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Chapter 2

Directing attention to a location in space results in retinotopic activation in primary visual cortex

Munneke, J., Heslenfeld, D.J., Theeuwes, J. (2008). Directing attention to a location in space results in retinotopic activation in primary visual cortex. *Brain Research*, 1222, 184 – 191

Abstract

It is well-known that directing attention to a location in space enhances the processing efficiency of stimuli presented at that location. Previous studies have shown that directing spatial attention manifests itself as an increase in spontaneous firing rate of neurons (the baseline signal) in extrastriate cortex at the retinotopic corresponding location. There has been considerable debate as to whether this preparatory effect of attention also occurs in human striate cortex (area V1). In the present study, participants had to direct attention to a cued location in space, while changes in blood oxygen level dependent (BOLD) signals were measured. We show that in conditions in which there was no change in sensory stimulation, modulations due to flexibly shifting spatial attention were present throughout early visual cortex (areas V1, V2 and V3). In all early visual areas, the increased BOLD signal in response to the cue was retinotopically specific. The present study shows that voluntary top-down attentional control modulates activity not only in extrastriate but also in striate cortex. This modulation occurs quickly and flexibly in a retinotopic fashion, and serves to facilitate target processing in a continuously changing environment.

Introduction

It has long been established that attention exerts influence on the visual system in order to cope with the vast amount of information that is passed on from the retina to the brain. Visual attention allows people to select information that is relevant for ongoing behaviour. Directing visual attention towards a location in space is thought to enhance the processing efficiency of objects presented within the attended area (Posner & Petersen, 1990). The effective utilization of spatial information is related to an attention mechanism that operates analogous to a “beam of light”. As a metaphor, Posner described visual selective attention as a “*spotlight*” that enhances the efficiency of the detection of events within its beam (Posner, 1980). Providing information about the location of an upcoming target usually involves a cueing procedure in which a cue indicates the location of the target. Such a cue may consist of a centrally presented arrow that points to the likely target location (e.g. Posner, 1980), or a word (e.g. “right” or “left”; Vecera & Rizzo, 2004) indicating the target location. Cueing in this way is typically referred to as “endogenous” or top-down, because participants are instructed to use this information in a top-down way to improve their performance. Typically, this preparatory effect of attention is revealed by performance benefits in responding to a target presented at the cued location relative to conditions in which no advance information about the target location is provided.

Previous studies have shown that the deployment of attention modifies neural activity in several areas in visual cortex (Moran & Desimone, 1985; Spitzer, Desimone, & Moran, 1988). Preparatory cueing effects modulate brain activity as early as visual area V2 and can be found in numerous other structures of the extrastriate cortex including areas V3, V4 and MT (Corbetta, et al., 2005; Hopfinger, et al., 2000; Kastner, et al., 1999; Luck, Girelli, et al., 1997). From these and from behavioural studies (e.g. Treisman & Gelade, 1980) it has become clear that attention plays an important role in early visual processing.

The preparatory signal evoked by spatial cueing manifests itself as an increase in spontaneous firing rate of neurons in those parts of visual cortex that code the cued location. Increases in activity based on location cueing have been labeled baseline shifts (Hopfinger, et al., 2000; Kastner, et al., 1999; Ress, et al., 2000). These shifts in baseline activity, which occur in a retinotopic fashion in visual cortex, are thought to reflect the

top-down signal from areas outside the visual cortex. Brain areas possibly responsible for the top-down signal are the superior eye fields (SEF), the frontal eye fields (FEF) and the superior parietal lobule (SPL), all of which modulate with the attentional effects in the visual cortex (Corbetta, 1998; Kastner, et al., 1999; Ruff, et al., 2006).

Deploying attention thus changes the excitability of sensory neurons in a spatially specific manner. Typically, only extrastriate cortex shows modulated activity as a function of where attention is directed (Giesbrecht, et al., 2003; Hopfinger, et al., 2000). Whether attention also modulates preparatory activity in the earliest part of the visual cortex, area V1, is still subject for debate. Although many studies showed that attention modulates the processing of sensory information in primary visual cortex (Brefczynski & DeYoe, 1999; Gandhi, et al., 1999; Martinez, et al., 1999; Silver, et al., 2005; Somers, et al., 1999; Tootell, et al., 1998; Worden & Schneider, 1996), conflicting results have been reported concerning preparatory attention following the presentation of a cue. A number of studies failed to show baseline shifts in V1 (Corbetta, et al., 2000; Corbetta, et al., 2005; Hopfinger, et al., 2000; Luck, Chelazzi, et al., 1997), whereas others did (Jack, et al., 2006; Kastner, et al., 1999; Ress, et al., 2000; Silver, et al., 2007). However, in none of these studies were the V1 modulations found to be evoked by a flexible allocation of preparatory attention to various regions in visual space. For example, Kastner et al. (1999) used a blocked design in which participants had to direct their attention to one location in space throughout a block of trials. Jack et al. (2006), Ress et al. (2000) and Silver et al. (2007) used a design in which participants had to report the presence of a ring-shaped target surrounding the fixation point. However, these tasks never required the participants to constantly shift attention to different locations in the visual field in order to detect the target. Therefore, even though the reported activations in V1 reflect preparatory attention, it is not clear whether such effects would be observed when participants shift attention to an unpredictable location in an endogenous way from trial to trial (e.g. Posner, 1980).

In the present study we used a variant of the classic Posner cueing task to direct attention to different locations in an endogenous fashion from trial to trial. An example of a trial is given in Figure 1. Participants were instructed to direct their attention covertly to the '2' or '8' o'clock position on an imaginary circle. Subsequently, a target display was presented which consisted of an annulus of many tilted line segments, plus a target

vertical or horizontal line at the indicated location. Participants had to decide by button press whether the target orientation was present at the indicated location. We determined whether under these trial-by-trial cueing conditions we would observe attention-related brain activity in V1 in a retinotopic fashion.

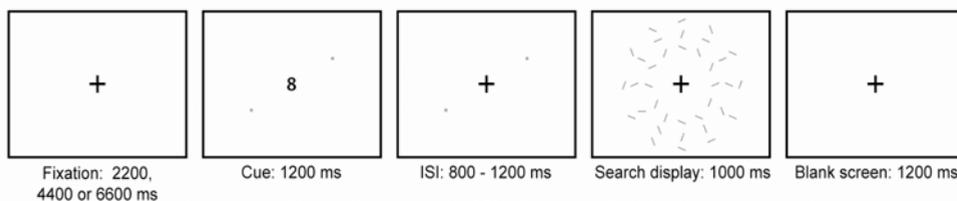
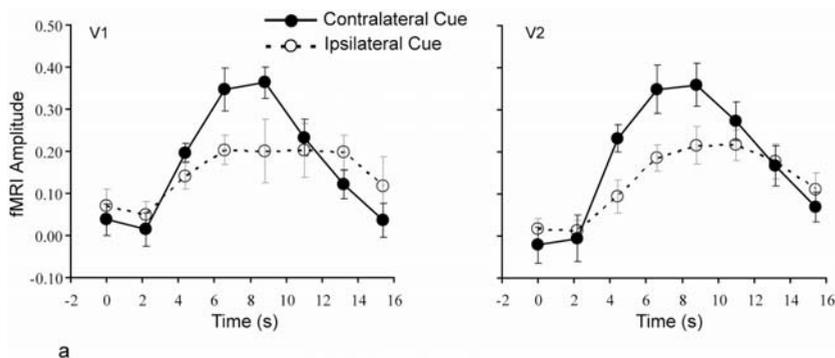


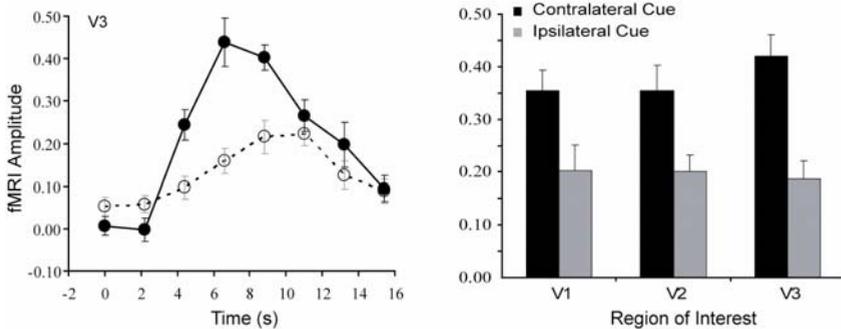
Figure 1. Experimental procedure: Participants focused on a centrally presented fixation point. A cue consisting of either a “2” or an “8” indicated the likely target location. Participants were told to covertly orient their attention to either the “2” or “8” o’clock position. A “0” (neutral cue) indicated that the target could appear at either location. The search display consisted of a cluttered field of slightly tilted line segments. One line segment was oriented either vertical or horizontal, the orientation determining the appropriate response. In 25% of the trials, the cue was not followed by a search display; these served to compute fMRI responses to cues and targets independently.

Results

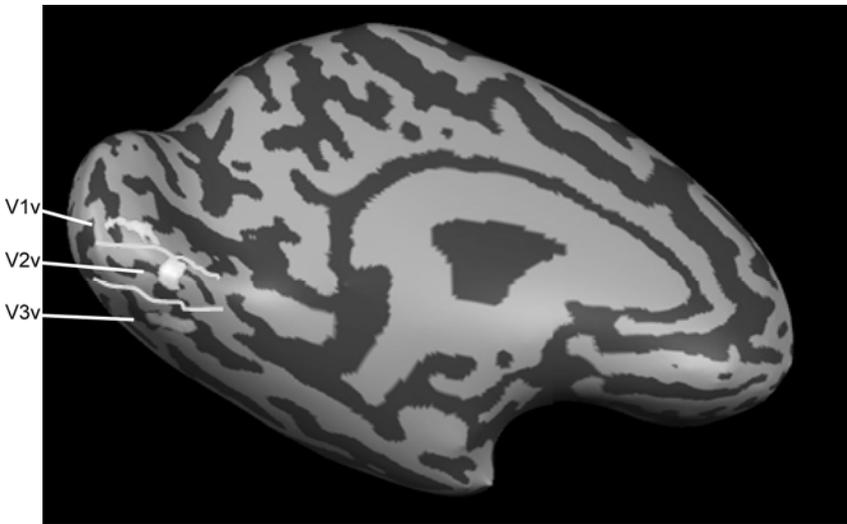
Behavioral Data

Participants performed significantly better when a target was validly cued, compared to performance on neutrally cued targets ($t(9) = 8.419, p < 0.001$). Mean d' was 1.95 for validly cued targets, compared to a d' of 1.16 for uncued targets. All participants showed a larger d' on trials in which the target was preceded by a valid cue.





b



c

Figure 2a). Cortical activation in response to all cues. Results of the deconvolution analysis. Activation evoked by cues indicating the contralateral visual field (such that the corresponding location is attended) was compared to activation evoked by cues indicating the ipsilateral visual field (such that the corresponding location is unattended). A significant increase in activation is seen throughout early visual cortex, including areas V1, V2 and V3. b) Difference in activity between contralateral and ipsilateral cues for the time period between 6.6 and 11 seconds for V1, V2 and V3. Error bars represent normalized standard errors (Loftus & Masson, 1994). c) Inflated hemisphere with ROIs from a typical participant.

fMRI Data

We determined the hemodynamic brain responses evoked by the cues in two ways. First, fMRI signals evoked by cues were separated from fMRI signals evoked by targets by means of a deconvolution analysis, separately for each participant and region of interest (ROI). Figure 2a shows the activity evoked by the cues, separately for each ROI and

averaged over participants and hemispheres. For each latency, we tested whether cues indicating contralateral targets (i.e., when the corresponding visual field location is attended) led to larger responses than cues indicating ipsilateral targets (when the corresponding visual field location is unattended) in the defined regions of interest. For V1 this effect was present between 6.6 and 11 seconds after cue-onset (smallest $F(1,9) = 5.700$, $p < 0.041$), in V2 and V3 the effect was present between 4.4 and 11 seconds after cue-onset (V2: smallest $F(1,9) = 7.675$, $p < 0.022$; V3: smallest $F(1,9) = 11.103$, $p < 0.009$). For the latencies during which all ROIs showed significant effects of cueing (between 6.6 and 11 seconds post-cue), the effect increased linearly over ROIs ($F(1,9) = 11.053$, $p = 0.009$; see Figure 2b, Table 1), indicating that the attentional modulation became larger in hierarchically higher areas in visual cortex.

ROI	Cue-Target (6.6s - 11s)			Catch trials (8.8s - 13.2s)		
	Ipsilateral	Contralateral	% Change	Ipsilateral	Contralateral	% Change
V1	0.202	0.355	75.75	-0.170	-0.076	55.37
V2	0.201	0.354	76.34	-0.193	-0.054	71.84
V3	0.187	0.420	124.74	-0.220	-0.001	99.57

Table 1. Normalized fMRI responses averaged over 10 participants between 6.6 and 11 seconds post-cue on cue–target trials and between 8.8 and 13.2 post-cue on catch trials, separately for each ROI and attention condition. In addition, the averaged percentage of signal increase is given, separately for each ROI. The left columns are derived from the cue-evoked responses as computed in the deconvolution analysis over all trials. The right columns are derived from the event-related averages of the catch trials only.

In a second, independent analysis, we computed event-related averages for the catch trials, i.e. those trials that were not followed by targets, separately for each ROI and participant, in order to determine effects of cueing without any further contribution from target displays. Figure 3a gives the event-related BOLD responses evoked by the catch trials, averaged over participants and hemispheres. Again, for each latency and ROI we tested whether cues indicating contralateral targets evoked a larger response than cues indicating ipsilateral targets. Increased activity to contralateral cues was found in V1 between 8.8 and 13.2 seconds post-cue (smallest $F(1,9) = 7.251$, $p < 0.025$); in V2 and V3 this effect was observed between 6.6 and 13.2 seconds post-cue (V2: smallest $F(1,9) = 8.365$, $p < 0.018$; V3: smallest $F(1,9) = 7.169$, $p < 0.025$). Again, a linear increase in activity

was observed over ROIs from 8.8 to 13.2 seconds ($F(1,9) = 16.437, p = 0.003$; see Figure 3b, Table 1). Note that this increase of activity towards higher visual areas was observed merely on the basis of a cue (i.e., in catch trials), without any further change in sensory input. Table 1 gives the normalized activity to contralateral and ipsilateral cues, as well as the percentage change, for each ROI and for both types of analyses.

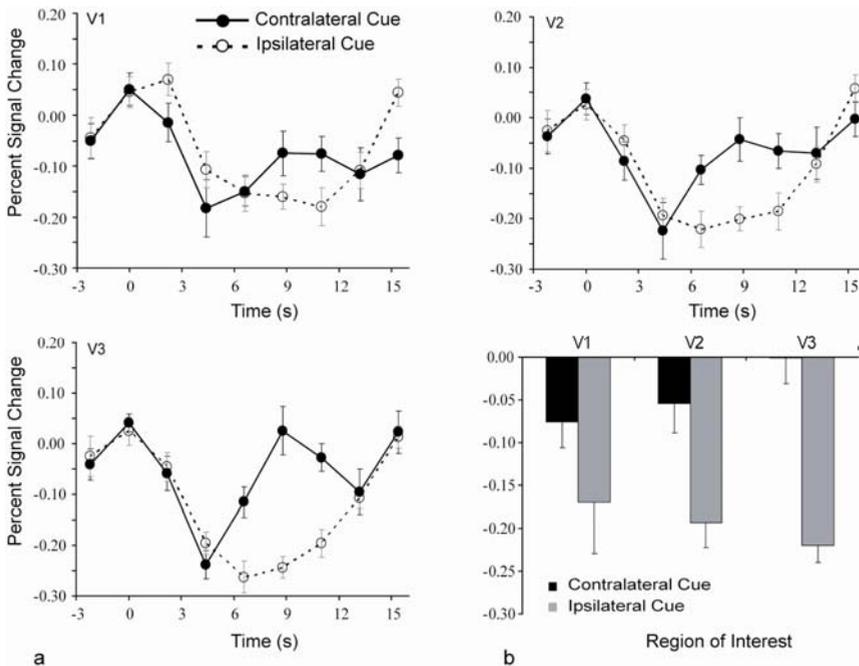


Figure 3a). Cortical activation in response to cues in catch trials, i.e. cues that were not followed by target displays. Activation evoked by cues indicating the contralateral visual field was compared to activation evoked by cues indicating the ipsilateral visual field, without any sensory contribution from target displays. Each curve represents the averaged time course of the fMRI signal, averaged across trials, hemispheres and participants. A significant decrease in activation is seen throughout early visual cortex, including areas V1, V2 and V3. b) Difference in activity between contralateral and ipsilateral cues for the time period between 8.8 and 13.2 seconds for V1, V2 and V3, for cues in catch trials. Error bars represent normalized standard errors (Loftus & Masson, 1994).

In order to examine whether the observed attentional effects were retinotopically specific, we also looked at activity in homologue regions corresponding to the remaining two quadrants (i.e., clock positions '4' and '10'), which were never cued. In none of those ROIs (V1, V2, V3) was significantly different activity observed in the hemisphere contralateral to the cued side, indicating that the effects of cueing were highly specific at

the corresponding retinotopic location in all three early visual areas (for V1, largest $F(1,9) = 2.737, ns$; for V2, largest $F(1,9) = 1.300, ns$; for V3, largest $F(1,9) = 3.122, ns$).

Discussion

The present study used a classic Posner cueing task in which on each trial participants directed attention to the location indicated by a centrally presented symbolic cue. Consistent with previous studies we found an improved sensitivity for detecting targets at the location indicated by the cue relative to conditions in which no location information was provided. In addition, we show that under these conditions there is increased activation in visual cortex contralateral to the side indicated by the cue. Moreover, this activity is retinotopic and seen in all visual areas including primary visual cortex. In other words, when participants endogenously shift their attention between regions in visual space, a change in activity was observed at the corresponding retinotopic locations in V1. The fMRI data show that after cue presentation, activation in retinotopically corresponding areas in V1 increases when the cue indicated the corresponding contralateral visual field location, even in catch trials in which no target stimulus was presented. We therefore conclude that the striate cortex is not a mere passive relay station for visual information but is actively involved in preparatory attentional processes. The current findings are consistent with the suggested metaphor (Posner, 1980) that compares directing attention to a spotlight that “illuminates” parts of the visual world around us. In line with this notion, our results suggest that directing the spotlight results in an increased activity in areas as early as V1.

The present findings are consistent with previous studies showing preparatory effects in striate cortex to targets or in more sustained paradigms. Previous fMRI investigations showed modulation of target-elicited neural activity as a function of attention (Brefczynski & DeYoe, 1999; Gandhi, et al., 1999; Martinez, et al., 1999; Silver, et al., 2005; Somers, et al., 1999; Tootell, et al., 1998; Worden & Schneider, 1996). Typically in these types of tasks, two or more stimuli were presented simultaneously, and participants were instructed to direct their attention to each location in turn and to detect or discriminate target stimuli presented at that location. These studies showed that spatial attention changes the sensory activity evoked by a target within both striate and

extrastriate cortex. In addition to these studies, effects of attention have also been demonstrated in V1 based on the mere preparation for a target, in the absence of further visual stimulation (Jack, et al., 2006; Kastner, et al., 1999; Ress, et al., 2000; Silver, et al., 2007). In these studies the observed modulations were obtained when participants directed their attention to the same location consistently over a whole block of trials. The current study extends these findings and shows that similar effects can be observed when observers shift attention flexibly on a trial-by-trial basis to unpredictable locations.

In contrast to the present finding, it should be noted that electrophysiological studies using event-related potentials (ERPs) suggested that spatial attention does not modify activity in primary visual cortex (Di Russo, et al., 2003; Martinez, et al., 1999; Martinez, et al., 2001; Noesselt, et al., 2002). These studies found modulations of fMRI responses to attended stimuli in V1 without accompanying effects on the electrophysiological C1 component. It was concluded that attentional effects in V1 are the result of delayed re-entrant feedback from higher visual areas. On the other hand, Kelly et al. (2008) using more sophisticated averaging procedures, showed that spatial attention can modulate the electrophysiological C1 response. Furthermore, several studies report a retinotopic decrease in EEG alpha power over occipital regions in spatial cueing tasks (Kelly, Lalor, Reilly, & Foxe, 2006; Thut, Nietzel, Brandt, & Pascual-Leone, 2006; Worden, Foxe, Wang, & Simpson, 2000), suggesting that early visual areas must be involved in attentional preparation. Our data show that spatial attention can modulate the fMRI V1 response even in catch trials which are not followed by a target display, and therefore not subject to re-entrant activation. This suggests that the fMRI V1 effects observed by Martinez and others may have contained early, genuine modulations as well, which may have been too small to be detected by standard ERP procedures.

In addition to signal increases in response to all cues (most of which were followed by search displays), we also observed fMRI signals in early visual areas in response to catch trials (in which no search display followed the cue). Note that the BOLD responses to catch trials (Figure 3a) are quite different from the BOLD responses to all cues (Figure 2a). As it was highly likely that a target display would follow the cue (catch trial probability was only 0.25), the observed difference in activity is most likely due to the absence of the expected search display. Davidson et al. (2004) reported decreased activity following the absence of an expected stimulus. Indeed, when no search display is presented in the

current task a decrease in activity is observed as well. However, the effects of attention are still present, showing a relative increase of brain activity at the corresponding retinotopic location.

The attentional modulation increased linearly over ROIs with the largest cueing effects occurring in V3. This trend is thought to be due to the increase in receptive field size of neurons in higher visual areas.

While in our study activity in V1 was clearly modulated by preparatory spatial attention, other studies have failed to find this V1 (e.g. Corbetta, et al., 2000; Corbetta, et al., 2005; Hopfinger, et al., 2000; Luck, Chelazzi, et al., 1997). This difference may be explained in a number of ways. First, it has been argued that the presence of distractors plays an important role in preparatory spatial attention. Serences et al. (2004) showed that cue-evoked preparatory attention is directly linked to a distractor-suppression component of attention. When observers know that there is a high likelihood that distractors accompany the target, cue-evoked activity may not only show an increase due to excitatory processes, but also an inhibitory effect suppressing distractor locations around the expected target. In the present study, the target was always embedded in distractors. The mere expectation that distractors will be present may have resulted in a stronger preparatory effect that is not seen in studies that present targets without distractors (e.g. Corbetta, et al., 2005; Luck, Chelazzi, et al., 1997). Second, task difficulty has been shown to influence activity in V1 as well. Ress et al. (2000) showed that decreased difficulty in target detection led to a loss in preparatory attentional effects in V1. This implies that only when attention is in high demand, V1 shows an effect of selective preparation. It is possible that studies that did not find preparatory effects in V1 did not use a task difficult enough to require such early selective modulation. In this view attention in V1 operates in a different fashion compared to regions in extrastriate cortex, which do show an effect of attention even when the demand for attention is relatively low.

In the current study, eye movements were recorded in order to establish whether subjects maintained fixation during the critical cue-target period. Eye movements during this period would lead to inflated performance and undesirable effects in early visual cortex. Due to technical constraints we could not use infrared eye-tracking, but resorted to the electro-oculogram (EOG). There was no effect of cue direction on the EOG traces,

but the method is not entirely optimal. It is sensitive to relative systematic eye movements, so it requires proper fixation at the beginning of a trial and enough trials with the same type of response. On the other hand, subjects needed to fixate at the center in order to identify the cue, and eye movements towards the target location would have moved that location out of the cortical regions of interest and would have weakened the attentional effects. Therefore we feel confident that our results are not caused by systematic confounding eye movements.

In sum, the present study shows that primary visual cortex is activated by preparatory spatial attention. By endogenously changing the focus of attention from trial to trial, a change in activity in primary visual cortex was observed at the corresponding retinotopic location. In combination with recent ERP work (Kelly et al., 2008) our findings suggest that primary visual cortex may operate as a locus of initial sensory gain control, prioritizing visual input from an attended location.

Method

Participants

Based on the results of an eye movement screening study, 10 healthy participants (3 male, mean age = 23.7) were selected to take part in the fMRI experiment. All participants were right-handed and had normal or corrected-to-normal vision. Informed consent was obtained before taking part in the experiment. Participants received a financial compensation. The protocol was approved by the ethical committee of the VU University Medical Center, Amsterdam, The Netherlands.

Stimuli and task

An example of an experimental trial is given in Figure 1. Participants were instructed to focus on a centrally presented fixation point, which was presented for either 2200, 4400 or 6600 ms. Following fixation, a cue appeared at the center of the screen for 1200 ms. The cue could be one of the digits '2', '8', or '0', and subtended 0.65 by 0.38 degrees. This digit instructed participants to covertly shift their attention to the corresponding location on an imaginary clock. Digits '2' or '8' indicated that the target could appear at the corresponding clock location; when '0' was presented, the target could appear at either of

these locations. The neutral condition served to estimate the uncued baseline performance. After cue presentation the screen went blank for a random duration of 800 – 1200 ms, during which participants were instructed to maintain attentional focus on the cued location. To help participants focus on the exact location in an otherwise blank display, two faint, one-pixel dots were presented throughout the trial indicating the two possible target locations. The search display, presented for 1000 ms, contained either a horizontal or a vertical line functioning as target stimulus. Participants responded manually if they detected one of the target orientations. The target was embedded in distractor stimuli, consisting of tilted lines, subtending 22 degrees from the horizontal or vertical position. Distractors were presented on three imaginary circles surrounding the point of fixation at a distance of respectively 4.14, 5.49 and 6.84 visual degrees. Targets were always presented on the middle circle so that they were fully surrounded by distractors. The difficulty of the task was adjusted online in order to maintain a steady performance level. Changes in task difficulty were achieved by increasing or decreasing the length of the line by two pixels after every ten trials. All lines were extended when performance dropped below 75% and shortened when performance was higher than 75%. After the target disappeared from the screen, a blank screen appeared for 1200 ms, during which the participant was still allowed to respond. After this period a new trial was initiated. The onset of each trial was synchronized to the onset of an fMRI volume (see below).

In 25 % of the trials, the cue was not followed by a target display. Instead a blank screen lasting 2200 ms was presented after which a new trial was initiated. These catch-trials were inserted to decorrelate fMRI-responses evoked by cues and targets within a trial (e.g. Ollinger, Corbetta, & Shulman, 2001; Ollinger, Shulman, & Corbetta, 2001). In total, 320 trials were presented to each participant, divided over 5 blocks. Participants were instructed to respond as accurately as possible. Stimulus presentation and response collection were controlled using E-Prime 1.1 (Psychology Software Tools).

EOG Screening Task

Before taking part in the fMRI experiment participants were carefully screened for their ability to shift attention but not their eyes, as eye-movements would confound the results

in the scanner. Participants were seated in a dimly lit room at a distance of 100 cm from the presentation screen. To measure eye movements, tin electrodes were placed at the outer canthi of each eye and above and below the right eye. Electro-oculogram (EOG) signals were averaged for each condition (cue left, cue right), providing the average deflection from the fixation point between cue and target presentation. Participants started with a practice block, and five experimental blocks were presented subsequently, identical to the task in the MRI scanner. Finally, one additional block of trials was presented during which participants were instructed to make an eye-movement towards the cued location. Figure 4 displays the averaged cue-locked EOG for all 10 participants participating in the MRI study, showing trials of the main task and trials in which eye-movements were required. As can be seen no eye-movements were initiated after cue presentation in the main task.

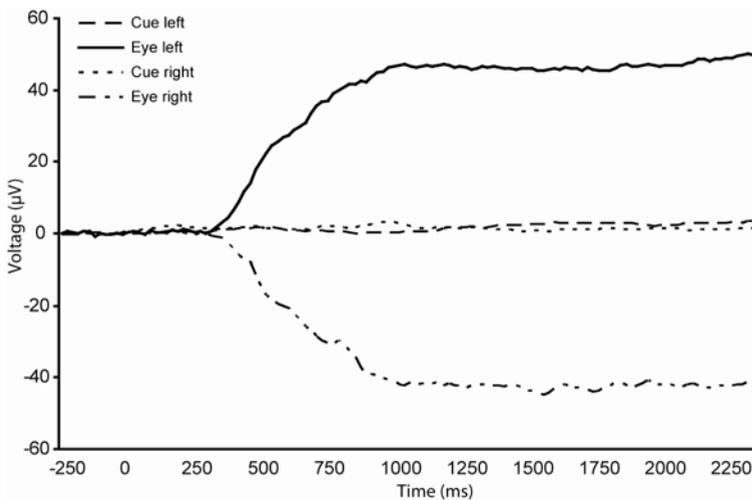


Figure 4. Horizontal EOG time-locked to the onset of the cue, averaged over all participants participating in the fMRI study. No eye movements were observed following the cue during the critical trial period (dotted and dashed line). For comparison, induced eye-movements to the left and right target location are added (solid and dash-dotted line). Target eccentricity was 5.5 degrees of visual angle.

Scan Acquisition

Imaging sessions took place in a 1.5 T Siemens Sonata scanner (Siemens Medical Systems, Erlangen, Germany), using an 8-channel phased-array head coil. Participants viewed the

stimuli through a mirror attached to the head coil. Functional data were collected using an EPI sequence scanning the whole brain in 24 near-axial slices. Scanning parameters for the main task were: TR = 2200 ms, TE = 55 ms, flip angle = 90°, slice thickness = 4 mm, gap = 0.8 mm, acquisition matrix = 64 x 64, in-plane resolution = 3.1 x 3.1 mm. All volumes were on-line motion corrected.

A 3-D anatomical scan was made at the end of the session, using a T1-weighted MP-Rage sequence. Scanning parameters were: TR = 2730 ms, TE = 3.43, TI = 1000 ms, flip angle = 7°, sagittal slice thickness = 1 mm, acquisition matrix = 256 x 224 pixels, in-plane resolution = 1 x 1 mm.

EOG was also recorded in the scanner between 2 carbon electrodes placed at the outer canthi of each eye, to ensure that participants did not make eye movements during the MRI sessions. Analysis of these data showed that participants were able to maintain fixation also during scanning. We tested the difference between EOG traces following leftward and rightward pointing cues and found no effect ($t(9) = 1.744, ns$).

Retinotopic mapping of visual areas

In two additional blocks, the vertical and horizontal meridian as well as the two target locations at clock positions '2' and '8' were stimulated with local flickering checkerboard patterns. The checks were counterphased at 10 Hz; each stimulus lasted 4s and was followed by the next after 8s. These localizer blocks served to identify the borders between visual areas V1, V2, V3, and the exact projection of the relevant visual field locations within these areas.

MRI Data Analysis

MRI data were analyzed using BrainVoyager QX 1.8 (Brain Innovation, Maastricht, The Netherlands). The first two volumes of each block were omitted in order to avoid differences in T1 saturation. The preprocessing of the remaining functional volumes consisted of slice scan-time correction, highpass filtering (0.01 Hz), slight spatial smoothing (3 mm FWHM Gaussian kernel), but no temporal smoothing.

The functional scans were automatically and if necessary manually coregistered to each individual anatomical scan and converted to Talairach space (Talairach & Tournoux,

1988) resulting in 4D functional data sets in Talairach space (e.g. Goebel, Muckli, Zanella, Singer, & Stoerig, 2001). Anatomical scans were also converted to Talairach space and segmented in order to separate the various tissues in each hemisphere. Based on the boundary between gray and white matter a model of the cortical surface was created. The segmented brains were then inflated, resulting in a smooth model of the cortical surface on which the functional data was projected. Based on the retinotopic data, regions of interest (ROIs) were defined in each of the 20 hemispheres corresponding to the projections of clock positions '2' and '8' in dorsal visual areas V1d, V2d, V3d in the right hemisphere, and ventral areas V1v, V2v, V3v/VP in the left hemisphere. Figure 2c shows a typical inflated left hemisphere and the three ROIs. In addition, based on the meridian activation, we also defined the homologue regions corresponding to clock positions '4' and '10', in order to determine the retinotopic nature of the attentional modulation.

Preparatory effects due to the cue were analyzed in these ROIs using two strategies: (a) We estimated the BOLD responses to all cues (both in catch-trials and trials in which target displays followed the cue) by means of a deconvolution GLM. A regressor was assigned to each of 8 volumes following the onset of all leftward, rightward and neutral cues, as well as following the onset of all left- and right-target displays. Note that the presence of catch trials (i.e., cue only) allowed us to decorrelate cue-related signals from target-related signals (e.g. Ollinger, Corbetta, et al., 2001; Ollinger, Shulman, et al., 2001). (b) We estimated the BOLD responses to the catch trials (i.e., only those trials in which cues were not followed by target displays) by computing event-related averages separately for each participant, ROI, and cue (i.e., the digit '2' or '8'). This allowed us to analyze BOLD responses to cues without any possible sensory contribution from target displays.

In both analyses, the resulting time series were averaged across hemispheres for each ROI (i.e., V1, V2, V3). Cueing effects were identified by comparing responses to cues indicating targets in the contralateral visual field (i.e., when the corresponding location was attended) with responses to cues indicating targets in the ipsilateral visual field (when the corresponding location was unattended), separately for each ROI and latency (i.e. fMRI volume).

Chapter 3

Spatial working memory effects in
early visual cortex

Munneke, J., Heslenfeld, D.J., Theeuwes, J. (2010). Spatial working memory effects in early visual cortex. *Brain and Cognition*, 72(3), 368-377.

Abstract

The present study investigated how spatial working memory recruits early visual cortex. Participants were required to maintain a location in working memory while changes in blood oxygen level dependent (BOLD) signals were measured during the retention interval in which no visual stimulation was present. We show working memory effects during the retention period in early visual cortex which were retinotopically organized in the sense that evoked BOLD responses were specific to the position of the remembered location on an imaginary clock. We demonstrate that this activity is similar to activity observed in conditions in which participants have to direct spatial attention to the same location. We suggest that during the retention interval modulation of neurons coding the remembered location evoke a baseline shift, providing converging evidence for the notion that spatial working memory may use spatial attention as a rehearsal mechanism.

Introduction

The ability to briefly maintain and interact with information held in memory is one of the pivotal qualities ascribed to “working memory”, and using this ability is functionally important for bridging the gap between perception and action. Over the years multiple models of working memory have been devised in an attempt to explain its many properties and functions (e.g. Baddeley, 1992; Baddeley & Hitch, 1974; Cowan, 1995). A widely accepted concept of working memory entails separate mechanisms for visuospatial and verbal storage of information, both of which have been studied extensively (for an overview see Jonides, Lacey, & Nee, 2005; Jonides, et al., 1996). Spatial working memory refers to the ability to store and interact with location-specific information of stimuli presented in the visual field over a brief period of time (for a recent review see Theeuwes, Belopolsky, & Olivers, 2009). Usually this ability is tested with a delayed recognition task (Awh, Jonides, & Reuter-Lorenz, 1998; Postle, et al., 2004; Smith, Jonides, & Koeppel, 1996). In a typical spatial delayed recognition task, participants are instructed to remember the location of an item presented on a display. After a delay during which the item is no longer present, a new item is presented and participants have to indicate whether the new item is presented at the remembered or at a different location. Delayed recognition tasks are used to study the properties and constraints of spatial working memory at a behavioural level, but are also used to study its effects at a neural level by looking at brain activity during the delay period. Due to the absence of visual stimulation during the delay period, observed neural activity is not confounded by sensory processes and therefore the observed neural activity is thought to reflect genuine working memory related processes.

Neural patterns during a working memory delay period are assumed to reflect memory related maintenance processes, ensuring an active representation of spatial information. Studies investigating the neural correlates of spatial working memory have demonstrated numerous regions in the parietal and frontal cortex which seem to reflect these maintenance processes, such as the prefrontal cortex (PFC), the frontal eye fields (FEF) and the posterior parietal cortex (PPC) (Curtis, 2006; Naghavi & Nyberg, 2005). However, some studies have questioned the interpretation of delay-period activity as purely mnemonic in nature. For example, Lebedev et al. (2004) had two monkeys (Macaca

mulatta) perform a task in which a saccade had to be made to either an attended or a remembered location. This study showed that neurons in prefrontal cortex of a monkey, that fired during a delay period, reflected maintenance processes only to a small extent, and that most cells in this region represented attended locations. They concluded that activity in prefrontal cortex observed during a delay period may exceed maintenance processes and that these processes may represent a broader scope of cognitive functions including spatial attention.

In line with Lebedev et al. (2004), spatial working memory is not the only source of activation in these areas in humans. Brain responses in the fronto-parietal network have also been observed in tasks involving spatial attention. Converging lines of research have suggested an intimate link between spatial working memory and spatial attention. Evidence for this suggested link comes from both behavioural and neuropsychological research. First, at a behavioural level it has been shown that processing visual information occurs more extensively at remembered locations compared to new locations, a finding similar to the observed enhanced processing of attended over unattended locations (Awh, Smith, & Jonides, 1995). Awh et al. showed that choice reaction times (RTs) to targets were faster when these targets were presented at a memorized location, compared to a non-memorized location, claiming that the speeded RTs were due to attentional enhancement of the processing of stimuli at the memorized location. In addition, when participants are unable to direct attention towards the remembered location, memory accuracy is attenuated (Awh, et al., 1998; Smyth, 1996) indicating that spatial working memory utilizes spatial attention mechanisms. Second, at a neural level a large overlap is observed in the cortical circuitry active during spatial working memory and spatial attention tasks in the fronto-parietal network (Awh & Jonides, 1998, 2001; Corbetta, 1998; LaBar, Gitelman, Parrish, & Mesulam, 1999). Furthermore, Jha (2002) showed that ERPs (N1 and P1) evoked by non-relevant probe stimuli during a delay-period in a working memory task were of equal magnitude independent of whether the probe stimuli were presented early or late in the delay period, suggesting that attention is deployed during the entire delay period. Taken together, these observations entail that both constructs may be conceptually different, but that the underlying neural mechanisms may be much more intertwined than commonly thought.

If spatial working memory evokes neural responses similar to spatial attention, then this overlap may not only occur in the fronto-parietal network, but in additional brain regions as well. Recently, an increasing number of studies on spatial attention have focused on the effects of attention on early visual processing in regions of the occipital cortex such as striate and extrastriate cortex. These studies indicate that the neural response to a visual event can be modulated by focused attention in striate and extrastriate cortex in a retinotopic fashion (Brefczynski & DeYoe, 1999; Gandhi, et al., 1999; Martinez, et al., 1999; Somers, et al., 1999). Moreover, in the absence of visual stimulation an increase in baseline activity can be observed in early visual cortex prior to the presentation of an expected visual event. Baseline activity refers to the spontaneous firing rate of neurons in the cortex and an attention-induced increase in baseline activity can be observed in both extrastriate cortex (Hopfinger, et al., 2000; Luck, Chelazzi, et al., 1997) and striate cortex (Jack, et al., 2006; Kastner, et al., 1999; Munneke, Heslenfeld, et al., 2008; Ress, et al., 2000). From these and other studies it has become apparent that visual cortex is involved in more than low-level processing of visual information.

If spatial working memory draws on the same neural circuitry as spatial attention, the question is whether visual cortex is also involved when remembering a location. In other words, does maintenance of spatial information in working memory elicit BOLD responses at retinotopic regions in early visual cortex? Previous research has shown some evidence that the visual cortex is modulated by remembering spatial information, but it is not always clear whether the observed activation pattern reflects working memory related maintenance processes or sensory processes caused by the stimuli presented during the task (Awh, et al., 1999). Moreover, the activation patterns observed were not retinotopic in nature, so the question as to what extent the observed effects are spatially specific to the target location remains (e.g. Courtney, Ungerleider, Keil, & Haxby, 1996). Postle et al. (2004) conducted a study which showed effects of spatial working memory in visual cortex; yet these effects did not reach statistical significance in primary visual cortex (V1) during the retention interval, despite being of a similar magnitude compared to effects of spatial working memory observed in extrastriate cortex.

Furthermore, in a recent fMRI study by Serences et al. (2009) multi-voxel pattern analyses (MVPA) showed that during the retention period of a working memory task, specific patterns of BOLD activation could be observed in V1 related to a to-be

remembered feature of a stimulus (colour or orientation). This result suggests that neural activation in early visual cortex may only reflect the coding of relevant features, but not the entire stimulus. A similar result was obtained by Harrison and Tong (2009) who were able to predict which of two gratings was held in working memory by the participant, based on classification of BOLD patterns. These studies show that early visual cortex is capable of maintaining to-be remembered information over a period of time during which the stimulus is no longer in view.

If visual cortex is capable of supporting working memory processes, this will add to the evidence linking the concepts of spatial working memory and spatial attention. A theoretical account of this overlap hypothesizes that maintaining location-specific information in spatial working memory is accomplished by shifts of spatial attention towards the memorized locations (Awh, et al., 1998; Awh, et al., 1999; Postle, et al., 2004; Smyth, 1996). Rehearsal of the stored spatial representation by covert shifts of attention acts as a functional mechanism similar to verbal rehearsal as a mechanism for storing information in verbal working memory (e.g. Baddeley, 1998). In both types of working memory, maintenance of the active representation is established by rehearsal of the task-relevant features of the stimulus. The existence of an attentional rehearsal mechanism in spatial working memory would explain the observation that the performance level in such a task is dependent on the attentional constraints of that particular task. Attentional rehearsal as a means for storage of spatial representations again emphasizes the strong behavioural link between the two concepts. However, at a neural level, the two constructs have mostly been studied separately and many questions concerning the overlap and functionality of observed neural activation during those tasks remain.

Although Awh et al. (2001; 1999) and Postle et al. (2004) observed effects of spatial working memory in early visual cortex; the method used in these studies leaves open some questions concerning the spatial specificity of the observed effects. Awh et al. and Postle et al. used full stimulation of both hemifields in order to define regions of interest in the visual cortex which makes the specificity of the observed effects within a hemifield hard to determine. This leaves open the question of whether the reported effects are truly retinotopic in nature or whether they reflect more general processes such as hemispheric arousal or alerting. In the current study we aim to further specify the effects observed by Awh et al. and Postle et al., investigating the spatial specificity of the observed effects and

the role primary visual cortex may play in attention and working memory. This is done by functionally defining the regions of interest (ROIs) in V1, V2 and V3 in a separate task based on target locations. Furthermore, ROIs based on nearby non-target locations were included in order to investigate whether the effects observed at target locations are spatially specific only for these locations or whether a larger part of the visual cortex is involved in spatial working memory.

Method

Participants

Sixteen paid volunteers participated in an fMRI experiment. All participants were healthy and had normal or corrected-to-normal vision. Based on eye movement data, three participants were excluded from further analyses, as systematic eye movements were observed during the task in the MRI scanner. Data from another subject was excluded from the analyses, because the behavioural results indicated that this subject was not able to perform the task in a proper fashion. All currently described analyses are based on data from the remaining twelve participants (1 male, mean age = 21.5 years). The protocol was approved by the ethical committee of the VU University Medical Center, Amsterdam, The Netherlands.

Stimuli and Task

Participants performed either a spatial working memory trial or a spatial attention trial. Trials were mixed within blocks. Figure 1 shows a typical trial for either task. Participants performed 64 trials of each task divided over eight blocks. An additional practice block of 16 trials (eight trials of each task) preceded the test blocks. Participants were instructed to maintain fixation at the central fixation point during the critical part of the trial, which started at cue onset and lasted until the manual response.

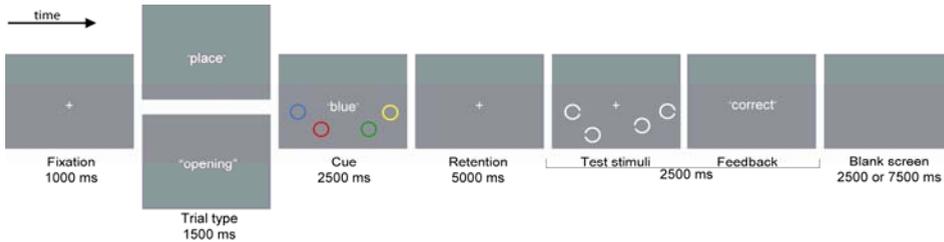


Figure 1. Time course of a typical trial. Participants were instructed to either perform a spatial working memory (“place”) or a spatial attention (“opening”) trial. Based on this instruction, participants had to remember the exact location of a colored circle in the working memory condition, or use this stimulus as a cue for an upcoming target in the attention task. After a 5 s retention interval, four new white circles appeared. In the working memory task, participants had to indicate whether the relevant white circle was present at the memorized location, whereas in the attention task participants had to indicate which side of the white circle contained a gap.

Working memory trials

At trial onset, participants focused the fixation cross ($0.6^\circ \times 0.6^\circ$) for a duration of 1000 ms, after which the word “place” appeared for 1500 ms, indicating that it was a memory trial. Following this instruction, a color word appeared (“red”, “blue”, “green”, “yellow”), which referred to one of four simultaneously presented colored circles (one *memory stimulus* and three distractor stimuli, in these colors). Participants had to remember the exact location of the circle indicated by the color word. For example, if the word “red” was presented, participants had to remember the location of the red circle. Following this display there was a five-second retention period during which only the fixation point was present in the middle of the screen. Subsequently four white circles (the test stimuli) appeared, all containing a small gap on the right or the left side. The gap was irrelevant in the working memory trials, but had a function in the attention trials (see below). The white test circles could appear either at the exact location of the colored circles, or with a small offset. On each trial, two test stimuli were positioned at the exact location of the previously presented colored circles, whereas the remaining two were positioned a small distance away from the location of the colored circles. The relevant test stimulus presented at the memory location had a 50% chance of being in the same location as the memory stimulus. All circles (diameter = 1.4°) were presented in the lower half of the visual field, centered on the positions of an imaginary clock at 4, 5, 7, and 8 hours, resulting in one stimulus per octant of the visual field. The test circles were presented for

a maximum period of 2500 ms, but disappeared when the participant responded with a button press. Importantly, in order to make sure that subjects were not verbally encoding the to-be-remembered location, the stimuli were not necessarily presented at the exact clock-positions, but could also be presented with a slight offset from this position, ensuring that participants had to store the actual location of the stimuli. Only the positions at 4 and 8 o'clock were used as memory locations, the remaining positions served as distractor locations.

Following the onset of the test stimuli, participants had to indicate whether the relevant test stimulus was presented at the exact location of the previous memory stimulus or whether it was presented with a small offset from this location. Responses to the trial were unspeeded and at the end of the trial feedback concerning the correctness of the response was given. After the response, a blank screen was presented for 2500 or 7500 ms before a new trial was initiated.

Spatial attention trials

Physically the attention task was identical to the working memory task. However instructions were different. If the word "opening" was presented at the beginning of the trial, instead of remembering the exact location of one of the colored circles, participants had to prepare for an upcoming target at that approximate location. Participants directed their attention covertly to the indicated colored circle which functioned as a location cue for the upcoming target. At the end of the trial, participants did not have to report the location of the test circle but had to report whether the opening of the test stimulus at the indicated location was on the left or the right side. Note that the cue itself was not indicative of the correct side of the target, but merely cued the location of the target stimulus. Other than the instruction word, properties and timing of stimuli were identical to the memory task. Again, only positions 4 and 8 were used as target positions, whereas positions 5 and 7 were used as distractor locations.

Task difficulty for both tasks was adjusted online in order to maintain a steady performance level. For both tasks, a moving performance average was calculated over the four most recent trials for each task separately. A cut-off score of 75% correct responses was used and task difficulty was adjusted when participants scored higher (i.e. trials were

made harder) or lower (i.e. trials were made easier) than the cut-off. Modulations in task difficulty for the memory trials were achieved by decreasing or increasing the distance between the location of the memory stimulus and the test stimulus by 2 pixels whenever participants performed above or below cut-off respectively. When the test stimulus was presented with an offset from the cued location, it was always presented on an imaginary line from fixation through the cued location, ensuring that no more than one stimulus per octant was presented. For the attention task, changes in difficulty were accomplished by decreasing or increasing the size of the gap in the test stimulus by 1 pixel whenever participants responded above or below cut-off respectively. For both tasks a performance level of 75% correct responses was aimed for. The initial difference in offset between target and test stimuli was 45 pixels (0.84°) and the initial gap size was 6 pixels (0.11°). Stimulus presentation and response collection were controlled using E-Prime 1.1 (Psychology Software Tools).

Even though the two tasks are perceptually similar and only differ in the instruction presented at the start of the trial, an important functional distinction underlying the tasks can be hypothesized. During a working memory trial, the exact stimulus location has to be memorized and carried over the delay period in order to make a comparison with the location of the newly presented target item. In other words, working memory trials contain a retrospective element in which a stimulus that is presented later in time has to be compared with a stimulus that has been presented at an earlier moment. In contrast, no such mechanism is required in the attention trials. As opposed to the retrospective nature of the working memory trials, attention trials contain only a prospective element, requiring preparation for an upcoming stimulus. Once the stimulus has been presented, no comparison has to be made with an item presented earlier in time, and a response can be given solely based on the presented target stimulus. Therefore, because of this functional distinction it may be argued that different neural processes may underlie the two tasks. However, if spatial attention is the means by which spatial working memory operates, both tasks may lead to very similar patterns of brain activity in visual cortex.

Scan Acquisition

Scanning sessions took place at the VU Medical Center using a 1.5 Tesla Siemens Sonata MRI scanner (Siemens Medical Systems, Erlangen, Germany). An 8-channel phased-array coil was used to obtain functional and structural images of the brain. An EPI sequence was used to obtain functional data of the entire brain. Scanning parameters for the main task were: number of slices = 25, TR = 2500 ms, TE = 60 ms, flip angle = 90°, slice thickness = 4 mm, gap = 0.8 mm, acquisition matrix = 64 x 64, in-plane resolution = 3.1 x 3.1 mm. To reduce the interfering effects of head movements during scanning sessions, all volumes were online motion corrected.

To obtain a 3-D anatomical scan a T1-weighted MP-Rage sequence was used at the end of the scanning session. Scanning parameters for the anatomical scan were: TR = 2730 ms, TE = 3.43, TI = 1000 ms, flip angle = 7°, sagittal slice thickness = 1 mm, acquisition matrix = 256 x 224 pixels, in-plane resolution = 1 x 1 mm.

During the scanning sessions horizontal electro-oculogram (EOG) was recorded by placing two carbon electrodes at the outer canthi of each eye. EOG was recorded (400 Hz) to ensure that participants did not make eye movements, as this would disrupt the patterns of functional activity obtained during the task. Analysis of these data showed that three participants were unable to maintain fixation during the critical scanning period (i.e. from cue onset, during the retention interval until target presentation). Data from these subjects were removed from further analyses. The remaining participants were able to maintain a steady gaze at the fixation point during the task.

Retinotopic mapping of visual areas

In order to map the borders between early visual areas (V1, V2, V3), the whole visual field was stimulated by presenting the participant with a slowly rotating checkerboard wedge. The wedge, with a width of 30 degrees, completed one rotation in 24 TRs. In total, eight rotations were presented in a single run; checks were counterphased at 9 Hz.

In a second task, target and distractor locations were stimulated with 9 Hz counterphased circular checkerboard patterns, presented at clock positions 4, 5, 7 and 8 (diameter = 3.2°). Each stimulus was presented for 1 TR (2280 ms) and was randomly followed by the next after an interval of 2 or 3 TR. This task served to identify the exact

visual field projections of the relevant locations in the experiment. Both tasks were combined (i.e., projections within the proper visual field borders) so that ROIs could be determined in striate and extrastriate cortex at the exact target location (see Figure 2)

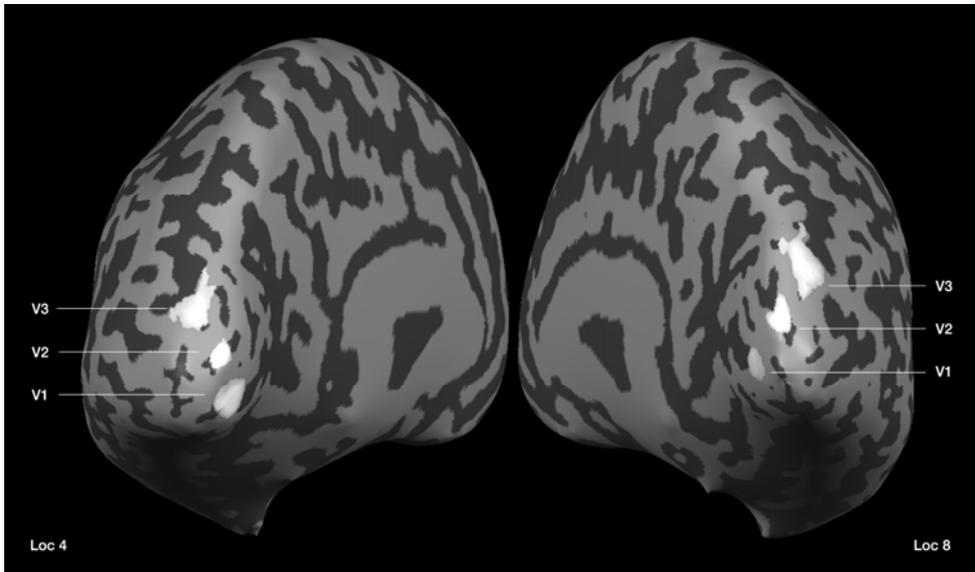


Figure 2. Inflated left and right hemisphere from a typical participant. Patterns of activation show representations of the right and left target location (at clock position 4 and 8) in V1, V2 and V3.

MRI Data Analysis

To analyze the MRI data Brainvoyager QX 1.10 (Brain Innovation, Maastricht, The Netherlands) was used. Because of differences in T1 saturation, the first two volumes of each run were removed. The remaining volumes were preprocessed, utilizing the following parameters: high-pass filtering (0.01 Hz), slice scan-time correction and a very gentle spatial smoothing (3 mm FWHM). Temporal smoothing (3s FWHM) was only applied to the data of the retinotopic mapping tasks and not to the data obtained in the main experimental task.

All preprocessed functional scans were coregistered to the individual anatomical scan and converted to Talairach space in order to obtain a 4D functional data set in Talairach space (Goebel, et al., 2001; Talairach & Tournoux, 1988). The 3D anatomical scan was converted to Talairach space and segmented, separating the various tissues of the brain. Based on the boundary between gray and white matter in the cortex, a

reconstruction of the cortical surface was created and inflated. Data from the retinotopic mapping experiments were projected on the inflated mesh to determine the ROIs in each of the 2 hemispheres for V1, V2 and V3 (see Munneke, Heslenfeld, et al., 2008).

The effects of spatial working memory and spatial attention in the visual cortex were investigated by determining the blood oxygen level dependent (BOLD) response by calculating event-related averages separately for each participant, task, and ROI. Event-related averaging provides a measure of BOLD signal change as a result of various events (i.e. cue onset, target onset) occurring in an experimental trial. In this analysis, the obtained time series were averaged across hemispheres for each ROI (i.e., V1, V2, V3). An advantage of the event-related average approach is that this type of analysis describes the BOLD response without any assumptions about amplitude or duration of this response, unlike a standard convolved GLM. In using this approach, the necessity to separate the different events in a trial can be circumvented when the duration between two events is sufficient. In the current study, cue and target presentation were separated by a delay period of five seconds, enabling a separation of cue and target related activity.

Effects of working memory and attention were investigated by comparing activity in ROIs evoked by cues indicating a relevant stimulus in the contralateral visual field compared to cues indicating a relevant stimulus in the ipsilateral visual field. This was done for both target and non-target locations. Because of the neural circuitry of the visual system, effects occurring in the retention period would lead to larger responses in the ROIs contralateral to the cued location.

Results

Behavioural data

Performance was calculated separately for both tasks. In the working memory task, average performance correct was 70%, whereas in the attention task it was 75%. All participants performed both tasks above chance level, which indicates that participants were performing the task as intended.

fMRI data

Targets. Hemodynamic brain responses evoked by the different events in each trial were determined from cue (color word) onset. The BOLD response was calculated using an event-related averaging procedure, reflecting percentage signal change in the BOLD response as a result of the different events in a trial. Event-related averages were calculated independently for each subject, task and region-of-interest. Figure 3 shows the averaged BOLD responses evoked during a trial for both tasks. At TR = 0, the cue is presented which results in the BOLD response peaking 5 seconds later (TR = 2). A decrease in activity can be observed in the 5 second interval following this peak (TR = 3 and TR = 4), which reflects the retention period. The BOLD response to the test stimulus can be observed peaking at 12.5 sec (TR= 5) and slowly dissipating afterwards.

In an initial, overall, within-subjects, ROI (V1, V2, V3) × task (memory vs. attention) × laterality (contralateral vs. ipsilateral) × TR (0 – 5) analysis, we found main effects of laterality ($F(1,11) = 39.642, p < 0.001$), ROI ($F(2,22) = 9.712, \epsilon = 0.921, p = 0.001$) and TR ($F(5,55) = 16.561, \epsilon = 0.499, p < 0.001$) showing that cues indicating a contralateral target location (i.e. the memory location or attended location) resulted in a larger BOLD response compared to cues indicating an ipsilateral target location (i.e. a non-memory location or unattended location), and that these responses varied over time and region of interest. No main effect of task was observed, suggesting a similar overall BOLD response in memory and attention trials ($F < 1$). Significant three-way interactions between ROI × laterality × TR ($F(10,110) = 4.835, \epsilon = 0.448, p = 0.002$) and task × laterality × TR ($F(5,55) = 3.894, \epsilon = 0.699, p = 0.012$) were observed, suggesting that the difference between contra- and ipsilateral activity changed differentially over TR and ROI for each task.

Significant interactions between laterality and ROI ($F(2,22) = 12.584, \epsilon = 0.993, p < 0.001$) and laterality and TR ($F(5,55) = 27.652, \epsilon = 0.424, p < 0.001$) indicated that the difference between contralateral and ipsilateral activity was not of equal magnitude for each ROI and TR. We therefore analyzed the effects of laterality and task independently for each ROI and TR. These follow-up analyses indicated significant differences between contralateral and ipsilateral activity in all ROIs, as indicated by main effects of laterality.

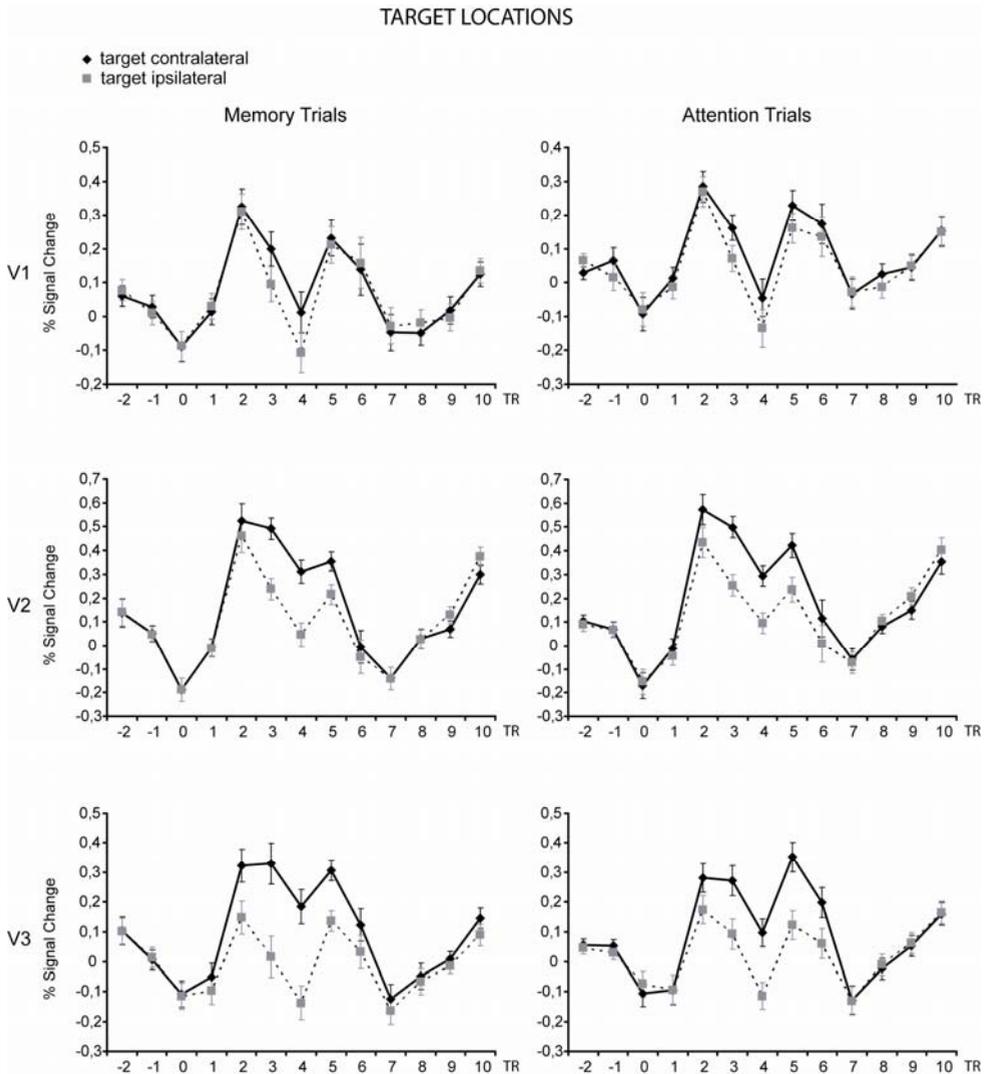


Figure 3. BOLD responses to trials of working memory (left column) and attention (right column) separately for each ROI (V1, V2 and V3) at target locations. The continuous line represents the BOLD response contralateral to the target location, whereas the dotted line represents the BOLD response ipsilateral to the target location. In all ROIs both tasks elicited a larger BOLD response during the retention period contralateral to the target location. Error bars represent the standard error of the mean corrected for within-subjects designs.

In V1 this effect became significant 7500 ms (TR = 3) post-cue and remained significant during the retention period and BOLD response evoked by the target stimulus (V1: smallest $F(1,11) = 11.476$, $p = 0.006$). Again, no main effects or interactions with task were

observed. In V2 and V3, similar results were obtained, but the difference between contralateral and ipsilateral activity became significant 5000 ms (TR = 2) post-cue (V2: smallest $F(1,11) = 9.620$, $p = 0.010$; V3: smallest $F(1,11) = 22.207$, $p = 0.001$), showing modulation of the cue. Additionally, interactions between laterality and task were observed in V3 during the retention period (TR = 3: $F(1,11) = 7.858$, $p = 0.017$; TR = 4: $F(1,11) = 7.219$, $p = 0.021$), which were caused by larger differences in the memory trials.

Non-Targets. In order to examine whether the observed BOLD responses were retinotopic in nature, the response at a non-target location in the same quadrant of the visual hemifield (contralateral) was compared to the non-target location in the opposite quadrant of the visual field (ipsilateral). The non-target locations corresponded to clock positions five and seven and these locations were never used as target locations. Again, repeated-measures analyses were conducted separately for each ROI (V1, V2 and V3) and TR (2-5). Contrary to the findings regarding the target locations, no main effect of laterality was obtained in V1 and V2 at the non-target locations (V1: largest $F(1,11) = 2.018$, $p = 0.183$; V2: largest $F(1,11) = 3.749$, $p = 0.079$), nor were main effects of task or interactions between task and laterality observed. A different pattern of results was obtained for V3. Similar to the observed patterns of BOLD activity at the target locations, a main effect of laterality was observed for all TRs in V3 (smallest $F(1,11) = 34.844$, $p < 0.001$). Furthermore, the analyses per TR and ROI showed significant interactions between task and laterality for certain TRs in V3. It was observed that during the retention period a larger difference between contra- and ipsilateral activity was observed in the memory task compared to the attention task. For TR = 3, the differences in percentage signal change were: Memory: 0.313% and attention 0.180% ($F(1,11) = 9.642$, $p = 0.010$). For TR = 4 these differences were: Memory 0.321% and attention 0.212% ($F(1,11) = 6.752$, $p < 0.025$). In both cases the interaction between task and laterality was caused by a larger difference between contra- and ipsilateral BOLD responses in the memory condition (see Figure 4).

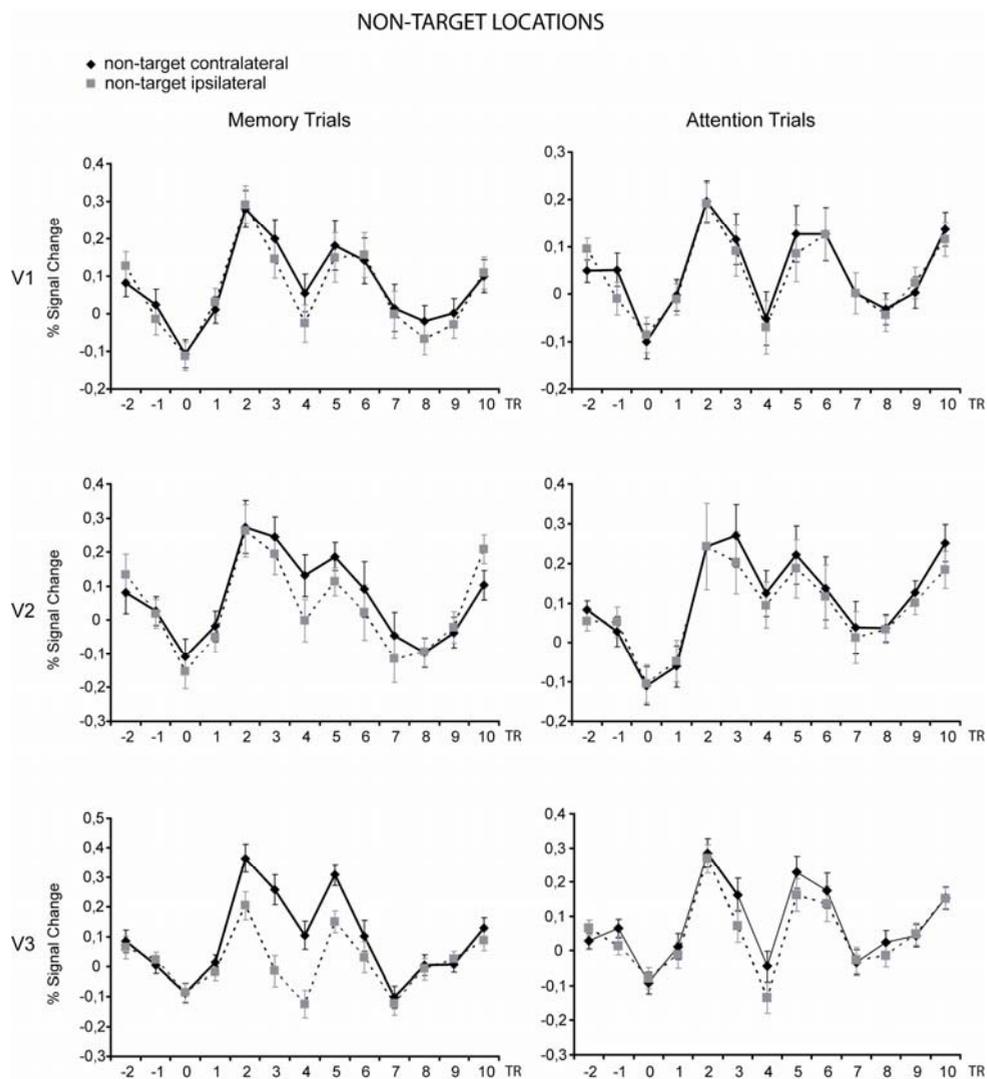


Figure 4. BOLD responses to trials of working memory (left column) and attention (right column) separately for each ROI (V1, V2 and V3) at non-target locations. The continuous line represents the BOLD response contralateral to the target side, whereas the dotted line represents the BOLD response ipsilateral to the target side. No difference between BOLD responses evoked at the non-target locations were observed for V1 and V2. Only in V3 did the difference between contra- and ipsilateral non-target locations reach statistical significance.

Targets vs. Non-Targets. Additionally, the difference between target and non-target locations was further analyzed by comparing the effects of working memory and attention at target versus non-target locations in the same contralateral quadrant. For example,

when clock position “4” was the indicated target location, a comparison between the ROIs reflecting location “4” and “5” was made. A repeated-measures ANOVA with location (target, non-target), ROI (V1, V2, V3), task (working memory, attention), and TR (0-5) showed a main effect of location, reflecting larger BOLD responses at target locations compared to non-target locations ($F(1,11) = 7.200, p = 0.021$). Furthermore, significant interactions between location and ROI ($F(2,22) = 14.282, \epsilon = 0.750, p = 0.001$), location and task ($F(1,11) = 6.483, p = 0.027$), location and TR ($F(5,55) = 4.344, \epsilon = 0.340, p = 0.033$) and location \times ROI \times TR ($F(10,110) = 4.911, \epsilon = 0.407, p = 0.002$) were observed, indicating that the effects of location were not the same for each ROI, task and TR. Post-hoc analyses per ROI and TR showed that the difference between the target and non-target locations during the critical period (TR 2-5) is strongest in V2 showing a larger BOLD response at the target location for all TRs (smallest $F(1,11) = 7.172, p = 0.021$). In V3 a small difference was found only at TR = 4 ($F(1,11) = 5.450, p = 0.04$). In V1 differences between target and non-target locations did not reach significance in the contralateral hemisphere during this period. Similar analyses for ipsilateral target and non-target locations showed a significant difference in BOLD amplitude between the target and non-target location in V1 for TR = 4 ($F(1,11) = 6.570, p = 0.026$). In V1 a larger BOLD response was observed at the non-target location compared to the target location ipsilateral to the cued side. Similar effects were not observed in V2 and V3 indicating that primary visual cortex was the only region in visual cortex showing decreased activation at the irrelevant target location compared to the non-target location.

Discussion

The present study aims to clarify and elaborate on previous work that shows that spatial working memory and spatial attention are mediated by early visual cortex. Looking only at target locations, it is shown that keeping a location in working memory results in an increased BOLD response in early visual areas V1, V2 and V3 at contralateral target locations, compared to ipsilateral target locations. More importantly, this response is retinotopically organized in the sense that responses were specific to the position of the remembered location on an imaginary clock. The increased activity was observed during the retention interval when no visual stimuli were present on the screen. These findings

suggest that the act of keeping a location active in working memory utilizes neural structures in early visual cortex.

An important feature of the present study is that we included two locations that contained a stimulus during cue and target presentation but which never needed to be kept in memory. For these non-target locations no difference was observed between the BOLD responses contralateral to the cued location compared to ipsilateral to the cued location in V1 and V2, suggesting that the modulation as a result of the spatial working memory instruction is retinotopic in primary visual cortex. In V3 a significant difference between contra- and ipsilateral non-target locations was observed. Even though this result may appear unexpected, it can be explained by the fact that the size of the receptive fields is relatively large in V3 (e.g. Smith, Singh, Williams, & Greenlee, 2001). When moving up the visual processing stream, receptive fields increase in size and in V3 they may be large enough to encompass both the target and non-target location, which makes it possible that target location effects are also present at nearby non-target location representations.

Importantly, when comparing BOLD responses at target and non-target locations within the quadrant contralateral to the cued side, qualitatively different results were obtained for V1, V2 and V3. Overall, a larger BOLD response was obtained for target locations than for non-target locations. This effect was most pronounced in V2, showing a larger BOLD response at target locations compared to non-target locations at all TRs. In V3 a larger BOLD response was observed at contralateral target locations. Unlike the effect in V2, this effect was only observed at one TR during the retention interval. The lack of an effect in V3 of equal magnitude and duration compared to V2 is most likely caused by overlapping receptive fields, encompassing both target and non-target location which may drown out the larger part of the effect.

No difference between contralateral target and non-target locations was observed in the primary visual cortex, suggesting that the previously reported effects in V1 between contra- and ipsilateral activity for target locations may be dependent on the ROIs ipsilateral to the cued side. Looking at the difference in BOLD amplitude between ROIs coding for target and non-target locations ipsilateral to the cued side, smaller responses were observed at the target location, compared to the non-target location. This deactivation at the uncued target location explains the initial difference between contra- and ipsilateral target locations.

Differences in BOLD amplitude contralateral to the uncued location, as is currently observed in primary visual cortex, have been observed in other studies. For example, Ruff and Driver (2006) showed in an fMRI study that foreknowledge about distractor presence resulted in BOLD effects only in visual cortex contralateral to the distractor location (i.e. ipsilateral to the target location), but did not influence target processing itself. This is in line with the current findings suggesting that the effects in V1 may be caused by a suppression mechanism attenuating the effects of the distractors in the ipsilateral visual field. Due to using only one location in the ipsilateral hemifield as a possible target location, it may be argued that this location gets suppressed more than the non-target location, resulting in less neural activation at the ipsilateral target location.

The cortical specificity of our findings, whether contra- or ipsilateral, rules out other possible explanations, such as alerting or other sources of arousal, as these would have resulted in a general increase of activity in ROIs coding for target and non-target locations in V1 and V2. We found spatially non-specific effects only in V3 suggesting that a non-target location next to a location held in memory leads to a larger BOLD response than a non-target location next to a target location not held in memory.

The present study supports the hypothesis that attentional rehearsal is the mechanism by which information is kept in spatial working memory as no differences were observed between BOLD responses reflecting the two tasks (Awh, et al., 1998; Awh, et al., 1999; Postle, et al., 2004). The current study shows a great resemblance between BOLD responses evoked by keeping a location in memory and BOLD responses elicited during a spatial attention task. Previous studies have shown that in both striate and extrastriate cortex, a neural response is elicited when spatial attention is allocated to a location of interest, showing sensory modulation of a stimulus (Brefczynski & DeYoe, 1999; Gandhi, et al., 1999; Somers, et al., 1999; Tootell, et al., 1998) and preparatory effects for an upcoming stimulus (Hopfinger, et al., 2000; Jack, et al., 2006; Kastner, et al., 1999; Luck, Chelazzi, et al., 1997; Martinez, et al., 1999; Munneke, Heslenfeld, et al., 2008; Ress, et al., 2000; Silver, et al., 2007). In the current study, similar effects during spatial working memory trials and spatial attention trials were obtained in V1 and V2, both tasks showing evoked BOLD responses of equal magnitude. This effect was observed in V3 for both tasks as well, but a difference in the size of the effect was observed between the two types of tasks, showing a larger effect in the spatial working memory task.

Previous studies have also provided evidence that spatial working memory recruits early visual areas. For example, Awh et al. (1999) showed that BOLD responses to a task-irrelevant flickering checkerboard, presented during the retention interval, were enhanced. Moreover, this effect was spatial in origin as there was more activity contralateral to the location kept in memory. Even though this study shows evidence for hemisphere-specific activity related to working memory, it should be realized that this is an effect in response to the test stimulus (i.e., the checkerboard). In other words, unlike what we show here, this study did not show an increase in activity in the absence of visual stimulation.

Postle et al. (2004) addressed the question whether neural activity in visual cortex would be present during the delay period in the absence of visual stimulation. Even in the absence of visual stimulation, Postle et al. observed an increased BOLD response evoked in extrastriate cortex as a result of keeping a location in memory. However, this baseline shift did not reach statistical significance in striate cortex during the delay period, leading to the conclusion that maintenance processes in spatial working memory are modulated in extrastriate cortex. Based on the quantitative effect observed in striate cortex, it could be hypothesized that a similar effect of spatial working memory might occur in striate cortex. Clearly, the current study shows that keeping a location in memory results in a modulation of activity in the absence of visual stimulation in both striate and extrastriate cortex.

Another possible cause for the larger modulation in primary visual cortex observed in the current study may be the role distractors play in attentional processing and, in line with the rehearsal theory, in spatial working memory maintenance processes. Serences et al. (2004) showed that when a target is likely to be accompanied by distractors, excitatory patterns of activation related to attentional enhancement of the target location can be observed, accompanied by an additional inhibitory component which is thought to reflect suppression of distractor interference. Desimone and Duncan (1995) showed that in the face of competition, attentional effects become larger as the attentional system has to suppress irrelevant information. The presence of distractors adds competition to the visual display and may therefore result in a larger preparatory response which could lead to the effects observed in V1 in the current study. In the study by Postle et al. no distractors were present, minimizing the need for resolving competition in the visual

display. Therefore, the absence of distractors may have resulted in a diminished preparatory effect due to which no effect in V1 was observed.

In a recent paper by Serences et al. (2009), it was hypothesized that maintenance during the delay period in a working memory task involved modulation of the sensory cortex coding the relevant feature of the stimulus (features were “color” and “orientation”). Multi-voxel pattern analysis (MVPA) showed that voxels in V1 coding color were significantly more active than voxels coding orientation during the retention period when color was the feature to be remembered. The reverse pattern was observed when orientation was the feature to be remembered. Even though no differences in BOLD amplitude between the response during the retention period and the response in a sensorily similar non-memory condition were observed, the MVPA showed that V1 plays a major role in maintenance of feature-specific information over a period in time. Our current findings add a spatial component to this data, indicating that voxels in V1 (and V2, V3) coding a to-be-remembered location show more activation than voxels coding a location not actively stored in working memory. Serences et al. conclude that the effects observed in V1 reflect actual maintenance processes and are not the result of attention-modulated sensory processes, encoding the to-be-remembered stimulus. A similar conclusion can be drawn from the current study. Based on the measured BOLD response in visual cortex, it is clear that during the retention period voxels coding the remembered location are significantly modulated at a time interval which does not coincide with sensory modulation. The BOLD response observed during the retention interval reflects an attentional baseline shift most likely indicating the manifestation of working memory-related maintenance processes.

In a study by Supèr et al. (2001), working memory related modulations in the primary visual cortex were investigated by having macaques make an eye movement towards a remembered stimulus. The Supèr et al. study showed that contextual modulation (i.e. the enhancement of the sensory response – in this case a task of figure-ground segregation) continues in V1 during a delay period, in the absence of the stimulus, but only when this information is needed at a later point in time. Nevertheless, the strength of the overall contextual modulation decreased over time, suggesting that the task required working memory processes. The results observed by Supèr et al. are not consistent with the current findings, as we did not observe this overall decline in working memory related

processes over time. This discrepancy may be explained by the fact that fMRI may be less sensitive than single-cell recording and therefore may not be able to reveal a subtle decline as reported by Supèr et al. Moreover, one should be careful when comparing BOLD responses as measured with fMRI in humans with neuronal spike trains as measured with single-cell recording in a monkey brain. Even though the responses measured by both techniques are assumed to reflect underlying neural processes, the physical processes underlying these measurements are entirely different and may therefore yield different results under similar conditions.

A recent study by Offen et al. (2009) also investigated the overlap between visual short-term memory (a component of visual working memory) for features and visual attention. It was shown that early visual cortex, including V1, showed spatially specific sustained activity during a delay period in tasks with high attentional demand, but not in a perceptually similar task utilizing spatial working memory. This dissociation between visual attention and visual working memory seems inconsistent with the current results as well as the notion of attention-based rehearsal as the mechanism by which working memory operates. However, as Offen et al. point out themselves, it is known that there are distinct mechanisms for spatial working memory and working memory for object features. Because Offen et al. used a feature-based working memory task, this may very well be the critical distinction between their study and the current study. This would indicate that the rehearsal mechanism only applies to location-based working memory processes as opposed to feature-based working memory processes.

The current findings suggest that the visual cortex, including V1, is actively involved in maintaining spatially specific properties of to-be-remembered information. These maintenance processes are most likely the result of a rehearsal mechanism in which covert shifts of top-down attention are made towards the memory location. The involvement of attentional processing explains why a spatial attention task resulted in similar patterns of activation in all ROIs. Therefore, it can be concluded that spatial working memory and spatial attention, even though conceptually different, are mediated by a similar functional neural network.

Chapter 4

Cueing the location of a distractor: An inhibitory mechanism of spatial attention?

Munneke, J., Van der Stigchel, S., Theeuwes, J. (2008). Cueing the location of a distractor: An inhibitory mechanism of spatial attention? *Acta Psychologica*, 129, 101 - 107.

Abstract

Presenting an irrelevant distractor increases reaction times to a target. The current study shows that cueing the location of an upcoming 'distractor' can help to reduce the effects the distractor has on target processing. It is hypothesized that this reduction is due to the active inhibition of the cued location. In two experiments in which the location of the distractor was cued in advance, a reduced effect of the distractor on target processing was observed. Analyses indicated that this effect was most likely caused by inhibition of the distractor location. The present findings suggest that inhibition plays an important role in visual-spatial selection processes and that this inhibitory mechanism can be controlled in a top-down fashion.

Introduction

Our capacity-limited brain is not equipped to dealing with the vast amount of sensory information that is presented to us at any given time. Therefore, a selection that separates the relevant from irrelevant information has to be made, allowing goal-directed behavior. Numerous studies have shown that focusing attention on locations or objects in the visual field improves this selection process (Luck, et al., 1996; Posner & Petersen, 1990; Theeuwes, 1989; Theeuwes & Van der Burg, 2007), which has led to the conclusion that attention is the necessary mechanism required for selection. When advance information regarding the location of relevant information in the visual field is available, attention can be deployed to this location prior to the actual presentation of relevant information. In a series of now classic experiments (Posner, 1978, 1980; Posner, et al., 1978; Posner, et al., 1980) it was shown that performance in detecting or discriminating a target significantly increased when the location of the target was previously cued. In a typical cueing task, participants are instructed to respond to the appearance of a target stimulus by making a key press. In one variety of this task, called “endogenous”, a central cue (typically an arrow) points to a possible target location, thereby allowing the participants to focus their attention on that location. After cue presentation the target will appear at the cued location (valid) in the majority of the trials, but will sometimes appear at an uncued location (invalid). The typical finding is that participants tend to respond faster and with higher accuracy to the target if it is presented at the cued location than when it is presented at the uncued location. These results reveal a benefit of location cueing: focusing attention on the cued location enhances processing of the target stimulus, which results in faster responses and higher accuracy.

Even though most studies have focused on cueing an upcoming target location, recently, a number of studies have begun to investigate the effects of cueing the location of an upcoming distractor (Ruff & Driver, 2006; Van der Stigchel, et al., 2006; Van der Stigchel & Theeuwes, 2006). The general idea behind these studies is that advance knowledge of the location of an upcoming distractor can help to reduce the interference of this stimulus on target processing. Previous research has shown that when an irrelevant distractor is presented with a target stimulus, the capture of attention by the distractor impoverishes processing of the target as reflected by slower reaction times to the target

(e.g. Schreij, et al., 2008; Theeuwes, 1992). Moreover, in a study by Theeuwes et al. (1998) it was shown that the eyes can also be captured by a new appearing irrelevant distractor.

One of the mechanisms thought to be responsible for a possible reduction of interference is inhibition of the distractor location. In an eye movement study by Van der Stigchel & Theeuwes (2006), participants were informed whether and where a distractor would appear. Participants were presented with a central cue consisting of a short arrow pointing towards the location of a possible distractor (80% probability) and a long arrow pointing towards the target location. When the target appeared, participants were instructed to make a speeded eye movement towards the target location. The rationale behind this study was that participants could actively inhibit the distractor location on the basis of a top-down expectancy of where the upcoming distractor would appear. The results of this study showed that by cueing the location of the distractor in advance, the eye movement towards the target location was affected, showing a trajectory which deviated away from the distractor location even when the distractor was absent. Because these deviations away from the distractor location have been attributed to active inhibition of this location (Sheliga, Riggio, Craighero, & Rizzolatti, 1995; Sheliga, Riggio, & Rizzolatti, 1994; Tipper, Howard, & Jackson, 1997), these results provide evidence for the idea that participants were actively inhibiting the distractor location on the basis of the distractor cue, even in trials in which the distractor did not appear.

The inhibition of irrelevant information is not only reflected in eye movement trajectories, but has also been found in a number of behavioral studies (e.g. Cave & Zimmerman, 1997; Wuhr & Frings, 2008). In the study by Cave & Zimmerman it was found that distractors presented close to the focus of attention received more inhibition than distractors presented further away. In their dual-task study, participants were instructed to give an unspeeded response reporting the presence or absence of a target letter within a circular array of (otherwise) non-target letters. In 50% of the trials a probe would appear after the presentation of the search array and participants would make a speeded response to the appearance of the probe. The probe could appear at a location previously occupied by either a target or a distractor letter. The results showed that reaction times to the probe were the fastest when the probe was presented at the target location. However, slowest reaction times were observed for probes appearing at distractor

locations with the least spatial separation between target and distractor, reflecting an inhibitory region surrounding the attended target location.

In a similar line of research it was found that probes presented close to salient stimuli (feature singletons) were inhibited resulting in lower probe discrimination sensitivity (d') at short distances from the feature singleton (Mounts, 2000b). Participants were shown a stimulus array containing multiple figure eight stimuli including one item that was made more salient (the singleton). The increased saliency of the singleton ensured an attentional focus at the singleton's location. After presentation of the search array, a probe was presented at a variable distance away from the singleton. When the probe was presented close to the salient item, d' was significantly lower than when the probe was presented further away, again reflecting the inhibitory surround of the focal point of attention. Importantly, inhibition of the probe location decreased with an increasing singleton-probe distance. In a follow up study by Mounts (2000a) it was reported that the inhibitory component is attentional in origin and can be top-down controlled by changing the participants' attentional set. When the target was a conjunction of features, this circle of inhibition disappeared and the color singleton itself became inhibited. Therefore, it is claimed that inhibition is at least up to a certain extent under top-down control.

Inhibition surrounding the focus of attention has been described as "localized attentional interference" and is more thoroughly investigated in a number of different studies (e.g. McCarley & Mounts, 2007; McCarley, Mounts, & Kramer, 2007; Mounts & Tomaselli, 2005). Importantly, these studies show that selective attention is not merely accomplished by enhancing the neural response coding for the attended location, but that inhibition of the surrounding area degrades the processing of items presented in this region. Both enhancing the attended location and the inhibition of the surround results in a bias favoring the attended location.

In a recent fMRI study by Ruff & Driver (2006) participants performed a speeded discrimination task in which an arrow was presented pointing to the location of the upcoming target. In the experimental blocks, the color of the arrow (either red or green) informed the participants whether a distractor would be present or absent. If a distractor was present, it always appeared at the opposite side of the screen. In control blocks, the target arrow did not provide information whether a distractor would appear or not. This

study showed that participants were generally slower when a distractor was present than when it was absent. However, on trials in which the upcoming distractor was cued, reaction times were faster compared to trials in which this information was not available. Another important finding of this study was that when there was advance knowledge that a distractor would not be presented, reaction times were similar to those found in the control block in which distractors were absent. This suggests that the differences found in the cued-distractor present condition are not attributable to an increase in arousal or other general effects. According to Ruff & Driver, advance knowledge of an upcoming distractor helps counteract the impact of this stimulus, resulting in faster responses to the target. However, they do not explain the mechanisms responsible for the decrease in detrimental effects caused by the distractor. The fMRI data showed that when a distractor was validly cued, activation in the corresponding hemisphere (which was never the hemisphere corresponding to processing of the target) arose, suggesting that an active process was taking place at the cued distractor location. Based on the inhibitory effects found in eye movement studies, it seems plausible that the effects found by Ruff & Driver are caused by top-down inhibitory effects, even though this explanation was not suggested in their paper. Cueing the location of the upcoming distractor may have resulted in active inhibition of the cued location, allowing for faster target detection.

Alternatively, the cue may function as a means for the participant to help distinguish which of the presented items is the target and which is the distractor. In general, looking for a target involves comparing all items, until a pre-defined shape has been detected. When a cue is presented indicating the location of an irrelevant stimulus, this comparison is no longer necessary for this irrelevant stimulus. In this account, the cue does not evoke inhibition at the distractor location, but helps the participant select the target from the presented items. This account does not necessarily invoke inhibitory processes at the distractor location.

The present study was set out to determine whether cueing the location of an upcoming distractor would evoke top-down inhibition of this location diminishing the effect of the presented distractor. The question arises whether it is possible to actively inhibit the distractor location purely on the basis of advance knowledge. In a first experiment the location of the distractor was cued on half the trials. When a cue was present, a distractor would appear at the cued location on half the trials. In the remaining

trials a distractor was not present. Participants were instructed to respond to the target, while making use of the distractor cue. Importantly, there were always four possible target locations, making the exact target location unknown. This design allows examining whether inhibition can occur as a result of advance information about the location of the distractor, independent of target cueing.

EXPERIMENT 1

In Experiment 1 we investigated whether cueing the location of a distractor can improve target processing. Participants were asked to judge the orientation of a target stimulus by making a two-choice response. At the start of each trial, the possible distractor location was indicated by a central cue. Participants were instructed to actively use this information. The aim of this study was to investigate whether locations can be inhibited on the basis of advance knowledge of the possible distractor location. If fewer attentional resources are allocated to the distractor, this should result in a faster response to the target.

Method

Participants

Twelve healthy participants (eleven female, mean age = 20.9 yrs) served as paid volunteers. All participants had normal or corrected-to-normal vision and were naive to the purpose of the experiment.

Stimuli

All stimuli were presented in grey on a black background, with the exception of the cue which was presented in an equiluminant type of red (11.4 cd/m). The target consisted of either a capital 'T' or an inverted capital 'T', whereas the distractor always took the shape of the two different targets superimposed, resulting in an 'I' shaped figure. Target and distractor were presented at a visual angle of 5.3° from the central fixation point and at a distance of either 10.6° or 7.5° from each other, depending on the location of both stimuli. The size of the target and distractor was 0.76° by 0.99°. The cue screen consisted of four arrows of which one could turn red, indicating the distractor location. All arrows

subtended a visual angle of 1.14° by 0.69° and were presented 1.07° degrees from the center of fixation. Stimulus presentation and response collection were controlled using E-Prime 1.1 (Psychology Software Tools, www.pstnet.com), running under Windows XP on an Intel Pentium 3 pc. A 19" CRT monitor was used to display the experiment.

Procedure

Participants were seated in a dimly lit cabin at a viewing distance of 75 cm from the monitor. Figure 1 shows the time course of a typical trial. First, a fixation screen was presented, containing the four centrally presented arrows with a fixation point in between. The arrows pointed to the four possible target and distractor locations.

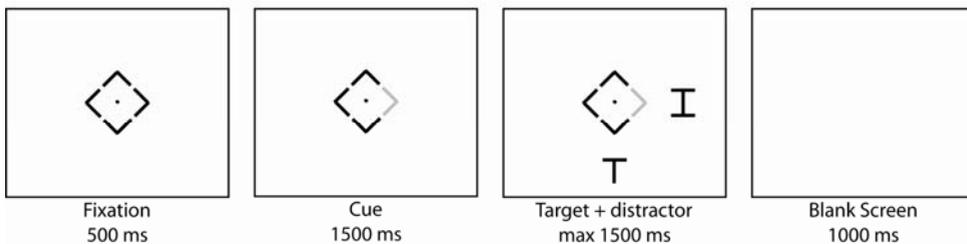


Figure 1. Time course of a typical trial in Experiment 1. Participants were presented with four arrows of which one could turn red 2000 ms after trial onset, indicating the location of the upcoming distractor. Participants responded to the identity of the target by pressing a key as fast as possible. Both cue and distractor could be present or absent resulting in a 2 x 2 design.

Participants were instructed to maintain fixated on the centrally presented fixation point during the entire trial. After 500 ms, on half the trials one of the arrows turned red, indicating the location of a possible distractor. When a location was cued, a distractor could appear at that location on 50% of the trials, whereas on the other 50% of the trials no distractor was present. In the event that the cue was not presented, a distractor could still appear on half the trials at one of the four locations. On the remaining trials only the target was displayed. The cue, which was presented for 1500 ms, was 100% indicative that the target would not appear at the corresponding location. If no cue was presented, the four arrows remained on screen for an additional 1500 ms in order to obtain similar time courses for cue present and cue absent trials. The target and distractor would remain on-screen for a maximum duration of 1500 ms, but would disappear when a response was

given, after which a black screen was presented for 1000 ms, signaling the start of the next trial. The entire experiment consisted of five blocks of 96 trials each, the first block being used as a practice block. Target and distractor locations were balanced over blocks. Participants responded as fast as possible to one orientation of the target with their left hand, while for the other orientation the right hand was used. The response hand was counterbalanced over participants.

Results

Reaction times smaller than 200 ms and larger than 1200 ms (0.69%) and reaction times on incorrect responses (4.92%) were excluded from the analysis. No significant effects of the experimental manipulations were found in the error scores.

A repeated measures analysis of variance (ANOVA) with “cueing” (distractor cued vs. distractor uncued) and “distractor” (distractor present vs. distractor absent) as factors revealed a main effect of cueing and distractor. Participants responded faster to the target when the location of the possible distractor was cued than when it was not cued (cued: mean = 568 ms, uncued: mean = 585 ms; $F(1,11) = 13.99$, $p < 0.005$; $MSE = 254.05$). Furthermore, participants were slower when a target was accompanied by a distractor than when a target was presented alone (distractor present: mean = 613 ms, distractor absent: mean = 540 ms; $F(1,11) = 59.24$, $p < 0.001$; $MSE = 1090.55$). Importantly, there was a significant interaction between Cueing and Distractor ($F(1,11) = 5.74$, $p < 0.05$; $MSE = 244.62$). Figure 2 shows that the distractor evoked a larger increase in reaction time when the cue was absent compared to when the cue was present. Indeed, additional t-tests showed that participants benefited from a cue when a distractor was present ($t(11) = 3.41$, $p < 0.01$) but not when a distractor was absent ($t(11) = 1.63$, $p > 0.10$).

Even though these results can be fully explained by an inhibition mechanism, reducing the interfering effects of the distractor, an alternative explanation might also account for the results. It could have been that the distractor cue functioned as a target cue, cueing the three remaining target locations. This would have allowed participants to shift their attention towards the three remaining locations or make an eye movement away from the cued location, instead of inhibiting the distractor location. In this

explanation, the mechanism responsible for the reduced influence of the distractor would not be inhibitory in nature, but excitatory.

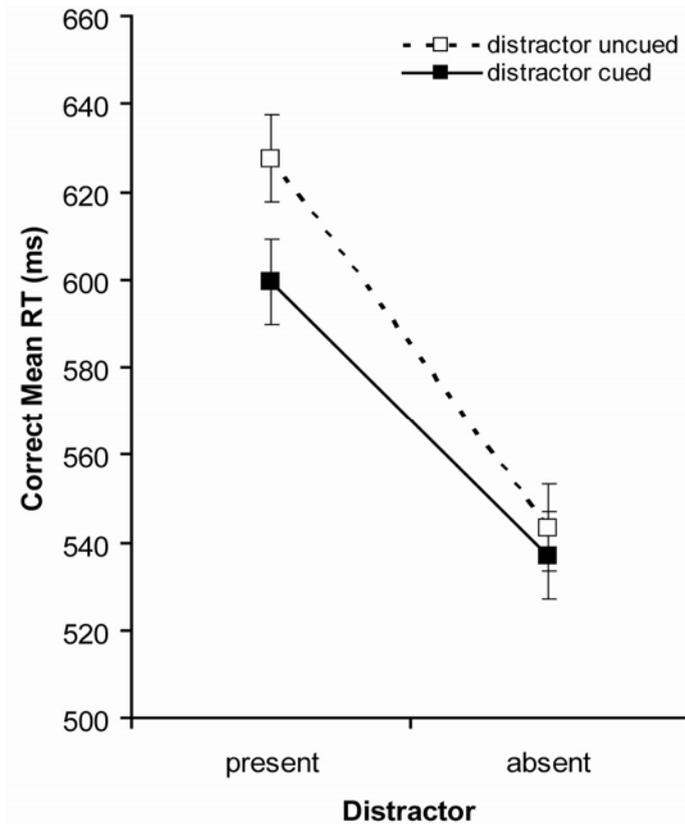


Figure 2. Mean response time (in ms) of Experiment 1 shown in two conditions. When a cue is present the distractor effect is reduced. Error bars represent 95% confidence intervals for the interaction between cueing and distractor presence, corrected for within subjects designs (Loftus & Masson, 1994).

To rule out this alternative account, we compared the effects of the cue on target-only trials. If participants used the distractor cue to attend to the remaining target locations, this should result in faster responses to the target when the distractor cue was present compared to when no distractor cue was presented. As reported above, in distractor absent trials there was no difference between the trials in which the distractor location was cued and the trials in which the distractor location was not cued. Moreover, if participants shifted their attention away from the cued location, this would result in a

difference between targets which were presented relatively close to the cued location and targets presented further away from this location (7.5 degrees and 10.6 degrees of visual angle respectively). An ANOVA with distractor (distractor present vs. distractor absent) and distance (target close vs. target far) as factors, revealed no significant effect of distance ($F < 1$). Again an effect of distractor was found ($F(1,11) = 32.70, p < 0.001; MSE = 1522.74$), but no significant interaction between distractor and distance was observed ($F < 1$). Therefore, a shift of attention away from the cued location as an explanation for the observed effect seems unlikely.

Discussion

In cueing studies it is often found that a target stimulus is processed faster when information about the target location is known in advance. In Experiment 1 we showed that cueing the location of a distractor diminishes the interfering effects of this distractor. We first replicated the distractor effect, showing that the presence of a distractor severely deteriorates performance on the target. We further showed that by cueing the location of a distractor, providing participants with advance knowledge of an interfering stimulus, the detrimental effects caused by the distractor decreased. Our results can be fully explained by a model in which inhibition is the main mechanism responsible for the results. By inhibiting the cued location, the information presented at this location does not receive the amount of attentional resources it would have received when a cue had not been provided. This lack of attentional resources results in less competition caused by the distractor thereby leaving the target automatically with more available resources, making the processing of this stimulus more efficient.

However, an alternative explanation can account for the observed effects as well. It is possible that participants do not use the cue to inhibit the distractor but to distinguish between which of the presented items is the actual target. If the cue is absent, participants can only find the target by distinguishing between the shapes of the presented items. When a cue is presented this is no longer necessary, because the cue provides sufficient information about which of the presented items is the target. In this situation no visual search is necessary because the target is the only element not presented at the cued location. This explanation might also account for the lack of

inhibition when no distractor is present. When no distractor is present, there is also no ambiguity as to which item is the target. Because of the lack of ambiguity the information provided by the cue is not necessary; hence the information provided by the cue is only used when a distractor is actually presented. Thus, the results of Experiment 1 could have been established either due to inhibition of the distractor location or due to the presence of a cue, reducing the need to search for the target stimulus. The set-up of Experiment 1 does not allow a separation of both mechanisms, but shows that advance knowledge of a distractor location reduces the interfering effects of items presented at that location.

To differentiate between the proposed inhibition account and the above mentioned “ambiguity” account, a second experiment was conducted in which information at the distractor location automatically influences target processing. For these ‘automatic’ distractors, there is always ambiguity except when information is actively suppressed. Therefore, a flanker-like design was adopted because it is known that compatible and incompatible flankers presented at non-target locations automatically interfere with target-processing despite prior information about the target and distractor locations (B. A. Eriksen & Eriksen, 1974; Miller, 1991). If the inhibition account is viable, the information at the cued location should disrupt target processing less, because the compatible and incompatible distractors are actively suppressed. If the ambiguity account is valid, distractor processing still occurs and the distractors will therefore influence target processing.

Furthermore, to exclude the possibility that the absence of an inhibitory cueing effect in the distractor-absent condition in Experiment 1 is due to a single target appearing as an abrupt onset, allowing this item to capture attention and dissolve the inhibition quickly, multiple elements were presented on every trial in Experiment 2. Besides a target and a distractor, neutral stimuli were presented which do not interfere with target processing.

EXPERIMENT 2

To differentiate between the two proposed mechanisms a second experiment was run in which the location of upcoming distractors was cued in a flanker-like task. A distractor

accompanied the target on every trial and could either be compatible or incompatible with the target.

Method

Participants

Fourteen healthy participants (nine female, mean age = 23.4 yrs) served as paid volunteers in this experiment and none of them had participated in Experiment 1. All participants had normal or corrected-to-normal vision.

Stimuli

All stimuli were presented on a dark grey background in a lighter shade of grey (12.08 cd/m) with the exception of the cueing arrow(s) which could turn red (7.96 cd/m). Targets consisted of the capital “B” or “F”, whereas the distractor was always indicated by the lower case letter “b” or “f”. Because of the response compatibility between the distractor and the target, it was thought that the distractor would have a strong effect on target performance. Neutral stimuli consisted of randomly selected upper or lowercase letters “x” and “k”. Distances between the fixation point and stimuli were similar to those in Experiment 1. The letter stimuli subtended a visual angle of 0.99 by 1.25 degrees.

Procedure

The time course of this experiment was similar to Experiment 1. The fixation screen, which was presented for 500 ms, consisted of four centrally presented arrows, pointing towards the possible target and distractor locations, with a central fixation point in between. In 50% of the trials, all arrows turned red and thereafter the elements were presented. In the remaining 50% of the trials, only one arrow would turn red, indicating the location of the upcoming distractor. A search display always consisted of a target, a distractor and two neutral stimuli. The different targets corresponded with two different response keys on a standard keyboard and response hand was counterbalanced over participants. Two thousand ms after cue presentation, the search display appeared and the participant was instructed to respond to the target as fast as possible. Target and distractors remained on screen for a maximum duration of 1500 ms, but disappeared when a response was given.

The distractor was compatible with the target in 50% of the trials and incompatible on the remaining trials. Note that again, the target never appeared at the cued location. The experiment consisted of three blocks of 96 trials, preceded by a short practice block of 48 trials.

Results

Reaction times smaller than 200 ms and larger than 1200 ms (2,38%) and reaction times on incorrect responses (6.12%) were excluded from the analysis. No significant effects of the experimental manipulations were found in the error scores.

A repeated measures analysis of variance (ANOVA) with “compatibility” (distractor compatible vs. distractor incompatible), “cueing” (distractor cued vs. distractor uncued) and distance (“close” vs. “far”) as factors showed a main effect of compatibility. Participants responded faster to a target when it was flanked by a compatible distractor compared to an incompatible distractor (compatible: mean = 647 ms, incompatible mean = 677 ms; $F(1,13) = 29.64, p < 0.001; MSE = 844.60$). A main effect of cueing was observed, indicating that participants respond faster when a cue was presented, than when the cue was absent (cue present: mean = 640 ms, cue absent: mean = 685 ms; $F(1,13) = 29.94, p < 0.001; MSE = 1827.32$). A main effect of distance was found, demonstrating that participants were faster to respond when target and distractor were presented further apart (distance close: mean = 669 ms, distance far = 656 ms; $F(1,13) = 5.20, p < 0.05; MSE = 895.47$).

As can be seen in Figure 3, the compatibility effect was larger in the distractor uncued condition compared to the distractor cued condition, indicated by a significant interaction between Cueing and Compatibility ($F(1,13) = 9.73, p < 0.01; MSE = 673.93$). Post-hoc testing showed that in both the cued and the uncued condition the compatibility effect was significant (Cued: $F(1,13) = 4.82, p < 0.05; MSE = 341.37$; Uncued: $F(1,13) = 56.35, p < 0.001; MSE = 270.83$). No other significant interactions were found in this experiment.

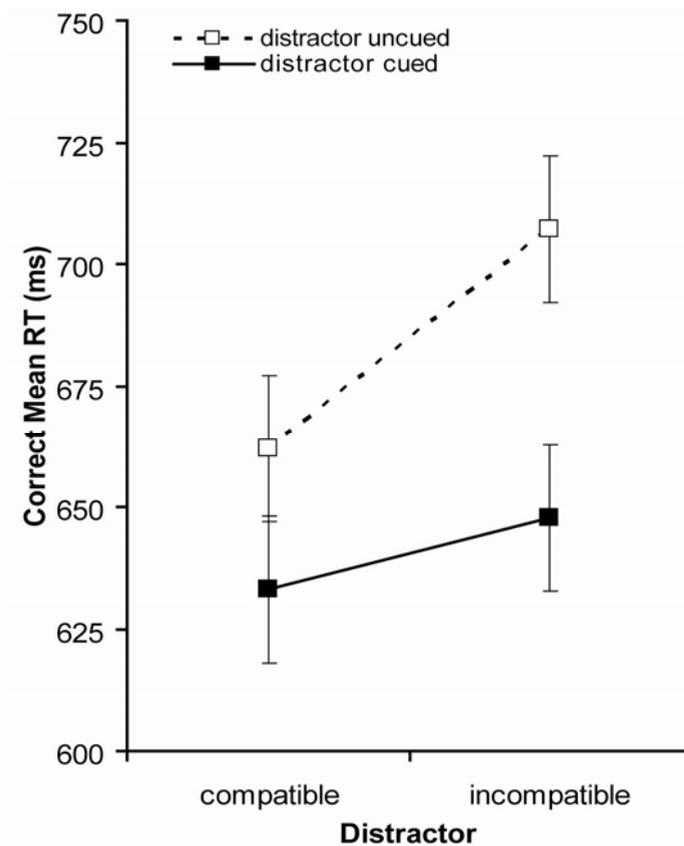


Figure 3. Cueing the location of a flanker-like distractor results in a reduced compatibility effect. Error bars represent 95% confidence intervals for the interaction between cueing and compatibility, corrected for within subjects designs (Loftus & Masson, 1994).

Discussion

Similar to Experiment 1, cueing the location of a distractor decreased the effect of the distractor on target processing. Because the nature of the distractor was such that it would automatically influence target processing, we were able to dissociate between two possible explanations. If the ambiguity account would be valid, distractor processing should still occur and therefore influence target processing. However, if the cue allows an active inhibition of the distractor, the interference it causes should be reduced. The data support the latter explanation, because the compatibility effect was very much reduced when the distractor location was cued in advance.

General discussion

Most cueing studies have focused on providing participants with advance knowledge of the location of an upcoming target stimulus. In the present study it was not the location of the target that was cued, but the location of an upcoming distractor. The results of Experiment 1 showed that cueing the distractor location led to faster response times to the target. This shows that the advance knowledge of the distractor location diminishes the interfering effect of the distractor suggesting an active inhibition of the distractor location. However, the results could also be explained by an alternative account in which ambiguity about the target is reduced because of the presence of the distractor cue.

Experiment 2 was conducted to separate the two proposed accounts. Experiment 2 showed that cueing the location of a distractor in a flanker-like experiment resulted in a reduced compatibility effect between target and distractor. Because compatible distractors on a non-target location automatically interfere with target processing despite prior information about the target and distractor locations (Eriksen & Eriksen, 1974; Miller, 1991), the strongly diminished compatibility effect makes a strong claim for an inhibition account. The ambiguity account cannot explain the results of Experiment 2. The cue can help to distinguish between target and distractor, yet when the presented distractor automatically influences target processing, inhibition of the distractor seems the most likely explanation of the current results. Whereas the ambiguity account does not seem to explain the results of Experiment 2, it can still explain part of the results of Experiment 1.

The present study provides evidence for the existence of an inhibitory mechanism of attention which can be controlled top-down, similar to the excitatory system used when a target location is cued. In the experiments described in this study, the location of the target was not cued, which suggests that the inhibitory mechanism can be controlled independently of the excitatory mechanism. The notion of two different functional systems for respectively excitation and inhibition is supported by an ERP study by Van der Stigchel, Heslenfeld & Theeuwes (2006) in which both target and distractor locations were cued in advance. The target and the distractor were endogenously cued by differently colored arrows, reflecting the possible location of target and distractor. Participants were instructed to make an eye movement towards the target as fast as possible. The results of

this study showed an early component called “right-lateralized inhibition positivity” (RLIP) hypothesized to reflect cue induced inhibition.

Ruff & Driver (2006) examined differences in brain activity on trials in which distractors were cued compared to trials in which distractors were uncued, using fMRI. Their results showed significant attentional modulation exclusively in the occipital lobe, contralateral to the cued distractor side, while no modulations were found contralateral to the cued target side. These findings support the notion that cueing the distractor location does not enhance target activation, but rather inhibits locations at which interfering information is expected.

Although we sought out to disentangle inhibition at the cued distractor location from excitation at the target location, we do not claim that these mechanisms do not act concurrently. Inhibition and excitation may be intimately linked and may act concurrently in order to enhance processing of relevant information in a noise filled environment. Moreover, at a neural level a closely linked connection between excitation and inhibition can be observed. For instance, in the cerebral cortex a distinction can be made between excitatory neurons, such as pyramidal cells, and inhibitory cells. However, both types of cells can be found active concurrently during spatially selective tasks (for an overview of the role of inhibition in neural and cognitive control mechanisms, see Houghton & Tipper, 1996). So, while we have solely focused on inhibitory mechanisms, we do not claim that excitatory mechanisms do not play a role in reducing the interfering effects of a distractor. The crucial finding is that the effects of a distractor can be eliminated by advance knowledge of its location. We believe that the current study provides sufficient evidence to claim that inhibition is one of the mechanisms involved.

It may be possible to explain the current results in terms of “tagging” processes. Tagging of irrelevant information was proposed by Neill, Valdes, Terry, & Gorfein (1992) as an alternative hypothesis to explain negative priming. Previously presented items which did not require a response could be tagged as irrelevant items. Whenever this item was later presented as a target, the tag would be retrieved resulting in a slower response to the target. In the current study a distractor always interfered with target processing and never needed to be responded to, therefore a “no-response” tag could accompany the internal representation of the distractor. Subsequently, whenever the distractor was presented the tag was retrieved from memory, suppressing the interference caused by

the distractor. This would facilitate search and result in faster reaction times in response to the target. This explanation might not necessarily involve an inhibitory component. However, if distractor stimuli are tagged in the current study, it would not matter whether the distractor would be preceded by a cue or not. In the current study it is found that cueing the location of a distractor has an effect on target processing. An explanation in terms of tagging therefore seems unlikely.

Inhibition of irrelevant information as the responsible mechanism for better target performance has been proposed before. In a series of experiments by Cepeda, Cave, Bichot & Kim (1998), in which a probe stimulus was shown at a location previously occupied by a target or a distractor or at an empty location, it was shown that probes were processed slowest at locations in which a distractor was previously displayed. Cepeda and colleagues make a strong case for inhibition of the distractor location by showing that response times to probes at previously empty locations produced the fastest reaction times, suggesting that distractor locations were indeed inhibited.

Furthermore, in a single-cell study by Moran & Desimone (1985) monkeys were taught to shift their attention to one of two stimulus locations within the receptive field of a single neuron in extrastriate area V4. At both stimulus locations a different stimulus was presented, one which elicited a high neural response, whereas the other elicited no neural response. In blocked order, monkeys focused their attention on one of the two stimuli. It was found that the neural response to the unattended stimuli was severely attenuated, whereas the response to the attended stimuli remained largely unaffected independent of the presence or absence of the irrelevant stimulus. Based on these results a filtering account of attention was proposed: Information presented at the focus of attention is processed, whereas the irrelevant information presented in the visual field is actively suppressed. In this model, inhibition of irrelevant information benefits the target processing as opposed to enhanced processing of the target location as found in classical cueing studies. The results found in the single-cell study by Moran & Desimone and the fMRI study by Ruff & Driver (2006) align with the data found in the present study. Inhibition of irrelevant information causes the relevant information to be processed faster. However, the question remains whether inhibition is the only cause of faster target processing or whether enhanced target processing plays a role as well. In an ERP study by Luck (1995) it was hypothesized that multiple separable mechanisms of visual-spatial

attention exert their influence during processes of attentional selection. Luck performed a cueing study in which an attention directing cue pointed to one of four possible target locations. Shortly after cue presentation, a small luminance target was presented immediately followed by a pattern mask. The presented cue could be valid, invalid or neutral. EEG was measured during task performance and afterwards two early ERP components called 'N1' and 'P1' were singled out, both of which are thought to reflect attentional modulation in the visual domain (Mangun & Hillyard, 1991). The results showed that valid cues were accompanied by an increase in the amplitude of the N1 component compared to the neutral cue, whereas an invalid cue was accompanied by a decrease in P1 amplitude compared to the neutral cue. Furthermore, no increase in P1 amplitude was found on valid trials and no decrease in N1 amplitude was found on invalid trials. Mangun & Hillyard (1991) have shown that P1 and N1 modulations can occur independently of each other, suggesting that spatial cueing invokes two separate attentional processes, one that suppresses information at unattended locations as reflected by a decrease in P1 amplitude and the other that enhances information processing at the attended location as reflected by a decrease in N1 amplitude. In the present study we found a benefit in target processing by cueing a distractor location without cueing the target locations. These results are in accordance with results found by Luck (1995) and Mangun & Hillyard (1991) showing that an inhibitory mechanism can function independently of a facilitatory mechanism.

In a classical cueing study it is thought that regions in the visual cortex corresponding to the cued location become active resulting in response enhancement (Corbetta, et al., 2000; Heinze, et al., 1994). This results in a bias in the competition between target and surrounding elements, leading to a faster and more thorough processing of the target. A similar but separable mechanism may be responsible for the inhibitory effects found in this study. Again, brain regions corresponding to the cued distractor location may become active, yet in a different way (possibly reflected by the reversed polarity compared with target cueing) which leads to a diminished processing of information presented at the cued location.

