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Differing causal roles for lateral occipital cortex and occipital face area in invariant shape recognition

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Abstract

The human extrastriate visual cortex contains functionally distinct regions where neuronal populations exhibit signals that are selective for objects. How such regions might play a causal role in underpinning our ability to recognize objects across different viewpoints remains uncertain. Here, we tested whether two extrastriate areas, the lateral occipital (LO) region and occipital face area (OFA), contained neuronal populations that play a causal role in recognizing two-dimensional shapes across different rotations. We used visual priming to modulate the rotation-sensitive activity of neuronal populations in these areas. State-dependent transcranial magnetic stimulation (TMS) was applied after the presentation of a shape and immediately before a subsequent probe shape to which participants had to respond. We found that TMS applied to both the LO region and OFA modulated rotation-invariant shape priming but, whereas the LO region was modulated by TMS for small rotations, the OFA was modulated for larger rotations. Importantly, our results demonstrate that a node in the face-sensitive network, the OFA, participates in causally relevant encoding of non-face stimuli.

Introduction

A hallmark of object recognition is the integration of individual features into a unified gestalt independently of variations in orientation, size and position of the object. Behavioral priming and adaptation effects indicate the existence of neural representations immune to these factors because they occur even when the orientation, size or position of an object changes but the configural relationship between features is held constant. Such neural representations may be present in extrastriate areas of the ventral visual cortex that in humans encode object and shape information (Grill-Spector, 2003; Ewbank *et al.*, 2005). One such region is the lateral occipital (LO) cortex (Malach *et al.*, 1995), which is the putative human homologue of the macaque inferotemporal cortex and contains shape-selective neuronal populations (e.g. Grill-Spector, 2003; Malach *et al.*, 1995). Neuroimaging evidence suggests that rotation invariance in the human LO cortex extends to approximately 60° (e.g. Eger *et al.*, 2006; Andresen *et al.*, 2009; Grill-Spector *et al.*, 1999). Another region that is implicated in shape and object processing is the occipital face area (OFA), located in the inferior occipital gyrus. The OFA is often regarded as a modular region exclusively devoted to face processing due to its preferential activation by face stimuli relative to objects (Gauthier *et al.*, 2000a). However, the OFA is also activated by non-face objects compared with textures (Gilaie-Dotan *et al.*, 2008), indicating that it is involved in the processing of non-face stimuli.

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Here we investigated whether rotation-invariant and shape-selective neuronal representations in the LO cortex and OFA played a causal role in shape processing. This was accomplished by using state-dependent transcranial magnetic stimulation (TMS), a technique that allows the causal roles and tuning properties of functionally distinct neuronal representations within a cortical area to be contrasted (see Silvanto & Muggleton, 2008a,b). In state-dependent TMS, a psychophysical paradigm such as adaptation (cf. Silvanto *et al.*, 2007; Cattaneo *et al.*, 2010b; Cohen Kadosh *et al.*, 2010) or priming (cf. Cattaneo *et al.*, 2010a) is used with the objective of inducing an activity imbalance between neuronal populations of different selectivities. If the subsequent application of TMS interacts with this initial state manipulation, this indicates that the stimulated region contains neuronal representations that were affected by the initial state manipulation (see also Silvanto & Pascual-Leone, 2008; Silvanto *et al.*, 2008 for reviews).

Here we used visual priming to manipulate the initial state of neurons that are selective for two-dimensional shapes. On each trial, a prime stimulus (one of four mirror-symmetric shapes, rendered as a chain of aligned Gabor patches) was presented in an upright position (i.e. with its axis of symmetry aligned with the vertical meridian). After a brief delay, participants were presented with a target stimulus (which was either the primed shape or one of the other shapes) embedded in a cluttered background of distracters, rotated either 20° or 70° from the prime stimulus.

Behaviorally, the participants' discrimination accuracy was higher on trials on which the target was the same as the prime stimulus for both target rotations, demonstrating a rotation-invariant priming effect. In the TMS conditions, TMS was applied over either the LO cortex or OFA during the delay between the prime and the target (cf. Campana

et al., 2002, 2006; Cattaneo *et al.*, 2008). If rotation-invariant neuronal representations are present in the LO cortex and OFA, we reasoned that the application of TMS over these regions should interact with the behavioral priming effect.

Materials and methods

Participants

Eight healthy, naive participants (five males and three females, aged 19–34 years) took part in the experiment. All had normal or corrected-to-normal vision. All participants gave written informed consent before participating in the study, which had been approved by the local ethics committee (Ethics Committee of University College London), and were treated in accordance with the Declaration of Helsinki.

Experimental stimuli

All stimuli were presented centrally on an SVGA 17-inch monitor set at 1024 × 768 resolution and a refresh rate of 60 Hz. Four different shapes were used in the experiment (see Fig. 1). Shapes were symmetrical with respect to the vertical axis and consisted of 24 Gabor elements (wavelength, 0.2°; SD, 0.2°), which were oriented to form a closed path. This path was described in polar coordinates by the function

$$\rho(\theta) = r(1 + a_1 \cos f_1\theta)(1 + a_2 \cos f_2\theta + \varphi)$$

where ρ is the radius at polar angle θ. The path is essentially a circle with radius r modulated by two cosines. The coefficients a_n and f_n are the amplitude and frequency, respectively, of cosine n and φ is the phase of the second cosine relative to the first. The coefficients defining the four shapes were chosen to ensure that the distance between neighboring elements was similar for the four shapes.

On each trial, the prime consisted of one of these shapes in its upright position (i.e. rotation of 0°) without noise. The target stimulus was one of these four stimuli, embedded in a background of randomly oriented Gabor elements placed on a jittered grid (Field *et al.*, 1993) and rotated either 20° or 70° to the left or right. On 'primed' trials, the target shape was the same as the prime shape. On 'non-primed' trials, the target shape was one of the other three shapes.

These rotations were chosen based on fMRI findings that rotation invariance in the LO cortex extends to no more than 60° (e.g. Eger *et al.*, 2006). These stimuli enabled us to keep the shape consistent under rotation while also rotating local elements to eliminate local facilitating effects and have been widely used in vision research (e.g. Ullman, 1992). Furthermore, in-plane rotations are a subset of

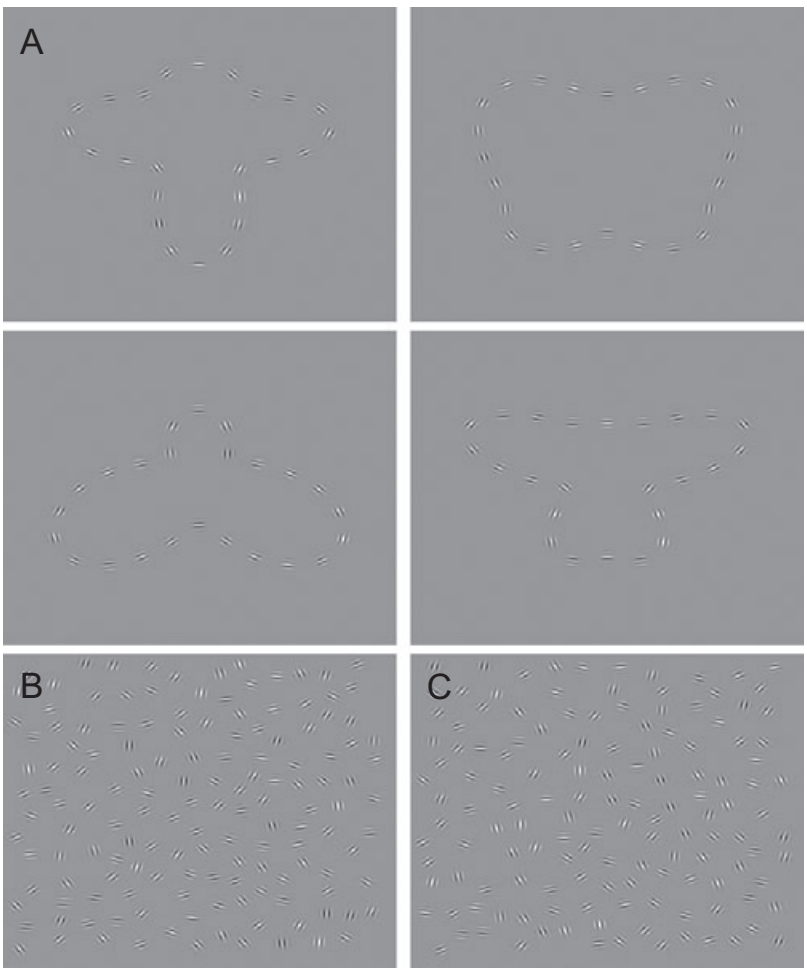

FIG. 1. Experimental stimuli. (A) The four shapes used in the experiment shown for the upright orientation (zero rotation) and without a background. On each trial one of these images appeared as a prime. Examples of two images shown as a target image in which the shape contour was embedded in a cluttered background of randomly oriented Gabor patches and rotated either 20° (B) or 70° (C) with respect to the upright. The participant's task was to indicate by means of a button press whether the shape was rotated clockwise or counterclockwise relative to upright.

rotations and viewpoints that the visual system has to overcome, and these are both processed in a similar manner and by the same populations (e.g. Logothetis *et al.*, 1995).

Behavioral task

Each trial began with a fixation cross, followed by a prime presented for 500 ms (see Fig. 2A for the timeline of an experimental trial). This was followed by a delay period of 500 ms, the target stimulus (250 ms) and a blank screen. On each trial, a 10 Hz triple-pulse TMS train was applied over either the LO cortex or OFA at 300 ms after the offset of the prime (such that the pulse train ended at target onset). Participants were asked to judge (by responding with the index or middle finger of the dominant hand) the direction of rotation of the target shape, which appeared within the central 16.5 × 16.5° of the visual field, was embedded in a cluttered background and never fully spatially overlapped with the prime (in order to prevent feature- and location-specific priming effects). The task was run in nine blocks of 64 trials (three blocks for each of the three TMS conditions: No TMS, LO cortex TMS and OFA TMS), the order of which was randomized by the software. In each block, there were 16 primed and non-primed trials for both the 20 and 70° conditions (half of which were rotated to the left and the other half to the right). The order of stimulus conditions (primed shape, rotation) was pseudo-randomized. Each of the four shapes appeared with equal frequency as prime within every block. There were thus a total of 48 primed and 48 non-primed trials for each TMS condition in the entire experiment. In the non-primed trials, the target stimulus was randomly selected to be one of the other three shapes used in the experiment. By embedding the target shapes in a cluttered background we ensured that the discrimination task was sufficiently difficult to reveal robust priming effects without the need to degrade the target image (such as reducing contrast or adding luminance noise). Moreover, this stimulus design mimics the challenges faced by rotation-invariant shape-selective target detection in a complex visual environment. The inter-trial interval was variable between 1.8 and 2 s.

fMRI localization of the occipital face area and lateral occipital cortex

A 1.5 T Siemens Sonata system was used to acquire T1-weighted anatomical images and T2*-weighted echo-planar images with BOLD contrast. Each echo-planar image comprised 32 axial slices (2 mm) with a 1 mm inter-slice gap covering the whole cerebrum with an in-plane resolution of 3 × 3 mm. The experiment was split into five runs, each consisting of 78 volumes. The first four volumes of each run were discarded to allow for T1 equilibration effects. Volumes were acquired continuously with a TR of 2.88 s/volume.

The functional localizer scan used a one-back paradigm to focus attention. The three categories of visual stimuli were faces, objects and scrambled images of the objects. Each image was presented for 360 ms with a 360 ms blank interval between images. Participants were instructed to press a key whenever they detected two images repeated in a row (one-back task) to ensure that participants were alert and attentive. Stimuli were presented in blocks of 40 items from within a category and a centrally presented red fixation cross was present throughout the experiment. The serial position of the categories was varied and all blocks were repeated, using a total of 80 different images per category.

All images were grayscale. In order to minimize retinotopic effects, we first generated Fourier-scrambled versions of the original images of all objects and faces and then superimposed each image onto these scrambled images. Object stimuli created in this manner were further Fourier-scrambled to generate the scrambled category. This ensured that each category occupied the same area of visual space and that the spatial frequency and orientation content of objects and scrambled objects were identical. The localizer stimuli were obtained from the Tarr object database (http://tarrlab.cnbc.cmu.edu/stimuli.html).

Functional imaging data were analyzed using SPM5 (http://www.fil.ion.ucl.ac.uk/spm). After deleting the first four volumes of each run to allow for T1 equilibrium effects, the functional images were corrected for slice acquisition time, realigned to the first image using an affine transformation to correct for small head movements and echo-planar image distortions unwarped using B0 field maps. The images were then smoothed with an 8 mm full-width half-maximum Gaussian filter and pre-whitened to remove temporal autocorrelation. The resulting images were entered into a participant-specific general linear model with three conditions of interest corresponding to the three

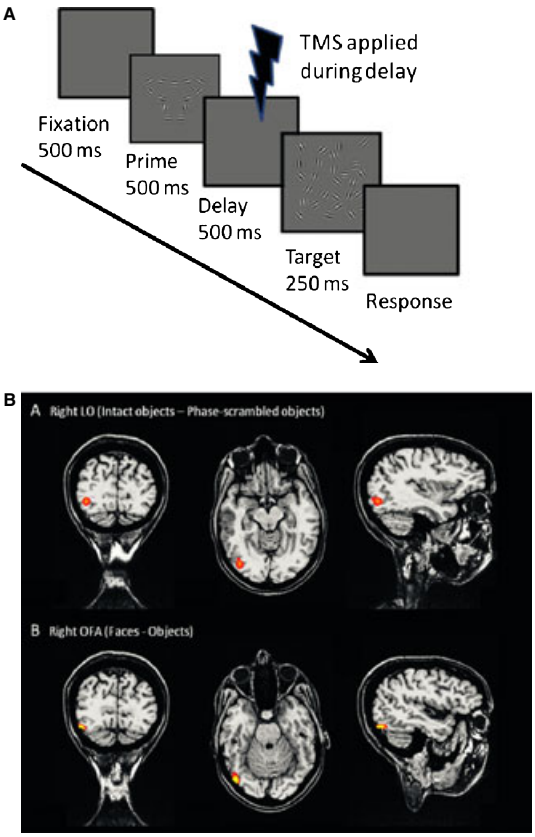

FIG. 2. (A) Timeline of an experimental trial. Each trial began with a fixation cross, followed by a prime presented for 500 ms. This was followed by a delay period of 500 ms, the target stimulus (250 ms) and a blank screen. On each trial, a 10 Hz triple-pulse TMS train was applied over either the LO cortex or OFA at 300 ms after the offset of the prime (such that the pulse train ended at target onset). Participants were asked to judge the direction of rotation of the target shape, which appeared within the central 16.5 × 16.5° of the visual field, was embedded in a cluttered background and never fully spatially overlapped with the prime (in order to prevent feature- and location-specific priming effects). On primed trials the target shape was identical to the prime shape. On non-primed trials the target was one of the remaining three shapes selected with equal probability. (B) The location of the LO cortex (Talairach coordinates of peak activation: 41, −79, −1) and OFA (47, −82, −13) in one representative participant. For illustration only, the activation clusters are shown using tkmedit from the FreeSurfer package (http://surfer.nmr.mgh.harvard.edu/fswiki). In all participants, the LO cortex and OFA were stimulated in the right hemisphere (as in previous studies, cf. Pitcher *et al.*, 2009).

categories of visual stimuli. Blocks were convolved with a canonical hemodynamic response function to generate regressors. In addition, the estimated motion parameters were entered as covariates of no interest to reduce structured noise due to residual head motion effects. Linear contrasts among the condition-specific regressors were used to identify the two TMS target sites within each participant's right hemisphere: the OFA by contrasting the activation associated with face presentation to the activation associated with object presentation and the LO cortex by contrasting objects to scrambled objects. The functional images were then registered to each participant's individual structural scan using a 12 parameter affine transformation to identify two TMS target sites right Occipital Face Area (rOFA) and right Lateral Occipital Cortex (rLO) in the right hemisphere.

Each TMS target site was individually identified in each participant by selecting the peak activation for that category in the LO cortical region. The target sites corresponded well with previously reported maps of object- and face-sensitive regions (Pitcher *et al.*, 2009; Hasson *et al.*, 2003). The mean coordinates of the target sites in Montreal Neurological Institute (MNI) coordinates were: LO cortex, 45 (SD ± 11), −82 (±12) and −2 (±16); and OFA, 46 (±12), −80 (±11) and −8 (±8). More importantly, the Euclidian distance between the LO cortex and OFA in Talairach space averaged across participants was 21.4 (±9.6) mm. Table 1 gives the MNI coordinates of the TMS sites and the Euclidian distances between them for each individual participant. Figure 2B depicts the locations of the OFA and LO cortex in one representative participant. These data show that good separation of the two stimulation sites was achieved in each individual participant, reflected in the functionally distinct effects of TMS reported below and in previous work (Pitcher *et al.*, 2009).

Transcranial magnetic stimulation

A Magstim Rapid stimulator (Magstim, Wales) and a 70 mm figure-of-eight coil were used for stimulation. A fixed TMS intensity (60% of maximum stimulator output) was used on the basis of a number of previous studies (e.g. O'Shea *et al.*, 2004, 2007; Silvanto *et al.*, 2005, Muggleton *et al.*, 2008), including studies on LO cortex and OFA function (Ellison & Cowey, 2006; Pitcher *et al.*, 2009). In the TMS conditions, a 10 Hz pulse train consisting of three pulses was applied on each trial during the delay between the prime and target. The first pulse of the pulse train was applied at 300 ms after the offset of the prime. The coil orientation was such that the coil handle was pointing upwards and parallel to the midline. Stimulation sites were localized using the Brainsight TMS-MRI coregistration software (Rogue Research Inc., Montreal, Quebec, Canada), utilizing individual high-resolution MRI scans for each participant. The right OFA and LO cortex were localized by overlaying individual activation maps from the fMRI localizer task for the face and object analysis (as described in full above), and the coil locations were marked on each participant's head. The TMS target coordinates were identified by selecting the voxel that exhibited the peak activation in each functionally defined area. As in a previous study contrasting the functions of the OFA and LO cortex, only the right hemisphere was stimulated (Pitcher *et al.*, 2009). Previous studies combining TMS with visual priming have used either single-pulse TMS (Cattaneo *et al.*, 2008, 2010a) or short pulse trains (e.g. Campana *et al.*, 2002, 2006); both approaches have obtained similar results. Here we used the latter approach as previous TMS studies on the LO cortex and OFA (cf. Pitcher *et al.*, 2009) also used brief pulse trains instead of single-pulse TMS. The stimulation parameters were within published safety guidelines (Wassermann, 1998).

TABLE 1. MNI coordinates and Euclidian distances (mm) between the LO cortex and OFA in the right hemisphere of individual participants

	OFA			LO cortex			
	x	*y*	*z*	*x*	*y*	*z*	Distance
S1	58	−81	4	63	−69	27	26.9
S2	46	−91	−12	37	−102	−8	14.3
S3	52	−77	−3	51	−86	11	17.0
S4	41	−79	−10	41	−95	−9	15.5
S5	21	−98	−6	53	−71	−15	42.4
S6	54	−67	−4	40	−74	−2	16.5
S7	54	−81	−10	48	−78	4	15.4
S8	43	−65	−22	29	−83	−22	23.0
Mean ± SEM	46 ± 4.2	−80 ± 3.9	−8 ± 2.8	45 ± 3.9	−82 ± 4.2	−2 ± 5.7	21.4

Results

Accuracy analysis

Figure 3 shows the mean (n = 8) priming benefit (defined as accuracy on primed trials minus accuracy on non-primed trials) for target discrimination. The priming benefit in the No TMS condition was statistically significant in two-tailed pairwise *t*-tests in both the 20° [t_7 = 2.36, P = 0.038] and 70° [t_7 = 2.40, P = 0.047] conditions; in both conditions, seven of the eight subjects showed this effect. A repeated-measures ANOVA with TMS site (No TMS, LO cortex, OFA) and stimulus rotation (20, 70°) revealed a significant interaction ($F_{2,14}$ = 7.09, P = 0.008); the main effects of TMS site ($F_{2,14}$ = 3.42, P = 0.062) and stimulus rotation ($F_{1,7}$ = 0.43, P = 0.53) were not significant. Pairwise two-tailed t-tests showed that LO cortex TMS reduced priming at the 20° condition relative to both the No TMS [t_7 = 2.55, P = 0.038] and OFA TMS [t_7 = 2.74, P = 0.029] conditions; there was no significant difference between the No TMS and OFA TMS conditions [t_7 < 0.0002, P = 0.99]. In contrast, in the 70° condition, OFA TMS reduced priming relative to No TMS [t_7 = 3.56, P = 0.009] and LO cortex TMS [t_7 = 3.18, P = 0.016] conditions, whereas there was no significant difference between the No TMS and LO cortex TMS condition [t_7 = 0.126, P = 0.903].

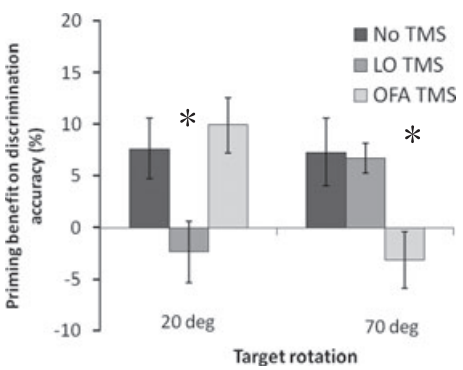

FIG. 3. The mean (n = 8) benefit of priming (defined as accuracy on primed trials minus accuracy on non-primed trials) on discrimination accuracy. A positive value indicates that accuracy was higher on primed trials relative to non-primed trials. In both the 20 and 70° conditions, seven of the eight participants showed the priming effect in the No TMS condition. Relative to the No TMS condition, LO cortex TMS reduced priming in the 20° condition, whereas OFA TMS had no significant effect. In the 70° condition, this pattern was reversed: OFA TMS reduced priming relative to No TMS, whereas LO cortex TMS had no significant effect. The error bars indicate ±1 SE from which the between-participants variance has been removed using the method of Loftus and Mason (1994). *Significant effects.

Effect of transcranial magnetic stimulation on primed vs. non-primed targets

Additional analyses were carried out in order to investigate whether TMS reduced the behavioral benefit of priming by impairing the detection accuracy on trials in which the target shape was the same as the prime (i.e. primed trials) or whether priming was reduced by facilitation of targets that were different from the prime (i.e. non-primed trials).

Figure 4A shows directly the effect of TMS on primed and non-primed trials by displaying the discrimination accuracy in the LO cortex TMS and OFA TMS conditions subtracted from the accuracy in the No TMS condition. In this figure a positive value indicates that TMS facilitated discrimination accuracy relative to the No TMS condition, whereas a negative value indicates that TMS impaired discrimination accuracy relative to the No TMS condition. Visual inspection of the data indicated that TMS generally reduced the behavioral benefit of priming by both reducing accuracy on primed trials as well as facilitating accuracy on non-primed trials. Figure 4B and C shows the raw discrimination accuracy for all of the TMS conditions (No TMS, LO cortex TMS, OFA TMS) for the 20 and 70° rotation conditions, respectively.

To further characterize these effects, a repeated-measures ANOVA on accuracy, in which prime-target congruency was added as a main factor, was carried out. There were thus three main factors: TMS site (No TMS, LO cortex, OFA) stimulus rotation (20, 70°) and prime-target congruency (primed, non-primed). The results indicated a three-way interaction ($F_{2,14} = 7.09$, $P = 0.008$). There was no main effect of rotation ($F = 1.978$, $P = 0.2024$) and no interaction between rotation and TMS site ($F_{2,14} = 0.42$, $P = 0.665$) or between rotation and congruency ($F_{2,14} = 0.432$, $P = 0.532$). The only significant pairwise t-test was the effect of LO cortex TMS on primed trials (relative to primed trials in the No TMS condition) in the 20° condition [$t_7 = 3.16$, $P = 0.016$]. This indicates that LO cortex TMS reduced the behavioral benefit of priming primarily by reducing accuracy on primed trials. Although there was a trend for increased accuracy for non-primed trials, this was not statistically significant. For OFA TMS neither the reduction of accuracy on primed trials nor the facilitation on non-primed trials reached significance, although a trend for both was present in the data.

Reaction time analysis

Reaction time analysis was performed on the median reaction times of correct responses. A behavioral benefit of priming was only present in the 20° rotation condition [where the median reaction times of primed and non-primed trials were 759 and 806 ms, respectively; $t_7 = 2.51$, $P = 0.04$]. For the 70° rotation condition, no significant priming benefit was observed [the median reaction times averaged across participants of primed and non-primed trials were 784 and 806 ms; $t_7 = 1.24$, $P = 0.26$]. A priming benefit analysis on median reaction times also revealed no effects of TMS. Specifically, a repeated-measures ANOVA with TMS site (No TMS, LO cortex, OFA) and stimulus rotation (20, 70°) revealed no significant main effects of TMS ($F_{2,14} = 0.07$, $P = 0.93$) or stimulus rotation ($F_{1,7} = 0.02$, $P = 0.89$) or an interaction ($F_{2,14} = 0.6$, $P = 0.56$). We also investigated whether TMS applied over either the LO cortex or OFA affected overall reaction times. A within-participants ANOVA with TMS site (No TMS, LO cortex TMS, OFA TMS) and target rotation (20, 70°) as main factors revealed no main effects of TMS site ($F_2 = 0.07$, $P = 0.93$) or target rotation ($F_{1,7} = 0.02$, $P = 0.89$), or an interaction

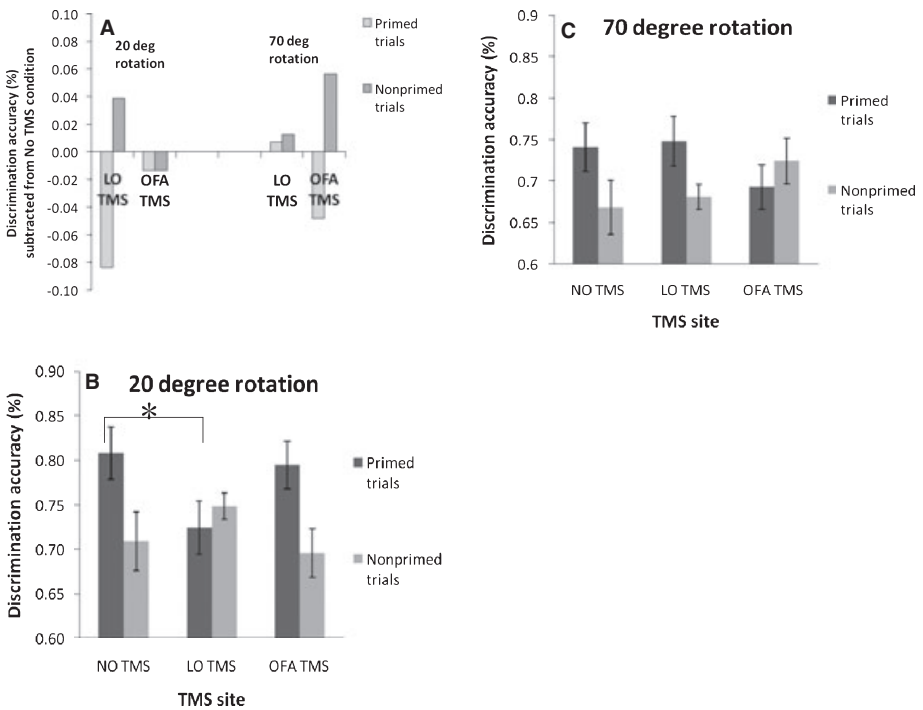

FIG. 4. The mean ($n = 8$) discrimination accuracies for primed and non-primed trials. (A) The effect of LO cortex TMS and OFA on primed and non-primed trials. In this analysis, discrimination accuracy in the LO cortex and OFA TMS conditions was subtracted from the accuracy in the NO TMS condition. A positive value indicates that TMS facilitated accuracy, whereas a negative value indicates a TMS-induced reduction in accuracy. A visual inspection of the data indicates that TMS generally reduced the behavioral benefit of priming by both reducing accuracy on primed trials and facilitating accuracy on non-primed trials. (B) Mean raw discrimination accuracy for the 20° rotation for each of the TMS conditions. (C) The mean raw discrimination accuracy for the 70° rotation for each of the TMS conditions. The error bars indicate ±1 SE from which the between-participants variance has been removed using the method of Loftus and Mason (1994).

($F_{2,14} = 0.61$, $P = 0.56$). In these reaction time analyses, data that were 4 SDs above the mean were removed as outliers.

Discussion

Behaviorally, the effect of visual priming was reflected as superior discrimination performance for target stimuli that were of the same shape as the prime relative to trials where the target was of a different shape from the prime (see No TMS condition in Fig. 1B). We found that TMS over the LO cortex reduced this behavioral benefit of shape priming in a fashion that depended on the degree of rotation. Priming was affected by LO cortex TMS only when the target was rotated 20°, with no significant effect when it was rotated 70°. This suggests a causal role for the LO cortex in rotation-invariant representations of 20° but not for 70°. This result is consistent with neuroimaging evidence suggesting rotation invariance of no more than 60° in this region (Eger *et al.*, 2006) although an exact comparison is hindered by differences in the type of rotation (in-plane vs. in-depth) and stimulus (real-world object vs. simple shape) in the two studies. Additional studies (e.g. Andresen *et al.*, 2009; Grill-Spector *et al.*, 1999) using fMRI adaptation with various types of stimuli have also shown that the LO cortex is sensitive to rotations of up to 60°, suggesting that rotation invariance in LO cortex will be confined to smaller angles. Single-cell recordings from the macaque inferotemporal cortex, which is the presumed homologue to the human LO cortex, show that the vast majority of object-responsive cells are view-dependent. However, a small minority of cells do show viewpoint invariance [4–9% (Perrett *et al.*, 1991), 9% (Logothetis *et al.*, 1995) and 9–14% (Booth & Rolls, 1998)]. Interestingly, the highest proportion of view-invariant neurons is shown when using images of real-world objects that monkeys are familiar with (Booth & Rolls, 1998), suggesting that neuronal rotation invariance might be an experience-driven process. Nevertheless, our finding of TMS-induced effects indicates, for the first time, that neuronal populations in the human LO cortex play a causal role in mediating object invariance because their stimulation with TMS altered behavior.

TMS applied over the OFA also reduced the behavioral effect of shape priming. In contrast to the LO cortex, priming was significantly reduced only for targets rotated 70°. Our results thus indicate that the OFA is causally involved in rotation-invariant representations for larger rotations, for which the LO cortex lacks invariance. This finding is important as it indicates that neuronal populations in the OFA play a causal role in non-face shape processing. In the context of the modularity debate, our results are consistent with the view that processing of different objects takes place in a widely distributed network (e.g. Haxby *et al.*, 2001) and challenge the strictly modular views of visual processing (Spiridon & Kanwisher, 2002) by providing evidence that an area that shows sensitivity for faces can also be causally involved in the processing of non-shape stimuli. Our findings are thus consistent with fMRI evidence that the OFA can be activated by non-face objects compared with scrambled objects (Gilaie-Dotan *et al.*, 2008), indicating that it is involved in the processing of non-face stimuli. Importantly, our results cannot be explained by non-specific effects of TMS on the OFA as we failed to find statistically significant effects for 20° rotations in OFA TMS (i.e. condition-specific effect) and for 70° rotations in LO cortex TMS (i.e. OFA region-specific effect for 70°). In other words, the OFA TMS effect for 70° rotations cannot be due to the TMS-induced activation spreading to the LO cortex because the application of TMS over the LO cortex did not affect priming for this rotation.

Indeed, previous work has also shown that the LO cortex and OFA can be selectively and differentially targeted by TMS (Pitcher *et al.*, 2009; see also Cohen Kadosh *et al.*, 2010, for TMS effects on OFA) and the separation that we achieved between the LO cortex and OFA foci (Table 1) is similar to Pitcher *et al.* (2009). The most relevant measure to assess the segregation of the TMS sites is the Euclidian distance between them for each individual participant. The distance between mean coordinates is not meaningful because it is affected by the large variability in the location of these brain areas between individuals. Taken together, the differential effects of TMS on priming that we observed indicate a causal role for neuronal populations in the OFA (as well as the LO cortex, see above) in invariant shape representation in the human brain.

It is important to note that our failure to identify any effect of OFA TMS at the 20° rotation does not mean that neurons in this region do not respond to stimuli with rotations of this magnitude; any neuronal representation invariant to a rotation of 70° is very likely to also respond to stimuli rotated by a smaller angle. However, the issue here is whether such neural responses are causally required for accurate detection or discrimination. Indeed, a benefit of state-dependent TMS is that it combines the fine functional specificity of priming paradigms with such an assessment of causality. Our results therefore show that shape-selective neuronal populations in the OFA are not necessary for the detection of shapes at small rotations (although they are likely to respond to such stimuli), possibly because such representations exist in other areas (such as the LO cortex, as our results indicate).

As human observers can easily overcome changes in the object viewpoint (viewing angle) (i.e. rotation invariance), it is reasonable to assume that there are neuronal populations in the human visual system that are invariant to such changes. One possibility for achieving such invariance is that a specific brain region processes objects in a view-independent manner, thereby exhibiting rotation invariance for all rotations. This can be achieved by either a view-independent representation (for supporting theories see Marr, 1982; Biederman, 1987) or interpolating over various view-dependent representations (Ullman, 1998; Bart & Ullman, 2008). Our results suggest an alternative possibility, where invariance is achieved in stages, such that smaller degrees of rotational invariance are associated with neuronal populations in different brain regions compared with those associated with larger degrees of rotational invariance. For example, outputs from the LO cortex, the involvement of which in small rotation invariance we have demonstrated here, could provide input into the OFA to support the invariant processing role for larger rotations that we demonstrate here. Although our findings cannot address such a speculation, they hint at hierarchical roles in the achievement of rotational invariance in the human brain that could be explored in future work.

Our findings have implications in a wider context beyond the question of rotation invariance as they have relevance to the modularity debate in visual object recognition. The modular view claims that different categories of objects are encoded in functionally segregated and specialized cortical areas (Fodor, 1983). In contrast, the distributed view of cortical function suggests that object discrimination depends on dispersed but functionally overlapping representations spread across the visual cortex (e.g. Haxby *et al.*, 2001). Our results are inconsistent with the modular view by providing the first positive evidence that the face-sensitive area (the OFA) plays a causal role in the processing of non-face shape stimuli. It has previously been argued that the failure to find effects of TMS over the OFA on object perception (Pitcher *et al.*, 2009) indicates a specialization of that area for face processing. One possible explanation for this earlier null finding (acknowledged by Pitcher *et al.*, 2009) may be that non-preferred shape stimuli evoke a relatively smaller neuronal signal in the OFA that is functionally less relevant or less sensitive to TMS disruption than the larger signals induced by preferred face stimuli. In

this view, the OFA effects were found here because our visual priming paradigm specifically enhanced signals in shape-selective neuronal populations prior to the application of TMS.

Another possible explanation could be related to the processing of mirror symmetry. Our stimuli (before rotation) exhibit mirror symmetry along the vertical axis, in a similar manner to faces. It could be argued that, at large rotations in our task, symmetry detection is more critical than at the small rotations where the task can be resolved by locally matching features of the shapes. Thus, if there is a preference in the visual system to facilitate processing of mirror-symmetrical shapes, the OFA may play a role in such a process. Sensitivity to mirror symmetry in the OFA could also explain the enhanced activation in this region commonly found for faces in imaging studies. Further research is needed to distinguish these explanations but, regardless of the exact content of information processed by the OFA, our data demonstrate that the OFA is involved in selectively matching shapes across large rotations.

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Abbreviations

LO, lateral occipital; OFA, occipital face area; TMS, transcranial magnetic stimulation.

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