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Issue: *Competitive Visual Processing Across Space and Time***Multimodal neuroimaging evidence linking memory and attention systems during visual search cued by context**

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Visual search can be facilitated by the learning of spatial configurations that predict the location of a target among distractors. Neuropsychological and functional magnetic resonance imaging (fMRI) evidence implicates the medial temporal lobe (MTL) memory system in this contextual cueing effect, and electroencephalography (EEG) studies have identified the involvement of visual cortical regions related to attention. This work investigated two questions: (1) how memory and attention systems are related in contextual cueing; and (2) how these systems are involved in both short- and long-term contextual learning. In one session, EEG and fMRI data were acquired simultaneously in a contextual cueing task. In a second session conducted 1 week later, EEG data were recorded in isolation. The fMRI results revealed MTL contextual modulations that were correlated with short- and long-term behavioral context enhancements and attention-related effects measured with EEG. An fMRI-seeded EEG source analysis revealed that the MTL contributed the most variance to the variability in the attention enhancements measured with EEG. These results support the notion that memory and attention systems interact to facilitate search when spatial context is implicitly learned.

Keywords: contextual cueing; visual search; attention; memory; hippocampus; EEG; fMRI; multimodal imaging

Introduction

Visual search for a target object among distracting items can be facilitated by contextual associations between co-occurring objects^{1–4} and spatial configurations that predict the target location.⁵ These contextual associations are learned over time, sometimes implicitly. For example, when target–distractor spatial configurations in search arrays are repeated, performance is improved relative to novel configurations, even when observers are unable to recognize the repeated displays.^{5–8} This so-called contextual cueing effect is not transient: behavioral evidence indicates that these implicit memories can facilitate search performance not only within the short term (i.e., single experimental sessions), but also in the long term, at least 1 week later.⁸

A number of studies have investigated the neural bases of implicitly learned context effects in visual search. In one study, patients with medial temporal lobe (MTL) damage did not show the benefit of context during search.⁶ Because the MTL and the

hippocampus have historically been implicated in long-term memory function,^{9,10} this finding points to the MTL memory system as an important mediator in the contextual cueing effect. The finding that contextual cueing can persist for up to 1 week⁸ is also consistent with the involvement of hippocampus-mediated long-term memory. However, these results have been controversial because the hippocampus is typically assumed to be critical for declarative memory operations, not implicit memory function.^{9–13} Nevertheless, recent functional magnetic resonance imaging (fMRI) evidence has shown that hippocampal blood-oxygen-level-dependent (BOLD) responses are modulated by implicitly learned repeated contexts,^{14–16} and we have recently shown that the magnitude of these contextual modulations early in learning can be predictive of subsequent short-term behavioral context effects observed within a single experimental session.¹⁶ It is unclear, however, whether these contextual modulations in MTL activity are also

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correlated with the long-term changes in behavior that have been measured at more distal points in time (e.g., 1 week later⁸).

The visual attention system has also been implicated in the contextual cueing phenomenon. Evidence supporting a role for attention comes from studies focused on contextual modulations of visual cortical functioning. Evidence from intracranial event-related potentials (ERPs) has shown that visual responses to old (i.e., repeated) search displays measured within the first approximately 200 ms of presentation are larger than the responses evoked by new spatial contexts.¹⁷ Scalp-recorded ERP studies have focused on the N2pc component, which is thought to reflect enhanced attentional selection of the search target within 200–300 ms of stimulus presentation.^{18–21} These studies have also shown that the N2pc is enhanced for repeated (old) contexts relative to new contexts.^{22,23} fMRI evidence has revealed modulated neural responses to old contexts in frontal, parietal, and occipital regions related to visual spatial attention.^{14,16,24} For example, in a recent fMRI study using brief lateralized search displays, we observed context-related enhancements in regions of visual cortex contralateral to the search display and in regions of the dorsal attention network.¹⁶ However, several studies have instead demonstrated behavioral and ERP evidence for the involvement of separate higher order response selection and decision processes more typically associated with prefrontal function and thus call the role of visual spatial attention into question.^{23,25–29}

On the basis of the existing evidence, it is clear that there are multiple potential mechanisms that may contribute to the contextual cueing phenomenon. One proposed explanation of implicitly learned contextual cueing is that repeated spatial context influences search by first triggering implicit memory, which then facilitates attention at the target location.⁷ Although there is evidence in support of the involvement of both memory and visual attention neural systems,^{14,16,22} open questions still remain. Specifically, it is unclear (1) how the fMRI measurements of the memory system relate to the attention-related effects measured with ERPs, and (2) how memory and attention systems are involved in both short- and long-term contextual learning.

These issues were addressed in this study by asking participants to perform a typical contextual cue-

ing task conducted in two sessions separated by 1 week. During Session 1, electroencephalography (EEG) and fMRI data were acquired simultaneously; in Session 2, only EEG data were acquired. The simultaneous neuroimaging approach allowed us to identify regions that were modulated by the search task with a high degree of spatial precision, while also allowing us to precisely measure the temporal dynamics of the context-related modulations. The goal was to conduct an fMRI-seeded source analysis of the EEG data from both sessions to answer two main questions: (1) To what extent are modulations of the MTL measured with fMRI in Session 1 related to behavioral and EEG contextual modulations both in the short- (Session 1) and long term (Session 2)? and (2) To what extent is the relationship between the fMRI and EEG data correlated with the behavioral contextual cueing effect?

Method

Participants

Sixteen volunteers were paid \$20/h or received course credit for participating in this study. The Human Subjects Committee at the University of California, Santa Barbara, approved the study procedures. All participants provided informed consent before the experiment. Two participants were removed from the analysis owing to behavioral response acquisition errors and two were excluded owing to EEG data file errors. The resulting 12 participants had a mean age of 21 years (11 right handed; 6 female).

Stimuli

The stimulus displays consisted of a target (the letter T, 1.5°) presented among distractors (the letter L, 1.5°). The color of the target and distractors was determined randomly and could be red, green, blue, yellow, or magenta. The target was oriented 90° clockwise or 90° counterclockwise. The orientation of the distractors was randomly selected from the pool of cardinal orientations (0°, 90°, 180°, 270°). The display was divided into an imaginary 5 × 4 grid (rows × columns), where each square in the grid was 2.4° × 2.4°. The grid was centered on the display vertically and positioned with the middle two columns offset 1.2° to the left and right of the vertical meridian (i.e., each hemifield contained a 5 × 2 grid). The offset ensured that no stimulus appeared at fixation and that the targets were lateralized, which

should maximize the chance of observing an N2pc. Otherwise, the locations of the targets and the distractors within the grid were randomly selected under the constraints described later. To prevent collinearity of the contours of adjacent items, the positioning of the search items within each position of the grid was jittered by $\pm 0.32^\circ$.

A set of eight unique displays was created for each subject and condition in which the location, orientation, and color of the distractors was fixed for a specific target location. These displays, referred to as “old” displays, were presented to the participant twice within each experimental block (once for each target orientation). An additional set of eight displays was created for each experimental block; in these displays, referred to as “new” displays, the location of the target was never the same as the location of the targets in any of the old displays. As with the old displays, each new display was presented twice within an experimental block.

Design and procedure

The experiment consisted of two sessions, with the search task procedure in both sessions being exactly the same. Each trial started with a central fixation cross for 250 ms, followed by a search array displayed until response or for a maximum of 1900 ms. Participants were instructed to indicate whether the target T was rotated to the left or right by pressing one of two buttons as quickly as possible. Responses were made with the right hand using a button box in Session 1, and with the < and > keys on a standard keyboard in Session 2. After the response, auditory feedback indicated whether the answer was correct (high-pitch beep) or incorrect (buzzer). Each trial lasted a total of 3 s. Participants were instructed to maintain fixation throughout the task and to adopt a passive search strategy, letting the unique item “pop” into mind. Instructions of this sort have been shown to facilitate the contextual cueing effect.³⁰ A sample trial sequence is shown in Figure 1A.

Each session consisted of eight experimental blocks, with each block including eight old displays with six items (one target + five distractors; small set) and eight old displays with 12 items (one target + 11 distractors; large set). The exact same number of new displays was also presented within each experimental block. To prevent response biases, each old and new display was presented twice within a block, once with the target rotated 90°

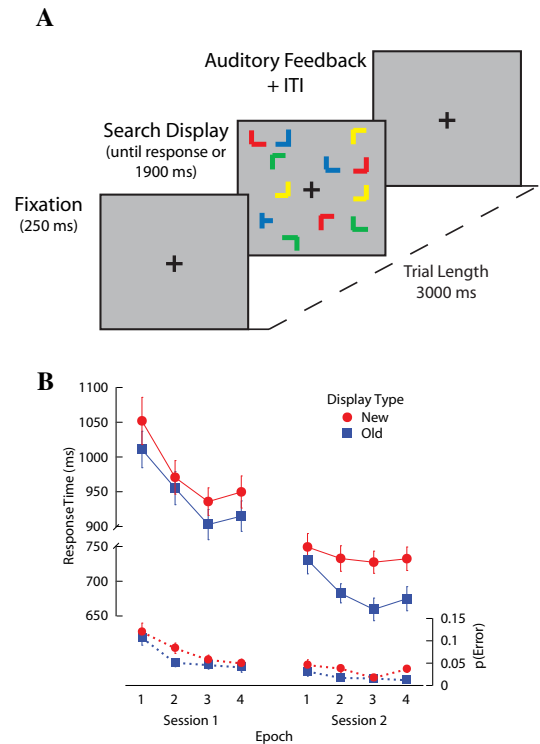


Figure 1. (A) Sample trial sequence. (B) Mean behavioral performance. Solid lines, response time; dotted lines, error rate. Error bars here and in other figures represent ± 1 standard error of the mean.

clockwise and once with the target rotated 90° counterclockwise. Half of each type of stimulus display included targets lateralized to the left and half were lateralized to the right. This design resulted in 32 old trials and 32 new trials per block. An additional 32 trials of the same duration (3000 ms), but in which no stimulus was presented, were randomly interleaved within the sequence of search trials to facilitate the event-related fMRI analysis.^{16,31–34}

In Session 1, EEG and fMRI data were acquired simultaneously. After a delay of 5–10 days (average = 7 days), participants returned for Session 2 in which EEG was recorded in isolation. The old displays presented in Session 2 were identical to those presented in Session 1. As in Session 1, the new displays were randomly generated for each block.

Immediately following Session 2, a surprise recognition task was given to the participants, in which they were presented the 16 old displays randomly intermixed with a freshly created set of new displays. Participants were asked to indicate whether

each display was old or new using a 10-point confidence scale (e.g., 1 = confident old; 5 = not confident old; 6 = not confident new; 10 = confident new). The continuous confidence ratings were converted to proportion correct by assigning confidence ratings of 5 or less as old responses and ratings of 6 or more as new responses.

fMRI data acquisition and preprocessing

Functional MRI data were acquired using a 3 Tesla Siemens TIM TRIO MRI scanner with a 12-channel head coil (Siemens, Munich, Germany). The functional data were acquired using a T2*-weighted gradient-echo sequence with a repetition time (TR) of 2 s, echo time (TE) of 30 ms, and flip angle (FA) of 90°, resulting in 37 contiguous slices at a 3 × 3 × 3.5 mm voxel resolution. For anatomical data, a T1-weighted 3D MPRAGE sequence with 1 mm isometric voxel resolution was used.

The fMRI data were preprocessed using Statistical Parametric Mapping 5 (SPM5; MathWorks, Natick, MA).³⁵ Slice timing and motion correction were first performed on the functional images. Anatomical scans for each subject were coregistered to the functional images and then spatially normalized using the Montreal Neurological Institute (MNI) template. The functional images were spatially normalized using the parameters from the anatomical normalization and then smoothed with an 8-mm isotropic Gaussian kernel.

EEG data acquisition and preprocessing

In Session 1, EEG and fMRI data were acquired simultaneously using an MRI-compatible Brain Products 64-channel EEG system (Brain Products, Gilching, Germany). The data were collected at a 1000-Hz sampling rate and re-referenced offline to the average of TP9/TP10 near the mastoids. MRI gradient artifacts in the EEG were corrected by creating an artifact template for each TR on the basis of triggers from the scanner. This template was subtracted from the raw EEG data³⁶ and the data were then down-sampled to 250 Hz. Care was taken to avoid removing relevant EEG signals from the data during MRI artifact correction by randomizing the initial search array onset after the first TR. This randomization combined with the 3-s trial length avoided synchronization between the gradient artifact and the task.³⁶ An additional artifact arising from the simultaneous fMRI acquisition was the ballistocardiogram (BCG) artifact, which was

corrected using a Matlab implementation of a Principle Component Analysis (PCA)-based method that finds the peak of the electrocardiogram signal, identifies an optimal basis set using the first four PCA components for each channel, and fits these to each artifact measured at each electrode.³⁷ Following these artifact corrections, the EEG data from Session 1 were treated identically to the EEG data from Session 2.

The EEG data in Session 2 were recorded using 64 scalp Ag/AgCl-sintered electrodes (BioSemi ActiveTwo; BioSemi, Amsterdam, the Netherlands). Additional electrodes were placed at the right and left mastoids, as well as 1 cm lateral to the left and right external canthi (horizontal), and above and below each eye (vertical) for the electro-oculogram (EOG). Data were sampled at 256 Hz and referenced offline to the average mastoid signal.

The resulting data from both sessions were filtered between 0.1 and 40 Hz and then epochs were extracted that included a 200-ms prestimulus period and a 700-ms poststimulus period. The prestimulus period was used to baseline the epochs and trials, in which any channel that showed a change in amplitude of 75 μ V or greater was classified as eye blink/movements artifacts and excluded from further analysis (<5% of trials). Finally, data were averaged across all trials for each stimulus type.

Data analysis

Two steps were taken to maximize the statistical power of our hypothesis tests. First, the eight experimental blocks of behavioral data were collapsed into four epochs for each session.^{5,16} Second, the set-size manipulation was initially included to assess the effect of context on search slopes, but a preliminary analysis revealed that, although there were main effects of set size on response time (RT), there were no interactions with any of the other factors of the design. Similar patterns emerged in the imaging data. As a result, all analyses were collapsed across set size. Additional dependent measure-specific analytical methods are described below.

Behavioral performance. RTs and error rates from the search task were analyzed using separate repeated measures ANOVAs. Recognition accuracy was analyzed using one-sample *t*-tests.

fMRI. The data were analyzed using an implementation of a general linear model that did not

make assumptions about the shape of the hemodynamic response.^{32,33} Six time points were modeled by a different parameter for each stimulus, resulting in a 12-s analysis window. The trial types modeled included correct trials only and were defined by epoch (1, 2, 3, or 4), display type (old or new), and set size (small or large), resulting in 16 trial types. Analyses were subsequently collapsed across set size to increase power. Contrasts focused on the estimated activity at the third and fourth time point of the analysis window. The main purpose of this analysis was to identify those regions modulated by the task, independent of the other factors of the design (i.e., stimulus versus baseline). Both activations (increases) and deactivations (decreases) were included because hippocampal and MTL regions often show a response that is below prestimulus baselines in these search tasks.¹⁶ The resulting contrasts allowed us to identify regions of interest (ROIs) to be correlated with behavioral performance and to seed source models of the EEG data in a statistically unbiased manner. Activations from all contrasts were thresholded at $P < 0.001$, uncorrected for individual voxels with an 11 contiguous voxel extent, which was selected on the basis of 1000 Monte Carlo simulations to ensure correction for multiple comparisons at $P < 0.05$ across the image volume.³⁸

To correlate the BOLD response with the behavioral contextual cueing effect, the BOLD time courses within the ROIs were converted to percent signal change relative to the response at the TR immediately preceding stimulus onset. In order to correct for the overlap in hemodynamic response to the search displays, the responses to stimulus-absent trials were subtracted from each time course.^{16,34} Finally, the difference in peak responses of the resulting ROI time course between old and new search displays was calculated using the average response from time points 3–4 and submitted to correlation analyses. To correct for multiple ROI comparisons, we also report the false discovery rate (FDR)–corrected q values in addition to standard P values.³⁹

ERP. The primary focus of the EEG data was the N2pc ERP component. To analyze the N2pc, the resulting epochs from lateral posterior electrode pairs P3/P4, P5/P6, and O1/O2 were used. The mean stimulus-evoked responses at electrode sites contralateral and ipsilateral to the target locations were

computed separately for each condition. Mean amplitudes were then computed to quantify and test hypotheses about the N2pc. This was done by computing the contra/ipsi mean amplitudes, averaging across the 200–300 ms time window.²² Then, the resulting ipsilateral mean amplitudes were subtracted from the corresponding contralateral mean amplitudes.

fMRI-seeded source analysis. To determine which of the regions modulated by the task accounted for the variance in the ERP data, we conducted source analysis constrained by the locations revealed by the fMRI contrasts. This analysis was conducted using the Brain Electrical Source Analysis (BESA) software (BESA GmbH, Gräfelting, Germany). The locations of the source dipoles were selected from activations from the fMRI data in Session 1, using the independent activation/deactivation contrasts to identify regions of activity. The source modeling procedure used a default four-shell ellipsoidal head model in which the locations of the dipoles were fixed but the orientation and amplitudes were allowed to vary. This process consisted of a least-squares fitting algorithm that considered the default criteria of source energy and variance in order to create a best-fit model that minimizes the residual variance between the observed EEG data and the dipole model.^{40,41} The models were fit at the individual subject level and then hypotheses were conducted at the group level.

Two source analyses were performed: the first served to validate the extent of contribution from the fMRI sources to the overall stimulus-evoked ERP (0–700 ms), whereas the second was focused on determining the sources that accounted for the difference in the size of the N2pc evoked by old and new displays. To isolate the N2pc component, the ERP data elicited by targets in the right visual field were subtracted from ERP data from targets in the left visual field.^{42,43} This subtraction was done separately for old and new displays. A second subtraction was done on the resulting ERP data from each session to isolate the difference in N2pc activity between old and new display types. To determine the relative contribution of each dipole source to the explained variance of the N2pc model, we conducted an additional analysis that measured the change in the explained variance when each source was removed from the model. This was accomplished by running

separate source models with each source independently removed from the model and recording the level of explained variance. For each source that was removed, we computed the proportion of variance accounted for by that source relative to the variance explained by the model with all sources. EV_{full} represents the explained variance of the model with all sources and $EV_{partial}$ represents the explained variance of a model with one source removed. Then the source-specific variance contribution can be computed using the following formula:

$$p(\text{source variance contribution}) = \frac{p(EV_{full}) - p(EV_{partial})}{p(EV_{full})}$$

This metric was computed for each source and subject. These values were then compared to a random permutation of the existing contribution values for each subject.

Results

Behavior

Search task. Overall mean RT on correct trials is shown in Figure 1B. Search times decreased across sessions ($F(1,11) = 440.10, P < 0.001$) and epochs ($F(3,33) = 17.60, P < 0.001$); however, the decline across epochs in Session 1 was greater than in Session 2 (session \times epoch: $F(3,33) = 21.33, P < 0.001$). RTs were faster for old than new displays (main effect of display type: $F(1,11) = 10.14, P < 0.01$). The effect of display type was more pronounced in later epochs, particularly in Session 2 (display \times epoch: $F(3,33) = 10.13, P < 0.001$; session \times display \times epoch: $F(3,33) = 10.06, P < 0.001$).

Mean error rates are shown in Figure 1B. Error rates were lower in Session 2, on trials with old displays, and at later epochs (main effects of session, display, and epoch: all F 's $> 16, P$'s < 0.01). The higher error rates in early epochs were more pronounced in Session 1 (session \times epoch: $F(3,33) = 7.87, P < 0.01$).

Recognition task. The mean proportion correct recognition of old displays was 0.57 (SEM = 0.04) and of new displays was 0.58 (SEM = 0.05). Neither were different than chance (old: $t(11) = 1.78, P > 0.10$; new: $t(11) = 1.74, P > 0.11$).

Neuroimaging

ERP. The mean contra- and ipsilateral waveforms and N2pc mean amplitudes measured at occipital

and parietal electrodes (see Methods) are plotted as a function of session and display type in Figure 2. Although the analysis of the mean amplitudes revealed only a marginal interaction between session and display type ($F(1,11) = 3.56, P = 0.09$), a planned comparison was performed in each session on the basis of prior evidence of N2pc effects in the same task.^{22,23} This analysis revealed a larger N2pc mean amplitude in response to old displays than to new displays in Session 2 ($t(11) = 2.66, P < 0.03, q < 0.05$), but not in Session 1 ($P > 0.88, q > 0.88$).

The lack of a robust N2pc in Session 1 is potentially problematic because this type of search task typically elicits the N2pc component.^{18,44,45} One possible explanation is that search is more variable in the early stages of learning and this variability may be masking the N2pc. Importantly, previous research has shown that the N2pc is attenuated during variable, inefficient search relative to less variable, efficient search.^{46,47} In the present context, if search variability is masking the N2pc, then RT variability might be associated with the size of the N2pc. To explore this possibility, we performed a rank-order analysis to assess whether individuals with less RT variability exhibited more robust N2pc mean amplitudes.^{48–50} In this procedure, all possible pairs of participants were compared with respect to their RT variability. For example, if in a given pair, Participant A had lower RT variability than Participant B and Participant A also had a larger N2pc mean amplitude, this would be considered a correct rank ordering (i.e., assigned a value of 1). Mean rank-order accuracy and standard errors were estimated using a jackknife method, leaving one participant out for each iteration.^{48–50} This analysis revealed that less RT variability in Session 1 was associated with larger N2pc effects significantly above chance (old: $M = 0.58, SEM = 0.04, t(11) = 2.10, P < 0.05$; new: $M = 0.65, SEM = 0.04, t(11) = 4.22, P < 0.01$).

Functional MRI. An ROI analysis was conducted on areas identified in an independent contrast of all stimuli regardless of condition. Regions of the MTL, precuneus, posterior cingulate, and frontal regions exhibited stimulus-evoked decreases in BOLD response (Fig. 3a), whereas the inferior parietal and occipital cortices exhibited stimulus-evoked increases in BOLD responses (Fig. 4a). The regions identified in these contrasts are listed in Table 1.

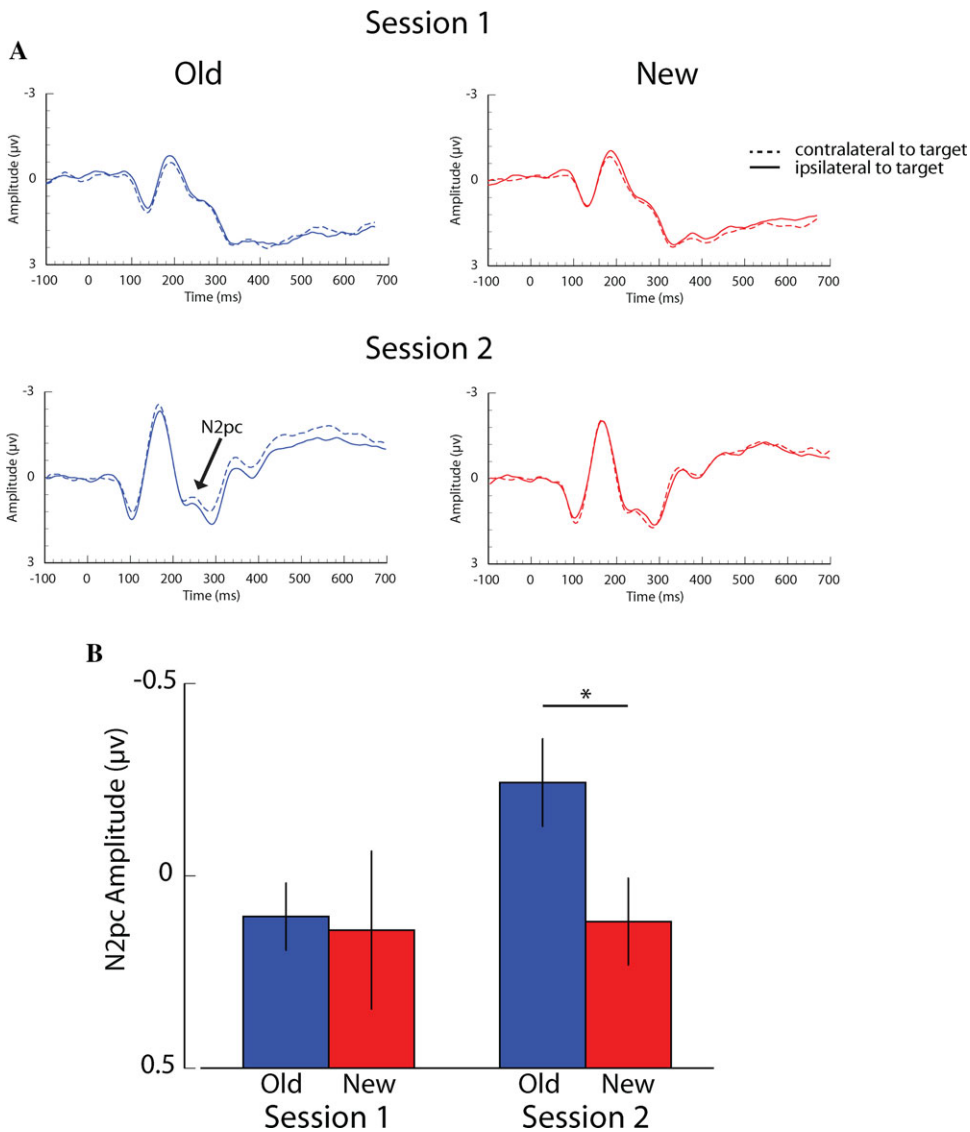


Figure 2. (A) Average ERP waveforms measured at occipital (O1/O2) and parietal electrodes (P3/4, P5/6). (B) Mean N2pc amplitude measured 200–300 ms poststimulus. * $P < 0.05$.

We have previously reported that the differential response to old and new displays in the MTL is correlated with the contextual cueing effect.¹⁶ To assess this correlation here, we computed the old–new difference in BOLD response and the contextual cueing effect in the MTL ROI revealed by the stimulus versus baseline contrast. The resulting scatter plots are shown in Figure 3B. The differential peak activations in the right MTL were significantly correlated to the RT contextual cueing effects in Session 1 ($r(10) = 0.73$, $P < 0.01$, $q < 0.03$) and in Session 2

($r(10) = 0.70$, $P < 0.02$, $q < 0.03$). Participants with larger differential responses to old and new contexts in Session 1 also had larger contextual cueing RT benefits, both within the same session and 1 week later. Although previous work has implicated MTL activation in recognition,¹² we found no correlation between MTL activity and performance on the explicit recognition task ($r(10) = -0.42$, $P > 0.17$).

We also correlated peak BOLD activity differences and contextual cueing for the other three cortical regions that reached the highest level of significance

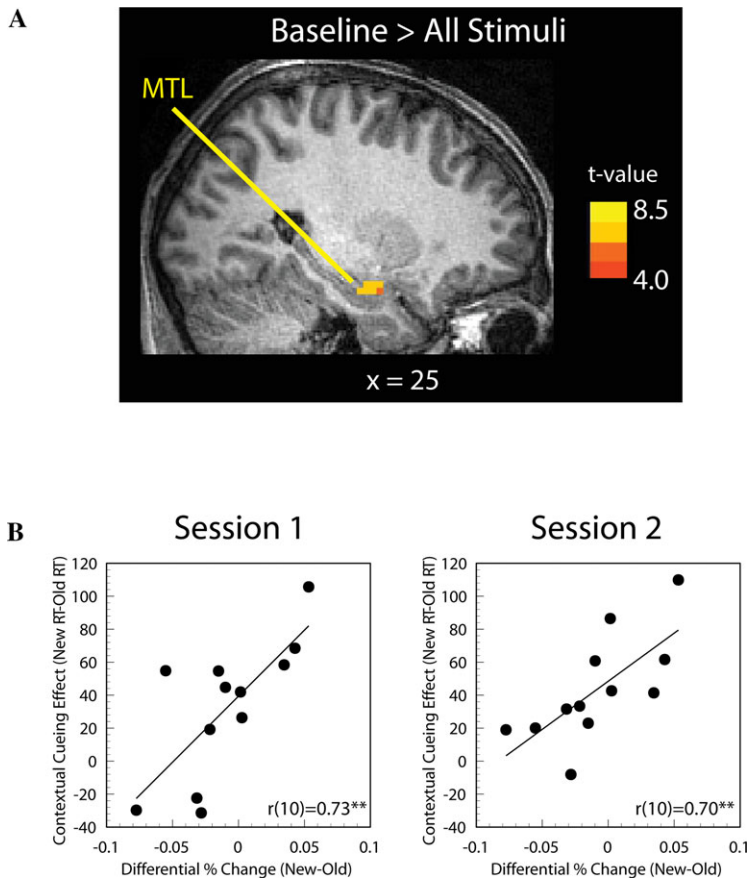


Figure 3. (A) Right medial temporal lobe (MTL) cluster that exhibited a significant deactivation compared to baseline ($P < 0.05$, corrected). (B) Correlation between the old–new difference in MTL response and the behavioral contextual cueing effect in Sessions 1 and 2. $**P < 0.05$, FDR—corrected for multiple comparisons.

in the stimulus contrasts. The resulting scatter plots are shown in Figure 4B. Differential activity from the right inferior parietal lobe (IPL) was not significantly correlated to behavior in Session 1 ($r(10) = 0.43$, $P > 0.16$, $q > 0.21$) and was only marginally related to behavior in Session 2 when corrected for multiple comparisons ($r(10) = 0.64$, $P < 0.03$, $q > 0.05$). The activation difference in the lingual gyrus was also not significantly correlated with the behavioral effect in Session 1 ($r(10) = 0.51$, $P > 0.08$, $q > 0.14$), but it was in Session 2 ($r(10) = 0.72$, $P < 0.01$, $q < 0.03$). In the superior temporal gyrus (STG), differential activations were not correlated with behavior in either Session 1 or 2 (both $r(10) < 0.39$, $P > 0.22$, $q > 0.25$). To ensure that correlations were not driven by BOLD activity tracking global RT changes, we also correlated the peak BOLD differences in all ROIs and mean RT across conditions and found no

significant correlations in either session (all $r(10) < 0.50$, $P > 0.09$, $q > 0.23$).

fMRI-seeded source analysis

To directly link the hemodynamic and electrophysiological responses in contextual cueing, a source analysis was performed using sources from the fMRI contrasts as dipole seeds. The stimulus activation sources included the STG (MNI xyz: 42, -42, 15), IPL (30, -48, 48), and lingual gyrus (-30, -78, -9) and their symmetrical pairs, as well as a single source in the superior frontal gyrus (SFG; 3, 3, 54); the stimulus deactivation sources included the left MTL (-30, 9, -21) region and its symmetrical pair, resulting in nine sources. Two initial analyses were performed. First, the dipole model was used to estimate the ERP responses to all stimuli. The mean proportion of variance explained across subjects was

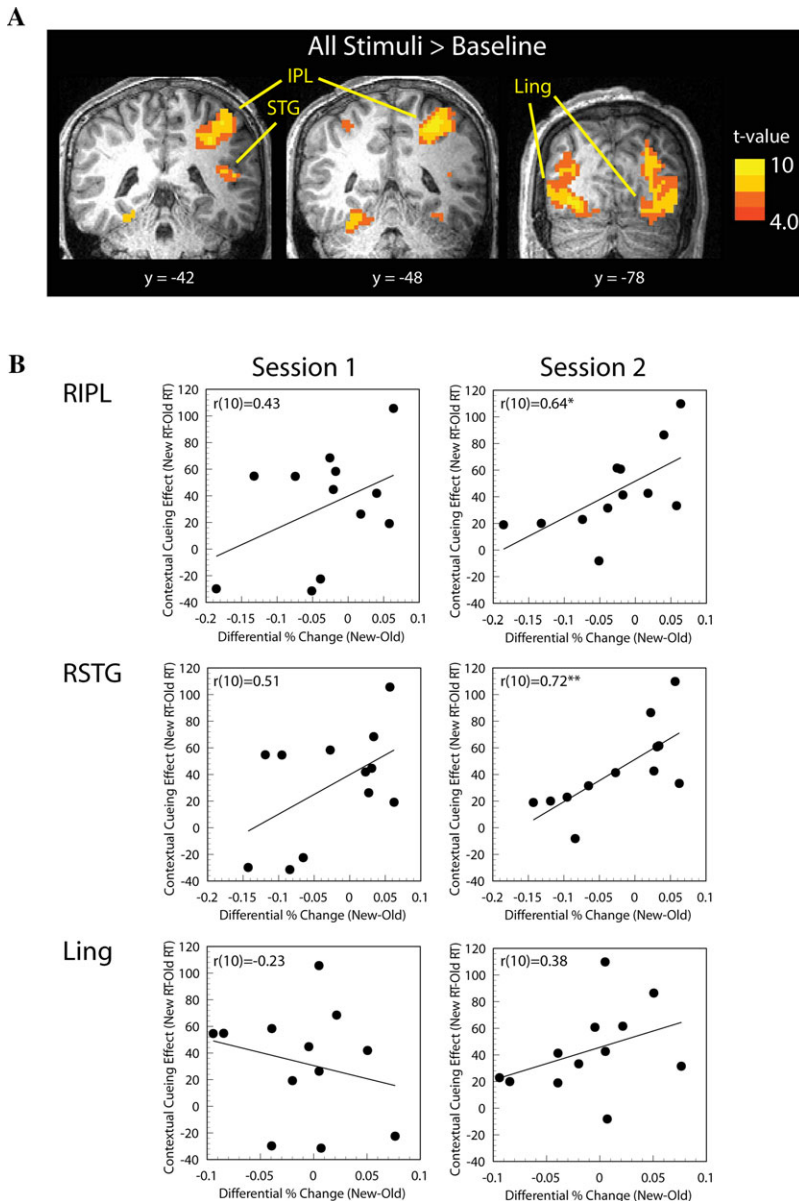


Figure 4. (A) Inferior parietal lobe (IPL), superior temporal gyrus (STG), and lingual gyrus (Ling) clusters exhibiting significant activations compared to baseline ($P < 0.05$, corrected). (B) Correlation between the old–new difference in IPL, STG, and Ling BOLD responses and the behavioral contextual cueing effect in Sessions 1 and 2. ** $P < 0.05$, FDR—corrected for multiple comparisons; * $P < 0.05$, uncorrected.

0.97 in Session 1 and 0.98 in Session 2 ERP responses. Second, the same sources were used to explain the difference between old and new N2pc ERP components. The average explained variance in the N2pc time range across subjects was 0.77 for Session 1 and 0.70 for Session 2. The mean proportion of explained variance is shown in Figure 5A.

To determine the relative contribution of each dipole source to the explained variance of the N2pc model, we conducted an additional analysis that measured the change in the explained variance when each source was removed from the model (see Methods). The mean relative contributions are shown in Figure 5B. When compared to a random per-

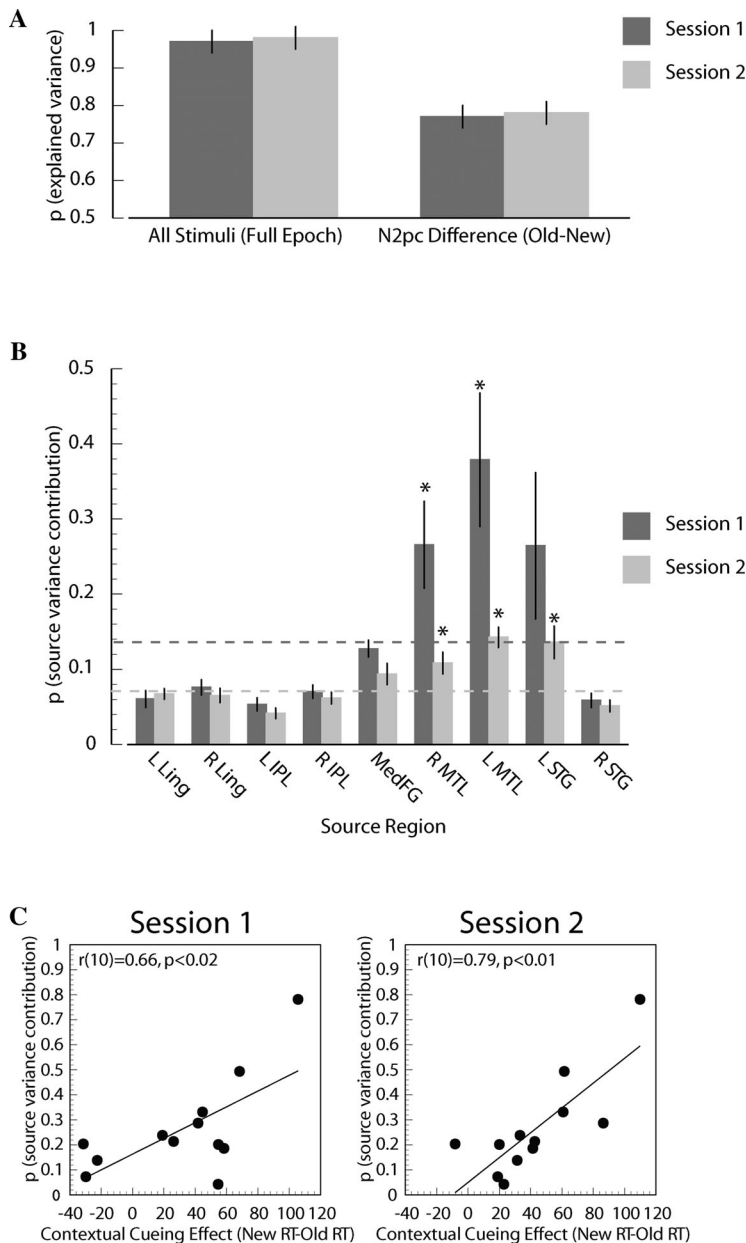


Figure 5. (A) The proportion of variance explained by the fMRI-seeded source models of the stimulus-evoked response and the old–new difference in N2pc amplitude. (B) The proportion of explained variance contributed by specific sources. Dotted lines indicate the proportion of variance explained after random permutation in Session 1 (dark line) and Session 2 (light gray). *Difference from random permutation, $P < 0.05$. L/R, left/right; Ling, lingual gyrus; IPL, inferior parietal lobe; MedFG, medial frontal gyrus; MTL, medial temporal lobe; STG, superior temporal gyrus. (C) Correlation between the proportion of variance explained by the rMTL and the behavioral contextual cueing effect in Sessions 1 and 2.

mutation of the existing source variance (Session 1: $M = 0.11$, $SEM = 0.02$; Session 2: $M = 0.07$, $SEM = 0.01$), the only seeded sources that showed a significant contribution to the head model in Session 1 were the left and right MTL, both $t(11) >$

2.59, $P < 0.03$. Although the contributions were lower overall in Session 2, the left and right MTL, along with the right STG, were the only sources with a significant contribution (all $t(11) > 2.41$, $P < 0.04$).

Table 1. The coordinates and statistics for the local maxima from the contrasts of all stimuli

Contrast	Region	X	Y	Z	T	Cluster size
Base > Stim	^a MTL	-30	9	-21	8.47	22
	Postcentral gyrus	-15	-45	72	6.58	47
	Posterior cingulate	6	-54	6	5.57	80
	Precuneus	-12	-81	39	5.46	30
	Frontal lobe	-21	30	39	5.28	34
	MTL (parahippocampus)	24	-6	-18	5.03	17
Stim > Base	^a IPL	30	-48	48	10.86	1988
	^a Lingual gyrus	-30	-78	-9	10.49	923
	Cerebellum	-21	-63	-45	7.88	24
	^a Sup temp gyrus	42	-42	15	7.39	183
	^a Sup frontal gyrus	3	3	54	6.63	88
	Insula	42	-6	6	6.12	15
	Med front gyrus	-48	0	42	5.78	104
	Inf front gyrus	51	3	36	5.68	15
	Sup temp gyrus	-63	-33	6	5.31	18
	Thalamus	18	-27	6	5.26	32
	Sup temp gyrus	-54	-15	6	4.98	15
	Midbrain	6	-27	-3	4.79	15

^aAsterisks indicate the regions used for the EEG source analysis.

Abbreviations: MTL, medial temporal lobe; sup, superior; inf, inferior; med, medial; front, frontal; temp, temporal.

We additionally assessed the extent to which individual variations in N2pc source contributions were related to the behavioral contextual cueing effect. The right MTL contribution was correlated with individual differences in contextual cueing in both sessions (Session 1: MTL: $r(10) = 0.66$, $P < 0.02$; Session 2: $r(10) = 0.79$, $P < 0.01$). Specifically, individuals with higher source contributions exhibited larger cueing effects, both within the same session and even 1 week later. The same was true for the STG (Session 1: $r(10) = 0.61$, $P < 0.04$; Session 2: STG: $r(10) = 0.76$, $P < 0.01$). Finally, individuals with higher left IPL source contributions had larger cueing effects, but only in Session 2 ($r(10) = 0.74$, $P < 0.01$).

Discussion

The purpose of this study was to investigate the link between memory and attention during search cued by context by addressing two questions: (1) To what extent are contextual modulations of the MTL measured with fMRI related to the contextual modulations measured with behavior both in the short- and long term? and (2) To what extent does the link between the search-related regions revealed

by fMRI and the contextual modulations measured with EEG explain the short- and long-term behavioral benefits of context?

MTL-behavioral correlations

Consistent with previous studies,^{14–16} we found that the old–new difference measured in the right MTL correlated with individual differences in the Session 1 behavioral contextual cueing effect. The novel finding was that MTL activity was also correlated with the contextual cueing effect observed 1 week later (Session 2). This finding may reflect the role of the MTL in the formation of associations early in learning—something that has also been observed in other tasks.^{51,52} The correlation with Session 2 behavior suggests that the MTL is also involved in the later expression of spatial context associations.

It is important to point out that the findings reported here are inconsistent with studies that have failed to find evidence for hippocampal involvement in implicit contextual memory.^{11–13} One potential reason for the conflicting evidence may be methodological: previous failures have typically assumed a canonical hemodynamic response function during analysis, which may be problematic.¹⁶

Another potential reason is theoretical: perhaps the traditional accounts proposing that the MTL and hippocampus mediate explicit declarative memory⁹ need to be revised in favor of a model in which the MTL integrates existing and new representations, both implicit and explicit.^{53,54} If true, the role of the MTL and hippocampus in contextual cueing may be to integrate the associations of target–distractor spatial configurations independent of awareness.¹⁶

Linking memory and attention using fMRI–EEG integration

The motivation of the multimodal imaging approach was to make a more direct link between the neural systems involved in memory measured with fMRI and contextual modulations of an ERP component commonly associated with attentional selection of a target among distractors (i.e., the N2pc). The key findings from the multimodal imaging data revealed that the MTL regions were the highest source contributors to the N2pc component from both sessions, and this level of contribution from the right MTL in Session 1 was directly related to the behavioral contextual cueing effect. This result not only provides evidence that the MTL is related to an ERP index of visual attention, but also that the efficacy of this MTL contribution to the N2pc contextual modulation is predictive of the eventual behavioral benefits owing to context. These findings are similar to those from a magnetoencephalographic (MEG) phase-locking study of object context that showed MTL activity linked to visual cortex activity within 200 ms.⁵⁵ Overall, these results fit well with the interpretation that the MTL memory system is activated by repeated contexts and interacts with visual attention to facilitate search.^{6,7,16,56}

The evidence reported here is consistent with the notion that the contextual cueing phenomenon is mediated by the interaction between the neural systems that support long-term memory, including the hippocampus, and the neural systems involved in attentional selection.^{55,57} However, there are three caveats that must be noted. First, although the multimodal imaging data demonstrated a relationship between attention and memory systems in contextual cueing, unequivocal conclusions about the direction of the relationship cannot be made. Second, the lack of a robust N2pc component in Session 1

is potentially problematic. Our control analysis revealed that RT variability was associated with the magnitude of the N2pc, suggesting that there was an N2pc present in Session 1, but that search variability at the individual level was masking the N2pc effects observed at the group level. Importantly, because the seeded-source modeling was done at the individual level, the analyses should be sensitive to small modulations of the N2pc present at the individual level that were not observed at the group level. Third, the behavioral effect of set size did not interact with the effect of context. This contrasts previous studies suggesting that context can change search slopes⁵ and may qualify the strength of the conclusion that attentional function is modulated by context. Nevertheless, the N2pc enhancement in Session 2 suggests that a neural index of attentional selection is modulated by context.

Conclusion

We report three key findings. First, when searching for targets embedded in repeated spatial configurations, BOLD modulations in the MTL—including in the hippocampus—observed during the early stages of learning are correlated with the behavioral benefits of context both in the short term (within session) and at distal points in time (1 week later). Second, relative to sources in parietal, frontal, and visual cortices, a dipole source positioned in the MTL explained the most variance in the contextual modulation of the N2pc ERP component and, again, this relationship is present both in the short term and at distal points in time. Finally, individual differences in the MTL contribution to contextual modulation of the N2pc were also correlated with the behavioral contextual cueing effect and, yet again, this correlation was present both in the short term and at distal points in time. Taken together, the links between fMRI, EEG, and behavior reported here, and the extant empirical evidence,^{6,14–17,24} provide strong support for the notion that both hippocampus-mediated memory and attentional selection processes are involved in the implicit learning of spatial configurations during search.

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Conflicts of interest

The authors declare no conflicts of interest.

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