation point (see Fig. 1), with the arrowheads pointing to the left or the right of the screen. The fixation cross was then presented alone for 600 to 700 ms (varied randomly across trials). The random values were added so activity related to the arrows would not systematically overlap activity related to the memory array. On each side of the screen, 1, 2, 4, or 6 colored disks were presented for 200 ms (always an equal number on each side), at randomly selected positions within a 3×4 imaginary grid. Colors were selected among 8 highly discriminable colors (black, dark blue, green, light blue, pink, red, white, and yellow). A color was never repeated on one side of the screen, but selection was independent across sides. The retention period was 1000 to 1100 ms (randomly selected from a rectangular distribution), followed by the test display. The test display consisted of a colored disk (one on each side of the screen), located at the position of one disk presented for encoding. This display was presented for 1500 ms. On 50% of the trials, the test disk had the same color as the one previously presented at this location; otherwise it was of one of the 7 remaining colors. Subjects had 1500 ms to answer by pressing one of two keys on an optically-coupled response pad (right index for "same," right middle finger for "different"). A colored disk was always presented simultaneously on the other side of the screen, with color and position varied in the same way as for the test disk, but independently. Feedback was provided after each trial by changing the fixation cross to a + or − sign, for a correct or an incorrect answer, respectively. The feedback was presented for 600 to 900 ms, chosen on the basis of the previous random interval to create an average interval of 4400 ms (range: 4350 to 4450, selected from a rectangular distribution) between the onset of each trial. Trials were presented in 20 blocks of 40 trials. Subjects initiated the block manually, allowing for a rest period as needed. Trial order was counterbalanced.

The amount of information maintained in VSTM was assessed using Cowan's k formula (Cowan, 2001) based on the behavioral results: (proportion of hits − proportion of false alarms) * the number of items presented. This formula is useful because it corrects for possible biases in the propensity to respond 'same' or 'different' (see also Pashler, 1988).

MEG and EEG recordings

A CTF-VSM whole-head 275-sensor MEG system in a magnetically shielded room was used for the recordings. Data were filtered with a 150 Hz low-pass filter and digitalized at 600 Hz during the recording. Bad MEG channels (3 or 4, depending on the subject) were excluded from the recording. EEG (PO7, PO8, right mastoid) was also recorded with reference to the left mastoid, and later algebraically re-referenced to the average of the mastoids. Bipolar EOG (electrodes placed at the left and right canthi for horizontal EOG and above and below the left eye for vertical EOG) was recorded in order to monitor eye blinks and eye movements. Bipolar ECG was also recorded. Trials with a correct or an incorrect response were included in the brain signal analyses.