

Independence of Anticipatory Signals for Spatial Attention From Number of Nontarget Stimuli in the Visual Field

C. Sestieri,^{1,2,3} C. M. Sylvester,⁴ A. I. Jack,³ G. d'Avossa,³ G. L. Shulman,³ and M. Corbetta^{1,2,3,4,5}

¹Department of Clinical Sciences and Bioimaging, G. d'Annunzio University and ²Institute for Advanced Biomedical Technologies, G. d'Annunzio University Foundation, Chieti, Italy; and ³Department of Neurology, ⁴Department of Radiology, and ⁵Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, Missouri

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Sestieri C, Sylvester CM, Jack AI, d'Avossa G, Shulman GL, Corbetta M. Independence of anticipatory signals for spatial attention from number of nontarget stimuli in the visual field. *J Neurophysiol* 100: 829–838, 2008. First published June 11, 2008; doi:10.1152/jn.00030.2008. Covertly attending to a location modulates the activity of visual areas even in the absence of visual stimulation. These effects are widespread, being found in the cortical representations of both attended and unattended portions of the visual field. It is not clear, however, whether preparatory modulations depend on subjects' expectation regarding the presence of additional nontarget stimuli in the visual field. Here, we asked subjects to endogenously direct attention to a peripheral location in the upper visual field, to identify the orientation of a low-contrast target stimulus, and we manipulated the number and behavioral relevance of other low-contrast nontarget stimuli in the visual field. Anticipatory (i.e., prestimulus) blood oxygenation level–dependent (BOLD) signal increments in visual cortex were strongest at the contralateral attended location, whereas signal decrements were strongest at the unattended mirror-opposite ipsilateral location/region of visual cortex. Importantly, these strong anticipatory decrements were not related to the presence/absence of nontarget low-contrast stimuli and did not correlate with either weaker target-evoked responses or worse performance. Second, the presence of other low-contrast stimuli in the visual field, even when potential targets, did not modify the anticipatory signal modulation either at target or nontarget locations. We conclude that the topography of spatial attention–related anticipatory BOLD signal modulation across visual cortex, specifically decrements at unattended locations, is mainly determined by processes at the cued location and not by the number or behavioral relevance of distant low-contrast nontarget stimuli elsewhere in the visual field.

INTRODUCTION

Spatial attention helps to reduce the high perceptual load that the brain's limited resources must deal with in every day vision. Behaviorally, covert spatial attention improves perception at an attended location relative to other locations in the visual field (e.g., Posner et al. 1980). Correspondingly, sensory-evoked neural activity in cortical regions representing attended locations is increased, whereas neural activity corresponding to unattended locations is decreased (Pinsk et al. 2004; Somers et al. 1999; Tootell et al. 1998).

Recent evidence suggests that covertly directing visuospatial attention to an upcoming stimulus location generates prestimulus (hence preparatory or anticipatory) activation of the portion of visual cortex representing the attended location (Hopfinger et al. 2000; Kastner et al. 1999; Luck et al. 1997; Müller and

Kleinschmidt 2004; Ress et al. 2000; Serences et al. 2004; Silver et al. 2007; Sylvester et al. 2007); in parallel, coupled deactivation of regions of visual cortex corresponding to unattended locations of the visual field have also been reported (Müller and Kleinschmidt 2004; Silver et al. 2007; Sylvester et al. 2007). However, it remains unclear whether these spatial attention–related preparatory modulations in visual cortex (both activity increases and decreases) mainly reflect the selection of information at the attended location or, also, the presence and behavioral relevance of potentially distracting information elsewhere in the visual field (Ruff and Driver 2006; Serences et al. 2004).

Sylvester et al. (2007) recently showed that attending to a location in the visual field produces a characteristic topography of anticipatory modulation in visual cortex. Two visual stimuli—a target and a nontarget stimulus—were presented on each trial in the upper visual field, at mirror-opposite locations across the vertical meridian. Sylvester et al. examined preparatory activity across visual cortex when subjects were cued to expect with 75% likelihood that the target would appear in one of the two upper field locations and the nontarget in the other mirror-opposite location. Preparatory activity showed a large increase at the cued location, but a decrease at other unattended locations of the visual field, with a peak near the mirror-opposite noncued location that contained a nontarget on most trials. This result was surprising, given that the nontarget was distant from the attended location (in the opposite hemifield) and barely visible (very low contrast). An intriguing question raised by those findings is whether the topography of anticipatory modulation of visual cortex involves an intrinsic (endogenous) gradient of activity with relative increments at the attended location and decrements at the mirror-opposite location in the visual field/cortex.

Here we tested this hypothesis by manipulating the number of expected nontarget stimuli in the visual field and their behavioral relevance (i.e., the probability that they were targets). As in Sylvester et al. (2007), subjects were randomly cued to a left or right upper visual field peripheral location where a low-contrast target was likely to appear (75% of the time, valid trials). In different blocks, the valid target was presented either alone (zero nontarget ["zero-NT"] condition), with one low-contrast nontarget at the mirror-opposite location ("one-NT" condition, identical to Sylvester et al.), or with three low-contrast nontargets, one at the mirror-opposite location

Address for reprint requests and other correspondence: M. Corbetta, Washington University School of Medicine, Department of Neurology, P.O. Box 8111, 660 S. Euclid Ave., St. Louis, MO 63110 (E-mail: mau@npg.wustl.edu).

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and the other two in the left and right lower visual field at the same eccentricity as the target ("three-NT" condition). One critical comparison tests for differences in preparatory signals when subjects know in advance that the target will be presented alone or with other nontarget stimuli. If the gradient of preparatory activity does not depend on the presence of other nontarget stimuli, then similar anticipatory modulation should be observed in the "zero-NT" and "one-NT" conditions at the cued and mirror-opposite location. Conversely, if the gradient reflects knowledge of an upcoming nontarget stimulus, then we predict stronger deactivation at the unattended location in the "one-NT" than that in the "zero-NT" condition.

Another question is whether knowledge of upcoming target probability modulates the topography and strength of anticipatory modulation at attended and unattended locations. On 25% of trials the target was presented at noncued locations (invalid trials). In the zero-NT and one-NT conditions, the invalid target always appeared in the mirror-opposite location (25% probability) in the upper visual field. In the three-NT condition, invalidly cued targets could appear with equal probability (8.3%) at the mirror-opposite location and the other two locations in the visual field. Therefore a comparison of preparatory signals in the one-NT and three-NT conditions at the mirror-opposite location tests whether these anticipatory signals are modulated by a priori knowledge about target probability.

METHODS

Subjects

Five subjects (four females, age range 23–30 yr, mean 27.6 yr), all right handed, with no history of neurological illness and normal or corrected-to-normal vision participated in the study. Subjects gave informed consent following the guidelines of the human studies committee at Washington University School of Medicine. The first author was one of the subjects.

Task

Subjects performed a spatially cued orientation-identification task (Fig. 1). Each trial started with an auditory cue directing the subject's attention to one of two peripheral locations. The cue was the word *one* or *two*, which indicated, respectively, the upper left or right visual

field location at 5° eccentricity at a polar angle of $\pm 45^\circ$. The cue correctly indicated the target location on 75% of the trials (valid trials). Following a stimulus-onset asynchrony (SOA) of 6.192 s (20% of the trials), 8.256 s (20%), or 10.320 s (60%), one or more low-contrast visual stimuli were presented for 100 ms. Both target and nontarget stimuli were Gabor patches obtained by multiplying a sinusoid with a spatial frequency of 3.5 cycle-per-degree and a circular Gaussian envelope with SD of 0.3° and a radius of 1.0°. An auditory report cue that specified the target location was given simultaneously with the target. Subjects reported the target patch orientation (left tilt, vertical, right tilt) using a three-choice button device and were told to be as accurate as possible, whereas no specific instructions were given concerning response speed.

On valid trials, in the zero-NT condition only the low-contrast target stimulus was presented; in the one-NT condition an additional low-contrast nontarget stimulus was presented in the contralateral (mirror-opposite) upper field location; in the three-NT condition a nontarget was presented at the mirror location and symmetrical locations in left and right lower visual quadrants (5° eccentricity; $\pm 45^\circ$ polar angle). On invalid trials, in the zero-NT and one-NT conditions the invalid target was always presented in the upper location mirror-opposite the cued location, whereas in the three-NT condition, the invalid target was presented with equal probability in either of the three noncued quadrants of the visual field. Therefore in the three-NT condition, each of the three noncued locations contained a target with probability 0.083 versus 0.25 for the noncued upper field location in the zero-NT and one-NT conditions. A random intertrial interval of 2.064 s (33% of the trials), 4.128 s (33%), or 6.192 s (33%) followed target presentation.

The number of nontarget stimuli was blocked (i.e., constant over the run) and subjects were always aware of block type. In addition, subjects typically performed three to four consecutive runs of the same condition before switching to a different condition, to keep the display configuration constant and to allow the subject to implement a strategy for that specific configuration. Subjects performed 45 runs over 4 days, for a total of 450 trials for each condition. Each run lasted about 7 min and contained 30 trials.

Practice sessions and target parameters

Prior to test scans, participants performed two preliminary behavioral training sessions in the scanner, each consisting of 600 trials, in which the contrast of the stimuli was adjusted to yield an accuracy of 70% for valid trials in the one-NT condition. During the scans, task difficulty and subjects' performance were equalized by adjusting the orientation of the oblique targets.

Apparatus

Stimuli were presented with a Power Macintosh G4 computer (Apple, Cupertino, CA) using Matlab software (MathWorks, Natick, MA) with the Psychophysics Toolbox (Brainard 1997; Pelli 1997). Images were projected to the head of the bore of the scanner via a liquid crystal display (LCD) projector (Sharp LCD C20X) and viewed with a mirror attached to the head coil. A magnet-compatible fiber-optic key-press device recorded the subject's responses. Eye position was measured in four of five subjects (not subject 1, author CS) with an ISCAN ETL-200 system (ISCAN, Burlington, MA) to verify that fixation was maintained in the interval between cue and stimulus presentation.

Behavioral methods

Behavioral data were first analyzed using repeated-measure four-way ANOVAs with Cue side (left, right), Validity (valid, invalid), Number of nontarget stimuli (zero-NT, one-NT, three-NT), and SOA (6, 8, 10 s) as factors and subject performance as the dependent

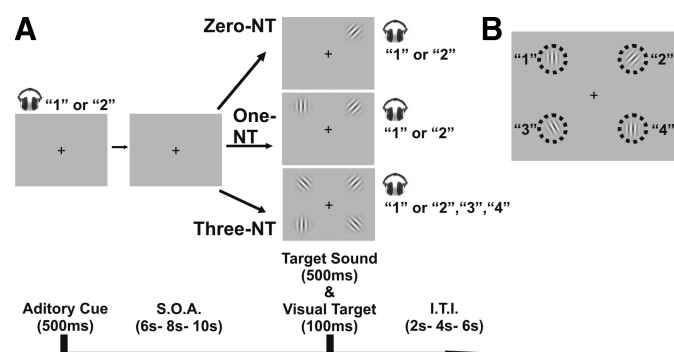


FIG. 1. The visuospatial attention task used in the practice sessions and the functional magnetic resonance imaging (fMRI) experiment. *A*: trial structure for the 3 versions of the task ("zero-NT," "one-NT," or "three-NT," where NT is nontarget). During the 2 practice sessions stimulus-onset asynchrony (SOA) was kept constant at 2 s, whereas in the fMRI task it varied among 6, 8, and 10 s. *B*: the association between spoken numbers and the peripheral locations where target or nontarget stimuli could have been presented.

variable. Separate analyses were performed for accuracy and reaction times. A subsequent analysis was confined to the data from the longest SOA (10 s) to be consistent with the functional magnetic resonance imaging (fMRI) analysis. Post hoc analyses were conducted using a two-tailed Duncan *t*-test.

Data acquisition

Images were acquired with a Siemens Allegra 3T scanner. Structural images were acquired using a sagittal MPRAGE T1-weighted sequence (TR = 1,810 ms, TE = 3.93 ms, flip angle = 12°, TI = 1,200 ms, voxel size = 1 × 1 × 1.25 mm). Blood oxygenation level-dependent (BOLD) contrast functional images were acquired with an asymmetric spin-echo echoplanar sequence (TR = 2,064 s, TE = 25 ms, flip angle = 90°, 31 contiguous 4-mm axial slices, 4 × 4-mm in-plane resolution).

Data analysis

The preprocessing and statistical analysis of fMRI data were performed using in-house software. The first four frames of each BOLD run were discarded from the analysis. Preprocessing included motion correction, within and between runs, and slice scan-time correction. Functional images were resampled at a voxel size of 3 × 3 × 3 mm and warped into a standardized atlas space (Talairach and Tournoux 1988). The BOLD responses for each voxel and subject were estimated independently using a general linear model (GLM). The regressors included a constant and a linear term, which accounted for baseline value and linear drift of the BOLD signal. Each event-related response was modeled using 11 to 13 delta functions, depending on SOA, starting with the cue onset. Separate regressors were used for each trial type [Number of nontarget stimuli (“zero-,” “one-,” “three-NT”) × SOA duration (6, 8, 10 s) × Cue side (left, right) × Validity (valid, invalid) × Accuracy (correct, incorrect)]. Individual subject data were then averaged across voxels within regions of interest (ROIs). Only trials with the longest SOA, which provided a sufficiently long duration to evaluate the evolution of the BOLD signal, were included in subsequent analysis.

Definition of regions of interest

ROIs in the visual cortex of each subject were defined using two passive localizers (Fig. 2). Five runs (5 min each) of a block paradigm with vertical and horizontal meridians were used to define borders of adjacent retinotopic areas in each hemisphere, in ventral (V1v, V2v, VP, V4) and dorsal (V1d, V2d, V3, V3a) visual cortex (Fig. 2A). Borders were hand-drawn on a flattened representation of each individual brain based on the contrast maps between horizontal and vertical meridian epochs, using Caret 5.3 software (Van Essen et al. 2001).

ROIs of the portion of visual cortex activated by the stimulus—eight runs (5 min each) of a passive block localizer—were included in which a single flickering (4 Hz) high-contrast Gabor patch (2° width) was presented for 12 s in each of the four possible target or nontarget stimulus locations in the main task (Fig. 2B). We also stimulated a foveal location with a central Gabor patch (1° width). We created contrast maps by comparing responses to each stimulus location, modeled by convolving a canonical hemodynamic response function with a square waveform of the stimulus duration, to the average responses to the other locations. ROIs for each visual area in each hemisphere were obtained by the conjunction of the active voxels defined by retinotopy and localizer maps (Fig. 2C). However, in the analyses subsequently discussed in RESULTS, the ROI corresponding to a stimulus location did not differentiate between different visual areas (e.g., V1, V2, etc.). Instead the regions of the different visual areas representing a stimulus location were combined into a single ROI.

BOLD time course analysis

For the analysis of preparatory activity (cue period only) BOLD signal change was estimated over the first six time points of regional individual trial time courses, corresponding to the entire preparatory period for the longest SOA. For the analysis of stimulus-evoked activity (target period only), BOLD signal was estimated over the subsequent seven time points corresponding to the entire target period. Cue and target period time courses were analyzed using repeated-measure ANOVAs in which the subject was treated as a random effect. ANOVAs of the cue period data included Number of nontarget stimuli (zero-NT, one-NT, three-NT), Hemisphere (left, right), Cue direction (contra, ipsi), Region (dorsal, foveal, ventral), and Time (time points 1–6) as factors, whereas ANOVAs of the target period data included Number of nontarget stimuli, Region, and Time (time points 7–13) as factors.

Predictive analysis

A procedure was developed to assess, on a trial-by-trial basis, how accurately BOLD preparatory activity covaries with cued location. This requires estimating the BOLD signal associated with left and right cues separately in each trial. Since the fast event-related design causes significant overlap in the BOLD signal for different events within a trial and across subsequent trials, it was not possible to exploit the same GLM that was used for the time course analysis.

Instead a three-step strategy was adopted. The first step was to remove all known sources of variability from the BOLD time series, with the exception of variability due to the locus of attention in the preparatory period of trials involving the longest SOA. A GLM was specified that included separate regressors for cue- and target-evoked responses and did not include separate regressors for the cued location. For the cue response, separate regressors specified the SOA, the number of expected stimuli, and the cued location (cued location only

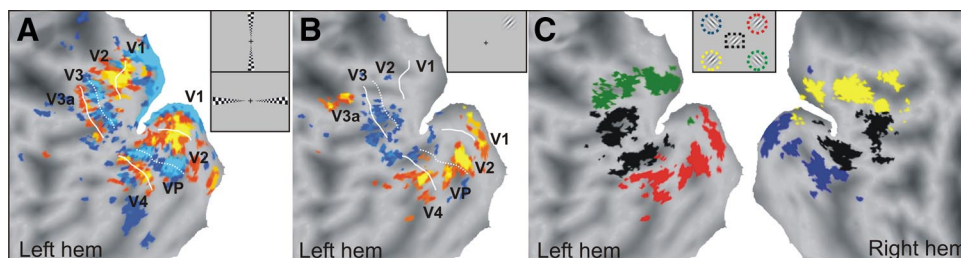


FIG. 2. Regions of interest (ROIs) in the visual cortex. A: the result of the retinotopy scans is superimposed on the flattened left hemisphere surface of a representative subject. The stimuli (vertical and horizontal meridians) used to obtain borders of visual areas are shown in the top right corner. B: an example of the results from the localizer scan in the same subject, which illustrates the portion of the ventral visual cortex of the left hemisphere activated by the presentation of a flickering high-contrast patch in the upper right visual field. C: the definition of the 3 ROIs in each hemisphere. The different colors correspond to the different peripheral locations in the visual field.

for trials with SOA of 6 and 8 s). For the target response, separate regressors specified Target location, Validity, and Number of peripheral stimuli.

Second, a residual data set was calculated, subtracting the estimated mean effects from the BOLD data. These residual BOLD data contained only systematic BOLD signals related to cue direction on the long SOA trials and variable signals that could not be further removed. We then averaged the time-point by time-point residual data set across the voxels within each ROI corresponding to stimulus location.

Third, this regional data set was entered into a further GLM in which each individual trial cue-evoked response was modeled as a separate event. The BOLD response for each cue was modeled as a scaled version of a particular waveform (the average difference in preparatory activity for left and right cues in the one-NT condition calculated in the standard time course analysis). To prevent any bias in the assessment of predictability, we considered only those trials belonging to the zero-NT and three-NT conditions. The larger the magnitude of this predictor in any zero-NT or three-NT trial, the more likely a left cue was presented on that trial.

We also derived trial-by-trial magnitudes for the difference in activity between homologous ROIs in opposite hemispheres. The time-point by time-point residuals of the right-hemisphere region were subtracted from the time-point by time-point residuals of the left-hemisphere region. Magnitudes were derived from this data set as from individual ROIs, as described earlier.

The overlap between the distributions of the BOLD response magnitudes evoked by leftward and rightward cues was assessed using a receiver-operator-characteristic (ROC) curve. To obtain the ROC curve, the conditional probabilities $P(\alpha > \text{crit} | R_{\text{left}})$ and $P(\alpha > \text{crit} | R_{\text{right}})$ were evaluated as a function of crit, where α is the derived magnitude (i.e., the magnitude calculated using the predictor time course), R_{left} indicates the subset of trials with leftward cues, and R_{right} is the subset of trials with rightward cues.

RESULTS

Behavioral results

Subjects attended to the upper field location indicated by the auditory spatial cue. Subjects were faster [$F(1,4) = 41.74$; $P < 0.005$] and more accurate [$F(1,4) = 8.393$; $P < 0.05$] during valid trials compared with invalid trials, indicating that they attended to the cued location. No interaction between the length of the cue–target interval period and any other task factor was observed, suggesting that attention was maintained at the target location throughout the cue–target interval.

Since our analyses focused on trials with the longest cue–target interval, we analyzed the behavioral data from this subset of trials separately (see Fig. 3).

The size of the validity effect increased as a function of the number of nontarget stimuli, as revealed by a significant two-way interaction of the Number of nontarget stimuli \times Validity for reaction times [$F(2,8) = 8.61$; $P < 0.01$]. A similar trend was observed for Accuracy [$F(2,8) = 3.82$; $P = 0.068$]. This effect was driven largely by invalid trials because the number of nontarget stimuli affected accuracy [$F(1,4) = 6.05$; $P < 0.05$] and reaction times [$F(1,4) = 13.82$; $P < 0.005$] on invalid trials but not on valid trials.

Therefore the presence or absence of low-contrast nontarget stimuli was irrelevant to the selection of validly cued visual stimuli. However, the number of nontarget stimuli influenced performance for invalidly cued targets. In other words, subjects were slower at reorienting attention from an incorrectly cued

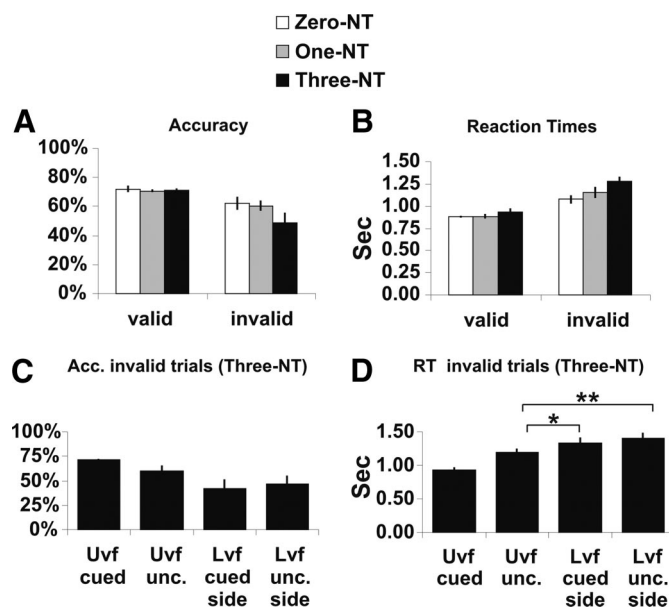


FIG. 3. Behavioral performance, averaged across the 5 subjects, for the 3 experimental conditions. Accuracy (A) and reaction times (B) for valid and invalid trials calculated using only trials with the longest SOA that were used for the fMRI statistical analysis. Accuracy (C) and reaction times (D) for valid trials (Uvf cued) and invalid trials presented at the other upper field location (Uvf unc.), at the lower field location of the cued side (Lvf cued side), and, finally, at the lower field location of the uncued side (Lvf unc. Side), for the “three-NT” condition only. Vertical bars represent SEs. * $P < 0.05$; ** $P < 0.01$. Lvf, lower visual field; Uvf, upper visual field; unc., uncued.

location when nontarget stimuli were present in the visual field. This effect may relate to the potentially distracting effect of nontarget stimuli or be related to probability uncertainty concerning target location. For instance, in the zero-NT and one-NT conditions only the mirror-opposite location could contain an invalid target, whereas in the three-NT condition the target could be presented in any of the unattended quadrants. Although report cues (in our case an auditory cue at the time of target presentation) are typically used to eliminate location uncertainty, we cannot rule out the possibility that the relative slowing in reorienting was due to the need to monitor three potential target locations instead of one.

We tried to address the issue of target location uncertainty by restricting the analysis to the zero-NT and one-NT conditions. In these conditions location uncertainty was matched because subjects knew that in the case of an invalid spatial cue the target would necessarily occur at the mirror-opposite location in the upper visual field. Interestingly, we still observed an interaction effect for reaction time between number of nontarget stimuli and validity [$F(1,4) = 8.01$; $P < 0.05$, three-way ANOVA (Cue side \times Validity \times Number of peripheral stimuli)], with slower reorienting when two stimuli (one target, one nontarget) were presented during an invalidly cued trial. However, even this result could reflect differences in the information available to reorient attention rather than the distracting effect of nontarget stimuli. As suggested by a reviewer this delay may reflect faster reorienting to the sudden onset of the target at the uncued location in the absence of competing nontarget stimuli in the visual field, or the need to rely on the auditory report cue to decide whether the target at the cued location was valid, or the delay necessary to disengage attention from the invalidly cued location.

Finally, in the three-NT condition, there was a significant difference in reaction times for invalid targets at the different uncued locations [$F(2,8) = 8.63$; $P < 0.01$] (see *bottom panel* of Fig. 3). Subjects were significantly faster for the invalid upper field location relative to the lower field locations on the cued ($P < 0.05$) and uncued sides ($P < 0.01$, Duncan post hoc t -test).

To summarize, subjects made use of the spatial cue, with more accurate and faster performance for valid compared with invalid trials. Increasing the amount of additional nontarget (low-contrast) stimuli did not affect the initial distribution of attention, as evidenced by the null effect of number of peripheral stimuli on identifying the orientation of valid targets, but did affect the reorienting of attention, as evidenced by poorer performance on invalid trials with the increase in the number of peripheral stimuli. However, this result could be also explained by increased uncertainty about the target location. In addition, on invalid trials, subjects appeared to preferentially shift to the unattended location in the upper visual field, as evidenced by significantly better performance at that location relative to other uncued locations.

Distribution of preparatory activity in visual cortex is independent of distant low-contrast nontarget stimuli

The primary question was whether the topography and strength of preparatory signals across visual cortex were influenced by knowing that additional stimuli would be presented at nontarget locations in the visual field, as well as the probability that these peripheral locations would become behaviorally relevant on invalid trials. We first characterized preparatory BOLD modulations across visual cortex, collapsing across the zero-NT, one-NT, and three-NT conditions. Figure 4 illustrates the time course of the BOLD signal over the whole trial (cue and target periods) for valid correct trials from the portions of visual cortex that represent the lower (*top row*), foveal (*middle row*), and upper visual field (*bottom row*) locations. Although we display the time course for the whole trial, all statistical analyses focus on the prestimulus, preparatory signals, which reflect purely endogenous signals.

As expected on the basis of previous data (Hopfinger et al. 2000; Kastner et al. 1999; Müller and Kleinschmidt 2004; Ress et al. 2000; Silver et al. 2007; Sylvester et al. 2007), activity was higher in the regions corresponding to the upper visual field locations when that portion of cortex was attended as compared with unattended [upper right location: $F(1,4) = 19.565$; $P < 0.01$; upper left location: $F(1,4) = 39.034$; $P < 0.01$]. Moreover, the BOLD signal was not only increased above resting baseline at attended locations, but was also decreased beneath resting baseline at unattended locations (compare black and gray curves in the *bottom panel* of Fig. 4).

The pattern of preparatory activity modulation across visual cortex did not depend on whether subjects expected none, one, or three additional peripheral stimuli [Number of nontarget stimuli, $F(2,8) = 0.627$, $P = \text{n.s.}$; Number of nontarget stimuli \times Region, $F(6,24) = 0.065$, $P = \text{n.s.}$]. Figure 5 illustrates signal time courses of preparatory activity across these three conditions in each of the four portions of visual cortex representing the locations of potential stimuli. Note the consistency of the cue signal from any individual region in the “zero-NT” (*left*), “one-NT” (*middle*), and “three-NT” (*right*)

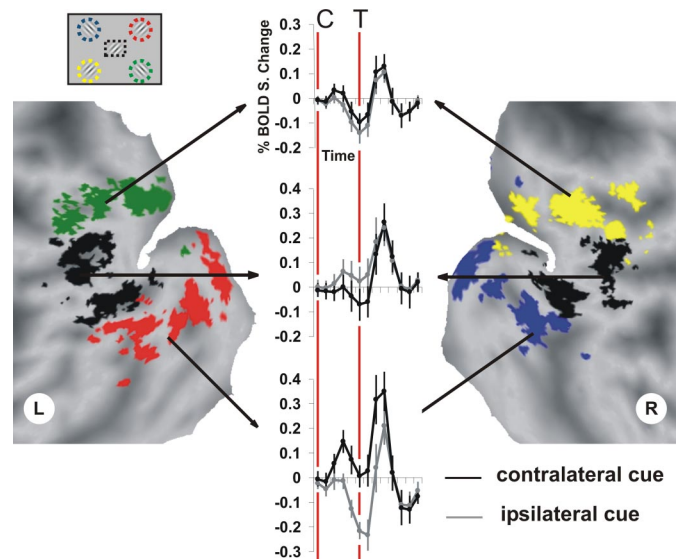


FIG. 4. Average blood oxygenation level-dependent (BOLD) signal time courses corresponding to the 13 time points following cue onset during valid correct trials with the longest SOA (10 s). Time courses were extracted from the ROIs representing the 4 possible target locations plus a foveal location, independently identified by the localizer. The 3 ROIs in the left and right hemispheres are highlighted in different colors and superimposed on the flattened hemisphere surfaces of a representative subject (located in the left and the right sides of the picture). Region colors correspond to the specific peripheral locations, illustrated above the left hemisphere representation. For display purposes, time courses have been collapsed for the different display conditions and left and right hemisphere ROIs. The two red vertical lines represent cue and target onset, respectively. Time courses from dorsal cortical regions (indicated by green and yellow areas on the flattened surface), corresponding to the lower visual field locations, are displayed in the *top row*. Ventral cortical regions (red and blue areas), corresponding to the upper visual field locations, are displayed in the *bottom row*. Time courses from ROIs representing the foveal regions (black areas) are shown in between. Black and gray time courses indicate BOLD responses for contralateral and ipsilateral cues, respectively. Vertical bars of the time courses represent SEs.

conditions. These results indicate that the distribution of preparatory activity across visual cortex did not depend on expectations concerning the presence of additional peripheral stimuli. It also did not depend on the likelihood that a noncued location contained a target, since there was no difference in preparatory activity in the upper field peripheral location in the one-NT condition (probability = 0.25) versus the three-NT condition (probability = 0.08). To test the robustness of these findings, the analyses were also conducted using all trials (valid, invalid, correct, and incorrect) rather than only valid correct trials. The same results were obtained.

The previous analysis concentrated on the mean effects of cue direction on the preparatory BOLD response. However, it is possible that the number of additional peripheral stimuli affected trial-to-trial variations in the cue-evoked response. To determine whether the number of nontarget stimuli had any effect on the variability of the cue evoked response, we estimated the cue-evoked response on a trial-by-trial basis and computed how accurately the BOLD signal reflected the cue instruction to attend to the upper left or the upper right target. ROC analysis showed that preparatory activity in the upper field location was equally reliable in indicating the location cued in the zero-NT (mean = 0.64 ± 0.05) and the three-NT (mean = 0.62 ± 0.02) conditions [$t = 1.429$, $P = \text{n.s.}$; two-tailed paired-sample t -test, Table 1, last row].

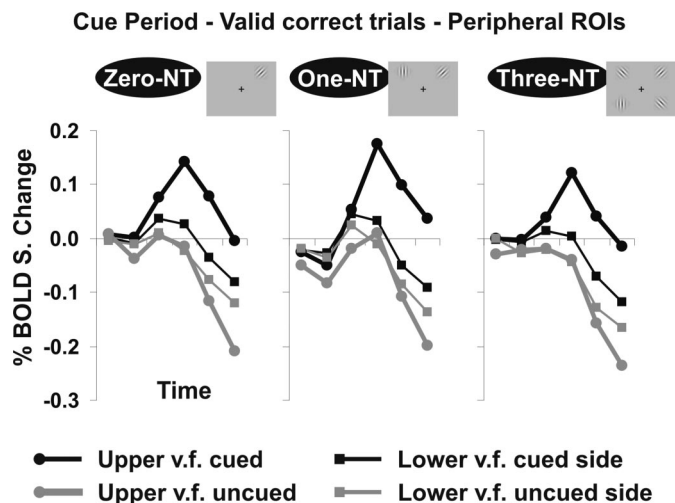


FIG. 5. BOLD signal time courses (valid correct trials only) during the preparatory period from the 4 peripheral ROIs [upper visual field (v.f.) cued location (thick black line), upper v.f. uncued (thick gray line), lower v.f. on the cued side (thin black line), and lower v.f. location on the uncued side (thin gray line)], each of the 3 display conditions displayed separately. The time courses from the 2 hemispheres are collapsed.

We conclude that preparatory activity does not depend on the number of expected low-contrast nontarget stimuli. This result is consistent with the behavioral finding that increasing the number of peripheral stimuli had no effect on task performance during valid trials [see also Doshier and Lu (2000) for a similar result]. Thus both behavioral and neuroimaging findings suggest that the expected number of low-contrast peripheral stimuli does not affect the preparatory orienting of spatial attention.

Preparatory activity is most suppressed mirror-opposite the attended location

Although the pattern of preparatory activity across visual cortex did not depend on the presence or absence of upcoming additional nontarget stimuli, the magnitude of preparatory activity varied significantly across the regions representing the different unattended locations [main effect of region, $F(2,8) =$

4.58, $P < 0.05$; Region \times Time, $F(10,40) = 4.021$, $P < 0.001$]. Preparatory BOLD activity was highest in the regions representing the attended location (thick black curve, Fig. 5) and lowest in the two regions representing locations in the opposite field (gray curves, Fig. 5).

Statistical tests confirmed that preparatory activity was significantly lower in the region representing the location mirror-opposite the attended location compared with the location in the ipsilateral [Region \times Time, $F(5,20) = 4.682$, $P < 0.005$] and the contralateral lower field location [Region \times Time, $F(5,20) = 2.922$, $P < 0.05$]. Furthermore, preparatory activity was significantly higher for the lower field location on the same side as the attended location compared with the other lower location [Region \times Time, $F(5,20) = 9.28$, $P < 0.001$].

Activity at the attended location was also more tightly linked with activity at the mirror-opposite location on a trial-by-trial basis. Recent work (Sylvester et al. 2007) demonstrates that the locus of spatial attention is best assessed as the difference in preparatory activity between locations in opposite hemifields. Figure 6 displays how well the difference in activity between locations in opposite hemifields indicated the locus of attention on a trial-by-trial basis (refer to Table 1 for individual values).

In the present data set, the difference in preparatory activity between the two upper field (mirror-opposite) locations better indicated the locus of attention, on a trial-by-trial basis, compared with the difference in activity between an upper field location and the lower field location in the opposite hemifield, both for the zero-NT condition ($P < 0.005$, two-tailed paired-sample t -test) and the three-NT condition ($P < 0.01$, two-tailed paired-sample t -test). This result did not depend on the number of expected nontarget stimuli, since a difference between conditions was never observed for any combination of signals (Table 1, bottom row).

Therefore the difference in activity between mirror-opposite locations best indicated the locus of attention regardless of whether subjects expected an additional peripheral stimulus to appear at the mirror-opposite unattended location. Because preparatory suppression was equal across the two locations in the opposite hemifield, this result suggests that trial-by-trial activity in mirror-opposite locations is more highly correlated than activity between nonhomologous locations. To summa-

TABLE 1. Cue direction predictive values

	Upper		Lower		Upper - Lower		Lower - Lower		Upper - Upper	
	Zero-NT	Three-NT	Zero-NT	Three-NT	Zero-NT	Three-NT	Zero-NT	Three-NT	Zero-NT	Three-NT
Subject 1	0.64	0.66	0.53	0.58	0.75	0.75	0.73	0.72	0.95	0.94
Subject 2	0.58	0.54	0.55	0.49	0.64	0.62	0.61	0.60	0.79	0.75
Subject 3	0.70	0.69	0.56	0.59	0.78	0.77	0.60	0.62	0.91	0.91
Subject 4	0.62	0.60	0.55	0.56	0.73	0.74	0.68	0.68	0.82	0.82
Subject 5	0.63	0.61	0.59	0.54	0.72	0.68	0.70	0.65	0.80	0.74
Mean	0.64	0.62	0.56	0.55	0.72	0.71	0.66	0.65	0.85	0.83
<i>P</i> value										
One-sample <i>t</i> -test	0.002	0.010	0.005	0.043	0.001	0.002	0.003	0.002	0.000	0.001
Paired <i>t</i> -test		n.s.		n.s.		n.s.		n.s.		n.s.

Predictive values calculated by ROC analysis, performed either for a single ROI or combining signals from different ROIs. The predictive value can be interpreted as the probability with which an ideal observer can predict the direction of the cue from the neural activity during the preparatory period. For each subject (rows), the different columns show values calculated for the "zero-NT" and the "three-NT" conditions for the single ROI representing the upper visual field locations, the single ROI representing the lower visual field locations, the subtraction of signals between ROIs representing the upper and the contralateral lower location, the subtraction between the two lower locations, and finally the subtraction between the two upper locations. The last two rows represent the probability associated with the one-sample t -test, testing the difference of the predictive value from chance level (0.5) and the probability associated with the paired t -test, testing differences between display conditions, respectively. n.s., not significant.

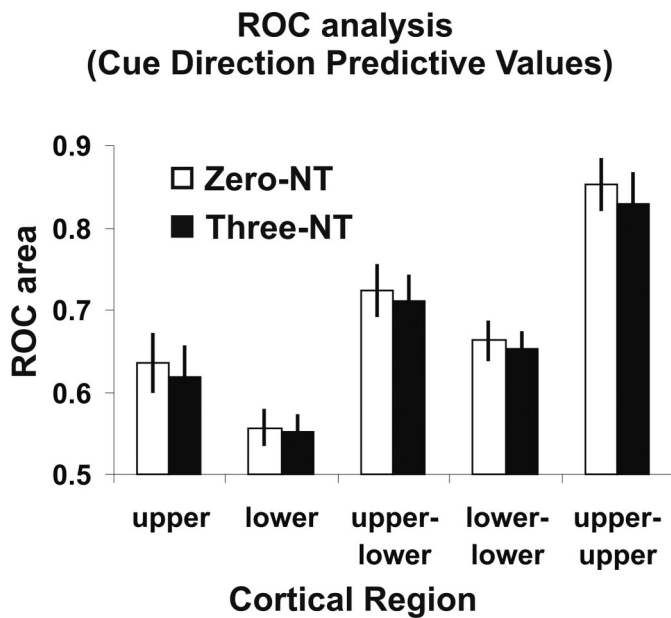


FIG. 6. Histogram of the receiver-operator-characteristic (ROC) values obtained in the predictive analysis of cue direction, “zero-NT” and “three-NT” conditions displayed separately. The bars correspond to (from the left): the single regions representing the upper v.f. locations, the single regions representing the lower v.f. locations, the subtraction of signals between regions representing the upper and the contralateral lower location, the subtraction between the 2 lower locations, and, finally, the subtraction between the 2 upper locations.

size, the time course and the predictive analysis indicated that the average and trial-to-trial suppression of the unattended location mirror-opposite to the attended location was not affected by the presence or amount of additional peripheral visual information.

Evoked activity for invalid targets depends on location

The behavioral results indicated that the number of nontarget stimuli had no impact on orienting of attention (valid trials), but that it did influence spatial reorienting of attention (as assessed by performance on invalid trials) because the response to invalidly cued targets appearing in the lower visual field was significantly slower than that for targets appearing in the upper field. Also, reorienting to an invalid target was slowest when the number of nontarget stimuli was largest. To study the neural correlates of spatial attention reorienting we studied target-evoked responses to invalidly cued targets in the different quadrants of visual cortex.

As shown in Fig. 7 activity was higher for invalid targets presented in the upper visual field compared with invalid target presented in the lower visual field. Consistent with the behavioral results, the BOLD signal target-evoked response in the three-NT condition was significantly different in the three visual ROIs corresponding to the three possible invalid locations [Region \times Time; $F(12,48) = 3.18$; $P < 0.01$]. In particular, at the signal peak (time point 3) the response was stronger in the region representing the upper field location compared with those representing the lower field locations ($P < 0.05$ and $P < 0.05$, respectively, two-tailed paired-sample t -test). This pattern of BOLD results in visual cortex is consistent with the slower reaction times to invalid targets pre-

sented in the lower field locations. Interestingly, across all possible target locations, the upper field location mirror-opposite to the attended location showed not only the largest preparatory deactivation during the cue period, but also the strongest stimulus-evoked response during target presentation.

Although target-evoked activity on invalid trials depended on the location of the target, it did not depend on the number of nontarget stimuli as confirmed by the lack of an interaction in a two-way repeated-measures ANOVA on the target responses with Number of nontarget stimuli (“zero-NT,” “one-NT,” “three-NT”) and Time (time points 7–13) as factors (Fig. 7). Therefore the decrease in performance at the upper field location on invalid trials as the number of peripheral stimuli increased was not reflected in the target-evoked response.

To summarize, both behavioral and neuroimaging results suggested that subjects preferentially reoriented their attention to the upper invalid location compared with the lower invalid location when the target was equally likely to occur in either location (three-NT condition). However, the invalid target response in the upper visual field did not depend on the number of nontarget stimuli.

DISCUSSION

Independence of anticipatory signals for spatial attention from number of nontarget stimuli in the visual field

Previous studies have reported that expecting a target at a peripheral location produces preparatory signal increases at the cued location (Hopfinger et al. 2000; Kastner et al. 1999; Luck et al. 1997; Müller and Kleinschmidt 2004; Ress et al. 2000; Serences et al. 2004; Silver et al. 2007; Sylvester et al. 2007) and decreases at unattended locations (Müller and Kleinschmidt 2004; Silver et al. 2007; Sylvester et al. 2007), including the location mirror symmetric of the opposite visual field. Moreover, the difference in response at cued and homologous uncued regions was highly predictive of the locus of attention when these responses were differenced (Sylvester et al. 2007). Our results confirmed these previous reports.

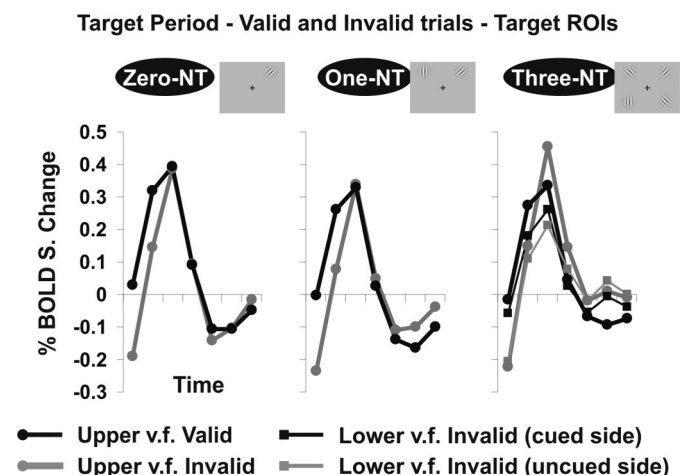


FIG. 7. BOLD signal time courses evoked by valid (thick black line) and invalid (thick gray line) target presentation from the corresponding ROIs representing the upper v.f. locations, in the 3 conditions. BOLD signal time courses evoked by invalid targets presented at lower v.f. locations (“three-NT” condition) obtained in the corresponding ROIs [lower v.f. location in the cued side (thin black line) and lower v.f. location in the uncued side (thin gray line)]. The time courses from the 2 hemispheres are collapsed.

We also found that the magnitude and spatial extent of preparatory BOLD signals in visual cortex, including signals at cued and uncued locations, were unchanged by whether subjects expected no, one, or three additional peripheral stimuli. Critically, BOLD decreases at the upper unattended location, which was homologous to the cued location, was independent of whether a peripheral stimulus was likely to appear at that location, indicating that the signal decrease at that location observed here and in Sylvester et al. was not caused by the expected presence of a nontarget stimulus. Similarly, the trial-to-trial predictability of the difference signal between the cued and homologous uncued location was also independent of the expected presence of a peripheral stimulus at the uncued location. Furthermore, preparatory signals were the same in regions of visual cortex representing both lower-field locations, irrespective of whether they were highly likely to contain a peripheral stimulus (three-NT condition, 91.7% of trials) or never contained a peripheral stimulus (zero-NT and one-NT conditions). Thus subjects appeared to allocate attention in the same manner across the visual field irrespective of whether or where additional peripheral stimuli might be presented along with the target. The observed invariance in preparatory signals was consistent with the invariance in task performance at the cued location. We also found that the probability that a non-cued location would contain a target did not affect preparatory signals. The same preparatory activity was observed at the mirror-opposite uncued location when the probability of a target at that location was 25% (zero-NT and one-NT conditions) or 8.3% (three-NT condition).

These results suggest that the spatial distribution of baseline signals generated by spatial attention is sometimes inflexible and is predominantly determined by the most likely stimulus location. Preparatory signals showing decrements at uncued locations may not reflect active suppression of potentially distracting information, but rather local or intrinsic mechanisms dependent on the selection of the attended location (see following text). This conclusion must be qualified by the observation that preparatory signals do reflect distracting stimuli when they are expected to be near the attended location (Serences et al. 2004). In our experiment the presence of distant low-contrast additional stimuli had an effect only on invalid trials, and further research is required to investigate the modulation of preparatory signals with adjacent or high-contrast distracters. Ruff and Driver (2006) reported that knowing that a distant high-contrast distracter would be presented in the visual field produced anticipatory activity *increases* in occipital cortex contralateral to the expected distracter. However, since these modulations were not shown to occur in retinotopically appropriate regions, they are difficult to compare with the signals described here, which were retinotopically specific.

Although varying the expected number of peripheral stimuli did not affect performance at the cued location, it had a very strong effect on performance at uncued locations. Performance on invalid trials decreased with the number of peripheral stimuli in the visual field. It has to be noted that this result could be explained by increased uncertainty about target location, even if it is observed when comparing conditions that share the same number of possible target locations.

The invariance of preparatory signals with the number of expected peripheral stimuli, noted earlier, indicates that the behavioral effect of the number of peripheral stimuli on invalid

trials was not caused by the spatial distribution of preparatory signals. This conclusion is bolstered by the fact that performance for invalid targets was best at the mirror location in the upper visual field, even though preparatory signals at that location showed the largest deactivation.

Visually evoked activity for invalid targets followed a pattern similar to that of the behavioral results, with the strongest response (even larger than for valid targets) to the invalid target at the mirror location in the upper visual field. Therefore whereas the expected number of peripheral stimuli did not influence preparatory processes, it did influence signals during the target period, most likely by affecting stimulus-driven reorienting of attention to unattended locations.

Mechanism underlying the allocation of spatial attention

The most straightforward interpretation of the present results is that attentional modulations result from a hemispheric competition that particularly affects portions of cortex representing the attended and mirror-opposite unattended location. Models of interhemispheric competition have been developed to explain the effect of neuropsychological syndromes such as neglect, in which spatial attention is biased toward the hemifield located ipsilateral to the lesion (Corbetta et al. 2005; He et al. 2007; Kinsbourne 1970). According to this model, there is an attentional processor in each hemisphere that is directed toward the opposite hemifield. These processes are in dynamic equilibrium through reciprocal inhibition. When the equilibrium is broken by a lesion, an attentional bias is generated by the lack of contralateral inhibition from the damaged hemisphere. Consistent with this hypothesis, behavioral recovery from neglect parallels both the reestablishment of contralateral evoked activity and the return to a normal interhemispheric functional connectivity in the posterior parietal regions belonging to the dorsal attention network (Corbetta et al. 2005; He et al. 2007).

Recent neuropsychological evidence (Duncan et al. 1999; Fink et al. 2000; Peers et al. 2005) also suggests the presence of reciprocal inhibition between spatial locations that are far apart. Interhemispheric models predict that an opposing attentional modulation should be observed in the contralateral hemisphere regardless of the presence of a peripheral stimulus, which is consistent with the results in the zero-NT condition.

The present results also indicate that contralateral inhibition seems to involve a special competitive interaction between mirror-opposite locations. Several lines of evidence support the existence of an intrinsic homotopic correlation. A higher number of callosal connections between cells representing homotopic versus heterotopic locations have been demonstrated in animals (Segraves and Rosenquist 1982) and humans (Dougherty et al. 2005). A recent functional connectivity study demonstrated that interhemispheric correlations in neural activity of the visual cortex persisted even in anesthetized monkeys (Vincent et al. 2007). In humans resting in complete darkness with eyes closed, Nir et al. (2006) observed a strong interhemispheric correlation between "mirror" cortical sites. The emerging idea is that these anatomical and functional connections are intrinsic and task independent.

The special relationship between homotopic cortical locations that is observed when subjects are at rest may also be

responsible for the critical relationship between upper visual field regions when subjects direct their attention to a specific upper field location, resulting in a strong attentional modulation with the opposite sign.

Alternatively, the mirror location could have played a special role in our study since the two attended locations were always in a mirror-symmetric position within the upper visual field across the vertical meridian. Thus the observed modulations could be task dependent and governed mainly by the particular distribution of cues. Even though it is not possible to rule out completely this second hypothesis, it seems implausible that subjects chose a suboptimal weighting strategy after an extensive degree of training on the task.

Difference in evoked activity between upper and lower fields

Results from the three-NT condition showed an upper field advantage, both in terms of reaction times and target-evoked activity, even though the three invalid locations shared the same probability of containing an invalid target. This result could be explained by an intrinsic upper field advantage in attention tasks. However, previous studies have shown that, if present, attentional and orientation discrimination advantages pertain to the lower field instead (He et al. 1996; Previc 1990). The lower field advantage is usually explained by the fact that the lower field is represented in the upper part of the primary visual cortex, which projects more heavily into the posterior parietal cortex (Maunsell and Newsome 1987), involved in spatial attention.

A more plausible reason for the observed upper field advantage is that reorienting was either biased to that location or more practiced to that location, since over the course of the experiment, it contained the largest number of invalid targets. Alternatively, the results could be explained if reorienting were easiest along a horizontal axis.

It is remarkable that a location that is highly suppressed—i.e., the location mirror-opposite to the cued location—subsequently shows a higher evoked response. A trial-by-trial analysis of both cue and target responses, however, would be necessary to demonstrate a true negative correlation between the activity during the cue and target periods. Nevertheless, this result is another sign that the location mirror-opposite to the cued location is treated in a special way with respect to other unattended locations.

Conclusions

The present results argue against the idea that preparatory signal decreases at unattended locations are necessarily related to expectations regarding potentially interfering information. Instead, the distribution of attentional modulation seems to be determined mainly by the attended location under conditions in which distant low-contrast peripheral stimuli are expected.

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Present addresses: A. I. Jack, Department of Cognitive Science, Case Western Reserve University, Cleveland, OH 44106; G. d'Avossa, Bangor Imaging Unit, Department of Psychology, Bangor University, Bangor, Gwynedd, UK LL57 2AS.

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