

JN-00974-2003

Final Accepted Version
JN-00974-2003.R2

A Push-pull Mechanism of Selective Attention in Human Extrastriate Cortex

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Abstract

Selective attention operates in visual cortex by facilitating processing of selected stimuli and by filtering out unwanted information from nearby distracters over circumscribed regions of visual space. The neural representation of unattended stimuli outside this focus of attention is less well understood. We studied the neural fate of unattended stimuli using fMRI by dissociating the activity evoked by attended (target) stimuli presented to the periphery of a visual hemifield and unattended (distracter) stimuli presented simultaneously to a corresponding location of the contralateral hemifield. Subjects covertly directed attention to a series of target stimuli and performed either a low or a high attentional load search task on a stream of otherwise identical stimuli. With this task, target-search related activity increased with increasing attentional load while distracter-related activity decreased with increasing load in areas V4 and TEO, but not in early areas V1 and V2. This finding presents evidence for a load dependent push-pull mechanism of selective attention that operates over large portions of the visual field at intermediate processing stages. This mechanism appeared to be controlled by a distributed fronto-parietal network of brain areas that reflected processes related to target selection during spatially directed attention.

Introduction

Converging evidence from single-cell physiology studies in monkeys and functional brain mapping studies in humans suggest that selective attention operates in extrastriate visual cortex by enhancing neural activity evoked by attended stimuli and by counteracting suppressive influences of nearby distracter stimuli that compete for neural representation (Tsotsos, 1990; Desimone & Duncan, 1995; Kastner & Ungerleider, 2000). As a result, the selected information is preferentially processed and the unwanted information from nearby distracters is effectively filtered out. This filter mechanism that occurs most strongly at the level of the receptive field (RF) is compatible with the idea that selective attention to a stimulus causes the RF to shrink around the attended stimulus, thereby leaving the unattended stimuli at nearby locations outside the RF (Moran & Desimone, 1985; Connor et al., 1996; Reynolds & Desimone, 1999). Importantly, this mechanism provides a neural correlate for an attentional ‘spotlight’ that operates across circumscribed regions of visual space (Eriksen & James, 1986; Tootell et al., 1998; Brefczynski & DeYoe, 1999). The size of the spotlight may be flexibly scaled to the different RF sizes of early and intermediate visual areas.

Less is known about the neural representation of unattended stimuli outside the focus of attention. Results from neuroimaging and behavioral studies suggest that the processing of unattended stimuli depends on the degree to which attentional resources are engaged by an attended stimulus (Lavie & Tsal, 1994; Rees et al., 1997). For example, Rees and colleagues (1997) demonstrated that activation in area MT evoked by

unattended moving stimuli was abolished when subjects performed a linguistic task of high attentional load relative to a low-load version of the task at fixation. In contrast, results from patients suffering from visuo-spatial hemineglect have shown that neural responses evoked by faces and object stimuli presented to the neglected hemifield were similar compared to those evoked by the same stimuli presented to the intact hemifield (Rees et al., 2000; Vuilleumier et al., 2001), suggesting that unattended stimuli undergo processing to advanced stages of category-specific object representations.

We have investigated the neural fate of unattended stimuli in an fMRI study in which attended (target) stimuli were presented to the periphery of the upper right quadrant of the visual field while unattended (distracter) stimuli were presented to a corresponding location of the contralateral hemifield. Thereby, neural activity evoked by target and distracter stimuli could be dissociated in visual areas with a quadrant or hemifield representation within the spatial resolution limits of fMRI. Target stimuli evoked activity in areas of left visual cortex, whereas distracter stimuli evoked activity in areas of right visual cortex. Subjects covertly directed attention to a series of sequentially presented target stimuli and performed either a low attentional load or a high attentional load search task while irrelevant distracter stimuli appeared in the contralateral hemifield. In both search tasks, stimuli were identical but appeared in different sequence. For the target-search related activity, we predicted that neural activity should increase with increasing attentional load (Spitzer & Richmond, 1991; Ress et al., 2000). For the distracter-related activity, the prediction was less clear, and several different possibilities were considered. First, neural responses evoked by distracter stimuli in the contralateral

hemifield may be suppressed in ventral extrastriate cortex depending on the attentional load of the task, as previously shown in dorsal extrastriate cortex (Rees et al., 1997). Second, neural responses evoked by distracter stimuli may not be affected in terms of attentional suppression, as suggested by studies of patients suffering from visuo-spatial hemineglect (Rees et al., 2000; Vuilleumier et al., 2001). And third, both mechanisms may operate at different processing levels. With our task, we found that target-related activity was enhanced to a similar degree and thus independent of attentional load in early areas V1 and V2, but increased depending on attentional load in areas V4 and TEO. Distracter-related activity was not affected by load in early visual cortex but decreased with increasing load in V4 and TEO. This finding presents evidence for a load dependent push-pull mechanism of selective attention that operates over large portions of the visual field at intermediate processing levels. This mechanism appears to be controlled by a distributed fronto-parietal network of brain areas that reflected target selection processes during spatially directed attention.

Methods

Subjects, visual stimuli and tasks

Nine subjects (five males; age: 22-38 yrs.) participated in the study, which was approved by the Institutional Review Panel of Princeton University. All subjects participated in the behavioral experiments; seven of them participated in the scanning experiments. Subjects were in good health with no past history of psychiatric or neurological diseases and gave their informed written consent. Subjects had normal or corrected-to-normal visual acuity.

Colorful complex images (each 2 x 2 degrees in size) were used that have previously been shown to activate human ventral visual cortex (Kastner et al., 1998, 1999). Pairs of stimuli were faded into each other by superimposing the stimuli and varying their contrast levels. Thereby, a wide range of ambiguous stimuli that were perceptually difficult to discriminate was generated. Two examples are given in Figure 1A. The stimulus to the left contains 100% stimulus A and 0% stimulus B, whereas the stimulus to the right contains 0% stimulus A and 100% stimulus B. The two stimuli in between contain 70% stimulus A/30% stimulus B and 30% stimulus A/70% stimulus B, respectively. Eight stimuli from a given pair (100/0%, 80/20%, 70/30%, 60/40%, 40/60%, 30/70%, 20/80%, 0/100%) were presented sequentially and in random order at 9.5° eccentricity in the right upper quadrant. The 50/50% stimulus was presented repeatedly as the distracter stimulus at a corresponding location in the opposite hemifield. Stimuli were presented for 250 ms followed by a 1000 ms blank period in blocks of 20 s. Subjects performed either a low attentional load or a high attentional load search, viewing the same stimuli but in different sequence (Fig. 1B). Both search tasks required subjects to covertly direct attention to the target location while maintaining fixation and to discriminate each of the sequentially presented stimuli. In the low-load condition, subjects counted the occurrence of a non-ambiguous (= 100/0%) stimulus following its initial presentation (Fig. 1B, see arrows). In the high-load condition, subjects counted the occurrences of stimuli that were identical to the previously shown stimulus (Fig. 1B, see arrows). This experimental design was aimed at varying parametrically mainly the perceptual processing load (and less so the cognitive load) at the target location, while

keeping all other parameters, notably the information processed at the target location, constant. Presentations of target and distracter stimuli were also tested in a fixation task condition during which subjects counted letters at fixation and ignored both stimuli (for details on the letter counting task, see Kastner et al., 1998, 2001). Presentation blocks during which either low load, or high load search or fixation tasks were performed were interleaved with blank periods of 14 s during which subjects performed the fixation task. It should be noted that differences in activity evoked at the target and distracter locations during the different attention tasks could not be attributed to fMRI adaptation due to repeated stimulus presentation in a block design. Sensory presentation conditions were kept constant during the different tasks, and only attentional processing load was manipulated. Therefore, any fMRI adaptation would have affected visually-evoked responses during the different conditions similarly. The blocks with directed attention to the display were indicated by a marker, an oriented line pointing to the target location, which was presented briefly close to fixation. After each scan, subjects reported the number of detected images or matches that they had counted at the target location in each attended block. Presentation blocks during which subjects performed search or fixation tasks were counterbalanced across the scanning session. Differences in processing load between the two search tasks were tested in behavioral sessions outside the scanner. Procedures during behavioral testing were identical to scanning procedures; only subjects were to respond by pressing a button instead of counting.

Eye movements were controlled during behavioral testing sessions. Display and viewing conditions were calibrated to match the conditions of the scanner experiments.

Head position and viewing distance were kept constant with a chin rest. Subjects' eye positions were monitored at a sampling rate of 60 Hz by a remote infrared eyetracking system (Model 504, Applied Science Laboratories, Bedford, MA, USA). Eye position data were output to disk in a standard NTSC (261x240) coordinate system for off-line analysis. Data of 7 subjects were converted from NTSC coordinates to degrees of visual angle (dva) that deviated from fixation. Fixation was defined in each run as the average eye position during the blank periods. The first blank period was discarded from each run for the two analyses performed. Horizontal eye position and vertical eye position were both sharply peaked and centered on the fixation cross. For the first analysis, analysis of variance tests were performed on the average eye position during each condition to determine if there was any relation between overall eye position and task condition. No significant differences in eye position were found for either the horizontal or vertical dimensions. Second, to check for the presence of saccades, the eye traces for each subject were imported to ILAB v.3.57 eye movement analysis software (Gitelman 2002) where blinks were removed using a pupil size and location filter and a region of interest (radius = 1.5 dva) was centered around fixation. On average, less than 1 saccade was detected per subject, as defined by any sample that left the region of interest. The times and endpoints for these rare eye movements did not relate to the task conditions. Of all the eye samples, 99.88% remained within the region of interest.

Data acquisition

Images were acquired with a 3 Tesla head scanner (Allegra, Siemens, Erlangen, Germany) using a standard head coil. Subjects were tested in two separate scanning

sessions, each lasting 2 hours. Functional images were taken with a gradient echo, echo planar sequence (TR = 2 s, TE = 30 ms, flip angle = 90°, 64 x 64 matrix). In session 1, sixteen contiguous, coronal slices (thickness = 4 mm, gap = 1 mm, FOV = 192 x 192 mm) were acquired in 12 series of 95 images each, covering activation areas in occipital, posterior temporal, and parietal cortex. In session 2, twenty-two contiguous axial slices were taken starting from the top of the brain (thickness = 4 mm, gap = 1 mm, FOV = 192-220 x 192-220 mm) and covering activation areas in frontal and parietal cortex. Seven subjects were scanned in session 1; five of the seven subjects were scanned in session 2. For each subject, retinotopic mapping was performed in a separate scanning session. Echo-planar images were compared with a co-aligned high-resolution anatomical scan of each subject's brain taken in the same session (FLASH, TR=150 ms, TE=4.6 ms, flip angle = 90°, 256 x 256 matrix). Another high-resolution anatomical scan of the entire brain (MPRAGE sequence; TR = 11.1 ms; TE = 4.3 ms; flip angle = 8°; matrix 256 x 256 voxels; three-dimensional resolution, 1 mm³) was taken to perform spatial normalization and to create cortical surface reconstructions using BrainVoyager software (Brain Innovation, Maastricht, Netherlands).

Visual stimuli were projected onto a translucent screen located at the back of the scanner bore at a distance of 60 cm from the subjects' eyes. Stimuli were viewed from inside the bore of the magnet via a mirror system attached to the head coil, providing a maximal visual angle of 28 x 36°.

Data analysis

Between-scan head movements were corrected by aligning each image to a reference image obtained in the middle of the session. Statistical analyses were restricted to brain voxels with adequate signal intensity (average intensity of > 20% of the maximum value across voxels). The first five images of each scan were excluded from analysis. Statistical analyses were performed using multiple regression in the framework of the general linear model (Friston et al., 1995) with National Institutes of Health Functional Imaging Data Analysis Program (FIDAP) software. Square-wave functions matching the time course of the experimental design were defined as effects of interest in the multiple regression model. The square-wave functions contrasted (1) epochs of visual presentations versus blank periods, and (2) epochs of visual presentations during search tasks versus fixation task. Activated voxels in visual cortex were identified based on the first effect of interest; activated voxels in frontal and parietal cortex were identified based on the second effect of interest. For each effect of interest, square-wave functions were convolved with a Gaussian model of the hemodynamic response (lag 4.8 s, dispersion 1.8 s) to generate idealized response functions, which were used as regressors in the regression model. Additional regressors were included in the model to partially factor out variance due to between-run changes in mean intensity and within-run linear changes. Statistical maps were thresholded at a Z score of 2.33 ($P < 0.01$) (degrees of freedom corrected for correlation of adjacent time points). Regions of interest (ROI) were located by identifying clusters of seven or more contiguous statistically significant voxels. Statistical significance ($P < 0.01$) of these clusters was assessed using random Gaussian field methods based on their spatial extent and peak height (Friston et al., 1994;

Poline et al., 1997). Statistically significant clusters of voxels were overlaid on structural T1-weighted scans taken in the same session and in the same plane. Activity in visual cortex was assigned to retinotopically organized areas based on retinotopic mapping, as described in detail elsewhere (Kastner et al., 2001). Briefly, areas V1, V2, and VP were identified by determining the alternating representations of the vertical and horizontal meridians, which form the borders of these areas. Areas V4 and TEO were identified by their characteristic upper (UVF) and lower visual field (LVF) topography. The UVF and LVF are separated in V4 and located medially and laterally on the fusiform gyrus, whereas this separation is not seen in the region anterior to V4, which we term TEO. SPL, IPS, and IPL in parietal cortex and FEF and SEF in frontal cortex, which are part of a distributed spatial attention network, were identified by their reported locations in the literature (for meta-analyses, see Kastner & Ungerleider, 2000; Pessoa et al., 2002). All time course analyses were performed on unsmoothed data. Time series of fMRI intensities, presented as group data, were averaged over all voxels in a given ROI, normalized to the mean intensity obtained during the control condition. For each subject, the ten peak intensities of the fMRI signal obtained during a given presentation block and task were averaged, resulting in mean signal changes. These values were further quantified by defining an attentional modulation index (AMI), which normalizes the attention effects relative to the fixation task condition, in which target and distracter stimuli were both ignored ($AMI_{High} = [ATT_{High} - FIX] / [ATT_{High} + FIX]$ where ATT_{High} and FIX refer to averaged responses during high load search, or fixation condition; accordingly, an AMI_{Low} was computed for responses during low load search). Statistical significance of time series data was determined by a random effects analysis using one-

sample, one-tailed t-tests; reported p -values refer to these statistical tests, if not specified otherwise. Interaction terms are only reported when significant. T-tests and ANOVAs were calculated to assess significance for behavioral data and activated volumes. For each subject, statistical maps and structural images were transformed into Talairach space (Talairach & Tournoux, 1988) using BrainVoyager software.

Results

Differences in attentional load between the two search tasks (see Fig. 1B) were established in behavioral experiments outside the scanner. Subjects ($N=9$) detected significantly more targets during the low load than during the high load search task and made fewer errors ($0.4\% \pm 0.02\%$ vs. $20.6\% \pm 1.8\%$; ANOVA, main effect of task: $p < 0.001$). Reaction times were significantly longer in the high load condition compared to the low load condition (446 ± 19 ms vs. 567 ± 29 ms; ANOVA, main effect of load condition: $p < 0.01$). Taken together, behavioral performance indicated that the processing load was effectively manipulated by the two search tasks. Behavioral performance in the search tasks was not different in the presence and in the absence of distracters in the contralateral hemifield, suggesting that distracter presentations did not interfere with search task performance.

Complex images presented at the target location evoked significant activity as compared to blank presentations in visual areas V1, V2, VP, and V4 of the left hemisphere in all subjects ($N=7$) and area TEO in six subjects. As the border between V2 and VP could not be distinguished unequivocally in some of the subjects, the

combined region will henceforth be referred to as V2. Stimuli presented at the distracter location significantly activated areas V1 and V2 of the right hemisphere in all subjects, area V4 in five subjects, and area TEO in two subjects. The locations of the activations were in the ventral parts of these areas, consistent with the locations of stimuli in the upper visual field. This is illustrated for a single subject in Figure 2A; in this subject, the upper visual field representation of dorsal area V3A was also activated by stimuli presented at the target location. Mean activated volumes were not different in left and right V1 and V2 (520 mm³ compared to 546 mm³ in V1; 642 mm³ compared to 617 mm³ in V2), but were significantly smaller in right than in left V4 and TEO (1369 mm³ compared to 581 mm³ in combined V4 and TEO; t-test, $p < 0.001$) with a significant interaction of activated hemisphere and area (ANOVA, main effect of hemisphere: $p < 0.01$; main effect of area: $p < 0.05$; interaction hemisphere x area: $p < 0.01$).

An analysis of the time series of the fMRI signal (Fig. 3) and the mean signal changes (Fig. 4A) averaged across subjects showed that in left V1 and V2 target search-related activity was enhanced, but to a similar degree during low load and high load search relative to the fixation task condition during which the same stimuli were ignored. Mean fMRI signals increased in V1 from 1.21% to 1.53% during low load search and to 1.41% during high load search (Fig. 4A; main effect of attention, $p < 0.01$; main effect of attentional load: n.s.), and in V2 from 1.25% to 1.44% and 1.58%, respectively (Fig. 4A; main effect of attention, $p < 0.01$; main effect of attentional load: n.s.). In left V4 and TEO (Figs. 3, 4A), target search-related activity was also enhanced relative to the control condition (main effect of attention: $p < 0.001$ for V4, TEO), but the attentional response

enhancement increased with increasing attentional load (main effect of attentional load: $p < 0.05$ for V4, TEO). Mean fMRI signals increased from 1.38% to 1.61% during low-load search and to 1.89% during high-load search in V4, and from 1.12% to 1.41% and 1.79%, respectively, in TEO (Fig. 4A). Hence, in V4 and TEO, fMRI signals evoked by target stimuli reflected the subjects' behavioral performance.

In right V1 and V2, distracter-related activity was not different across the three different task conditions (Fig. 3 and 4A). Mean signals in V1 and V2 were 1.16% and 1.23% during fixation, 1.21% and 1.34% during low load search, and 1.18% and 1.30% during high load search (Fig. 4A), suggesting that visual processing in early visual cortex was mediated by bottom-up mechanisms and did not depend on attentional load. In right V4 and TEO, however, distracter-related activity was attenuated depending upon the attentional load (Fig. 3 and 4A). Mean signal changes combined for V4 and TEO were 1.70% during fixation, 1.68% during low load search, and 1.45% during high load search (main effect of attentional load: $p < 0.01$). Thus, in areas at intermediate but not at early processing stages, the attentional load-dependent suppression of distracter-related activity mirrored the attentional load dependent enhancement of target search-related activity, as also reflected in the attentional modulation index shown in Figure 4B (ANOVA; AMI for target-related activity: main effect of task: n.s.; main effect of area: n.s.; interaction task x area: $p < 0.01$; AMI for distracter-related activity: main effect of task: $p < 0.05$; main effect of area: $p < 0.05$).

Areas in frontal and parietal cortex activated during high and low load search relative to the fixation task condition are depicted for a single subject in Figure 2B. Across all subjects (N=5), areas in the frontal eye field (FEF), the supplementary eye field (SEF), the superior parietal lobule (SPL), the intraparietal sulcus (IPS), and the inferior parietal lobule (IPL) were found to be consistently activated. These areas have been previously described to form a distributed fronto-parietal spatial attention network (see Kastner & Ungerleider, 2000; Pessoa et al., 2002 for references). In addition, areas in the middle and inferior frontal gyrus, and in the insula were consistently activated. We will focus our analysis on activity in areas of the attention network, which are more likely to reflect the attentional manipulations associated with the different tasks and not other differences between pattern discrimination and letter identification. The locations of FEF, SEF, SPL, IPS, and IPL in Talairach space were found to be similar as described previously (Kastner et al. 1999) [FEF: -31, -9, +50; +42, -8, +48; SEF: +1, +6, +51; SPL: -16, -72, +42; +13, -70, +42; IPS: -35, -51, +36; +34, -53, +35; IPL: -48, -43, +39; +47, -42, +40]. Areas in the FEF, SPL, IPS, and IPL were activated bilaterally without hemispheric differences. Mean signal changes averaged across subjects and hemispheres are shown in Figure 4C for SPL, IPS, IPL, FEF, and SEF. In all areas, activity increased with increasing attentional load, thereby reflecting subjects' behavioral performance. In this respect, target search-related activity in areas of the fronto-parietal cortex was similar compared to response patterns in left V4 and TEO (main effect of attention: $p < 0.001$ for IPS and $p < 0.01$ for FEF, SEF, SPL, and IPL; main effect of attentional load: $p < 0.05$ for FEF, SEF, SPL, IPS, and IPL). However, unlike in these extrastriate areas, activity was entirely suppressed in the fronto-parietal network, when subjects performed the fixation

task and ignored target stimuli (Fig. 4C). Thus, areas of the fronto-parietal attention network were activated only when target stimuli were attentionally selected, but not when the same stimuli were ignored, supporting the idea that these areas are involved with target selection and distracter suppression during spatially directed attention rather than sensory-driven processes (Everling et al., 2002; Moore & Armstrong, 2003; Schall & Thompson, 1999).

Discussion

We investigated the neural representation of attended and unattended stimuli under conditions of varying perceptual load by having subjects perform either a detection or a discrimination task of identical target stimuli while presenting unattended stimuli simultaneously. By varying the processing requirements for identical stimuli, the perceptual load of information processing at the target location was primarily manipulated (Lavie, 1995). The low load and high load search tasks were designed as 0-back and 1-back tasks to keep the cognitive load in terms of working memory (WM) requirements relatively constant, as shown previously for similar 0- and 1-back WM tasks (Nystrom et al., 2000). With this task, we found that target search-related activity was enhanced during search tasks independent of attentional load in early cortical areas V1 and V2, whereas distracter-related activity was not affected by the load manipulation. In intermediate areas V4 and TEO, target search-related activity increased and distracter-related activity decreased depending on attentional load. Activity in a fronto-parietal network of brain regions reflected processes related to target selection and distracter suppression during spatially directed attention. In behavioral studies outside the scanner,

we found that eye movements were not systematically correlated with the different task conditions and were therefore an unlikely source to account for the response modulation found in visual, parietal, and frontal cortex. Taken together, these results provide evidence for a long-ranging and load dependent push-pull mechanism of selective attention operating at intermediate processing stages of visual cortex. This mechanism may serve to partially filter out unwanted information over large spatial scales.

For the target search-related activity, we predicted that neural activity should increase with increasing attentional load in visual cortex based on previous results from single cell physiology and neuroimaging (Spitzer & Richmond, 1991; Rees et al., 1997). In support of our hypothesis, such response pattern was found in intermediate areas V4 and TEO, where the load-dependent increases of neural activity reflected the subjects' behavioral performance. In these areas, neural activity was also strongly correlated with the response patterns of higher-order fronto-parietal areas known to be involved in processes of target selection during spatially directed attention (Everling et al. 2002; Schall et al. 1999). In contrast, load-independent enhancement of neural responses to attended stimuli was found in early areas V1 and V2. There are several different possibilities to interpret the dissociation of attentional effects at early and intermediate processing levels. First, the dissociation may be related to the visual stimuli used in our study. The colorful patterned stimuli activated ventral extrastriate cortex presumably more optimally than early visual cortex. Differential effects of attention depending on task difficulty have been obtained in V1 with achromatic grating stimuli that are better suited to activate early visual areas (Rees et al., 2000). Second, our findings may indicate

a dissociation of attentional functions at different processing stages within the visual system. The load-independent effects may be related to a more general attentional gain control mechanism that affects visual processing as early as in the LGN (O'Connor et al. 2002), whereas the load-dependent effects may be more closely related to the attentional selection process. Importantly, because of the dissociation of attention effects in early and intermediate visual areas, it is not likely that the effects merely reflected an addition of attention-related baseline increases to visually-evoked activity (Kastner et al. 1999; Ress et al. 2000).

For the distracter-related activity, we probed two alternative but not mutually exclusive hypotheses. One prediction was that distracter-related activity may be suppressed dependent on the attentional load of the task at hand, based on previous results from neuroimaging studies in dorsal extrastriate cortex (Rees et al., 1997). Another prediction was that distracter-related activity may not be affected by attention, based on results from neglect patients (Rees et al., 2000; Vuilleumier et al., 2001). Our results provide evidence that both mechanisms operate at different processing stages. Consistent with the results from neglect patients, distracter-related activity was not affected by attention in early visual cortex suggesting that visual processing was mediated considerably by bottom-up mechanisms. Consistent with accounts of attentional load (Lavie & Tsal, 1994), distracter-related activity was attenuated depending on attentional load at intermediate processing stages. It is conceivable that fMRI adaptation effects due to repeated presentation of the same stimulus contributed to the overall responses evoked at the distracter location. However, because the sensory

presentation conditions at the distracter location were kept constant across all attention tasks, it is unlikely that adaptation effects accounted for the dissociation of the load dependent suppression of distracter-related activity between early and intermediate visual areas. Taken together, our results show that attentional-load dependent suppression of distracter-related activity operates not only in dorsal extrastriate cortex, as previously shown (Rees et al. 1997), but also in ventral extrastriate cortex and that the suppression appears to be correlated with a load-dependent facilitation of neural responses evoked by attended stimuli. Indeed, the load-dependent suppression of distracter-related activity mirrored the load-dependent enhancement of target search related activity in areas V4 and TEO.

Notably, the suppressive mechanism operated over large portions if not the entire visual scene suggesting that the focus of attentional selection may be surrounded by extensive suppressive zones (LaBerge and Brown 1989; Vanduffel et al., 2000; Smith et al., 2000; Tsotsos et al. 2001). This result may provide a neural basis for psychophysical studies that have implicated suppressive surrounds around the locus of attentional selection based on poorer performance in discriminating and slower reaction times in responding to distracter stimuli (Bahcall and Kowler 1999; Caputo and Guerra 1998; Cave and Zimmerman 1997; Cutzu & Tsotsos, 2003). How may such a long-ranging mechanism be implemented at the neural level? There are at least three possibilities that need to be considered. First, visual stimuli presented to the contralateral hemifield have been shown to influence the processing of stimuli within receptive fields (RFs) of the ipsilateral hemifield in V4 (Desimone et al., 1993). Such long-ranging and context-

dependent extra-RF modulation of neural responses is thought to be mediated by transcallosal connections in this area (Van Essen et al., 1982). Selective attention may operate in visual cortex by affecting local circuits that mediate context modulation, as previously shown in V1 (Ito & Gilbert, 1999). Second, it has been demonstrated that microstimulation of the FEF can enhance neural activity in V4 at target locations and suppress activity at distracter locations (Moore & Armstrong, 2003). Thus, the attention effects obtained in extrastriate cortex in the present study may be under feedback control of higher-order areas of the fronto-parietal attention network that mediate both target selection and distracter suppression (Everling et al., 2002; Schall & Thompson, 1999). And third, results from computational neuroscience have shown that long-ranging suppressive mechanisms may result from feedback between visual areas flowing from higher to lower areas (Tsotsos et al., 2001). FMRI studies demonstrating that attention effects increase in magnitude from early to later processing stages in visual cortex (e.g. O'Connor et al., 2002) provide evidence in support of such a feedback mechanism that reverses the visual processing hierarchy. It should be noted that these possibilities are not mutually exclusive.

Our results add to a growing number of physiology, lesion, and neuroimaging studies (DeWeerd et al., 1999; Gallant et al., 2000; Kastner et al., 1998; Moran & Desimone, 1985; Reynolds et al., 1999; Recanzone & Wurtz, 2000) that demonstrate an important functional role for areas V4 and TEO in the spatial filtering of distracters. In single-cell recording studies, it has been demonstrated that spatially directed attention can influence the competition among multiple stimuli in favor of one of the stimuli by

modulating competitive interactions in extrastriate areas V2, V4, and MT, thereby filtering out unwanted information from nearby distracters (Moran & Desimone, 1985; Reynolds et al., 1999; Recanzone & Wurtz, 2000). Consistent with these results, studies in a patient with an isolated V4 lesion (Gallant et al., 2000) and in monkeys with lesions of areas V4 and TEO (DeWeerd et al., 1999) have demonstrated significant performance deficits in an orientation discrimination task in the presence, but not in the absence of distracters, suggesting a deficit in the efficacy of the filtering of distracter information. The present findings suggest that, in addition to filter mechanisms that operate at the level of the RF, attention can also attenuate distracter-evoked activity from areas beyond the RF. Future studies are needed to clarify whether intra- and extra-RF mechanisms for the filtering of unwanted information constitute separate entities, or are interdependent. Further, the relation of these spatial attention effects to previously demonstrated long-ranging feature-based attention effects needs to be explored (Saenz et al., 2002; Treue and Martinez Trujillo, 1999).

Acknowledgments

We thank D. M. Beck and K. A. Schneider for valuable discussions and H. M. Fehd for help with manuscript preparation. Supported by a NSF Graduate Research Fellowship to M.A.P. and by grants from NIMH (RO1 MH64043, P50 MH62196) and the Whitehall Foundation to S.K.

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Figure Legends

Figure 1: *Experimental design.* A: Pairs of complex images ($2 \times 2^\circ$ in size) were superimposed at varying contrast levels (as indicated for the 4 stimuli) to provide a range of ambiguous stimuli that were perceptually difficult to discriminate. B: A series of 16 attended (target) stimuli (6 shown for each load task) from a given pair were presented sequentially at 9.5° eccentricity to the right upper quadrant, while unattended (distracter) stimuli were presented to a corresponding location of the contralateral hemifield. Stimuli were presented for 250 ms followed by a 1000 ms blank period in blocks of 20 s. Subjects performed either a low attentional load search of a non-ambiguous stimulus in a 0-back task or a high attentional load search, which required them to distinguish between stimuli in a 1-back task. In both conditions, the same stimuli were presented but in different sequences. Arrows indicate correctly identified stimuli in the two tasks.

Figure 2: *Activated areas in visual, parietal, and frontal cortex.* A: Areas in visual cortex activated by presentations of complex images relative to blank periods presented on a flattened surface reconstruction of a single subject's occipital cortex. Area boundaries as identified by retinotopic mapping are indicated by broken (horizontal meridian representation) and solid (vertical meridian representation) lines. Target-related activity (left-hand side) was found in areas V1, V2, VP, V4, TEO, and V3A of the left hemisphere. Distracter-related activity (right-hand side) was found in V1, V2, VP, and V4 of the right hemisphere. The star indicates regions of foveal representations. B: Areas in frontal (FEF) and parietal (SPL, IPS, IPL) cortex activated during search tasks

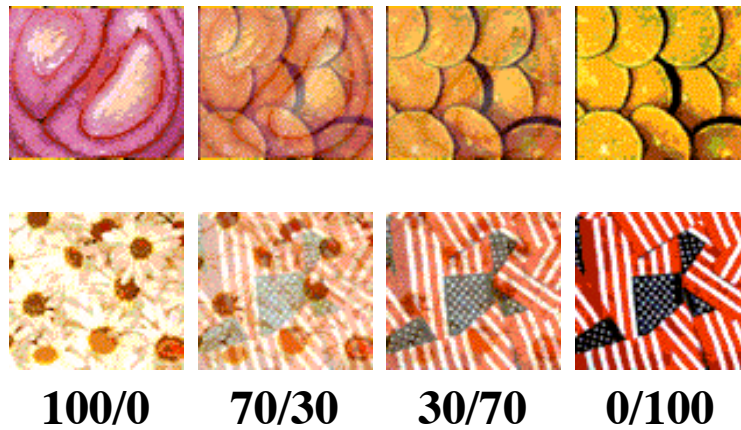
relative to the fixation task, thereby revealing regions involved with the spatial attention tasks at the target location. Activations are depicted on inflated left and right hemispheres of a single subject.

Figure 3: *Time series of fMRI signals in visual cortex.* Time series of fMRI signals for target search-related activity and distracter-related activity in combined areas V1/V2 and V4/TEO averaged across scans and subjects. Time courses are shown during the fixation task, when both stimuli were ignored (FT), and during the low load (LLS) and high load search (HLS) tasks. In V1 and V2, target-related activity was enhanced for attended relative to fixation conditions to a similar degree during the two search task conditions. Distracter-related activity was not affected by the load manipulation. Conversely, in V4 and TEO, target-related activity was greater during the high load as compared to the low load search condition; distracter-related activity was suppressed depending upon attentional load.

Figure 4: *Mean signal changes and attentional modulation index in visual, frontal and parietal cortex.* A: Mean signal changes in right [R] and left [L] V1, V2, V4, and TEO, averaged across subjects. For each subject, the ten peak intensities of the fMRI signal obtained during visual presentations of the fixation task (FT), the low load search (LLS), or the high load search task (HLS) were averaged. Target search-related activity was evoked in left visual cortex; distracter-related activity was evoked in right visual cortex. B: Attentional response modulation on visual stimuli as quantified with an attentional modulation index (AMI), which normalizes the activities obtained during the two search

task conditions relative to the activity obtained in the fixation task condition. In V1 and V2, attentional response enhancement of target-evoked activity was similar; distracter-related activity was not affected by attention. In V4 and TEO, attentional enhancement effects on target stimuli increased with increasing attentional load, whereas suppressive effects on distracter stimuli were found with increasing load. C: Mean signal changes in SPL, IPS, and IPL of parietal cortex and FEF and SEF of frontal cortex were computed as described in A. Activity was entirely suppressed when target stimuli were ignored and increased during target search with increasing attentional load, thereby reflecting target selection processes. Vertical bars indicate SEM.

A



B

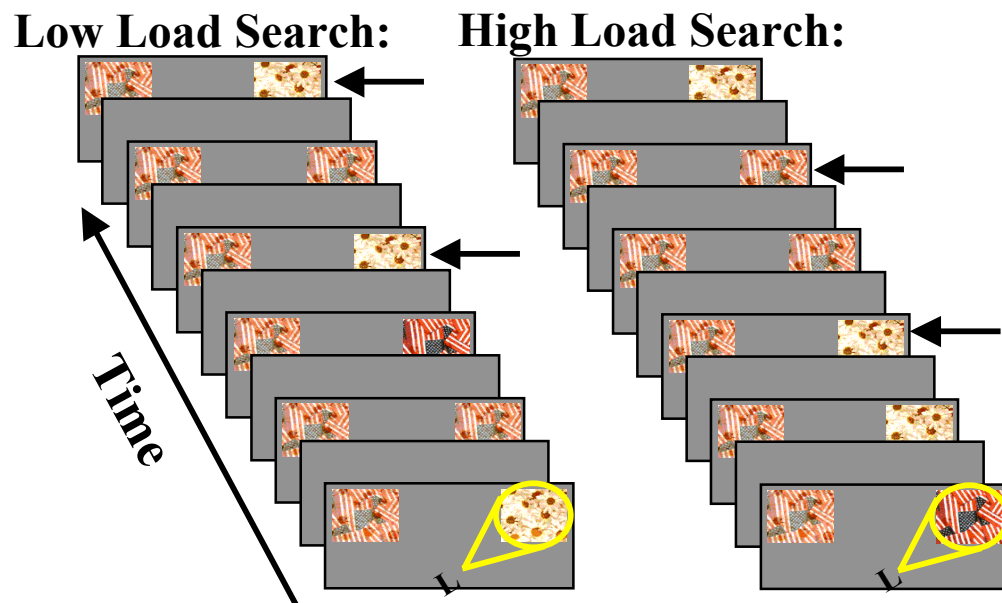
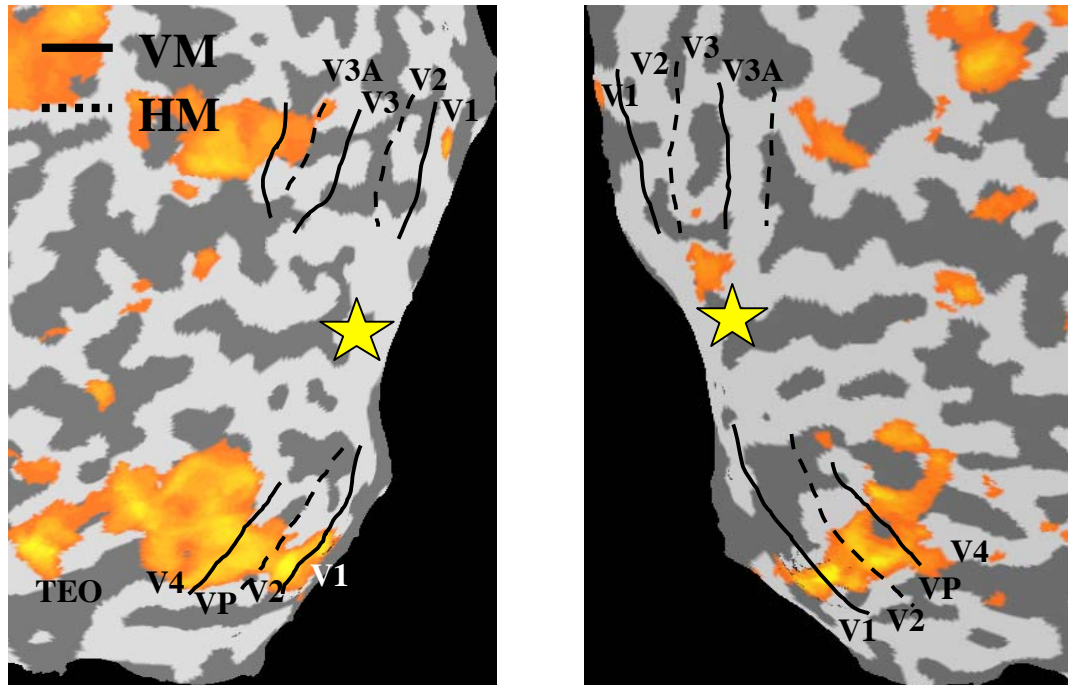


Figure 1

A



B

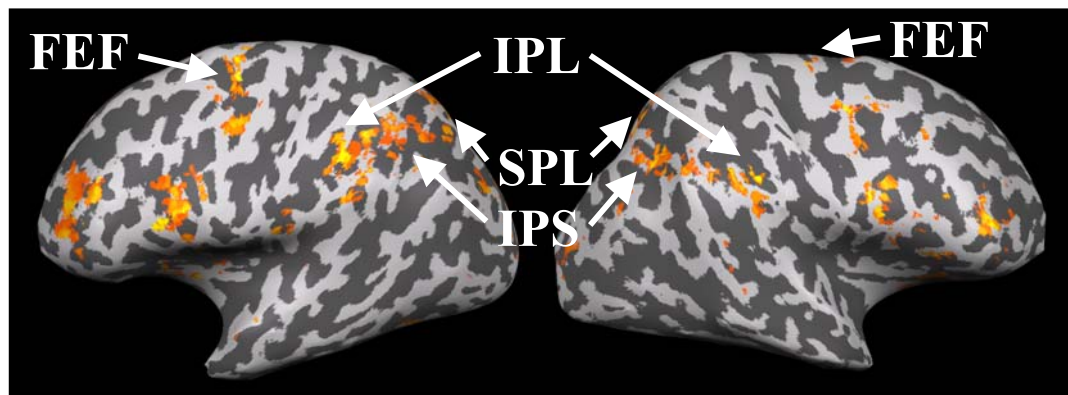


Figure 2

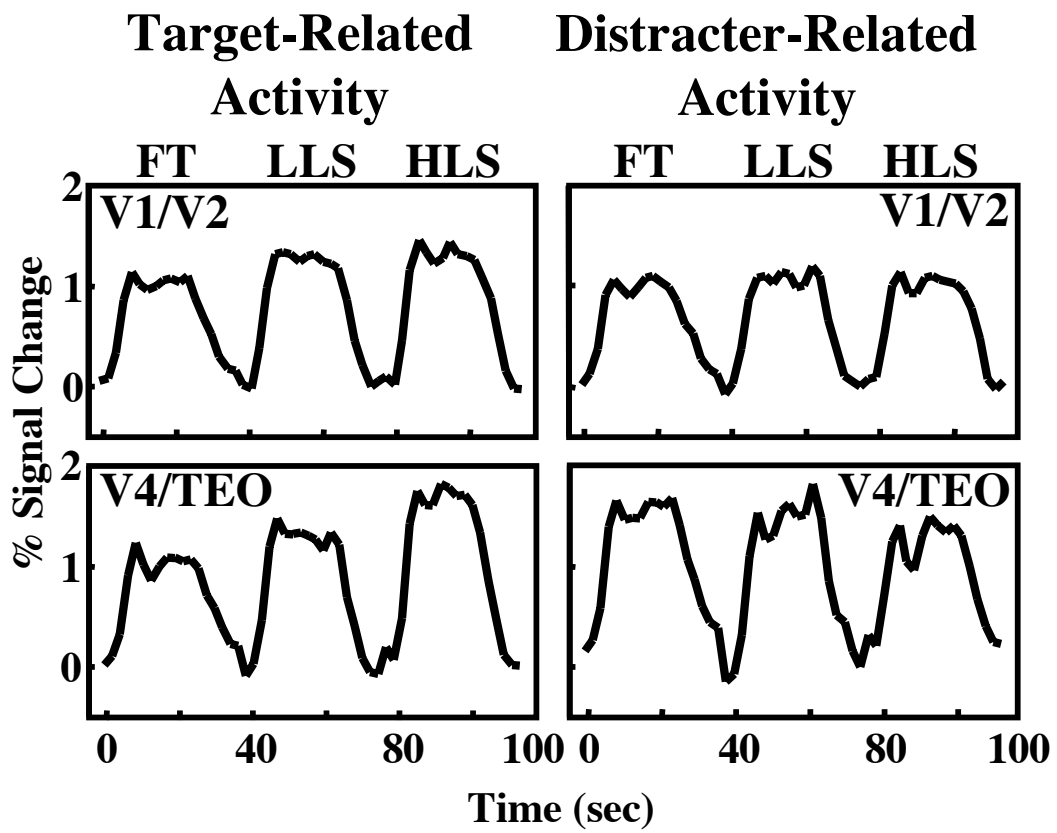


Figure 3

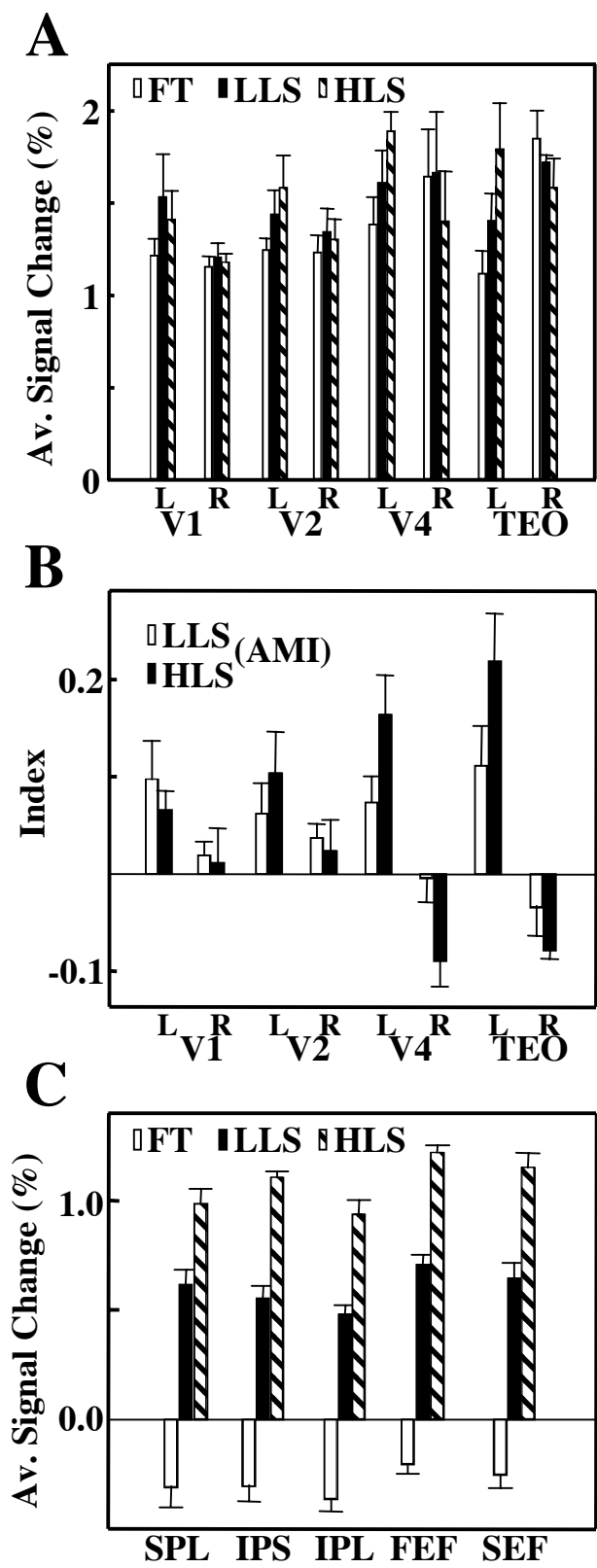


Figure 4