

INHIBITION OF ORIENTING DURING A MEMORY-GUIDED SACCADIC TASK SHOWS A MEXICAN-HAT DISTRIBUTION

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Abstract—Recent behavioral studies in monkeys and humans have shown that holding an item in spatial working memory may lead to sustained and spatially selective prolongation of reaction times (RTs) to visual stimuli presented during the memory delay. In order to resolve the seeming contradiction between these findings and current theories on the interaction of working memory and attentional orienting, it has been hypothesized that memory-dependent modulation of orienting may be the net effect of superposed facilitatory and inhibitory mechanisms. Their relative strength during the memory delay may determine whether RTs to visual stimuli presented during the memory delay are shortened or prolonged. Here, we expand on this hypothesis by investigating the spatial distribution of memory-dependent inhibition with behavioral data from normal human subjects. The experiment consisted of a combination of an oculomotor spatial working memory task (memory-guided saccade task, 6-s delay) and a visual discrimination task (performed 1500, 2500, or 3500 ms after presentation of the memory cue). RTs to discrimination stimuli were analyzed as a function of memory-guided saccade amplitude. By fitting polynomial approximations to our data we show that the spatial distribution of memory-dependent inhibition of orienting significantly differs from a monotonic gradient across the visual field. Instead, we demonstrate the existence of a central inhibitory peak surrounded by a facilitatory annulus, forming a transient “inverted Mexican hat” profile, which mirror-images findings from recent studies on the spatial distribution of attention. These findings are consistent with the hypothesis of a highly flexible modulation of orienting in which both the signs and spatial distribution of memory-dependent bias signals are adapted to behavioral demands. © 2008 IBRO. Published by Elsevier Ltd. All rights reserved.

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An important prerequisite of spatially directed behavior is the ability to modulate visual processing at distinct locations of the visual field. It is well-known that, following the onset of a visual stimulus, there is transient facilitation of orienting to subsequent stimuli at its location (Posner,

1980; Posner and Cohen, 1984). This attention effect usually lasts some hundreds of milliseconds and is followed by a transient inhibitory after-effect termed “inhibition of return” (IOR) (Posner and Cohen, 1984; Klein, 2000). The time courses of these phenomena are not fixed but rather change according to stimulus characteristics and top-down factors. Among other cognitive factors, working memory appears to exert an important influence on attentional orienting to visual stimuli (Awh and Jonides, 2001). For example, during a spatial delayed match-to-sample task, holding an item in working memory shortened reaction times (RTs) to discrimination stimuli presented at the location of to-be-remembered items up to some seconds after memory cue offset (Awh et al., 1998). In line with these findings, studies have shown enhanced neural activity in visual cortices during the delay of working memory tasks (Awh et al., 2000; Super et al., 2001; Bisley and Goldberg, 2003; Postle et al., 2004).

However, results from recent experiments suggest that working memory does not always facilitate behavioral responses to stimuli presented at remembered locations. Surprisingly, accurate memory of a spatial stimulus in an oculomotor working memory task (memory-guided saccade task) yielded sustained and spatially selective *prolongation* of RTs to visual stimuli presented during the memory delay (Ostendorf et al., 2004; Krishna et al., 2006). This RT prolongation was not observed in control conditions where the spatial stimulus was passively perceived or presented in a position distinct from the subsequent visual stimulus (Ostendorf et al., 2004; Krishna et al., 2006). It has been speculated that this unexpected and memory-dependent RT prolongation may result from prolonged IOR (Ostendorf et al., 2004; Krishna et al., 2006). In order to reconcile the conflicting findings of different working memory effects on orienting, it has been claimed that facilitation and inhibition may simultaneously be present during working memory and that changes of their relative strength may actually determine whether RTs to visual stimuli presented during the memory delay are shortened or prolonged (Ostendorf et al., 2004).

The hypothesis of parallel memory-dependent top-down mechanisms of facilitation and inhibition implies that their spatial characteristics may be similar, albeit with opposite signs. For spatial attention, previous models compared its spatial distribution with a metaphorical “spotlight” of facilitated processing (Posner, 1980) that may be adjusted in size like a “zoom-lens” (Eriksen and St. James, 1986). However, recent studies strongly suggest a more complex spatial pattern. Experiments in humans and monkeys revealed a central zone of facilitation at the attended

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Abbreviations: AIC, Akaike’s information criterion; ANOVA, analysis of variance; IOR, inhibition of return; ISI, interstimulus interval; RT, reaction time.

location surrounded by adjacent zones of inhibited processing, forming a Mexican-hat-like distribution of behavioral parameters and neuronal activity (Cutzu and Tsotsos, 2003; Müller and Kleinschmidt, 2004; Schall et al., 2004; Müller et al., 2005; Hopf et al., 2006).

Here, we have investigated the spatial distribution of memory-dependent inhibition of orienting. We asked whether a more detailed analysis of the data from Ostendorf et al. (2004) would yield a spatial pattern of RTs which complements the findings from studies of attention. In contrast to preceding studies (Ostendorf et al., 2004; Krishna et al., 2006), we chose a new approach and analyzed RTs to visual stimuli presented during the delay of a memory-guided saccade task as a direct function of subsequent memory-guided saccade metrics. Analyzed this way, the spatial pattern of memory-dependent inhibition of visual discrimination differed from a spotlight or monotonic gradient distribution. Instead, we found a transient “inverted Mexican hat” profile with a central zone of inhibited processing surrounded by adjacent zones of facilitation. We infer that the general principle of center-surround organization also applies to inhibitory top-down effects on visual orienting. Depending on the behavioral context, the brain appears to flexibly recruit facilitatory and inhibitory bias signals for orienting during working memory.

EXPERIMENTAL PROCEDURES

Subjects and experimental setup

Ten naïve, right-handed human subjects were tested with a modified memory-guided saccade task (four males, mean age 24.4 years, range 21–27 years). All subjects gave informed consent prior to participation in the study which was approved by the local ethics committee and conducted in accordance with the Declaration of Helsinki. Eye movements were recorded by infrared-oculography of the right eye at a frequency of 200 Hz (AMTech eyetracker, Weinheim, Germany). The system had a spatial resolution of $<0.3^\circ$ and a horizontal linear range of more than 20° bilaterally. The subject's head was fixed to the recording system by means of a chinrest and a bite bar. During recording sessions calibration trials were performed regularly. A 22-inch CRT-monitor (Vision Master Pro 510; Iyama Electric, Nagano, Japan; refresh rate: 110 Hz) was used for stimulus presentation at a viewing distance of 50 cm in an otherwise darkened room. Stimuli were green (luminance 30 Cd/m²) and were presented on a homogeneous gray background (luminance 3 Cd/m²).

Behavioral paradigms

The rationale of the experiment is to combine a memory-guided saccade task and a visual discrimination task in which the relative positions of memory cue and discrimination target are varied from trial to trial (Fig. 1). In some trials, memory cue and discrimination target coincide, in others they did not. Memory-dependent modulations of orienting should manifest themselves in different RTs between these trial types. Consequently, the approach in previous studies was to analyze RTs to discrimination targets as a function of memory cue position (Ostendorf et al., 2004; Krishna et al., 2006). However, presenting a memory cue in a position of the visual field means neither that its position is precisely encoded in working memory nor precisely responded to by a memory-guided movement. Since accuracy of memory-guided saccades is correlated with neuronal activity supporting spatial working memory representations (Funahashi et al., 1989), analyzing RTs to dis-

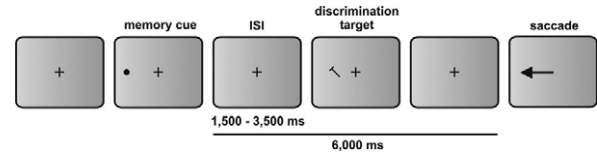


Fig. 1. Schematic of the task. While fixating on a central fixation cross, subjects were presented a peripheral cue at 6° , 9° , or 12° to the left or right. Subjects were required to remember the position of the cue and to perform an eye movement toward the remembered cue position after a delay of 6 s (memory-guided saccade); 1500, 2500 or 3500 ms after the memory cue, a discrimination target was presented at 9° in the same or opposite visual hemifield. Subjects indicated by a speeded manual response whether the discrimination target was a rotated “T” or “L.”

crimination targets as a function of memory-guided saccade amplitude should allow for a more direct brain-behavior-correlation. This approach was pursued in the present study which presents a re-analysis of the data from the memory condition of Ostendorf et al. (2004).

The sequence of events was as follows (Fig. 1): While fixating on a central fixation cross (diameter: 0.5°), subjects were presented a peripheral cue (diameter: 0.4°) for 500 ms at 6° , 9° , or 12° horizontally to the left or right. Subjects were instructed to remember the cue position for a delay of 6 s. The subsequent offset of the fixation cross served as signal to execute a memory-guided saccade to the remembered cue position. At variable interstimulus intervals (ISIs) of 1500, 2500, or 3500 ms after the first cue, a rotated “T” or “L” (diameter: 0.76°) was presented in the same or opposite visual hemifield at 9° . Subjects performed a speeded discrimination of this stimulus by pushing a button with their right (T) or left (L) index finger. Discrimination stimuli were presented for up to 1 s, with presentation being terminated by the response. “T” and “L” stimuli were equally distributed across the investigated stimulus positions and ISIs to avoid any bias from individual right-left differences in RTs. The experiment consisted of a total of 432 trials in pseudorandom order, split into three sessions of six blocks each. Sessions were recorded on consecutive days. Prior to testing, subjects received separate training of the memory-guided saccade task and the discrimination task followed by a test block of the final experimental condition.

Data analysis

Saccades were analyzed with EYEMAP-Software (AMTech) using a velocity criterion for determination of saccade onset ($35^\circ/\text{s}$). The first saccade after fixation offset entered analysis. Trials in which eye movements occurred during stimulus presentation or delay period ($10.0 \pm 1.8\%$) were excluded from analysis. For analysis of RTs to discrimination targets, trials with false responses ($5.1 \pm 1.2\%$) and responses longer than 1000 ms ($0.92 \pm 0.31\%$) were eliminated. All further statistics were done with SPSS software, version 12.0.1 (SPSS Inc., Chicago, IL, USA). Throughout the manuscript, means are given with standard errors.

In our first study, a significant decrease of RTs with increasing ISI was found, presumably because of the rising probability of a discrimination to be performed (mean RTs at 1500 ms ISI: 578 ± 23 ms; 2500 ms ISI: 540 ± 20 ms; 3500 ms ISI: 522 ± 17 ms; Ostendorf et al., 2004). For further analysis, we individually normalized RTs by z-transformation (Dorris et al., 1999). This approach allows for a reliable separation of memory-dependent changes in discrimination performance from the memory-independent effects of ISI on RTs. Normalization of RTs moreover neutralizes any bias arising from memory-independent inter-individual RT differences. Consequently, analysis of variance (ANOVA) of normalized RTs revealed a significant interaction of factors task, hemifield, ISI, position ($F_{4,72} = 3.4$, $P = 0.013$), but no significant effect of ISI alone ($F_{2,36} = 0.83$, $P = 0.45$).

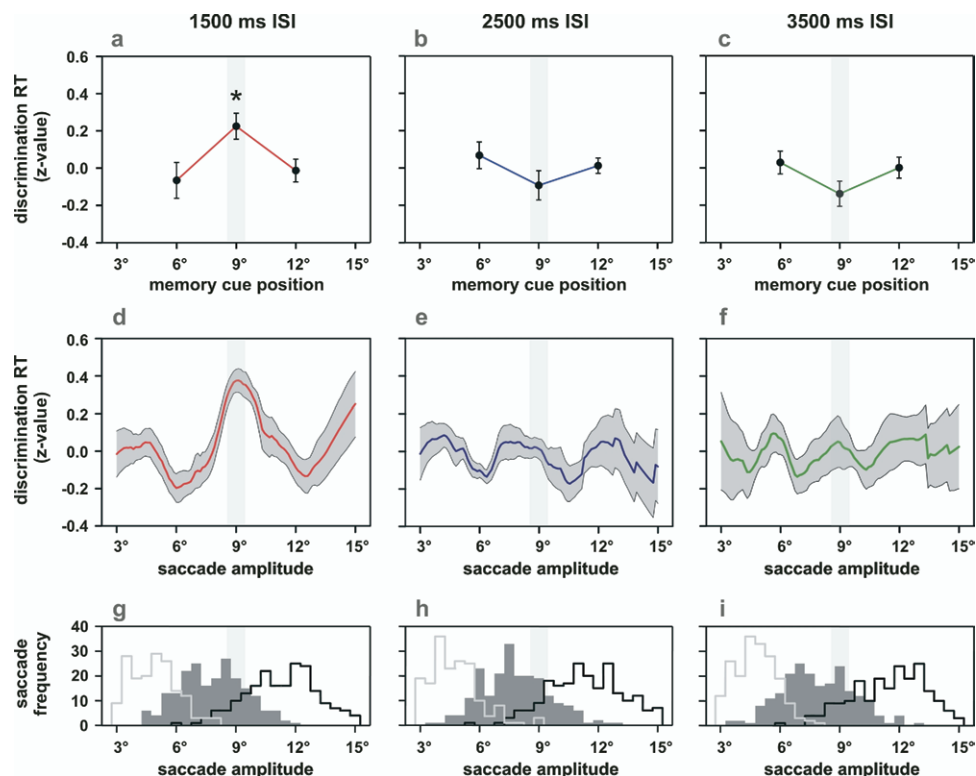


Fig. 2. Spatial distribution of RTs for letter discrimination and spatial distribution of memory-guided saccade amplitudes from 10 subjects, separately for three ISIs. Gray shaded bars at 9° indicate position of discrimination stimulus. (a–c) RTs as a function of memory cue position; abscissa: memory cue position in degree; ordinate: mean normalized RTs \pm SEs for letter discrimination; * $P \leq 0.035$ difference with 6° and 12°. (d–f) RTs as a function of memory-guided saccade amplitude; abscissa: saccade amplitude in degree; ordinate: normalized RTs for letter discrimination; mean curves \pm SEs indicate averaged locally weighted non-linear regression curves. Note the Mexican-hat pattern of RT distribution at 1500 ms ISI. (g–i) Distribution of saccade amplitudes; abscissa: saccade amplitude in degree; ordinate: frequency of saccades; light gray: saccades with memory cue at 6°, dark gray: saccades with memory cue at 12°.

In our previous report, spatially selective inhibition of visual discrimination was exclusively present in trials where memory cue and discrimination target were presented in the same visual hemifield (Ostendorf et al., 2004). In these trials, a clear inhibitory peak of RTs was observed, provided that the position of the discrimination target (9°) and the position of the memory cue coincided (mean RT prolongation 25.0 ms compared with trials in which memory cues were presented at 6 or 12°). In the present study, analysis focused on these memory-dependent effects. Trials in which discrimination target and memory cue were presented in opposite hemifields were therefore not included. Hence, analysis was based on a total of 2160 trials.

A locally weighted non-linear regression was performed in each subject for each ISI (LOWESS; window width 5°) with saccade amplitude as independent variable and normalized RTs as dependent variable. Then, individual regression curves were averaged for each ISI. Model functions for the averaged regression curves were compared by using partial F tests. For non-hierarchical comparisons of models, Akaike's information criterion (AIC) was used:

$$n \times \ln(\text{RSSQ}/df) + 2 \times k + n + 2$$

where n is the sample size, k is the number of parameters in the model, RSSQ is the error sum of squares and df its degrees of freedom in the respective model (Stone, 1998). If model selection is based on the AIC criterion, the model with the smallest AIC has to be selected.

RESULTS

As can be seen in the amplitude histograms in Fig. 2g–i, saccade endpoints in the memory-guided saccade task were frequently hypometric and showed considerable scatter around memory cue positions. It is also evident that the distribution of saccade amplitudes around cue positions is not random but rather shows three separable peaks located in the vicinity of memory cue positions. A repeated measures ANOVA confirmed that there was a significant effect of memory cue position on saccade amplitudes ($F_{2,18} = 7.9$, $P = 0.003$) but no significant effect of ISI ($F_{2,18} = 2.4$, $P = 0.12$) and no significant interaction of ISI with memory cue position ($F_{4,36} = 2.0$, $P = 0.11$). It may thus be inferred that subjects remembered cue positions well at all ISIs and that there was no differential proactive interference of the discrimination target with memory of the spatial cue. By contrast, a repeated measures ANOVA showed a significant main effect of ISI on latencies of memory-guided saccades with longer latencies in trials with 3500 ms ISI (mean at 1500 ms ISI: 246 ± 16 ms; 2500 ms ISI: 252 ± 20 ms; 3500 ms ISI: 299 ± 19 ms; $F_{2,18} = 22.1$, $P < 0.001$), indicating an interaction of the discrimination cue at 3500 ms ISI or the corresponding manual response with the execution of the memory-guided saccade. Con-

sistent with the observations of others (Bell et al., 2000; Kalesnykas and Hallett 1994) we observed a trend for longer latencies in trials with memory cues presented at small eccentricities (mean at 6° memory cue position: 274 ± 20 ms; 9°: 263 ± 17 ms; 12°: 260 ± 19 ms). However, this tendency did not achieve statistical significance ($F_{2,18} = 3.4$, $P = 0.06$). Most important, there was no significant interaction of factors ISI and memory cue position ($F_{4,36} = 0.4$, $P = 0.79$), indicating that different RT distributions at different ISIs cannot be attributed to a specific interaction of the discrimination cue or the corresponding manual response with the prepared memory-guided saccade.

Complementing our previous report (Ostendorf et al., 2004), we observed a significant peak in normalized RTs to discrimination stimuli presented at the position of the memory cue in trials with 1500 ms ISI in the memory-guided saccade task (Fig. 2a; mean z-value 0.23 ± 0.07 at 9° vs. -0.01 ± 0.06 at 12°, $P = 0.013$; and vs. -0.07 ± 0.09 at 6°, $P = 0.035$, paired *t*-tests). In trials with 2500 and 3500 ms ISI, no inhibition was observed (Fig. 2b, c; $P > 0.05$ for all comparisons, paired *t*-tests).

A different picture emerged when normalized RTs from the memory-guided saccade task were analyzed as a function of saccade amplitude. Although averaged regression curves in trials with 1500 ms ISI still showed a clear inhibitory peak (Fig. 2d; peak at 9.3° saccade amplitude, mean z-value 0.38 ± 0.06) which clearly coincided with the position of the discrimination target (centered at 9°, spatial extent from 8.6° to 9.4°), the slope of the curve outside this central region differed from a simple gradient distribution. Flanking the central inhibitory peak, two facilitatory troughs were observed (at 6.2° and 12.8° saccade amplitude, mean z-values -0.2 ± 0.08 and -0.13 ± 0.09 , respectively), thus forming a slightly asymmetrical center-surround distribution of normalized RTs. Compared with the slope of the curve joining the mean RTs at 6°, 9° and 12° (Fig. 2a), the RT differences between the inhibitory peak and the facilitatory troughs (Fig. 2d) were higher (0.58 and 0.51 vs. 0.30 and 0.24, respectively). This Mexican hat-like pattern largely disappeared in trials with 2500 and 3500 ms ISI. We deem it unlikely that this effect is due to differences in saccade amplitude distributions between ISIs as their characteristics were almost indistinguishable between ISIs (Fig. 2 g–i). However, from further inspection of these histograms it is also clear that, due to hypometria and scatter in saccade amplitudes, saccades with 9° amplitude occurred both in trials with memory cues located at 9° and in trials with memory cues located at 12°. In order

to analyze whether there was a differential contribution of both trial types to the central inhibitory peak, we identified those trials which contributed to the slope of the RT regression curve in Fig. 2d at mean z-values of ≥ 0.2 . No significant difference was found between normalized RTs of such trials with 9° and 12° memory cues (mean z-value from 59 trials with 9° memory cue: 0.21 ± 0.14 , and from 50 trials with 12° memory cue: 0.3 ± 0.15 , $P = 0.66$, unpaired *t*-test).

Next, we asked which mathematical function best explains the observed spatial RT distribution at 1500 ms ISI. Contrary to similar investigations of the spatial distribution of IOR (Bennett and Pratt, 2001), we decided not to fit a double gaussian function to our data as the behavior of this function requires assumptions about approaching a baseline for very small or very large saccade amplitudes. In our data there was only limited information for such a line at small saccade amplitudes and no information for large saccade amplitudes. We therefore decided to fit the data contributing to the Mexican-hat-shaped central part of the regression curve by polynomials. From the data it was evident that the spatial distribution of RTs decreased from maximum values around 9° saccade amplitude to some minimum values. We hypothesized that a clear increase from these minimum values can be observed with further distance from the central peak. This hypothesis was tested by comparing a fit with a polynomial of degree 2 (quadratic curve with one maximum value only) to a fit of a polynomial with degree 4 (curve with one maximum value and two minimum values). Thus, we calculated the following polynomial model curves with X_{center} equal to $X - 9^\circ$:

$$Y = \beta_0 + \beta_2(X - X_{\text{center}})^2 \quad (1)$$

$$Y = \beta_0 + \beta_2(X - X_{\text{center}})^2 + \beta_4(X - X_{\text{center}})^4 \quad (2)$$

The fit for the term with degree 4 (2) was significantly better compared with a simple quadratic function (1) ($P < 0.001$, partial *F*-test, Table 1, Fig. 3). Model (2) includes an increase of RTs at saccade amplitudes outside the central zone of the Mexican-hat-shaped RT distribution and therefore approximates the observed values significantly better than model (1). While both models yield symmetric curves around a center of 9° saccade amplitude, it is evident from Fig. 3 that the fit of the model can be improved by taking into account the asymmetry of the observed values. Since we presented stimuli horizontally, asymmetry of observed values is likely to occur as both the cortical representation of visual stimuli and attention effects have been shown to change with stimulus eccentric-

Table 1. Statistical comparison of polynomial model functions

| No | Covariates | Model SSQ | df | Error SSQ | df | F | R ² | AIC |
|----|--------------------|-----------|----------------|-----------|----|-------|----------------|------|
| 1 | x^2 | 0.585 | 2 ^a | 1.607 | 72 | 13.10 | 0.26 | -204 |
| 2 | x^2, x^4 | 1.209 | 3 ^a | 0.982 | 71 | 29.14 | 0.54 | -238 |
| 3 | x, x^2 | 0.864 | 2 | 1.327 | 72 | 23.43 | 0.38 | -219 |
| 4 | x, x^2, x^3, x^4 | 1.962 | 4 | 0.229 | 70 | 149.8 | 0.89 | -344 |

SSQ, sums of squares.

^aOne extra degree of freedom for centering around 9°.

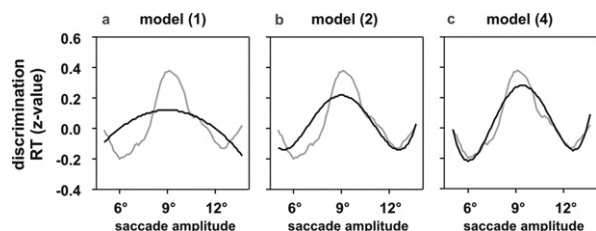


Fig. 3. (a–c) Polynomial model curves and observed values; abscissa: memory cue position in degree; ordinate: mean normalized RTs for letter discrimination; black curves: model curves, gray curves: observed values. For explanation of models, see Results. Note superior fit of model 4 in c, which models a Mexican-hat’s “brim” and asymmetry.

ity (Daniel and Whitteridge, 1961; Rovamo and Virsu, 1979; Carrasco et al., 2003; Shani and Sagi, 2005). We therefore calculated the following additional polynomial model curves which allow for asymmetries:

$$Y = \beta_0 + \beta_1(X - X_{\text{center}}) + \beta_2(X - X_{\text{center}})^2 \quad (3)$$

$$Y = \beta_0 + \beta_1(X - X_{\text{center}}) + \beta_2(X - X_{\text{center}})^2 + \beta_3(X - X_{\text{center}})^3 + \beta_4(X - X_{\text{center}})^4 \quad (4)$$

AIC values for model (3) were slightly smaller than for model (1) (Table 1) with a negligible improvement in fit of the corresponding model curve (not included in Fig. 3). The best fit was observed with model (4) which includes both the Mexican hat’s “brim” and the asymmetry in amplitude-RT-relationships ($P < 0.001$ compared with model (3) and $P < 0.001$ compared with model (2), partial F -test, Table 1). In addition, AIC values for this model were considerably smaller than for models (1), (2) and (3), indicating that among the models tested, model (4) best describes the observed values.

DISCUSSION

This study investigated the spatial characteristics of inhibition of orienting during working memory. We therefore studied the spatial distribution of RTs to discrimination targets presented during the delay of a memory-guided saccade task. We show that when RTs are analyzed as a function of memory-guided saccade amplitude, their spatial distribution differs significantly from a simple gradient distribution. Rather, our findings support a center-surround organization of inhibitory modulation of orienting. In the following section we will discuss how these findings relate to previous studies of attention and IOR.

Computational modeling and single-neuron studies in monkeys have suggested that central excitation and surround inhibition is a constituent element of processing in several cortical regions of the visual system, e.g. in V1 (Ringach et al., 2003; Kang et al., 2003), V4 (Moran and Desimone, 1985), area MT (Olavarria et al., 1992) or the frontal eye fields (Schall et al., 2004). In humans, recent functional imaging studies have shown that modulation of early visual cortices by visuo-spatial attention shows a similar organization with enhanced neural activity evoked

by visual stimuli presented at attended locations and suppressed neural activity in an adjacent annular zone surrounding the attention focus (Müller and Kleinschmidt, 2004; Hopf et al., 2006). Complementing these studies, behavioral evidence for a Mexican-hat-like distribution of visuo-spatial attention has been presented recently. In a detection task, human observers showed decreased detection accuracy of target letters presented close to a cued location and a gradual increase of detection accuracy for remote locations (Cutzu and Tsotsos, 2003). In a letter discrimination task, RTs have been shown to be selectively prolonged for distracter letters presented at small separations to the target letter (Müller et al., 2005). The radius of the observed inhibitory zone in these studies measured 1.3° to 4° of visual angle and thus corresponds at least roughly to our results ($\sim 3^\circ$ separation between central inhibitory and peripheral facilitatory troughs) despite differences in stimulus characteristics and likely differences in task demands. Thus, a similar dimension of the hat’s “brim” is compatible with a functional relationship between the mirror-image spatial distribution of RT changes in these and our studies. Alternatively, this similarity may simply be an artifact resulting from similar spacing of targets and distracters between studies. For example, in our study, facilitatory troughs were located closely to the position of memory cues other than 9° , i.e. closely to 6° and 12° . It is unlikely that arbitrary positioning of memory cues in our experiment matches the spatial tuning of memory-modulated visual processing purely by chance. In our first report we have speculated that the observed spatially selective inhibition of covert attention shifts during a working memory task may be a means to promote flexible orienting to novel visual information (Ostendorf et al., 2004). If this holds true, the coincidence of facilitatory troughs with concurrent memory cue positions in our experiment may support the idea that the width of the observed inhibitory zone may be flexibly adjusted according to task demands, a finding that is reminiscent of the “zoom lens” hypothesis derived from studies of spatial attention (Eriksen and St. James, 1986; Turatto et al., 2000). However, a verification of this hypothesis will require additional experiments with variable spacing of memory cues.

What precisely causes the inhibition observed here? We have argued previously that the close relationship between RTs and saccade amplitude points to a memory-related process (Ostendorf et al., 2004). Indeed, recent computational studies suggest that spatially selective memory-related neuronal activity involves both local excitation and long-range inhibition, forming a Mexican hat profile of neural activity (Wang, 2001; Fall et al., 2005). The spatial pattern observed in our experiment may thus be interpreted as a behavioral fingerprint of a neuronal network coding the location of the memory cue. Single-unit studies have shown that during a memory delay, such activity coexists in prefrontal neurons coding either the sensory coordinates of the memory cue or the motor coordinates of the related memory-guided movement (Funahashi et al., 1993; di Pellegrino and Wise, 1993). The relationship between saccade metrics and discrimination

RTs is intuitively suggestive of a prospective oculomotor rather than a sensory code of spatial working memory, mediating the observed modulation of visual discrimination. The presence of significant inhibition in the early phase of the memory delay is not necessarily incompatible with this hypothesis as the fixed length of the memory delay in our paradigm allows for advance preparation of an oculomotor response. However, since the coordinates of the preceding memory cue and the following oculomotor response coincided in our paradigm, it is not possible to definitely relate the inhibitory effect to a motor or sensory-based or representation in spatial working memory. In either case, we observed similar inhibitory effects in trials with a 9° memory cue and 9° amplitude saccades and in trials with a 12° memory cue and 9° amplitude saccades. Thus, inhibition appears not to be correlated with accuracy of the mnemonic representation per se but to be associated with the metrics of the upcoming oculomotor delayed response. This represents a non-trivial finding as it is controversial whether attention is bound to the saccade target or to the actual landing point of a saccadic eye movement (Deubel and Schneider, 1996; Collins and Doré-Mazars, 2006). A similar relationship between 9° saccade amplitude and discrimination RTs in both trial types furthermore suggests a fairly stable association between the mnemonic representation at 1500 ms ISI and the contingent oculomotor response 4500 ms later. It may thus be speculated that the main part of accuracy losses in our task may already take place during transformation of the sensory cue to a mnemonic representation or early during the memory maintenance period, which is supported by previous behavioral findings on memory-guided saccade performance across different delays (Gnadt et al., 1991; White et al., 1994).

It has been argued previously that the observed memory-dependent inhibition is a special case of IOR, with sustained prolongation of RTs to visual targets either resulting from prolonged inhibitory top-down processes or from weakened facilitatory modulation (Ostendorf et al., 2004; Krishna et al., 2006). This view claims that the time-course of behavioral effects is the sum of attentional facilitation and IOR, with the relative strength and time-course of either component being flexibly adapted to current behavioral demands. Indeed, like for attention (Awh et al., 1998; Awh and Jonides, 2001), there is psychophysical evidence that IOR is significantly modulated by top-down factors including working memory (Lupianez et al., 2001; Khatoon et al., 2002; Castel et al., 2003; Tipper et al., 2003; Klein et al., 2006). In our experiment, this would mean that the necessity to inhibit a premature eye movement to the memory cue during the delay may have led to enhanced IOR, overriding a parallel but weaker attentional facilitation. Alternatively, IOR in our experiment may have simply been delayed compared with the control condition. We cannot decide between these possibilities as the shortest ISI in our experiment was 1500 ms and the switch from initial attentional facilitation to subsequent IOR is likely to occur with shorter ISIs (Klein, 2000). However, provided that inhibition in our experiment is coupled to inhibition of

premature overt orienting to the memory cue (Ostendorf et al., 2004), the necessity of this function becomes less important as the delay proceeds and the execution of a memory-guided saccade approaches. This may explain why our findings are limited to the 1500 ms ISI. Whether the lack of significant inhibition at longer ISIs results from a decrease in IOR or an increase in concurrent facilitation cannot be inferred from our data. Concerning the spatial distribution of inhibition, we have argued in our previous report (Ostendorf et al., 2004) that the pattern of RTs at 1500 ms ISI in our experiment closely matches the gradient distribution of IOR observed in monkeys performing cue-saccade paradigms (Dorris et al., 1999) and in humans performing tasks requiring manual responses (Pratt and Abrams, 1999; Bennett and Pratt, 2001). At first glance, the finding of a Mexican-hat distribution in the present investigation weakens this analogy but leaves open the possibility that an analysis with RTs binned against saccade amplitudes rather than against stimulus positions may yield a more complex spatial pattern of inhibition in simpler attentional orienting tasks as well.

Taken together, we have presented evidence for a Mexican-hat-like spatial pattern of memory-dependent inhibition of orienting that mirror-images spatial characteristics of attention. These findings support the hypothesis of a highly flexible modulation of visual processing in which the signs of memory-dependent bias signals are flexibly adapted to particular behavioral demands. The presumed parallelism of sustained facilitation and inhibition of orienting may have implications for studies correlating behavioral parameters with neuronal activity. For example, during a working memory task there may be sustained increases of neuronal activity in visual areas suggesting facilitated processing of visual stimuli. However, RTs to these stimuli may not necessarily be shortened, because of concurrent memory-dependent inhibition of orienting. Further experiments with paradigms dissociating stimulus positions and memory-guided oculomotor responses and with paradigms employing more memory cue positions may clarify the origins and spatial flexibility of the observed inhibition.

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