Similar effects of repetitive transcranial magnetic stimulation of MT+ and a dorsomedial extrastriate site including V3A on pattern detection and position discrimination of rotating and radial motion patterns

Benjamin M. Harvey
Visual Development Unit, Department of Experimental Psychology, Oxford University, Oxford, UK, & Department of Experimental Psychology, Utrecht University, Utrecht, Netherlands

Oliver J. Braddick
Visual Development Unit, Department of Experimental Psychology, Oxford University, Oxford, UK

Alan Cowey
Department of Experimental Psychology, Oxford University, Oxford, UK

Our recent psychophysical experiments have identified differences in the spatial summation characteristics of pattern detection and position discrimination tasks performed with rotating, expanding, and contracting stimuli. Areas MT and MST are well established to be involved in processing these stimuli. fMRI results have shown retinotopic activation of area V3A depending on the location of the center of radial motion in vision. This suggests the possibility that V3A may be involved in position discrimination tasks with these motion patterns. Here we use repetitive transcranial magnetic stimulation (rTMS) over MT+ and a dorsomedial extrastriate region including V3A to try to distinguish between TMS effects on pattern detection and position discrimination tasks. If V3A were involved in position discrimination, we would expect to see effects on position discrimination tasks, but not pattern detection tasks, with rTMS over this dorsomedial extrastriate region. In fact, we could not dissociate TMS effects on the two tasks, suggesting that they are performed by the same extrastriate area, in MT+.

Keywords: rTMS, V3A, MT+, motion processing, position discrimination

Citation: Harvey, B. M., Braddick, O. J., & Cowey, A. (2010). Similar effects of repetitive transcranial magnetic stimulation of MT+ and a dorsomedial extrastriate site including V3A on pattern detection and position discrimination of rotating and radial motion patterns. *Journal of Vision, 10*(5):21, 1–15, http://journalofvision.org/content/10/5/21, doi:10.1167/10.5.21.

Introduction

Our recent psychophysical studies (Harvey & Braddick, 2008) have revealed different spatial summation characteristics for pattern detection and position discrimination tasks performed on rotating, expanding, and contracting patterns. This raises the possibility that distinct neural systems might be involved in the two tasks. fMRI results (Koyama et al., 2005) have shown a retinotopic organization of activation of visual area V3A, related to the position of the center of radial motion in the visual field. V3A is also differentially activated by the degree of contour curvature in stationary and moving forms (Caplovitz & Tse, 2007). Since the center of a motion pattern corresponds to the position of maximum curvature, this curvature sensitivity could be used to locate the center of motion. Finally, Beardsley and Vaina (2005) report a stroke patient who is unable to determine the direction of radial motions but is still able to localize the centers of these patterns accurately. Together, these results raise the possibility that an area other than MT+ may be involved in representing the position of the center of radial and perhaps circular motion and that this area may be V3A in humans. The present study aimed to test whether transcranial magnetic stimulation (TMS) could provide evidence to support this distinction between the functions of these two areas. Furthermore, because macaque V3A is not motion sensitive (Orban et al., 2003), and so is apparently not functionally homologous to human V3A in this respect, this also provided a way to confirm the motion processing role of human V3A with a technique other than fMRI.

However, in macaques, MST has also been implicated in position discrimination of optic flow patterns (Duffy & Wurtz, 1995), and several models of heading discrimination propose a population-coded representation of heading in MST (Lappe & Rauschcker, 1993; Page & Duffy, 2003; Perrone & Stone, 1998). It is therefore possible that the closely related task of discriminating

doi: 10.1167/10.5.21 Received August 5, 2009; published May 12, 2010 ISSN 1534-7362

center of motion position in humans relies on population encoding of this location in MT+.

While MT+ has a well-established role in detection and direction discrimination of rotating, expanding, and contracting patterns in humans (Morrone et al., 2000; Smith, Wall, Williams, & Singh, 2006; Wall, Lingnau, Ashida, & Smith, 2008), the role of V3A in detection of these patterns is much less well established. fMRI studies show human V3A to be highly sensitive to coherent motion (Braddick, O'Brien, Wattam-Bell, Atkinson, & Turner, 2000; Sunaert, Van Hecke, Marchal, & Orban, 1999; Tootell et al., 1997) and the activation of V3A, like that of MT, varies with the speed of the motion stimulus (Chawla et al., 1999; Chawla, Phillips, Buechel, Edwards, & Friston, 1998). Also, as with MT+, rTMS over V3A can induce subjective slowing of the perceived speed of motion stimuli, often accompanied by performance deficits in speed discrimination tasks (McKeefry, Burton, Vakrou, Barrett, & Morland, 2008). rTMS over MT+ or V2/V3 (at a site which probably also includes V3A) disrupts the perception of first- or second-order unidirectional motion (Cowey, Campana, Walsh, & Vaina, 2006). However, this may well result from disruption caused by rTMS of either site leading to disruption of the other via direct anatomical links between the two areas. Despite all of these roles of V3A in motion perception, it does not seem to respond selectively to optic flow structure (Greenlee, 2000).

This study aims to clarify whether a dorsomedial area of extrastriate cortex, which is sensitive to global motion, is functionally involved in position discrimination of the centers of rotating, expanding, and contracting motions or in detection of these patterns. When stimulated with TMS, this extrastriate area almost certainly includes V3A. However, due to the limited spatial resolution of TMS, we do not claim to target V3A specifically. Indeed, this may not be possible with TMS. This study also looks for different TMS effects on these pattern detection and position discrimination tasks, which might support different neural substrates underlying the performance of the two tasks.

Methods

Observers

Four observers participated in the experiment. BH, JS, and CB had normal vision, while AC had corrected-to-normal vision. BH, JS, and CB were very experienced with psychophysical tasks very similar to the tasks performed here during TMS. Informed consent was obtained from subjects under the requirements of approval by the local UK NHS research ethics committee (COREC No 06/Q1607/52).

Apparatus and stimuli

Stimuli were generated online by a Pentium 4 computer with a Radeon 7000 graphics card. They were displayed on an Iiyama S901 CRT monitor in a 13.33° × 10.00° (16.66° diagonal) rectangular region. Sequences were generated online at 60 Hz and at 1600 × 1200 resolution using custom software written in Lua (Ierusalimschy, 2003). Each stimulus consisted of 3000 circular white dots (diameter 4.4 min of visual angle) on a black background. Stimuli were viewed binocularly at a distance of 89 cm. All dots moved at the same speed of 1.9°/s, irrespective of distance from the center of motion. No radial speed gradients were used, and so motions did not simulate the motion of a rigid object. The choice of velocity and lack of a speed gradient is discussed more fully by Harvey and Braddick (2008).

Dots had a lifetime of five frames (0.083 seconds). To minimize coherent stimulus flicker, dots were replaced asynchronously by randomly distributing initial dot lifetimes among the first five frames of the display sequence.

Incoherently moving dots followed the same motion pattern as coherently moving dots, but with respect to a randomly placed center of motion, so that for rotating patterns, the local curvature of single dot paths gave no information about the center of motion. If the movement of a coherently moving dot crossed the boundaries of the coherent part of the display, reached the center of motion, or at the end of the dot's lifetime, it was replaced at a new, random position with a full, five-frame lifetime.

In radial motion stimuli, if the starting locations of dots had been randomly distributed, there would have been a net movement of randomly placed dots towards or away from the center of motion. This would respectively increase or decrease dot density at the center of motion. Therefore, in radial stimuli, the random location was assigned to the third (middle) frame of the dot's lifetime.

Because TMS was administered unilaterally in the right hemisphere, its effects had to be tested with stimuli whose partially coherent regions were confined to the lower left quadrant of the visual field. This partially coherent area was in the center of the display, but subjects fixated a cross 3.33° to the right and 2.49° above of the center of the display, i.e., 4.16° diagonally from the center, and made perceptual judgements about motion patterns in a 5° diameter circular region in the lower left field quadrant (Figure 1). Outside of this partially coherent central region, the display contained only non-coherent dynamic noise.

Subjects performed both pattern detection and position discrimination tasks, following a two-alternative forced-choice design. In the position discrimination task, the display always contained an area of partially coherent radial or rotational motion, with the center of motion positioned either above or below the center of the display. The subject responded whether they perceived the center of motion above of below the center of the display, using

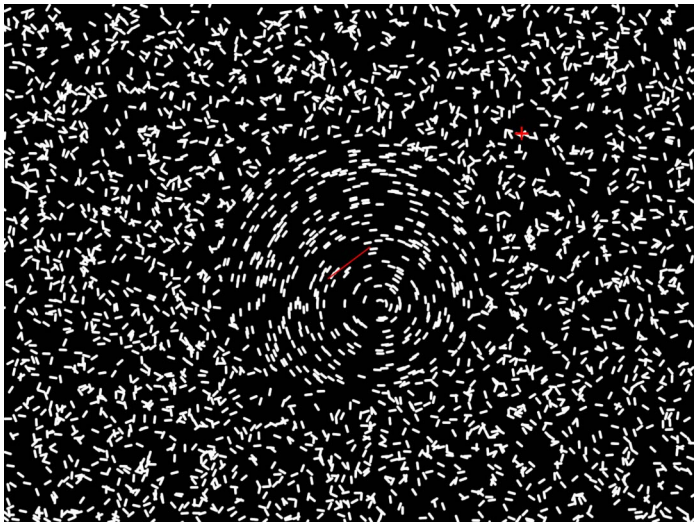

Figure 1. Static representation of moving stimuli used. Fixation cross shown in upper right side of stimulus, with partially coherent motion pattern in center of display.

the up and down arrow keys on a standard keyboard. In the pattern detection task, the display either contained an area of partially coherent radial or rotational motion (again with the center of motion positioned either above or below the center of the display) or non-coherent, random motion only. Subjects indicated whether or not they perceived a partially coherent motion pattern using the left and right arrow keys on the keyboard to signal coherent and non-coherent motion respectively. In this pattern detection task, subjects ignored the position of the center of motion.

In both pattern detection and position discrimination tasks, the center of motion of the partially coherent pattern was positioned either above and left or below and right of the center of the display. Both of these positions were the same distance from the fixation point to avoid eccentricity-dependent differences of threshold between them. For observer AC, these possible centers of motion positions were 3.0° apart; for BH, CB, and JS, this separation was 2.0°. These different values were selected as being about the smallest distances at which each subject could perform position discriminations with partially coherent motion patterns. The same locations were also used for pattern detection tasks to ensure that the positional uncertainty required for the position discrimination displays was not a source of difference between the two tasks.

In order that subjects were clear about where to attend in the display, the center of the display was marked with a red dot between stimulus presentations. This positional cue allowed subjects to focus their covert attention to the partially coherent part of the stimulus. During stimulus presentations, this dot changed to a red line 1° in length, bisecting the two possible positions of the center of motion, providing a reference point for the position judgments.

The coherent dots in the display moved in rotating, expanding, or contracting patterns around the center of motion. The direction of rotating motion was randomized between clockwise and counterclockwise so that subjects could not judge position from the direction of movement at a point between the two possible center positions. While there was no indication that subjects used this strategy in this or previous experiments, it was preferable to avoid the possibility by randomizing direction. As the same is true of expanding and contracting patterns, they also had to be randomized in the sequence of presentations. However, there are considerable differences between the processing of expanding and contracting motion patterns, (Harvey & Braddick, 2008), and the present experiment showed marked differences in coherence thresholds between these patterns. We therefore presented expansion and contraction stimuli in mixed blocks but analyzed the data from these two types of trial separately.

Stimuli were presented at a coherence level at which subjects could perform the task correctly on 80–90% of trials without TMS (given in Table 1), allowing performance to decrease with TMS administration without falling to chance. Subjects' head position was restrained by a chin and forehead rest. They responded using the arrow keys on a standard computer keyboard. After practice trials had been successfully completed, test trials were conducted in blocks of 24, plus repeats for any trials which were rejected because of eye movements. After any trial in which TMS might have been delivered (i.e., was

	80–90% correct response coherence level without TMS (%)					
	Rotation		Expansion		Contraction	
Subject	Detection	Pos. disc.	Detection	Pos. disc	Detection	Pos. disc.
AC	23	37	35	31	45	29
BH	20	30	25	35	20	26
CB	20	58	24	38	29	32
JS	35	63	25	50	32	65

Table 1. Summary of coherence levels used for each subject in each stimulus condition. Coherence levels at which subjects responded correctly on 80–90% of trials were chosen. Pos. disc. = position discrimination.

delivered in the TMS test conditions, was not delivered in the no-TMS controls), an enforced pause of six seconds was started in which subjects could respond, but could not start another trial.

The blocks of 24 trials always contained the same numbers of each condition being tested, presented in a randomized order. For example, position discrimination for rotating patterns contained two conditions, with the center of motion above or below the center of the display, so each was presented in twelve of the trials. A summary of the conditions in each block is presented in Table 2.

Grouped across all test runs, subjects had 60 trials per condition, e.g., 60 partially coherent and 60 non-coherent trials. These were combined for each decision type, i.e., coherence detection, to give a score out of 120. Scores under different TMS conditions were compared using chi-squared tests on a table of correct vs. incorrect answers. For demonstration of TMS effects, performance with TMS over MT+ or the dorsomedial extrastriate (V3A) site was compared to performance with TMS over the vertex.

For pattern detection in mixed expanding and contracting conditions, three conditions were used: a single non-coherent condition provided the "signal absent" trials for both expansion and contraction detection. This minimized the number of trials and in particular the amount of TMS required. It did result in twice the number of partially coherent trials as non-coherent stimulus trials. Subjects were informed of these different proportions; the data gave no evidence of any resulting bias towards "partially coherent stimulus" responses. As each subject was presented with 120 "partially coherent stimulus" trials and 60 "non-coherent stimulus" trails, response frequencies should match these figures if there was no bias towards either response due to this unusual ratio. Chi-squared tests of the observed frequency of "partially coherent stimulus" and "non-coherent stimulus" responses, grouped across all subjects in no TMS and vertex TMS conditions showed no significant difference from the expected rates ($p = 0.18$).

As different numbers of trails per condition were present in each type of block, different numbers of blocks were performed for each condition. For both tasks with rotating stimuli, with only two conditions being tested (and therefore 12 trails per condition per block), five blocks were performed to make sixty trails overall. As four conditions were being examined for the position discrimination task with expanding and contracting stimuli, allowing only six trials per condition, ten blocks were performed. For pattern detection with expanding and contracting stimuli, three conditions were being examined, allowing eight trials each. Thus, 7.5 blocks were performed, seven blocks of 24 trails and one block of 12 trials.

Blocks were presented in a randomized order for task, motion type, and TMS condition. All tasks, motion types and TMS condition combinations were performed once in randomized order and then performed again in another randomized order. Subjects were told verbally which motion type and task was to be shown before each trial block started, for example, "rotation, yes/no" or "radial, up/down."

TMS parameters

TMS was delivered at one of three sites (MT+ site, dorsomedial extrastriate V3A site, or vertex) or was not delivered (no TMS condition). In the no TMS condition, the TMS generator was not activated, and the coil was not held near the subject's head. TMS sites were tested in separate blocks, whose order was randomized.

TMS pulses were generated by a Magstim Rapid generator with four capacitor booster modules used to provide enough current for repetitive TMS. Magnetic fields were generated through a 70-mm Magstim figure-eight butterfly coil. The coil was held by hand over a marker placed on a surgical cap to maintain coil position accurately throughout the session. In each trial, trains of six evenly spaced pulses were delivered within 500 ms (12 Hz), the period of stimulus presentation. The first pulse was delivered just before the first frame was displayed, and the last pulse delivered approximately 417 ms after stimulus onset, i.e., 83 ms before stimulus offset. Pulses (each pulse less than 1 ms) were delivered between frames

Motion type	Task	Separated conditions	Response	Randomly varied but analyzed together	Trials per condition per block
Rotation	Detection	Partially coherent/ non-coherent	Partially coherent/ non-coherent	Clockwise/CCW/up/down	12
Rotation	Pos. disc.	Up/down	Up/down	Clockwise/CCW	12
Exp./Con.	Detection	Expanding/contracting/ non-coherent	Partially coherent/ non-coherent	Up/down	8
Exp./Con.	Pos. disc.	Expanding/contracting/ up/down	Up/down		6

Table 2. Summary of conditions used in each type of trial block. Exp. = expansion; Con. = contraction; Pos. disc. = position discrimination; CCW = counterclockwise.

to avoid affecting the stimulus display monitor during its 60 Hz scan cycle, i.e., after every fifth frame.

Pulses were delivered unilaterally on the right side of the head, and so perceptual tasks were performed in the corresponding left half of the visual field.

The sites used for TMS vary slightly between subjects because of individual differences in gross brain anatomy. The positions and orientations of the coil and the strength of the magnetic field were determined functionally by phosphene elicitation (Cowey & Walsh, 2000; Walsh & Cowey, 2000). Subjects sat in a darkened room wearing a snugly taped surgical cap. After fixating the fixation cross on the display, they closed their eyes and kept their gaze on the same position. When the subject was ready, he pressed a key and a train of six TMS pulses was generated at 12 Hz. These stimulation parameters have been used effectively in previous rTMS studies (Cowey et al., 2006). Phosphenes were reliably elicited above a threshold of 65–70% of the maximum stimulator output, depending on the subject and stimulation site. Effective stimulation sites for phosphene elicitation were typically only about 1–2 cm in diameter. For a further 1 cm around these sites, much weaker phosphenes could still be elicited.

The phosphenes elicited to determine the MT+ and dorsomedial extrastriate (V3A) TMS stimulation sites were required to have a characteristic moving, flickering achromatic appearance and cover much of the lower left quadrant of vision, including the center of the display area. This site for MT+ was always at, or close to, 3 cm above the inion and 4–5 cm lateral from the mid-line. Our dorsomedial extrastriate site was always 5 cm above the inion and 1–2 cm lateral from the mid-line. Here, it is harder to be sure that phosphenes were produced as a result of V3A stimulation as V3 and V2 are very close to the stimulation site and stimulation of either of these could have elicited phosphenes. However, the limited spatial resolution of TMS means that all three of these areas were probably stimulated by TMS no matter how stimulation sites were chosen, although V2 least of all because it is furthest from the dorsal surface. Furthermore, the phosphenes elicited to determine the TMS site for our dorsomedial extrastriate site were always perceived as moving and achromatic, which would not be the expected appearance for phosphenes elicited by stimulation over V2. For vertex TMS, no phosphenes were produced, and indeed a site with no specific neurological effects was needed. The vertex site was therefore defined as the point half way between the inion and the bridge of the nose, on the midline of the scalp, defined as the point equidistant from the right and left tragus.

It may have been desirable to position TMS coils by reference to fMRI loci using a neuronavigated TMS procedure. This approach is increasingly common, with the increasing availability of fMRI and the use of both TMS and fMRI in many studies. The technique used in this study involved hunting for TMS coil positions that optimally elicited phosphenes with perceptual characteristics expected from previous TMS studies and the known response properties of the targeted area. While fMRI-based neuronavigation is certainly desirable when fMRI loci have been found, recent studies from several labs have used a similar hunting technique to localize MT+ effectively (Grossman, Battelli, & Pascual-Leone, 2005; Laycock, Crewther, Fitzgerald, & Crewther, 2007; Silvanto, Cowey, Lavie, & Walsh, 2005).

V3A has not been so thoroughly studied with TMS as MT+. Due to the limited spatial resolution of TMS, it probably is not possible to specifically target V3A, even if fMRI loci are known. As such, this study instead targets a dorsomedial region of extrastriate cortex where TMS also produces strongly moving phosphenes. Several lines of evidence suggest that V3A was being effectively targeted. First, the known location of V3A in humans from fMRI studies (Caplovitz & Tse, 2007; Koyama et al., 2005) is in close proximity of this location to our coil position. Also, importantly, the phosphenes elicited at or very near the chosen dorsomedial extrastriate site used often extended into the upper visual field. This is in agreement with V3A's hemifield retinotopic map, although our ideal phosphene was primarily in the lower left quadrant of the visual field as this was where our test stimulus was presented. Such a phosphene would be unlikely to be produced by stimulation of V2 or V3, which have only quarter-field representations (Wandell, Dumoulin, & Brewer, 2007). For other nearby areas, the motion characteristics of the phosphenes suggest they are not produced by stimulation of V7. V7 does not seem to be highly motion selective in humans, responding instead to object information and processing of structure from disparity (Georgieva, Peeters, Kolster, Todd, & Orban, 2009; Konen & Kastner, 2008). While V6 is sensitive to motion and contains a full hemifield representation (Fattori, Pitzalis, & Galletti, 2009), its mid-sagittal position in the dorsal parieto-occipital sulcus makes TMS effects unlikely as V6 should not be close enough to the coil to show TMS effects.

Finally, since TMS experiments were completed, subjects AC and BH have had retinotopic fMRI scans collected. As the locations of TMS sites were recorded for each subject during TMS administration, the locations of these sites can be determined relative to brain areas defined by visual field maps. This is discussed fully in the next section.

Overall, it seems very likely that the stimulated region includes V3A, which may simplify interpretation of our results.

TMS coil orientations were systematically varied to find the most effective orientation for eliciting phosphenes. However, the orientation with the handle parallel to the floor and pointing just above the right ear was as good as any other orientation for stimulation over MT+ and our dorsomedial extrastriate site in all of the subjects used here. The direction of maximal current flow in the figure of eight coils was along the central axis, towards the

handle. For stimulation over the vertex, some orientations produced uncomfortable sensory or motor twitches in some subjects, so these were avoided.

In the first experiments performed, the field strength used was just below the phosphene elicitation threshold. However, the performance of subjects CB, BH, and JS was not consistently affected by stimulation over some sites at this level. Therefore, a higher level was used in later experiments, about 5% of maximum field strength above the phosphene elicitation threshold for each site. While this produced phosphenes in the dark with eyes closed, during presentation of the stimulus, which was much brighter than the phosphenes, no phosphenes were visible. It is therefore implausible that any TMS effects would be attributable to visual masking of the stimulus by the phosphene, as the phosphene was not perceptible during stimulus presentation. To further ensure that visual masking was not occurring, motion patterns were produced that resembled phosphenes elicited from MT+ and our dorsomedial extrastriate site. These motion patterns consisted of large dim gray dots with short lifetimes (two to four frames, chosen at random) moving in random directions to imitate MT+ phosphenes. The patterns moved less quickly to imitate dorsomedial extrastriate site phosphenes, and had shorter lifetimes (one to two frames, chosen at random). Subjectively, these patterns looked very much like the phosphenes produced with the eyes closed by TMS on each site. These patterns were overlaid on the test stimuli and again were not perceptible. Performance of BH was tested with and without these overlaid motion patterns, and no differences in performance were seen.

Vertex TMS field strength could not be determined by this approach as it was not expected to produce any visual effect. Instead the level selected was the same as the highest level used on either the MT+ or dorsomedial extrastriate sites.

Retinotopic mapping of TMS sites

Since TMS experiments were completed, subjects AC and BH have had retinotopic fMRI scans collected. As the locations of TMS sites were recorded for each subject during TMS administration, the locations of these sites can be determined *post hoc* relative to brain areas defined by these visual field maps. As our dorsomedial extrastriate site is most difficult to interpret and because visual field maps are particularly clear in the early extrastriate areas near this stimulation site, we will focus on this site. For MT+, visual field maps can be hard to acquire clearly and our method for finding the TMS site for MT+ is well established.

Visual field maps were acquired for BH for the purposes of another study. For AC, they were acquired for this study, and so AC placed oil capsules over the TMS sites used, making them clearly visible on his anatomical scans. For BH, TMS sites were determined approximately relative to the anatomical landmarks used when positioning the TMS coils.

For AC, magnetic resonance data were acquired on a 3-T whole-body scanner (Varian Unity Inova, Palo Alto, CA), with a head insert gradient coil (Magnex, Oxford, UK). For BH, data were acquired on a Philips Achieva 3T scanner (Philips Medical Systems, Best, Netherlands) with a Quasar Dual gradient set. For both subjects, T1-weighted anatomical MRI data sets were acquired in the same session. Functional images were aligned with the anatomical MRI by a mutual information rigid-body alignment technique (Ashburner & Friston, 2003).

Gray and white matter was segmented from the anatomical MRI using custom software and hand-edited to minimize segmentation errors (Teo, Sapiro, & Wandell, 1997). The cortical surface was reconstructed at the gray-white matter border and rendered as a smoothed 3D surface (Wandell, Chial, & Backus, 2000).

The visual stimuli were generated in the Matlab programming environment using the PsychToolbox (Brainard, 1997; Pelli, 1997). We used conventional rotating wedge and expanding ring sections of a high-contrast, moving, dartboard pattern (DeYoe et al., 1996; Engel, Glover, & Wandell, 1997; Sereno et al., 1995). For AC, the dartboard pattern was exposed by slowly moving apertures either in the shape of a rotating wedge or an expanding ring aperture follow a periodic pattern and complete a full cycle in 24 seconds. A total of 6 cycles per scanning run were shown for rings apertures and 10 cycles per scanning run for wedge apertures. Volumes were acquired every 3 seconds.

For BH, the dartboard pattern was exposed by rotating wedge or expanding ring apertures moving in discrete steps at every volume acquisition, with each step moving 1/16th of a cycle. Again, a complete cycle took 24 seconds to display. A total of 6 cycles per scanning run were shown for both wedge and ring apertures. Volumes were acquired every 1.5 seconds.

fMRI analysis was performed in the VISTA software package, which is freely available at (http://white.stanford.edu/software/). For each voxel, the harmonic phase of the responses to the stimulus cycles gave estimates of visual field eccentricity (ring stimuli) and polar angle (wedge stimuli) preferences.

When visual field maps had been made for each subject, regions of interest (ROIs) were created as 10 mm diameter spheres below the TMS administration sites (Figure 2). These reflect the likely areas affected by TMS administration at our dorsomedial site.

The visual field maps were then rendered onto the 3D surface of the smoothed gray-white matter border, along with the sphere ROIs. The places where the sphere ROIs intersected with the gray-white matter border were thus shown on an inflated rendering of the visual field map structure of the occipital lobe. These gave estimates of the regions of the occipital lobe that were affected by TMS, in

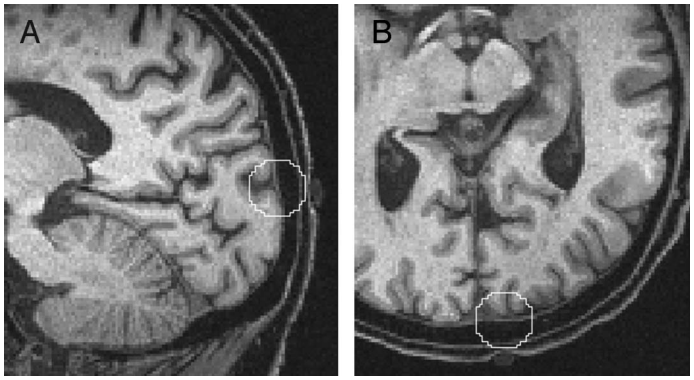

Figure 2. Location of the dorsomedial TMS site, marked with an oil capsule on the scalp in an anatomical MRI scan for subject AC, shown in sagittal (left) and axial (right) views. The 1-cm-diameter sphere under the capsule shows the area most strongly affected by TMS at this site.

relation to visual field maps. The visual field maps were used to define the brain areas near the TMS site (Sereno et al., 1995). The intersections of early visual areas and TMS sites can thus be seen in Figure 3. For both subjects, V3A, dorsal V3, and (to a lesser extent) dorsal V2 were the areas within the TMS site.

This shape is only intended to give an approximate idea of the areas affect by TMS and should not be read as an accurate biophysical model of TMS affects and their precise locations and strengths. Considering the *post hoc* nature of this analysis technique and the lack of sufficiently high precision in the positional estimate of the affected area, we present this affected area as a fairly conservative estimate of the areas affected by TMS and their intersection with more precisely defined brain areas.

Eye movement tracking

As unilateral TMS only affects one half or quadrant of the visual field, it was important to ensure that the partially coherent part of the stimuli fell inside this quadrant. Fixation near the center of the display, where the coherent motion was presented, would improve performance by bringing coherent motion into field areas unaffected by the TMS. Therefore, eye movements were monitored as described below, and trials containing eye movements larger than 0.8° were automatically rejected. All rejected trials were then repeated at the end of the block. If trials from many conditions within the same block were rejected, the order of their repeats at the end of the block was randomized and repeats were conducted until all trials required within the block had been accepted. Typically fewer than five of the 24 trials within a block (17%) were rejected. If more than eight trials (33%) were rejected, the entire block was repeated after allowing the subject a few minutes to rest.

Eye movements were recorded online by an Eyelink II eye tracking system from SR Research. The original head mounting for this system prevented placement of the TMS coils against the skull; it was therefore disassembled from the headset and mounted firmly on the forehead and chin headrest.

This arrangement meant that the small head movements that were possible with respect to the head rest would be registered as large eye movements by the eye tracking cameras fixed to the head rest. As the function of eye tracking here was simply to exclude invalid trials, this artifact would have simply led to the rejection of some valid trials, which should not have distorted the results.

To avoid rejecting trials because of head shifts between stimulus presentations, the registered position of the fixation point was recalibrated during fixation just before the first frame of the stimulus presentation. Gaze position

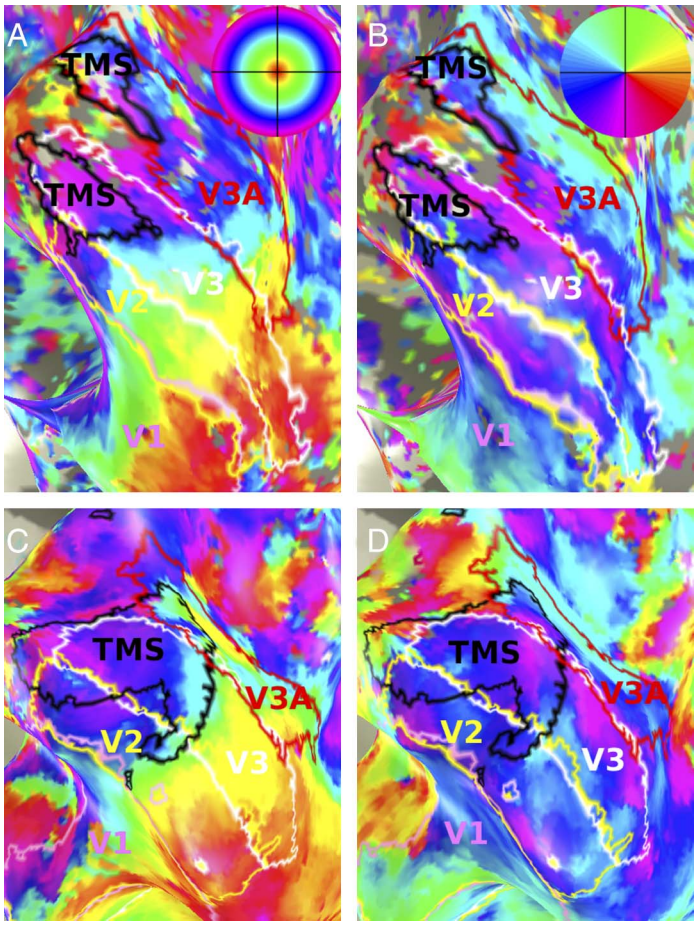

Figure 3. Intersection of the dorsomedial TMS site represented by the sphere in Figure 2 (black outline) with the flattened cortical surface. Panels A and B show eccentricity and polar angle maps respectively for subject AC. Panels C and D show the same for subject BH. Colored circles give visual field map relationships to the color map representations used. Visual areas dorsal V2 (yellow outline), dorsal V3 (white outline), V3A (red outline), and V1 (pink outline), as determined by reversals in visual field maps, are also shown.

was then read after each frame by the stimulus-generating computer. Any deviation exceeding 0.8° from the initial fixation position led to the trial being rejected immediately, minimizing the number of TMS pulses delivered.

Subject AC had considerable experience performing psychophysical tasks and TMS studies in which fixation was required, and it was unlikely that he would make many eye movements. This subject was tested first, before technical issues with the eye tracking setup were resolved, and so eye movement tracking was not done for this subject.

Results

For both tasks and all subjects, and for rotating, expanding, and contracting motions, significantly more errors were produced when TMS was applied over MT+ than when applied over vertex. No difference was seen between vertex TMS and no-TMS conditions. For AC only, for both tasks and for rotating, expanding, and contracting motions, significantly more errors were made when TMS was applied over the dorsomedial extrastriate site (including V3A) than when applied over vertex. The effect of TMS over this site for AC was typically smaller than the effect of TMS over MT+, although this difference was not always seen and was often small. No subject reported experiencing any phosphenes in conjunction with TMS, confirming that the impairments were not simply a result of visual masking (Figure 4).

Erroneous responses were also separated into two halves depending on which stimulus was being show when the error was made. For example, in the pattern detection task, "partially coherent" responses to a non-coherent stimulus were analyzed separately from "non-coherent" responses to a partially coherent stimulus (Figure 5). Likewise, in the position discrimination task, "down" responses to an up stimulus were analyzed separately from "up" responses to a down stimulus (Figure 6). When counts of errors made in these different situations were examined, no pattern of errors was seen that was consistent between subjects or stimulus motion direction conditions. This shows that TMS affected perception of both partially coherent and non-coherent stimuli in the pattern detection task and both positions in the position discrimination task. However, no condition was consistently and statistically significantly affected across motion types and subjects.

Discussion

In this experiment, very similar TMS effects were seen for pattern detection and position discrimination tasks in each subject. For BH, CB and JS, TMS over MT+ affected performance in both tasks for all motion patterns, while TMS over the dorsomedial extrastriate site (including V3A) affected neither. For AC, TMS over MT+ or the dorsomedial extrastriate site affected both tasks for all motion patterns, although the effects of the dorsomedial stimulation were smaller.

Overall, these results provide no evidence that neuroanatomically distinct areas are responsible for processing the two types of task. MT+ function seems to be necessary for both tasks, while functional integrity of dorsomedial extrastriate cortex, including V3A, is not necessary for either task in three of the four subjects tested. However, this is not to say that MT+ is necessarily performing all of the computations necessary for both tasks, merely that information represented in MT+ contributes to the performance of both tasks. For an area so important in the motion processing pathway, this is perhaps not surprising.

The effect of MT+ stimulation on position discrimination tasks and the lack of a stimulation effect at the dorsomedial extrastriate site that was consistent in, or specific to, position discrimination tasks, suggest that V3A does not play a critical role in discrimination of motion position discrimination. This speaks against the possible model whereby analysis of contour curvature in V3A (Caplovitz & Tse, 2007) leads to a retinotopic representation of center of motion position (Koyama et al., 2005), which could be used for center of motion position discrimination.

The dominant effect of TMS over MT+ on position discrimination performance suggests that center-of-motion position, or information from which this is derived, is computed in MT+. This result supports any model in which motion represented in MT+ is used to derive center of motion position. A similar result has been found on the effect of TMS over MT (McGraw, Walsh, & Barrett, 2004), where TMS modulated errors in localization of stationary stimuli that are normally found after motion adaptation. This result shows that the adaptation effect on stimulus localization relies on MT (but not V1), implicating MT in the representation of stimulus position. Both studies suggest that position discrimination performance relies on the extrastriate motion processing areas in MT+.

Both this study and the MT motion adaptation study (McGraw et al., 2004) question the assertion that the large receptive fields and extensive spatial summation in MT+ might prevent accurate position discrimination. Instead, it supports a position discrimination mechanism such as those in models of heading discrimination that implicate a population-coded representation in MST (Lappe & Rauschcker, 1993; Page & Duffy, 2003; Perrone & Stone, 1998).

Whether a more explicit representation of heading or center-of-motion position is then derived from this population code remains an interesting question that several recent studies have began to address, particularly

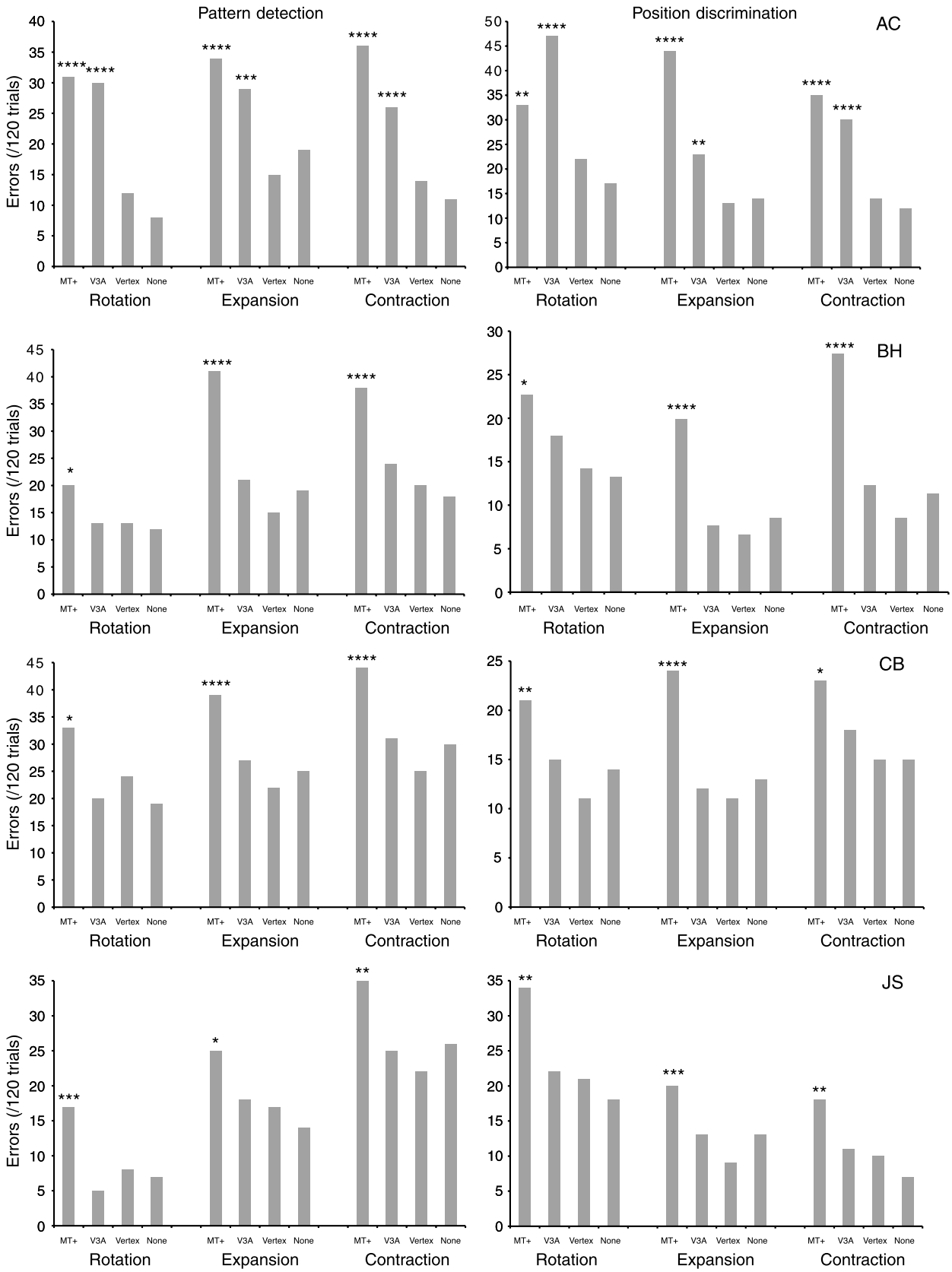

Figure 4. Counts of errors given in pattern detection and position discrimination tasks during various TMS conditions, with rotating, expanding, and contracting stimuli for subjects AC, BH, CB, and JS. "V3A" is shorthand for the dorsomedial extrastriate site. Statistical comparisons of total counts of correct responses, compared against vertex TMS, were made with a chi-squared test. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

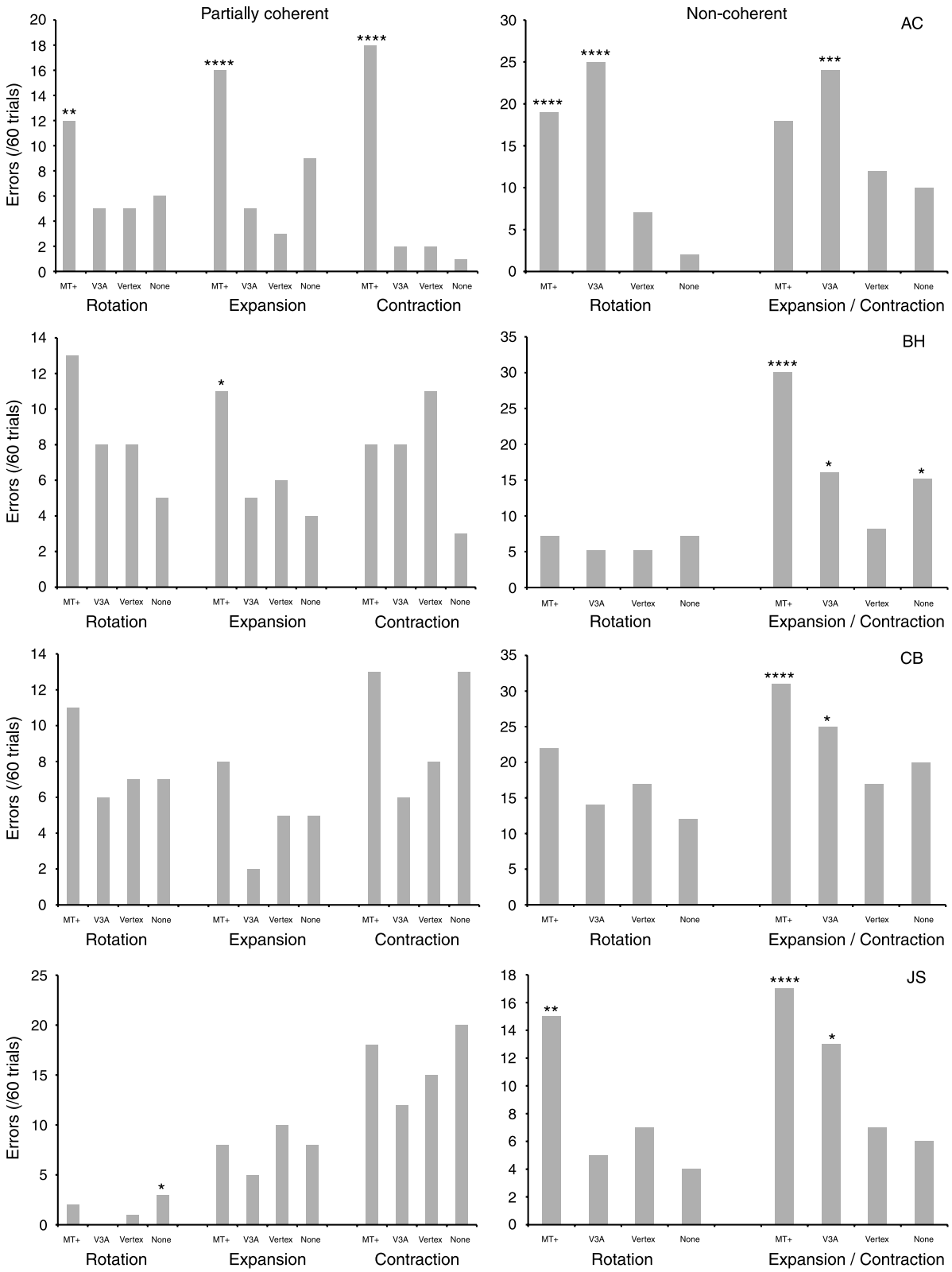

Figure 5. Counts of errors given in the pattern detection task, analyzed separately when errors were made for a partially coherent stimulus (left panels) or a non-coherent stimulus (right panels). Results are shown for various TMS conditions, with rotating, expanding, and contracting stimuli for subjects AC, BH, CB, and JS. "V3A" is shorthand for the dorsomedial extrastriate site. Statistical comparisons of total counts of correct responses, compared against vertex TMS, were made with a chi-squared test. Note that the non-coherent stimulus for expanding and contracting stimuli was the same set of trails, as these conditions were mixed, and so results here are given together. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

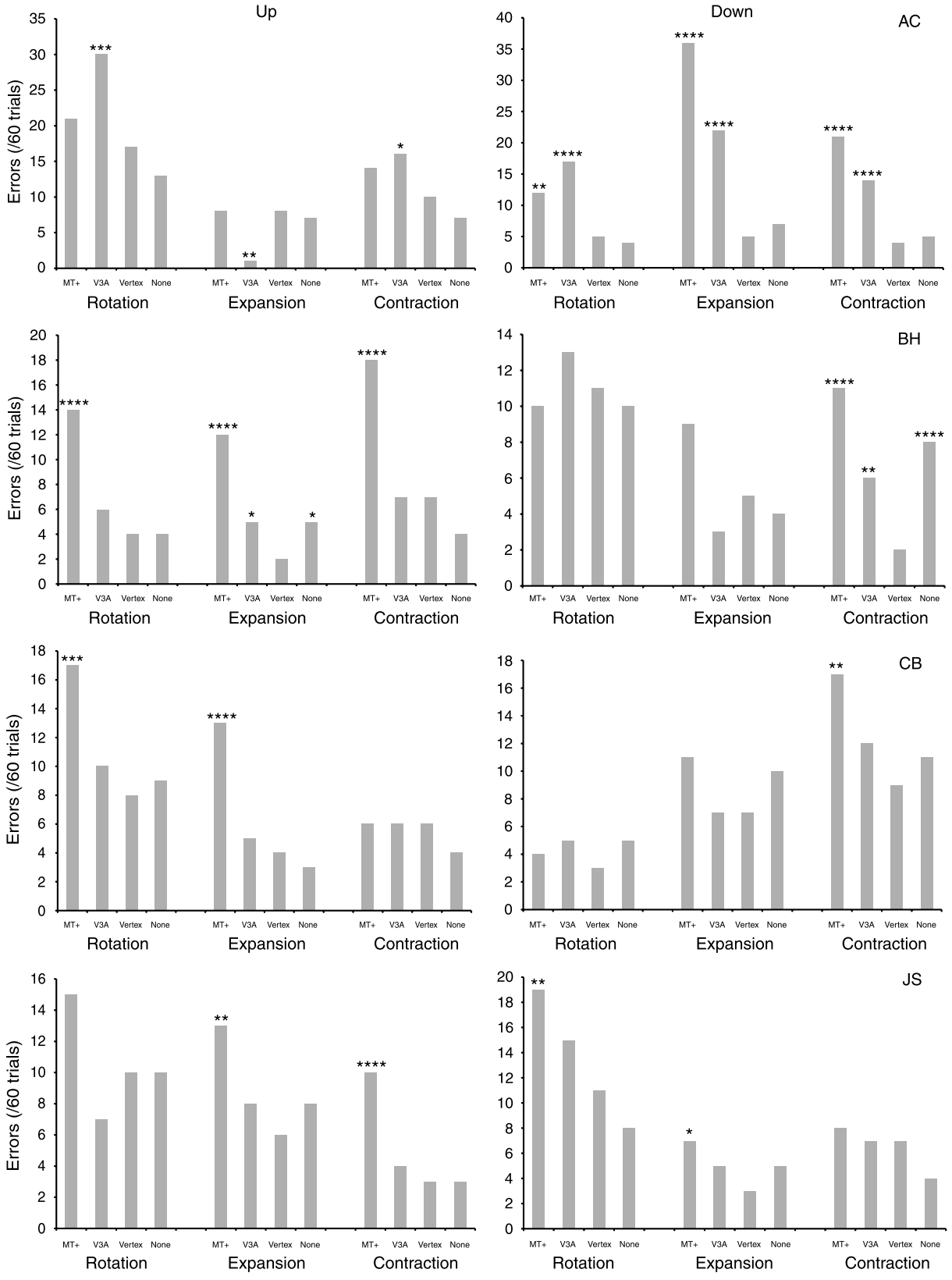

Figure 6. Counts of errors given in the position discrimination task, analyzed separately when errors were made with the center of the motion pattern up (left panels) or down (right panels) relative to the center of the display. Results are shown for various TMS conditions, with rotating, expanding, and contracting stimuli for subjects AC, BH, CB, and JS. "V3A" is shorthand for the dorsomedial extrastriate site. Statistical comparisons of total counts of correct responses, compared against vertex TMS, were made with a chi-squared test. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

with regard to area VIP. Macaque VIP neurons respond more selectively than MST neurons to preferred headings and maintain these responses despite changes in gaze (Bremmer, Duhamel, Ben Hamed, & Graf, 2002; Duhamel, Bremmer, BenHamed, & Graf, 1997; Zhang, Heuer, & Britten, 2004). These heading responses seem to be clustered in a columnar organization (Zhang & Britten, 2004). Furthermore, an area putatively identified as the human homologue of VIP gives a stronger BOLD response to optic flow stimuli with a single center of motion than one containing several centers, while MST does not (Wall & Smith, 2008). As any representation of heading in VIP would almost certainly derive inputs from MT+, TMS over MT+ would affect this heading representation. While VIP has been investigated with regard to heading representation in these studies, Wall and Smith (2008) used time-varying stimuli that included all directions of spiral motion, not just expanding motions. Therefore, it is possible that centers of rotating and contracting motions are represented in the human homologue of VIP in a similar way as those for expanding motions from which heading is derived. Unfortunately, the distance from the skull of the VIP homologue in the human brain makes it a poor target for TMS studies designed to stimulate it selectively (Figure 7). Furthermore, likely anatomical links between MT+ and VIP would make a clear interpretation of results difficult. These factors would therefore make it very difficult to use TMS to examine the role of VIP in discrimination of center of motion position, particularly in any way that could distinguish between TMS effects on VIP and MT+.

In both tasks and for all motion patterns, TMS over dorsomedial extrastriate site (including V3A) affected AC's performance but not that of the other three subjects. There are several ways to account for this difference, which may provide hypotheses for further experimentation. While providing interesting discussion, these hypotheses are not meant to provide an answer, and we do not have strong evidence as yet to distinguish among them. First, V3A and its surrounding areas are in a very convoluted part of the brain's surface. As such, small variations in brain morphology and the position of V3A on the surface of this area could lead to large differences in its distance from the skull and therefore on its susceptibility to TMS. If AC's V3A was much closer to the skull, it might be much easier to disrupt its activity by TMS. Also, AC was very experienced in TMS studies, including functional localization of brain areas by phosphene elicitation, and so perhaps the V3A stimulation site was located more accurately in his case. On the other hand, TMS over this site did elicit moving phosphenes in all subjects, so must have had at least some effect on motion processing in this region. Furthermore, retinotopic mapping of BH and identification of the area probably affected by TMS at this site confirms that V3A lay within the TMS site for this subject, and no effects of TMS over V3A were seen.

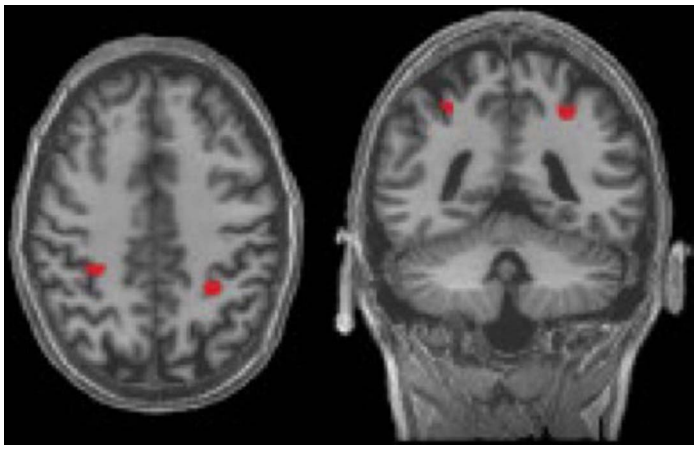

Figure 7. Deep location of area VIP in the human brain from fMRI studies. Taken from Wall and Smith (2008).

In a TMS study of unidirectional motion perception (Cowey et al., 2006), TMS over either MT+ or V2/V3 disrupted performance at direction discrimination. The V2/V3 site was very similar to the dorsomedial extrastriate site used in the present experiment. These authors suggest the V2/V3 effect results from direct connections between V2/V3 and MT+, as are seen in macaques. They suggest that stimulating either site disruptively affects the other. If this is true, it is strange that the present experiment did not show a consistent effect of stimulation at a similar site. However, this experiment used rotational and radial motions rather than unidirectional. So while MT (the likely neural substrate for effects on unidirectional motion perception) and V2/V3 may be directly linked, MST (the likely substrate for rotational and radial motion perception) and V2/V3/V3A may not be. If MST and V2/V3/V3A may only be linked via MT, TMS effects may not spread so strongly between these areas. A further and possibly important difference between the two experiments is that Cowey et al. (2006) were testing direction discrimination in displays where the moving elements were clusters of pixels of different luminance contrast presented on a static but similarly high contrast background. The entire displays were much "noisier" than in the present experiment.

Also, AC is considerably older than all of the other subjects, which could have affected his susceptibility to TMS or his ability to accurately and robustly perceive the stimuli. However, Cowey et al. (2006) used young subjects and still found TMS effects over V3A/V3/V2, so his age is probably irrelevant.

Finally, and perhaps most importantly, BH, CB, and JS were very experienced in psychophysical experiments with the types of stimuli used here, while AC was not. These three subjects had spent over one hundred hours each as subjects in psychophysics experiments involving pattern detection and position discrimination of these types of pattern, in RDK displays, over the previous

2 years. Although AC had participated in many TMS and psychophysics studies, many involving motion perception, he had not participated in studies that used this type of RDK display, used rotational and radial motion patterns, or performed position discrimination tasks.

Experience in a task is known to affect neural activity in several ways. The number of areas activated by global motion and the intensity of activation as shown by fMRI are greatly reduced after subjects become more familiar with the displays (Vaina, Belliveau, des Roziers, & Zeffiro, 1998). The exception was MT+, which showed more intense activation with experience. It seems that cortical processing here becomes more refined to the areas best suited to this task. It is therefore feasible that while V3A is useful for the tasks in this experiment for less experienced subjects, experience may reduce its importance, and concomitantly the effect of TMS over V3A. Furthermore, TMS over parietal cortex affects performance on novel, but not learned, conjunction search tasks (Walsh, Ashbridge, & Cowey, 1998). When the task is well learned and a strategy is adopted, TMS effects can disappear. Thus, experienced subjects may be resistant to TMS over certain sites, perhaps as these are activated more in inexperienced subjects.

Overall, these results failed to show different TMS effects on pattern detection and position discrimination tasks. They show that processing in MT+ is necessary for both tasks, whereas the dorsomedial extrastriate site (including V3A) is not for most subjects. That TMS over the latter site has significant effects on all tasks for one subject suggests that it may be important, although perhaps only before a subject becomes very experienced at a task. However, there was no evidence even here that the role of this site differed between the two tasks.

Acknowledgments

This work was supported by an MRC research studentship to BMH and by MRC grants G7908507 and G0601007 to OJB and G0601975 to AC.

Commercial relationships: none.
Corresponding author: Benjamin M. Harvey.
Email: b.m.harvey@uu.nl.
Address: Room 16.24, Department of Experimental Psychology, Heidelberglaan 2, Utrecht, Netherlands.

References

Ashburner, J., & Friston, K. J. (2003). Rigid body registration. In W. D. Penny (Ed.), *Human brain function* (pp. 635–655). London, UK: Academic Press. [Google Books]

Beardsley, S. A., & Vaina, L. M. (2005). How can a patient blind to radial motion discriminate shifts in the center-of-motion? *Journal of Computational Neuroscience, 18,* 55–66. [PubMed]

Braddick, O. J., O'Brien, J. M., Wattam-Bell, J., Atkinson, J., & Turner, R. (2000). Form and motion coherence activate independent, but not dorsal/ventral segregated, networks in the human brain. *Current Biology, 10,* 731–734. [PubMed]

Brainard, D. H. (1997). The psychophysics toolbox. *Spatial Vision, 10,* 433–436. [PubMed]

Bremmer, F., Duhamel, J. R., Ben Hamed, S., & Graf, W. (2002). Heading encoding in the macaque ventral intraparietal area (VIP). *European Journal of Neuroscience, 16,* 1554–1568. [PubMed]

Caplovitz, G. P., & Tse, P. U. (2007). V3A processes contour curvature as a trackable feature for the perception of rotational motion. *Cerebral Cortex, 17,* 1179–1189. [PubMed]

Chawla, D., Buechel, C., Edwards, R., Howseman, A., Josephs, O., Ashburner, J., et al. (1999). Speed-dependent responses in V5: A replication study. *Neuroimage, 9,* 508–515. [PubMed]

Chawla, D., Phillips, J., Buechel, C., Edwards, R., & Friston, K. J. (1998). Speed-dependent motion-sensitive responses in V5: An fMRI study. *Neuroimage, 7,* 86–96. [PubMed]

Cowey, A., Campana, G., Walsh, V., & Vaina, L. M. (2006). The role of human extra-striate visual areas V5/MT and V2/V3 in the perception of the direction of global motion: A transcranial magnetic stimulation study. *Experimental Brain Research, 171,* 558–562. [PubMed]

Cowey, A., & Walsh, V. (2000). Magnetically induced phosphenes in sighted, blind and blindsighted observers. *NeuroReport, 11,* 3269–3273. [PubMed]

DeYoe, E. A., Carman, G. J., Bandettini, P., Glickman, S., Wieser, J., Cox, R., et al. (1996). Mapping striate and extrastriate visual areas in human cerebral cortex. *Proceedings of the National Academy of Sciences of the United States of America, 93,* 2382–2386. [PubMed] [Article]

Duffy, C. J., & Wurtz, R. H. (1995). Response of monkey MST neurons to optic flow stimuli with shifted centers of motion. *Journal of Neuroscience, 15,* 5192–5208. [PubMed]

Duhamel, J. R., Bremmer, F., BenHamed, S., & Graf, W. (1997). Spatial invariance of visual receptive fields in parietal cortex neurons. *Nature, 389,* 845–848. [PubMed]

Engel, S. A., Glover, G. H., & Wandell, B. A. (1997). Retinotopic organization in human visual cortex and

the spatial precision of functional MRI. *Cerebral Cortex, 7,* 181–192. [PubMed] [Article]

Fattori, P., Pitzalis, S., & Galletti, C. (2009). The cortical visual area V6 in macaque and human brains. *The Journal of Physiology, 103,* 88–97. [PubMed]

Georgieva, S., Peeters, R., Kolster, H., Todd, J. T., & Orban, G. A. (2009). The processing of three-dimensional shape from disparity in the human brain. *Journal of Neuroscience, 29,* 727–742. [PubMed]

Greenlee, M. W. (2000). Human cortical areas underlying the perception of optic flow: Brain imaging studies. *International Review of Neurobiology, 44,* 269–292. [PubMed]

Grossman, E., Battelli, L., & Pascual-Leone, A. (2005). Repetitive TMS over posterior STS disrupts perception of biological motion. *Vision Research, 45,* 2847–2853. [PubMed]

Harvey, B. M., & Braddick, O. J. (2008). Psychophysical differences in processing of global motion and form detection and position discrimination. *Journal of Vision, 8*(7):14, 1–18, http://journalofvision.org/content/8/7/14, doi:10.1167/8.7.14. [PubMed] [Article]

Ierusalimschy, R. (2003). *Programming in Lua*. Rio de Janeiro: Lua.org. [Article]

Konen, C. S., & Kastner, S. (2008). Two hierarchically organized neural systems for object information in human visual cortex. *Nature Neuroscience, 11,* 224–231. [PubMed]

Koyama, S., Sasaki, Y., Andersen, G. J., Tootell, R. B., Matsuura, M., & Watanabe, T. (2005). Separate processing of different global-motion structures in visual cortex is revealed by fMRI. *Current Biology, 15,* 2027–2032. [PubMed]

Lappe, M., & Rauschcker, J. P. (1993). A neural network model for the processing of optic flow from ego-motion in higher mammals. *Neural Computation, 5,* 374–391.

Laycock, R., Crewther, D. P., Fitzgerald, B. P., & Crewther, S. G. (2007). Evidence for fast signals and later processing in human V1/V2 and V5/MT+: A TMS study of motion perception. *Journal of Neurophysiology, 98,* 1253–1262. [PubMed] [Article]

McGraw, P. V., Walsh, V., & Barrett, B. T. (2004). Motion-sensitive neurones in V5/MT modulate perceived spatial position. *Current Biology, 14,* 1090–1093. [PubMed]

McKeefry, D. J., Burton, M. P., Vakrou, C., Barrett, B. T., & Morland, A. B. (2008). Induced deficits in speed perception by transcranial magnetic stimulation of human cortical areas V5/MT+ and V3A. *Journal of Neuroscience, 28,* 6848–6857. [PubMed]

Morrone, M. C., Tosetti, M., Montanaro, D., Fiorentini, A., Cioni, G., & Burr, D. C. (2000). A cortical area that responds specifically to optic flow, revealed by fMRI. *Nature Neuroscience, 3,* 1322–1328. [PubMed]

Orban, G. A., Fize, D., Peuskens, H., Denys, K., Nelissen, K., Sunaert, S., et al. (2003). Similarities and differences in motion processing between the human and macaque brain: Evidence from fMRI. *Neuropsychologia, 41,* 1757–1768. [PubMed]

Page, W. K., & Duffy, C. J. (2003). Heading representation in MST: Sensory interactions and population encoding. *Journal of Neurophysiology, 89,* 1994–2013. [PubMed]

Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: Transforming numbers into movies. *Spatial Vision, 10,* 437–442. [PubMed]

Perrone, J. A., & Stone, L. S. (1998). Emulating the visual receptive-field properties of MST neurons with a template model of heading estimation. *Journal of Neuroscience, 18,* 5958–5975. [PubMed]

Sereno, M. I., Dale, A. M., Reppas, J. B., Kwong, K. K., Belliveau, J. W., Brady, T. J., et al. (1995). Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Science, 268,* 889–893. [PubMed]

Silvanto, J., Cowey, A., Lavie, N., & Walsh, V. (2005). Striate cortex (V1) activity gates awareness of motion. *Nature Neuroscience, 8,* 143–144. [PubMed]

Smith, A. T., Wall, M. B., Williams, A. L., & Singh, K. D. (2006). Sensitivity to optic flow in human cortical areas MT and MST. *European Journal of Neuroscience, 23,* 561–569. [PubMed]

Sunaert, S., Van Hecke, P., Marchal, G., & Orban, G. A. (1999). Motion-responsive regions of the human brain. *Experimental Brain Research, 127,* 355–370. [PubMed]

Teo, P. C., Sapiro, G., & Wandell, B. A. (1997). Creating connected representations of cortical gray matter for functional MRI visualization. *IEEE Transactions on Medical Imaging, 16,* 852–863. [PubMed]

Tootell, R. B., Mendola, J. D., Hadjikhani, N. K., Ledden, P. J., Liu, A. K., Reppas, J. B., et al. (1997). Functional analysis of V3A and related areas in human visual cortex. *Journal of Neuroscience, 17,* 7060–7078. [PubMed] [Article]

Vaina, L. M., Belliveau, J. W., des Roziers, E. B., & Zeffiro, T. A. (1998). Neural systems underlying learning and representation of global motion. *Proceedings of the National Academy of Sciences of the United States of America, 95,* 12657–12662. [PubMed]

Wall, M. B., Lingnau, A., Ashida, H., & Smith, A. T. (2008). Selective visual responses to expansion and

rotation in the human MT complex revealed by functional magnetic resonance imaging adaptation. *European Journal of Neuroscience, 27,* 2747–2757. [PubMed]

Wall, M. B., & Smith, A. T. (2008). The representation of egomotion in the human brain. *Current Biology, 18,* 191–194. [PubMed]

Walsh, V., Ashbridge, E., & Cowey, A. (1998). Cortical plasticity in perceptual learning demonstrated by transcranial magnetic stimulation. *Neuropsychologia, 36,* 363–367. [PubMed]

Walsh, V., & Cowey, A. (2000). Transcranial magnetic stimulation and cognitive neuroscience. *Nature Reviews, Neuroscience, 1,* 73–79. [PubMed]

Wandell, B. A., Chial, S., & Backus, B. T. (2000). Visualization and measurement of the cortical surface. *Journal of Cognitive Neuroscience, 12,* 739–752. [PubMed]

Wandell, B. A., Dumoulin, S. O., & Brewer, A. A. (2007). Visual field maps in human visual cortex. *Neuron, 56,* 366–383. [PubMed]

Zhang, T., & Britten, K. H. (2004). Clustering of selectivity for optic flow in the ventral intraparietal area. *Neuroreport, 15,* 1941–1945. [PubMed]

Zhang, T., Heuer, H. W., & Britten, K. H. (2004). Parietal area VIP neuronal responses to heading stimuli are encoded in head-centered coordinates. *Neuron, 42,* 993–1001. [PubMed]