

Is delayed foveal feedback critical for extra-foveal perception?

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Abstract

Recent neuroimaging evidence suggests that visual inputs arising beyond the fovea can be ‘fed back’ to foveal visual cortex to construct a new retinotopic representation. However, whether these representations are critical for extra-foveal perception remains unclear. Using transcranial magnetic stimulation we found that relatively late (350-400msec) disruption of foveal retinotopic cortex impaired perceptual discrimination of objects in the periphery. These results are consistent with the hypothesis that feedback to the foveal retinotopic cortex is crucial for extra-foveal perception, and provide additional evidence for ‘constructive’ feedback in human vision.

1. Introduction

Feedback is a ubiquitous concept in cognitive neuroscience, being implicated as the engine of attentional selection (Desimone and Duncan, 1995; Duncan et al., 1997; Kastner and Ungerleider, 2000), mental imagery (Kosslyn et al., 2001; Kosslyn et al., 1999) and visual awareness (Lamme, et al., 1998; Ro et al., 2003). Established accounts of feedback emphasise top-down modulation of pre-activated feedforward representations (Ress and Heeger, 2003; Super et al., 2001). Recently, however, multivoxel pattern analysis of fMRI data has provided evidence that peripheral object information can be decoded from visual cortical regions that represent central *foveal* space (Williams et al., 2008). These data point to the existence of a feedback mechanism that does more than simply modulate existing activity: it constructs a new representation.

Although this previous fMRI study is suggestive of a ‘constructive’ feedback mechanism (Williams, et al., 2008), definitive evidence remains lacking. In particular, it is not known whether peripheral object information in the foveal retinotopic cortex is causally constitutive in shaping perception, or whether such activity is a redundant by-product of activity elsewhere. Furthermore, the temporal resolution of the BOLD measurement is too low to definitively distinguish a foveal feedback hypothesis from several competing explanations, including cross-activation via horizontal cortical connections (Gilbert, 1993; Lamme, Super, et al., 1998) and hemodynamic point spread (Arthurs and Boniface, 2003; Logothetis, 2008).

We contrasted these accounts in the present study using the complementary approach of transcranial magnetic stimulation (TMS) together with an almost identical behavioural task to Williams et al. (2008). If foveal visual cortex is crucial for processing extra-foveal stimuli then disrupting it should impair the ability to discriminate peripheral visual objects. Moreover, if peripheral discrimination requires foveal *feedback*, then the critical timecourse of behavioural effects should be substantially delayed relative to the well-established feedforward timing of the visual system (~40-120msec; e.g. Amassian et al., 1989; Corthout et al., 1999; Kammer et al., 2005; Lamme and Roelfsema, 2000). In Experiment 1 we tested these hypotheses by applying TMS over the posterior termination of the calcarine sulcus between -150ms and +500ms relative to stimulus onset. To anticipate, TMS significantly impaired discrimination accuracy when given 350-400ms after stimulus onset. In Experiment 2 we confirmed that calcarine TMS disrupted early processing of foveal stimuli, and we also tested whether late disruption of visual perception was specific for peripheral stimuli.

2. Methods

2.1 Experiment 1

2.1.1 Participants

Eighteen neurologically healthy, right-handed volunteers were recruited in Experiment 1 (9 females; mean age = 26.2 years). All participants had normal or corrected-to-normal vision and were initially screened for medical contraindications to TMS and MRI. The study was approved by the Human Research Ethics Committee at the School of Psychology, Cardiff University.

2.1.2 Apparatus

Experimental sessions were conducted in a darkened laboratory. Visual stimuli were presented at a mid-sagittal viewing distance of 65cm, on a 21-inch CRT monitor (60 Hz vertical refresh rate; 1024×768 resolution; black background). Throughout the experiment, the participant's head was fixed within a chinrest. Eye gaze was monitored on all trials with a Cambridge Research Systems video eye-tracking system, mounted in the chin rest (250 Hz sampling rate). Trials in which gaze deviated more than 2° from fixation or in which eye-blinks occurred were discarded. These criteria resulted in the exclusion of 1.1% of trials due to blinks, and 0.1% of trials due to saccades. The total percent of eye errors did not differ significantly between TMS sites (1.14%; $t(16)=0.67$, $p = .51$).

2.1.3 TMS and MRI parameters

Cortical stimulation was administered with a Magstim Super Rapid² system using a figure-of-eight coil (70mm) with the handle oriented upright to induce current flow along the superior-inferior axis. The TMS coil was fixed in position using a clamp and tripod and participants wore foam earplugs throughout the experiment.

In different sessions, TMS was applied to the posterior termination of the calcarine sulcus (the *foveal* site) or to an occipital control region (the *non-foveal* site; see Figure 1). On each trial, a double-pulse of TMS was applied at one of seven possible times relative to target onset (-150/-100, -50/0, +50/100, +150/200, +250/300, +350/400, +450/500 msec), at either a high 'effective' intensity or a low 'ineffective' intensity (120% or 40% motor threshold obtained via a single-pulse protocol, as described previously; Ruff et al., 2006; Schenkluhn et al., 2008; Varnava et al., 2011). Mean stimulator output for low and high intensities was 20% and 58%,

respectively. An initial test at the start of each session confirmed that the high intensity TMS did not elicit phosphenes.

[Insert Figure 1 about here]

To control for spatial priming effects we also delivered TMS prior to target onset. Our rationale for doing so was that activation of foveal retinotopic space (via TMS) might cue attention away from peripheral stimuli, providing an obvious explanation for any perceptual deficit. To address this issue, TMS was applied from 150msec before target onset, when any such attentional priming effects should be maximal (Müller and Rabbitt, 1989).

Prior to testing, structural MRI scans of each participant were acquired in a 3T whole-body GE scanner. Target sites for TMS were localised in each participant's scan using MRICro imaging software (Rorden and Brett, 2000). Neuroanatomical definitions for each site were based on occipital sulcal landmarks. The foveal (posterior calcarine or 'p-calcarine') site was defined as the hemispheric mid-point between the posterior termination of the left and right calcarine sulci. The non-foveal (non-calcarine control) site was referenced to a location ~15mm superior to the p-calcarine site, beyond the termination of the calcarine sulci. On average, the non-calcarine site was localised 15.7mm rostral to the foveal site on the cortical surface ($SD = 2.4\text{mm}$) and 16.8mm rostral on the scalp surface ($SD = 2.3\text{mm}$). The mean scalp-cortex distance for the p-calcarine ($M = 12.4\text{mm}$, $SD = 2.6\text{mm}$) and non-calcarine sites ($M = 11.6\text{mm}$, $SD = 1.9\text{mm}$) did not differ significantly [$t(16)=1.4$, $p = .19$]. At the beginning of each testing session, one region of interest was coregistered to the scalp surface using MR coregistration software (MRIReg) and a magnetic tracking device (miniBIRD 500, Ascension Tech).

2.1.4 Stimuli and Procedure

In the discrimination task (Figure 1a), participants decided whether two 'spiky' stimuli presented in opposite diagonal locations were the same or different. Participants responded with the index or middle finger of their right hand to indicate a 'same' or 'different' response, respectively. Participants were instructed to maintain fixation throughout each trial and respond as accurately as possible, with no emphasis on speed.

Target stimuli were selected randomly from a set of 1296 pre-generated ‘spiky’ stimuli, which vary by six levels along four dimensions (Op de Beeck et al., 2006). Prior to receiving TMS, the duration of the target stimulus was titrated in each participant to yield 70-75% discriminations ($d' = 1.0 - 1.5$), with the constraint that the duration could not exceed 150msec ($M = 78\text{msec}$, $SD = 39\text{msec}$). If a participant could not perform at a sufficient accuracy level for the longest duration, then the titration was repeated using a more constrained set of spiky stimuli in which the minimal difference between stimuli on ‘different’ trials was increased. On average, participants achieved 74.4% ($d' = 1.40$) performance during low-intensity TMS of foveal and non-foveal sites.

Each trial was self-initiated by button press and commenced with the onset of the central fixation stimulus (grey square, $0.15^\circ \times 0.15^\circ$, 500msec). The target array was then presented, which consisted of the two ‘spiky’ stimuli in opposite diagonal locations ($1.85^\circ\text{H} \times 1.65^\circ\text{W}$, each at 7° eccentricity). An indefinite response window was then followed by a fixed inter-trial interval of 750 msec, after which the participant could initiate the next trial via button press.

The diagonal configuration of spiky stimuli was held constant throughout each block of trials, and alternated between blocks. Each block contained 116 trials, including four initial ‘practice’ trials (not analysed), followed by 112 experimental trials. Within each block containing TMS, four trials were presented per level of TMS intensity (low, high), TMS onset time relative to target onset (-150/-100, -50/0, +50/100, +150/200, +250/300, +350/400, +450/500), and target type (same, different). Participants completed a total of eight such blocks per TMS site (p-calcarine, non-calcarine), thus yielding a total of 64 trials per TMS intensity, TMS onset time, and TMS site. The order of stimulation sites was blocked between sessions and counterbalanced across participants, with at least 24 hours between subsequent sessions.

Prior to receiving TMS, participants initially completed the same task during ‘Sham’ TMS, in which the coil was aligned perpendicular to the occipital scalp. The Sham condition was undertaken with the same parameters as the active sites, and simulated some of the sensory artefacts that accompany real TMS. These artefacts can distract or alert participants independently of cortical stimulation (Sawaki et al., 1999). Participants completed a total of eight Sham blocks prior to active TMS, divided between sessions for each of the TMS sites.

Following completion of the experiment, the Sham blocks were compiled into a baseline that included the same number of trials per TMS intensity and TMS onset time as the active sites.

2.1.5 Data Analysis

The principal dependent variable was the d' of target discrimination. The hit rate (HR) was defined as the proportion of correct 'same' responses on 'same' trials, while the false-alarm rate (FAR) was defined as the proportion of 'same' responses on 'different' trials. To provide a full account of the results, we undertook a combination of linear and non-linear analyses.

2.1.5.1 Non-linear regression analyses

Based on previous studies that have revealed at least two critical periods of processing in visual cortex (e.g. Camprodon et al., 2010; Corthout et al., 1999; de Graaf et al., 2011; Heinen et al., 2005; Koivisto et al., 2010; Laycock et al., 2007; Silvanto et al., 2005a; Stevens et al., 2009), we modelled individual data using a double inverted Gaussian function, which permits up to two distinct TMS-induced epochs after target onset. This approach has the advantage of detecting both early and late effects of TMS on performance and can also capture individual differences in the critical timecourse of visual processing. A similar analytic approach to considering event-related TMS data was recently reported by Stevens et al. (2009).

Specifically, the following Gaussian model was fit to d' values separately in each participant at each level of TMS site (p-calcarine, non-calcarine, sham) and TMS intensity (low, high).

$$y = y_0 + a_1 e^{\left[-0.5 \left(\frac{x-x_1}{b_1} \right)^2\right]} + a_2 e^{\left[-0.5 \left(\frac{x-x_2}{b_2} \right)^2\right]} \quad (1)$$

where y_0 = the intercept of the model,

a_1, a_2 = peak amplitude (change in d' from y_0) for the first and second periods, respectively;

x_1, x_2 = time of the first and second peaks; and

b_1, b_2 = full width half maximum (FWHM) bandwidth of the first and second periods.

The values of each parameter in each participant were permitted to vary freely in each model according to the following data-driven (1-3) and *a priori* (4-7) constraints:

- 1) $(d'_{\max} \times -1) < y_0 < d'_{\max}$
- 2) $(d'_{\max} \times -1) < a_1 < d'_{\max}$
- 3) $(d'_{\max} \times -1) < a_2 < d'_{\max}$
- 4) $-200 < x_1 < 550$ (limited to ± 50 msec beyond the range of TMS onset times)
- 5) $-200 < x_2 < 550$
- 6) $5 < b_1 < 200$
- 7) $5 < b_2 < 200$

where d'_{\max} = the maximum d' value per participant for the specific combination of TMS site and TMS intensity.

According to this modelling approach, an influence of TMS on performance is denoted by the values of a_1 (first period) and a_2 (second period) to which t -tests can be applied. If these differed significantly from zero in a group analysis then the secondary parameters were also considered (x_1 , x_2 , b_1 , b_2).

2.1.5.2 Linear analyses

In addition to the non-linear regressions, we also undertook more conventional ANOVA analyses. Two-way repeated-measures ANOVAs including factors of TMS site (p-calcarine, non-calcarine, sham) and TMS onset time (-150/-100, -50/0, +50/100, +150/200, +250/300, +350/400, +450/500) were undertaken separately for trials involving low or high intensity TMS, and for d' and response bias (c : the overall tendency to respond 'same' or 'different' independently of discrimination sensitivity). Where appropriate, analyses of simple main effects were corrected for multiple comparisons using the Holm-Bonferroni procedure (Aickin and Gensler, 1996).

2.2 Experiment 2

2.2.1 Participants

Ten volunteers were recruited in Experiment 2 (6 females; mean age = 23.9 years), one of whom had also participated in Experiment 1.

2.2.2 Apparatus

Equipment for visual presentation and eye-tracking was identical to Experiment 1. Trials in which gaze deviated more than 2° from fixation or in which eye-blinks occurred were discarded, resulting in the exclusion of 2.0% of trials due to blinks and 1.0% of trials due to saccades.

2.2.3 TMS and MRI Parameters

General TMS and MRI methods were identical to Experiment 1, with the exception that TMS was now applied to the p-calcarine site only. On each trial, a double-pulse of TMS was delivered at one of two possible times relative to target onset (+50/100 or +350/400 msec) at a high or low intensity (120% or 40% MT). Mean stimulator output for low and high intensities was 19% and 58%, respectively.

2.2.4 Stimuli and Procedure

Participants completed the same task as in Experiment 1, but including blocks requiring discrimination of foveal or peripheral stimuli. All stimulus characteristics for peripheral targets were identical to Experiment 1. For foveal targets, the stimulus height and width were reduced in general accordance with the foveal vs. peripheral (7°) cortical magnification factor (Duncan and Boynton, 2003; 0.5°H × 0.4°W) and centred 0.5° from fixation along the same diagonal vectors as the peripheral targets.

Prior to receiving TMS, the duration of the target stimulus was titrated in each participant to achieve 70-75% discriminations ($M = 83\text{msec}$, $SD = 16\text{msec}$). To ensure comparability of TMS effects, the duration of foveal and peripheral targets was matched within each participant. On trials with low-intensity TMS, average discrimination accuracy was 71.3% for foveal targets ($d' = 1.2$) and 69.6% for peripheral targets ($d' = 1.1$). These durations did not differ significantly [$t(9) = 0.71$, $p = .50$ for % correct; $t(9) = 0.81$, $p = .44$ for d'].

As in Experiment 1, the diagonal configuration of targets was held constant within blocks and alternated between blocks, with the order of alternation counterbalanced across participants. Each block contained 68 trials, including four initial ‘practice’ trials (not analysed) followed

by 64 experimental trials. Participants completed four blocks each with foveal or peripheral stimuli. Each set of four blocks was presented in a continuous sequence, with the order (foveal-peripheral or peripheral-foveal) counterbalanced across participants. In total, 64 trials were obtained per participant at each level of Target location (foveal, peripheral), TMS intensity (low, high) and TMS onset time (+50/100, +350/400 msec).

Following the main experiment, participants completed an additional phosphene test with the coil held in the same position over the p-calcarine site. During this procedure, participants were blindfolded and single pulse TMS was systematically increased in intensity until either the phosphene threshold was reached, the TMS became uncomfortable, or the intensity reached 100% stimulator output. If phosphene threshold was reached, the participant was then asked to report the location and approximate size of the percept.

2.2.5 Data Analysis

Three-way repeated-measures ANOVAs were undertaken for d' and c , including factors of Target location (foveal, peripheral), TMS intensity (low, high) and TMS onset time (+50/100, +350/400).

3. Results

3.1 Experiment 1

Trials in which participants responded prior to TMS were excluded from analysis (<0.1%), and the results for one participant were excluded entirely due to overall chance-level performance during low-intensity TMS. The outcome of the non-linear regression analysis is reported in Table 1 and Figure 2a. The models accounted for 83-92% of the variance in each sub-condition of TMS Intensity (low, high) and TMS site (p-calcarine, non-calcarine, sham). As shown in Table 1, the average peak amplitude (a : the change in d') differed significantly from zero only when high-intensity TMS was applied to the p-calcarine site at the later of the two possible Gaussian phases [parameter a_2 : $t(16) = -3.43$, $p = .003$]. On average, TMS in this condition reduced d' by 0.69 ($SE = 0.20$) relative to the condition-specific intercept ($y_0 = 1.44$, $SE = 0.08$). This drop in d' was observed in 15/17 participants and corresponds to a TMS-induced reduction in discrimination sensitivity of 46.9%. The average time of this peak for the p-calcarine site was 332.2 msec after target onset ($SE = 20.5$) with an average bandwidth (FWHM) of 59.8 msec ($SE = 16.5$). Site-specific comparisons between the average modelled d' at each time point revealed similar effects (see Figure 2a). Additional paired t -

tests showed that a_2 for the p-calcarine *high*-intensity TMS trials was significantly reduced relative to a_2 for the corresponding *low*-intensity TMS trials [$M = 0.15$, $SE = 0.25$; $t(16) = 2.4$, $p = .029$], and was also reduced relative to the high-intensity TMS trials for both the non-calcarine control site [$M = 0.21$, $SE = 0.30$; $t(16) = 2.5$, $p = .022$] and the sham control condition [$M = 0.02$, $SE = 0.24$; $t(16) = 2.1$, $p = .048$].

[Insert Table 1 about here]

Conventional linear analyses produced a similar outcome. A two-way ANOVA of mean d' on high-intensity TMS trials, including factors of TMS site (p-calcarine, non-calcarine, sham) and TMS onset time (-150/-100, -50/0, +50/100, +150/200, +250/300, +350/400, +450/500) revealed no significant main effects (both $p > .16$) but did uncover a significant two-way interaction of TMS site \times TMS onset time [$F(12, 192) = 1.81$, $p = .049$]. As shown in Figure 2b, analysis of simple main effects (Holm-Bonferroni corrected) revealed that stimulation of the p-calcarine site at +350/400msec ($d' = 1.05$) reliably impaired performance relative to both the non-calcarine control site ($d' = 1.43$; $p = .004$) and the sham control condition ($d' = 1.52$; $p = .002$). This impairment in performance during p-calcarine TMS was consistently observed across participants (Figure 2c).

[Insert Figure 2 about here]

In contrast, detection sensitivity at +350/400msec did not differ significantly between the sham and non-calcarine control conditions ($p = .48$), and no significant differences between p-calcarine, non-calcarine and sham conditions were observed at any other TMS onset times. An additional paired t -test indicated that performance at +350/400msec for the calcarine site ($d' = 1.05$) differed significantly from the average d' of the six remaining calcarine TMS onset times ($d' = 1.28$; $t(16) = -2.54$, $p = .022$). The corresponding two-way ANOVA of d' on low-intensity TMS trials revealed no significant interaction or main effects (all $p > .11$) and was therefore not considered further. However, at +350/400msec, calcarine TMS did significantly reduce d' on high-intensity TMS trials ($d' = 1.05$) compared with the corresponding low-intensity TMS trials ($d' = 1.34$; $t(16) = -2.68$, $p = .016$).

To what extent is the time-specific reduction in performance during p-calcarine stimulation associated with changes in response bias, that is, the tendency to judge the targets as ‘same’ or

‘different’? To answer this question we conducted the same two-way ANOVAs as above but on the c parameter extracted from signal detection analysis (Figure 2d). For low-intensity TMS trials, no significant interaction or main effects were observed (all $p > 0.1$). For high-intensity TMS trials, no significant interaction [$F(12, 192) = 0.34, p = .98$] or main effect of TMS time was detected [$F(6, 96) = 1.94, p = .08$]. However, now a significant main effect of TMS site was observed [$F(2, 32) = 4.30, p = .029$], driven by significantly higher c (tendency to respond ‘different’) on trials with calcarine ($M = -0.07, SE = .05$) or non-calcarine TMS ($M = -0.1, SE = .04$) compared with the sham control condition ($M = -0.16, SE = .05$; both $p < .016$). The reason for this effect is not clear; it could potentially reflect a general influence of high-intensity active TMS on arousal, or perhaps a change in bias with practice (since sham blocks were always completed at the beginning of the p-calcarine and non-calcarine sessions). Importantly, however, since c did not differ between the p-calcarine and non-calcarine sites ($p = .49$), it cannot explain the site- or time- specific effects of p-calcarine TMS on d' .

3.2 Experiment 2

Trials in which participants responded prior to TMS were excluded from analysis ($<0.1\%$). A three-way ANOVA of mean d' , including factors of Target location (foveal, peripheral), TMS intensity (low, high) and TMS onset time (+50/100, +350/400) revealed a significant three-way interaction [$F(1, 9) = 7.2, p = .025$]. Analysis of simple main effects revealed that effect of p-calcarine stimulation depended on target location and TMS onset time (see Figure 3). For foveal targets, high-intensity (vs. low-intensity) TMS significantly impaired discrimination accuracy at +50/100msec ($p = .019$) but not at +350/400msec ($p = .765$). For peripheral targets, however, the opposite result was observed: consistent with Experiment 1, TMS impaired discrimination accuracy at +350/400msec ($p = .018$) but not at +50/100ms ($p = .398$). The corresponding ANOVA of response bias (c) revealed no significant main effects or interactions (all $p > 0.1$).

[Insert Figure 3 about here]

Following the main experiment, phosphenes were successfully elicited in 2 of 10 participants during single-pulse TMS of the p-calcarine site, at 81% and 84% stimulator output. In both cases the reported phosphene was foveal and did not overlap with the locations of the peripheral targets. These phosphene thresholds were substantially higher than the high-intensity output for these participants in the main experiment (46% and 56%, respectively).

This was expected, as the TMS coil was deliberately oriented vertically in both experiments precisely to minimise the likelihood of phosphene induction, which typically most effective when the handle is positioned horizontally to induce current flow in a lateral-medial direction (e.g. Kammer et al., 2001).

4. Discussion

In Experiment 1 we found that TMS applied near the posterior (foveal) calcarine sulcus can disrupt the encoding of stimuli presented in the visual periphery, approximately 300-400msec after stimulus onset. In Experiment 2 we further observed that p-calcarine stimulation during the expected feedforward window (+50/100msec; Kammer et al., 2005a) selectively impaired discrimination of foveal but not peripheral targets; whereas stimulation during the later period (+350/400ms) selectively impaired discrimination of peripheral but not foveal targets. The timecourse of this peripheral impairment appears too late to be explained by feedforward processing or horizontal cortical connections (Lamme and Roelfsema, 2000). Furthermore, the early impairment of foveal discrimination (combined with the foveal phosphene reports) indicates that p-calcarine TMS successfully disrupted foveal retinotopic cortex. Taken together, therefore, the specificity of these findings in terms of neuroanatomy, timing, and retinotopic location is consistent with the hypothesis that foveal cortex is a crucial recipient of late feedback signals from the visual periphery.

The present results raise a number of questions about the content and functionality of foveal feedback. Existing fMRI evidence indicates that representations of the visual periphery in foveal cortex contain only task-relevant information (Williams, et al., 2008), encoding the behaviourally relevant shape, but not the irrelevant colour, of peripheral objects. This evidence, combined with the current TMS results, suggests that constructive feedback reflects more than a mere artefact of visual processing or the point spread of the haemodynamic response (Arthurs and Boniface, 2003; Logothetis, 2008). Instead, constructive feedback appears to be an instrumental component of visual perception, required whenever task goals require covert allocation of attention to objects in peripheral space.

Since our behavioural task required covert selection of the visual periphery, might our TMS results be explained by the same feedback mechanisms that are known to support attention? (Desimone and Duncan, 1995; Duncan, et al., 1997; Kastner and Ungerleider, 2000; Pessoa et

al., 2003). Conventional accounts of feedback, including those implicated in attention, involve modulation of existing feedforward representations; however our data indicate that p-calcarine TMS did not interfere significantly with early feedforward processing of peripheral stimuli. Furthermore, the critical epoch we observed in primary visual cortex (+350-400msec) is ~100msec later than would be expected solely by re-entrant attentional modulation (Juan and Walsh, 2003; Martinez, 1999; Martinez et al., 2001; Noesselt et al., 2002) and raises the possibility that foveal feedback, while likely dependent on goal-directed attention, may incur additional computational costs. Consistent with previous explanations of late occipital feedback (Heinen et al. 2005), this computation could potentially relate to perceptual decision-making processes, implemented by a constructive feedback mechanism that exploits the fine-grained spatial resolution of foveal cortex to ‘rebuild’ and discriminate between extra-foveal representations. Recent evidence raises the possibility that this top-down process may be linked to visual working memory (Harrison and Tong, 2009; Serences et al., 2009) and mental imagery (Stokes et al., 2009). Within either of these domains, foveal visual cortex may serve as a dynamic workspace, or ‘scratchpad’, for increasing the precision of perceptual decisions (Baars, 1988). Interestingly, late TMS in Experiment 2 did not reliably impair discrimination of foveal stimuli (Figure 3a). While this null effect should be treated with caution, it nevertheless suggests that this ‘scratchpad’ may be especially important for resolving extra-foveal representations, perhaps in advance of a goal-directed saccade that would foveate the stimulus under naturalistic conditions.

The existence of foveal feedback implies the actions of a key source (or sources) that transmit behaviourally relevant information to the foveal cortex. Key candidates include the lateral occipital complex (LOC: Pitcher et al., 2009), extrastriate cortex (Pascual-Leone and Walsh, 2001; Silvanto et al., 2005b) as well as parietal and frontal areas (Chambers and Mattingley, 2005; Corbetta et al., 2008; Stokes, et al., 2009). The ability to measure foveal feedback with fMRI, and now with TMS, opens a number of promising avenues for combining these methods in future studies, for instance, by determining the effect of LOC stimulation on peripheral information encoded in foveal V1. More broadly, further studies of the mechanism by which top-down sources modulate striate cortex (Ruff, et al., 2006; Silvanto et al., 2009) are likely to have important implications for understanding the nature of foveal feedback in visual information processing.

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Table 1. Mean and SEM of coefficients resulting from the Gaussian non-linear regressions. Only high-intensity TMS of the calcarine site during the late phase significantly reduced discrimination accuracy. * $p < 0.05$ following Holm-Bonferroni correction for twelve comparisons (strictest $\alpha = .00416$).

TMS	Site	R^2	y_0	Period	Peak Amp ($a_1 a_2$) $\Delta d'$	Peak Time ($x_1 x_2$) msec	Bandwidth ($b_1 b_2$) msec
High	Calcarine	0.83 (0.04)	1.44 (0.08)	1 st	-0.05 (0.33)	N/A	N/A
				2 nd	-0.69 (0.20)*	332.2 (20.5)	59.8 (16.5)
	Non-calc	0.88 (0.02)	1.40 (0.09)	1 st	0.49 (0.38)	N/A	N/A
				2 nd	0.21 (0.30)	N/A	N/A
	Sham	0.90 (0.02)	1.27 (0.11)	1 st	0.02 (0.23)	N/A	N/A
				2 nd	0.02 (0.24)	N/A	N/A
Low	Calcarine	0.91 (0.02)	1.23 (0.09)	1 st	0.43 (0.37)	N/A	N/A
				2 nd	0.15 (0.25)	N/A	N/A
	Non-calc	0.83 (0.03)	1.37 (0.10)	1 st	0.42 (0.26)	N/A	N/A
				2 nd	0.29 (0.33)	N/A	N/A
	Sham	0.92 (0.02)	1.18 (0.13)	1 st	0.64 (0.39)	N/A	N/A
				2 nd	-0.07 (0.37)	N/A	N/A

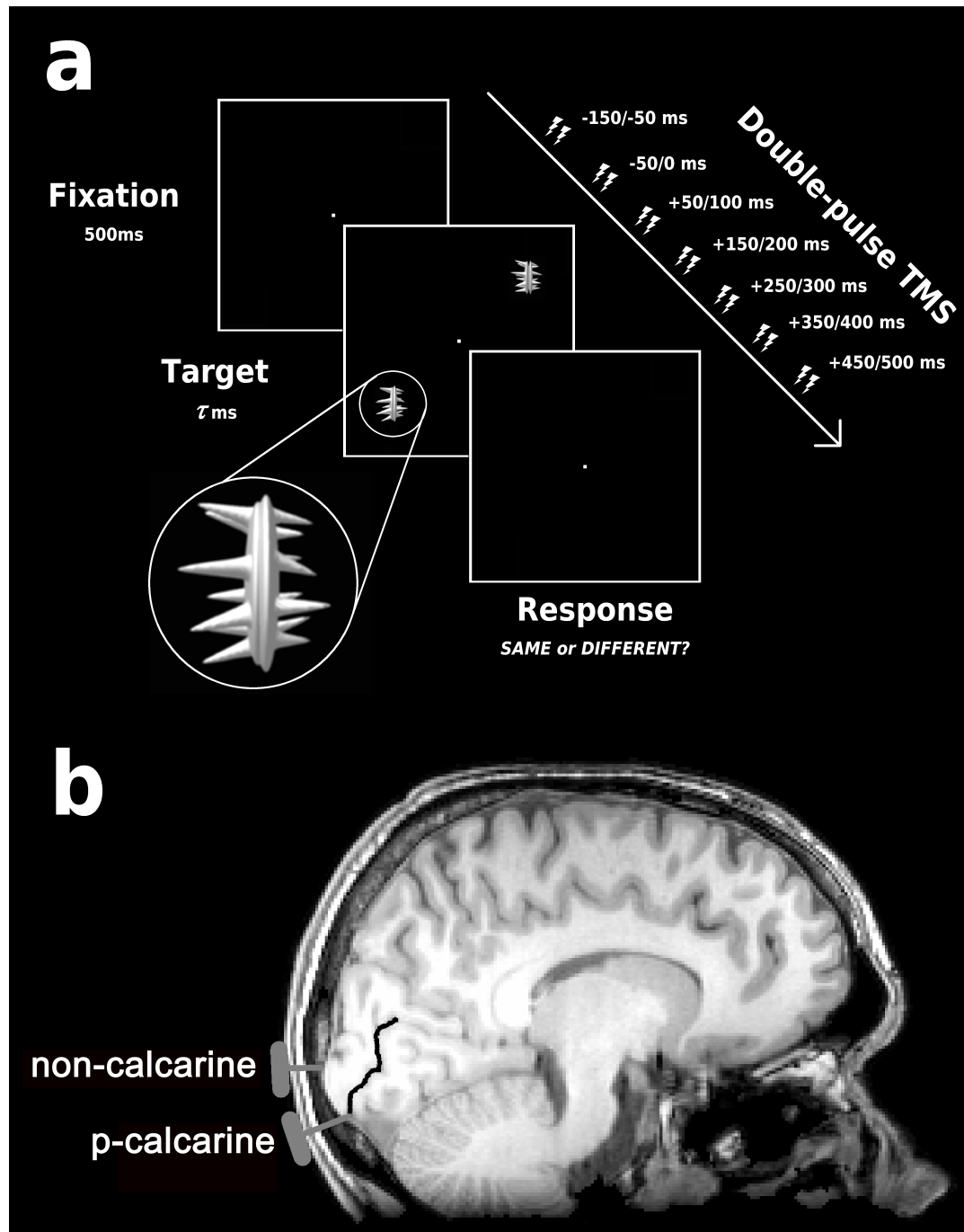


Figure 1. Experimental paradigm and sites of cortical stimulation. (a) Schematic of visual displays in Experiment 1. The target array consisted of two objects presented in opposite diagonal locations, drawn randomly from a set of ‘spiky’ stimuli (Williams, et al., 2008); 7° eccentricity; diagonal configuration alternated between blocks). On each trial, participants decided whether the two objects were the same or different. Prior to the TMS experiment, the duration of the target array (τ) was adjusted on an individual basis to yield 70-75% correct discriminations. In Experiment 2, the task and stimulus sequence was broadly identical with the exception that stimuli were presented either on the fovea or in the periphery, with TMS was applied to the p-calcarine site at either +50/100 or +350/400msec. **(b)** TMS sites in one participant. The p-calcarine site (foveal representation) was defined as the posterior termination of the calcarine sulcus (black line). The non-calcarine control site was localised ~15mm rostral to the calcarine site. All regions were localised within individual MRI scans.

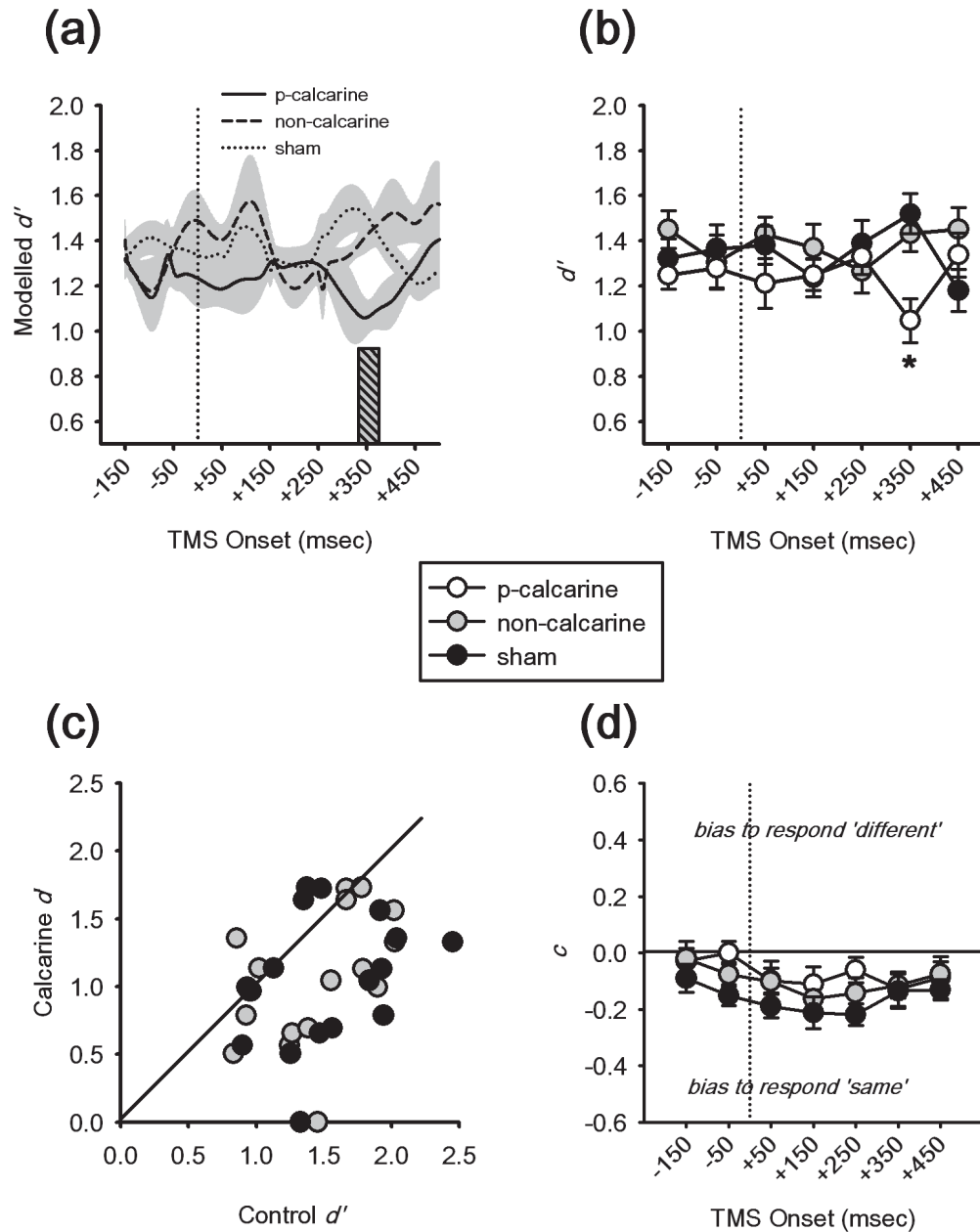


Figure 2. The effect of occipital TMS on perception of peripheral stimuli in Experiment 1. **(a)** Average double-Gaussian models of d' during high-intensity TMS in the p-calcarine, non-calcarine and sham conditions. The grey shaded regions indicate ± 1 SE of the average model at each TMS onset time. The hatched bar indicates the range of TMS onset times at which the average modelled d' , during p-calcarine TMS, differed significantly from both the non-calcarine and sham conditions (by paired-samples t -test with Holm-Bonferroni corrections). See Table 1 for average Gaussian coefficients. **(b)** Average d' for high-intensity TMS trials as a function of TMS onset time and TMS site. Consistent with the non-linear analysis, TMS at a relatively late onset time (+350/400msec) impaired discrimination accuracy (*). **(c)** Individual results at the TMS onset time of +350/400msec. Data points falling to the right of the unity line indicate a reduction in d' caused by calcarine stimulation. **(d)** Average response bias for high-intensity TMS trials according to TMS onset time and TMS site. Overall, TMS of the p-calcarine and non-calcarine sites reduced the tendency to respond 'same' (relative to sham); however this general effect did not interact with TMS onset time. Error bars in all panels are ± 1 SEM.

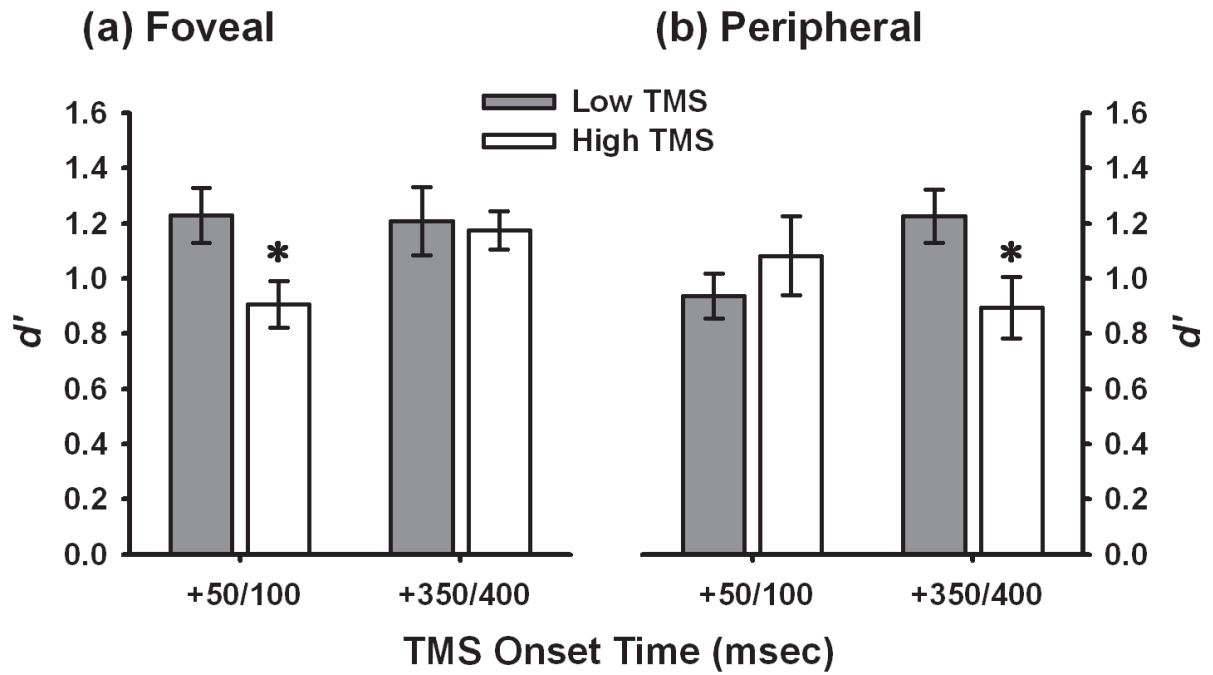


Figure 3. The effect of p-calcarine stimulation on foveal and peripheral perception in Experiment 2. (a) Average d' for foveal stimuli plotted according to TMS intensity and TMS onset time. Only early TMS (+50/100ms) impaired performance. **(b)** Average d' for peripheral stimuli plotted according to TMS intensity and TMS onset time. Only late TMS (+350/400ms) impaired performance. Error bars are ± 1 SE of the mean. * $p < .05$ for comparison of low- vs. high-intensity TMS.