The Journal of Neuroscience, January 14, 2015 • 35(2):731–738 • 731

Behavioral/Cognitive

The Causal Role of the Occipital Face Area (OFA) and Lateral Occipital (LO) Cortex in Symmetry Perception

Silvia Bona,[1,2,3,8] **Zaira Cattaneo,**[4,5,6] **and Juha Silvanto**[1,7]

[1]Brain Research Unit, O.V. Lounasmaa Laboratory, School of Science, Aalto University, 02150 Espoo, Finland, [2]Advanced Magnetic Imaging Centre, Aalto Neuroimaging, OV Lounasmaa Laboratory, School of Science, Aalto University, 00076 Espoo, Finland, [3]BioMag Laboratory, HUS Medical Imaging Center, Helsinki University Central Hospital, 00290 Helsinki, Finland, [4]Department of Psychology, University of Milano-Bicocca, 20126 Milan, Italy, [5]Brain Connectivity Center, National Neurological Institute C. Mondino, 27100 Pavia, Italy, [6]Milan Center for Neuroscience, 20126 Milan, Italy, [7]University of Westminster, Faculty of Science and Technology, Department of Psychology, W1B 2HW London, United Kingdom, and [8]Department of Behavioural Sciences, University of Helsinki, 00014 Helsinki, Finland

Symmetry is an important cue in face and object perception. Here we used fMRI-guided transcranial magnetic stimulation (TMS) to shed light on the role of the occipital face area (OFA), a key region in face processing, and the lateral occipital (LO) cortex, a key area in object processing, in symmetry detection. In the first experiment, we applied TMS over the rightOFA, its left homolog (leftOFA), rightLO, and vertex (baseline) while participants were discriminating between symmetric and asymmetric dot patterns. Stimulation of rightOFA and rightLO impaired performance, causally implicating these two regions in detection of symmetry in low-level dot configurations. TMS over rightLO but not rightOFA also significantly impaired detection of nonsymmetric shapes defined by collinear Gabor patches, demonstrating that rightOFA responds to symmetry but not to all cues mediating figure-ground segregation. The second experiment showed a causal role for rightOFA but not rightLO in facial symmetry detection. Overall, our results demonstrate that both the rightOFA and rightLO are sensitive to symmetry in dot patterns, whereas only rightOFA is causally involved in facial symmetry detection.

Key words: bilateral symmetry; fMRI-guided TMS; lateral occipital cortex; occipital face area; symmetry detection; visual cortex

Introduction

Bilateral vertical symmetry plays an important role in the visual world and it is also an important cue in face processing (Simmons et al., 2004; Rhodes et al., 2005; Chen et al., 2007; Anderson and Gleddie, 2013). Previous neuroimaging studies on symmetry detection have mostly used low-level stimuli such as dot configurations. These studies have implicated various extrastriate visual areas, in particular the lateral occipital region (Sasaki et al., 2005; Tyler et al., 2005), and the functional significance of the lateral occipital (LO) cortex in symmetry detection with such stimuli has been demonstrated by recent transcranial magnetic stimulation (TMS) studies (Cattaneo et al., 2011; Bona et al., 2014). In contrast, the detection of facial symmetry appears to involve the occipital face area (OFA) (Chen et al., 2007), a region in the lateral inferior occipital gyrus and a key node in face processing (Haxby et al., 2000; Rossion et al., 2003; Kadosh et al., 2011; Pitcher et al., 2011; for review, see Atkinson and Adolphs, 2011). Interestingly, the rightOFA shows differential activation between faces and asymmetric scrambled images but not between faces and symmetric scrambled images whereas the fusiform face area (FFA) does so for both contrasts (Chen et al., 2007). However, the causal role of OFA in symmetry perception has not been investigated.

In the present study, we focused on the following issues: first, does the rightOFA play a causal role in symmetry detection, and if so, is its role restricted to facial symmetry? Second, is the object-selective region LO, which has been implicated in symmetry processing of nonface stimuli (Sasaki et al., 2005, Tyler et al., 2005; Bauer et al., 2014; Bona et al., 2014), also causally involved in facial symmetry detection? These questions were addressed by the use of fMRI-guided TMS, a tool that can reveal the functional necessity of cortical regions in a cognitive function (Pascual-Leone et al., 2000; Walsh and Cowey, 2000; Sack et al., 2009; Sandrini et al., 2011).

In Experiment 1, we assessed whether the rightOFA is involved in detection of symmetry in low-level dot configurations (Experiment 1a). RightLO was included as a stimulation site because of its established sensitivity to symmetry in such stimuli (Sasaki et al., 2005; Tyler et al., 2005; Bona et al., 2014). The left hemisphere homolog of OFA (leftOFA) was used as a control site, as done in a previous TMS study (Pitcher et al., 2007), because

Received Sept. 8, 2014; revised Oct. 13, 2014; accepted Oct. 20, 2014.

Author contributions: S.B., Z.C., and J.S. designed research; S.B. performed research; S.B. and Z.C. analyzed data; S.B., Z.C., and J.S. wrote the paper.

J.S. is supported by the European Research Council (336152), Emil Aaltonen Foundation, and the Academy of Finland (266789), and Z.C. is supported by a Fund for Investments on Basic Research and Italian Ministry of Education, University, and Research (RBFR12F0BD). We thank Gillian Rhodes for providing the original symmetric and normal faces, Cathy Mondloch and her colleagues for providing the original stimuli for the "Jane Face task," Carlo Toneatto for his help in programming the experimental scripts and creating the stimuli, and Fariba Sharifian and Simo Vanni for their help in fMRI data analysis.

The authors declare no competing interests.

Correspondence should be addressed to Zaira Cattaneo, Piazza dell'Ateneo Nuovo 1, 20126 Milano, Italy. E-mail: zaira.cattaneo@unimib.it.

DOI:10.1523/JNEUROSCI.3733-14.2015

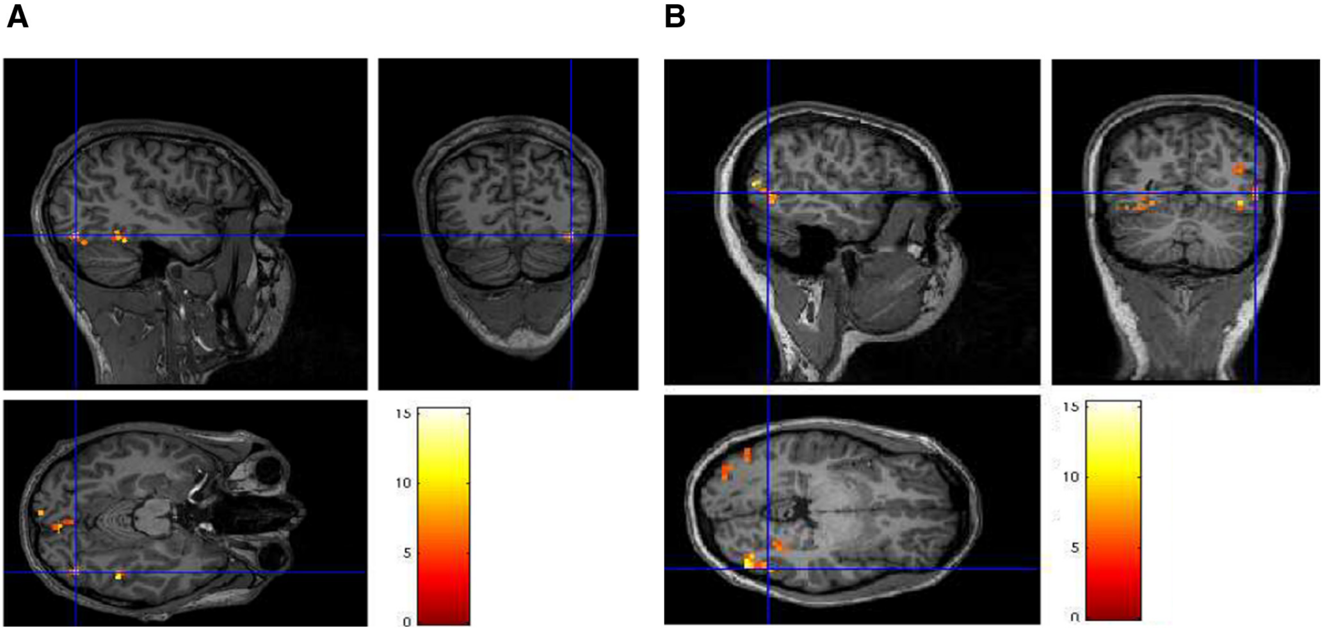

Figure 1. Activation peak for faces versus objects in rightOFA (***A***) and objects versus scrambled objects in rightLO (***B***) of a representative participant from axial, sagittal, and coronal view, respectively (from bottom left in clockwise direction). See Materials and Methods for the mean MNI coordinates of our sample ($n = 14$).

this region is functionally less significant for face perception than the rightOFA. Specifically, lesion studies indicate that the integrity of leftOFA is not necessary for the encoding of facial identity (Landis et al., 1988; Wada and Yamamoto, 2001; Uttner et al., 2002), and TMS evidence indicates that it is not causally involved in discrimination of face parts (Pitcher et al., 2007).

To assess the selectivity of OFA to symmetry (independently of other cues mediating figure-ground segregation) a control experiment (Experiment 1b) involving the detection of nonsymmetric shapes defined by collinear Gabor patches (GPs) was performed. In Experiment 2, we investigated the role of the rightOFA and rightLO in facial symmetry detection (Experiment 2a). A standard face discrimination task (the "Jane faces" task; Mondloch et al., 2002) was run as a control experiment (Experiment 2b) to confirm the specificity of rightOFA stimulation across the previous experiments.

Materials and Methods

Participants

Fifteen students (9 males, mean age = 25.1; SD = 2.5) with normal or corrected-to-normal vision from Aalto University, Espoo (Finland) were recruited for the experiments. One participant was excluded because of unreliable localization of rightOFA and leftOFA (see next section), therefore, the final sample consisted of 14 subjects (8 males, mean age = 24.8; SD = 2.4). All participants were right-handed (Oldfield, 1971) and provided a written informed consent before participation. The study was approved by the local ethics committee and participants were treated in accordance with the Declaration of Helsinki. Participants were paid for their participation. The study consisted of three sessions. In the first session, fMRI localization was performed. The TMS studies were performed in the last two sessions. Experiments 1a and 1b were performed in the first session, and Experiments 2a and 2b in the second session. The sessions were separated by at least 1 week.

fMRI localization of LO and OFA

fMRI localization was performed using a 3 T Signa Excite scanner (General Electric Medical Systems) equipped with a 30-channel receiver head coil. For each participant, the session consisted of three runs (one for LO and two for OFA). RightLO was identified as the activation peak of cluster of voxels that responded more strongly to gray-level images of objects than to scrambled versions of the same pictures (for a similar procedure, see Bona et al., 2014). Scrambled objects were generated from the original object images by randomly selecting an equal number of square tiles arranging them in a 16 × 16 grid of the same dimensions as the object images. Functional images were acquired in a single run lasting 432 s with gradient echo sequence (23 slices with 3.5 mm slice thickness, RT = 2 s, echo time = 30 ms, voxel size = $3.125 \times 3.125 \times 3$ mm^3, flip angle = 75). A high-resolution T1-weighted MPRAGE anatomical scan was also acquired for each participant. RightOFA and its homologous in the left hemisphere (leftOFA) were defined as the activation peak of the cluster of voxels that responded more strongly to gray-level images of faces than to objects. Functional images were acquired over two runs, each lasting 271.2 s. Otherwise, the same parameters as for rightLO localization were used. SPM8 MATLABTM toolbox (http://www.fil.ion.ucl.ac.uk/spm; cf. Friston et al., 2007) was used for data preprocessing, parameter estimation, and visualization. After excluding the first four slices of each run to obtain a stable magnetization, the functional images were corrected for interleaved acquisition order and head movements. During the parameter estimation, the data were high-pass filtered with 128 s cutoff, and noise autocorrelation was modeled with the AR(1) model. The data were coregistered with the high-resolution anatomical images.

RightLO was successfully localized in all participants. In one participant neither leftOFA nor rightOFA could be localized; this participant was excluded from the study. LeftOFA could not be localized in five of the remaining participants, in line with previous fMRI studies reporting face-related activation in this region in approximately half of the sample (Rossion et al., 2003; Haist et al., 2010). As mentioned in the Introduction, this LO region has not been found to be necessary for various aspects of face processing, such as the detection of facial identity (Landis et al., 1988; Wada and Yamamoto, 2001; Uttner et al., 2002) and has been used as a control site for rightOFA before (cf. Pitcher et al., 2007).

When leftOFA could not be localized, in the TMS sessions the coordinates of rightOFA were used as a reference in the left hemisphere. The mean MNI coordinates were as follows: rightOFA: 46 (SD: 4.6), −75 (SD 5.4), −3 (SD: 5.2); rightLO: 44 (SD: 4.6), −79 (SD 5.6), −10 (SD: 5.8); leftOFA (calculated only for the nine subjects from whom we obtained a significant activation): −43 (SD: 4.1), −82 (SD: 4.3), −7 (SD: 6.9). Figure 1 shows the rightOFA and rightLO sites in one representative partic-

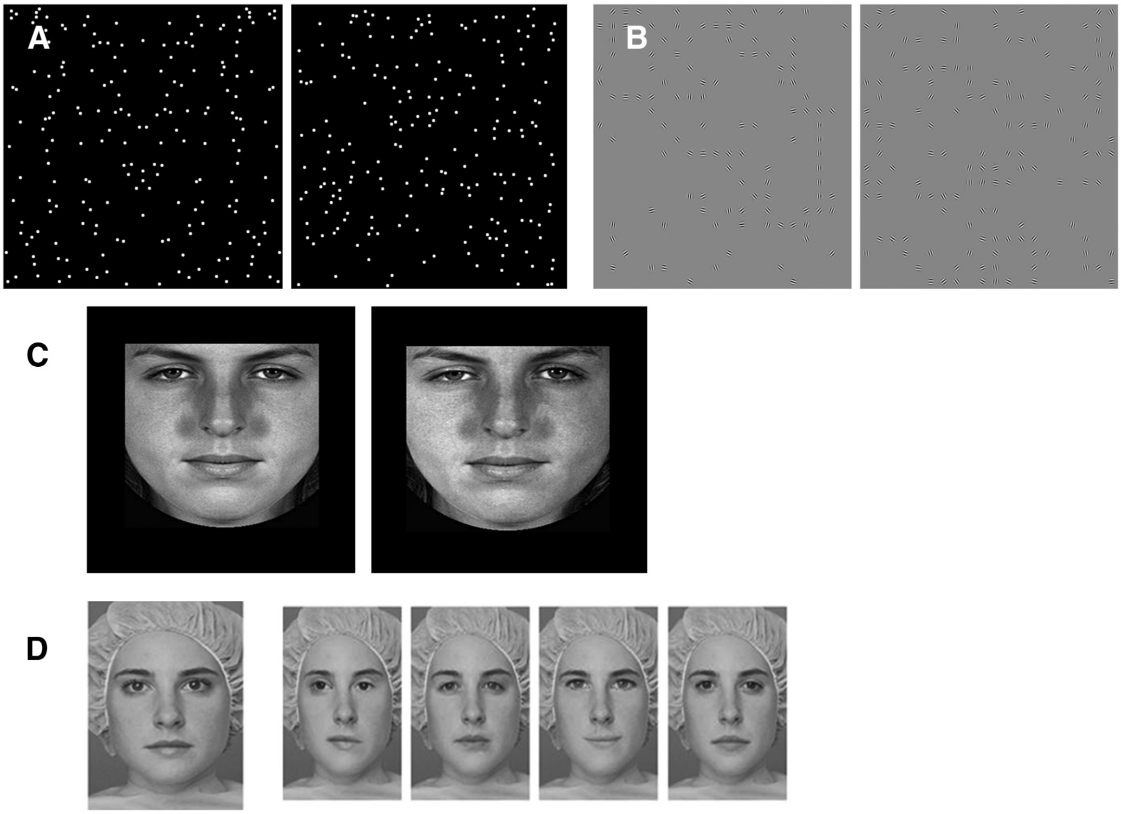

Figure 2. Examples of stimuli used in the experiments: In Experiment 1a (left to right: a symmetric and an asymmetric dot pattern (***A***); in Experiment 1b (left to right: a stimulus with a visible shape and with no visible shape (***B***); in Experiment 2a (left to right: a symmetric and an asymmetric face) (***C***); and in Experiment 2b, the featural set of the Jane faces task Mondloch et al., 2002) (***D***).

ipant. These coordinates are consistent with prior studies (Pitcher et al., 2009, 2012; Schwarzkopf et al., 2010; Nagy et al., 2012).

TMS stimulation

A Nextim stimulator was used to deliver TMS pulses via a biphasic figure-of-eight coil. The sites of stimulation were localized using the eXimia NBS neuronavigation system (Nextim), a coregistration software that allows real-time fMRI-guided positioning of the coil (Säisänen et al., 2008). During the stimulation, the coil was placed tangentially over the activation peaks obtained from participants' fMRI localizers, such that the coil handle was pointing upward and parallel to the midline, similarly to previous studies stimulating LO and OFA (Pitcher et al., 2009; Gilaie-Dotan et al., 2010). On each trial, a 3-pulse TMS train with a frequency of 10 Hz and an intensity of 40% of the maximum stimulator output was delivered over the target sites. These stimulation parameters were taken from our previous study (Bona et al., 2014) in which we assessed the involvement of LO in detecting symmetry with the same stimuli as used here in Experiment 1a. Vertex was defined as the midway point between the inion and the nasion and equidistant from left and right intertragal (Pitcher et al., 2007), and has been widely used as a control site in TMS studies as it controls for nonspecific somatosensory effects of TMS without eliciting unintentional neural effects on task performance (Azañón et al., 2010; Dilks et al., 2013; Ganaden et al., 2013). Here, vertex was used as the baseline against which the effects of OFA and LO TMS were compared.

Experimental tasks

Experiment 1A: symmetry detection in dot patterns

This study aimed to investigate the role of the rightOFA in symmetry processing in dot patterns. The stimulation sites were rightOFA, rightLO, leftOFA, and vertex (baseline).

Stimuli. The stimuli were the same as used in Bona et al. (2014), and similar to those used by Sasaki et al. (2005). A total of 120 vertically symmetric stimuli and 120 asymmetric stimuli were created, all consisting of 198 white dots on a black background. The patterns were relatively sparse, with the dots covering 1.8% of stimulus area. Each stimulus had a diameter of 16” of visual angle, and dot diameter was 0.16”. The luminance of the white dots was 199.82 cd/m^2 and the luminance of the background was 1.12 cd/m^2. Symmetry was present along the vertical axis (with the vertical axis of symmetry coinciding with the vertical midline of the display). Stimuli were generated by first placing half of the dots randomly onto the left side of the stimulus, and then reproducing the same arrangement on the right side so that the resulting image was symmetric (with each dot on the left side of the image having a corresponding symmetric dot in the right hemispace). For asymmetric stimuli, the dots were distributed in a pseudorandom manner over both the left and right half of the stimulus, with the constraint that the same number of dots appeared to the left and to the right of the midline. Figure 2*A* shows an example of a symmetric and a nonsymmetric pattern.

In all experiments, stimuli were presented on an 18 inch monitor with a display resolution of 1600 × 1200. Subjects were seated at a view distance of 60 cm, with their heads stabilized by using a chin rest. Stimuli and task were controlled by E-prime v2.0 (Psychology Software Tools).

Procedure. Figure 3 (left panel) depicts the time line of an experimental trial. In each trial a black fixation cross appeared in the middle of the screen for 500 ms, followed by the target (i.e., a symmetric or an asymmetric dot pattern) presented for 75 ms. The TMS pulse train (3 pulses at 10 Hz, i.e., pulse gap of 100 ms) was administered at target onset. Participants were required to indicate whether the target stimulus was symmetric or asymmetric with a button press, using their right index and middle finger. Participants were instructed to respond as accurately and quickly as possible. Each block consisted of 80 trials (40 symmetric and 40 asymmetric targets, presented in random order). Four blocks were run, one for each stimulation site (rightLO, rightOFA, leftOFA, and vertex). The order of blocks was randomized across participants. Prior to the experi-

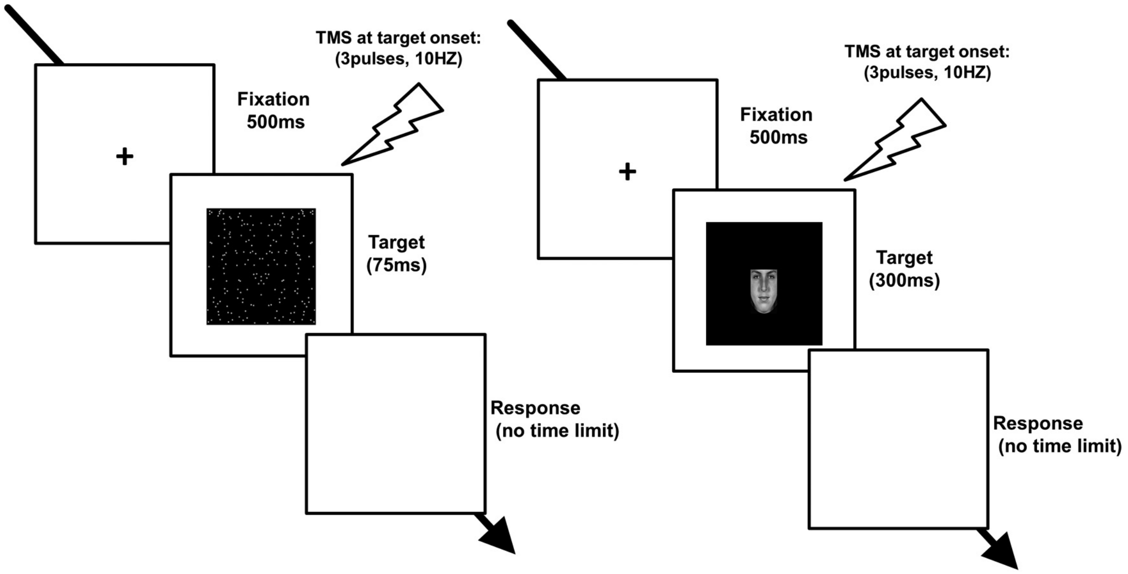

Figure 3. Time line of an experimental trial in Experiments 1a (left panel) and in Experiment 2a (right panel). In Experiments 1a and 1b, each trial began with a black fixation cross for 500 ms, followed by the target presented for 75 ms. Participants were required to indicate whether the stimulus was symmetric or asymmetric (Experiment 1a) or whether the stimulus embedded a shape or not (Experiment 1b). The TMS pulse train (3 pulses, 10 Hz) began concurrently with the target onset. In Experiment 2a the stimulus consisted of a face and participants had to indicate whether the face was either perfectly symmetric or slightly asymmetric.

ment, participants performed a brief practice session (with no TMS) consisting of 40 trials (20 symmetric and 20 asymmetric).

Experiment 1b: detection of shapes defined by collinearity of GPs

This study was run to test whether possible effects of OFA and LO-TMS on symmetry detection in Experiment 1a depended on these regions being involved in figure-ground segregation mechanisms also based on other grouping cues (such as collinearity). TMS was applied over rightOFA, rightLO, leftOFA, and vertex (baseline), as in Experiment 1a. As in Kourtzi et al. (2005), our stimuli consisted of shapes defined by a closed contour of similarly oriented Gabor elements that were embedded in a background of Gabor elements. These stimuli (Fig. 2*B*) yield the perception of a global figure in a textured background rather than simple paths (i.e., open contours).

Stimuli. The stimuli consisted of GP patterns (grayscale values ranging from 13 to 165) presented on a gray background (gray value 89; Bona et al., 2014). Each Gabor element was defined as the product of a sine wave (i.e., odd phase) luminance grating (frequency of 3.75 cycles/deg) and a 2D Gaussian envelope (SD of 0.19" in both dimensions). The luminance of the GP ranges from a minimum luminance 1.74 cd/m^2 to maximum luminance of 64.72 cd/m^2. The background luminance was 17.24 cd/m^2. Each pattern had a diameter of 16" of visual angle and the GP diameter was 0.8". GPs were distributed on an invisible 20 × 20 grid. The number of GPs in the patterns ranged from 120 to 210. The minimum center-to-center distance between the Gabor elements was 0.8." A first set of 40 stimuli was created in which GPs were carefully distributed and oriented to delineate a closed contour (with all contours defining unfamiliar shapes) embedded in a random GP background (similar to Kourtzi et al., 2005). The contour was built up from a variable number of GPs that always corresponded to the 40% of the total number of GPs present on screen (the remaining 60% GPs were random background). A second set of 40 stimuli was generated consisting of GPs randomly distributed and oriented: for each stimulus of the first set, a corresponding random pattern was created for the second set, so that GP patterns in the two sets were fully matched in terms of the total number of GPs they contained. Figure 2*B* shows an example of a stimulus with and without the embedded shape.

Procedure. The task involved shape detection; participants were required to indicate, with a button press, whether the target stimulus contained a shape. Participants were instructed to respond as accurately and quickly as possible. An experimental block contained 80 stimuli (40 with a visible shape and 40 with no shape, randomly presented). Four blocks were performed, one for each TMS site (rightOFA, rightLO, leftOFA, and vertex).

Experiment 2a: symmetry detection in faces

This study aimed to investigate whether the rightOFA and rightLO are causally involved in detecting symmetry in faces. The stimulation sites were rightOFA, rightLO, and vertex (baseline). We chose not to include any active stimulation sites in the left hemisphere as we were primarily interested in the role of the rightOFA and rightLO. The same stimulation sites were used in the study by Pitcher et al. (2007).

Stimuli. Stimuli were adapted from Rhodes et al. (1998; Experiment 2) and consisted of 26 normal faces (13 males) and their perfectly symmetric versions. All faces displayed a neutral expression and were presented in frontal view. The perfectly symmetric versions were obtained by blending each face with its mirror image (for a detailed description, see Rhodes et al., 1998, 2005). Faces measured ~10.5 × 14.5 degrees of visual angle and were centrally presented, embedded in a black semi-oval masking the hair (Fig. 2*C*). The mean luminance of the stimuli was 84.91 cd/m^2 and the background luminance was 0.82 cd/m^2.

Procedure. Figure 3 (right panel) shows the time line of an experimental trial. The procedure was as in Experiment 1a, with the exception that faces rather than dot patterns were used as stimuli, and participants had to indicate whether or not faces were symmetric. Each face was presented for 300 ms; stimulus duration was chosen on the basis of a prior pilot study showing that with this duration baseline accuracy is high (~90%). The experiment consisted of three blocks, one for each stimulation site (rightOFA, rightLO, and vertex). Each block consisted of 46 trials (23 symmetric and 23 asymmetric targets, presented in random order). The order of the TMS blocks was randomized across subjects. Triple-pulse 10 Hz TMS at 40% of the maximum stimulator output was given as in Experiment 1. Participants were instructed to respond as accurately and as quickly as possible. Before the experiment, participants performed a practice no-TMS block consisting of 20 trials (10 symmetric and 10 asymmetric).

Experiment 2b: facial feature discrimination (Jane task)

This experiment was run to confirm correct localization of rightOFA and rightLO. If the stimulation sites were accurately localized, then TMS over

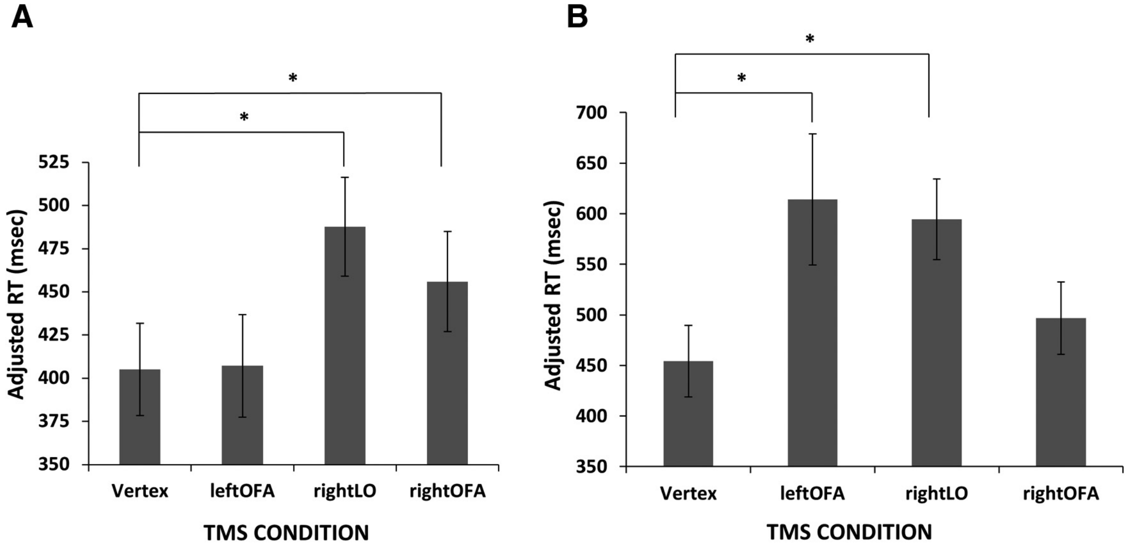

Figure 4. The mean ($n = 14$) inverse efficiency (i.e., RT/accuracy) for each TMS condition in Experiment 1a (***A***), which assessed symmetry detection in dot patterns, and Experiment 1b (***B***), which assessed shape detection. The asterisks indicate significant pairwise comparisons (Bonferroni–Holm corrected). Error bars represent ± 1 SEM. In Experiment 1a, TMS significantly impaired symmetry detection in dot patterns when applied over rightOFA and rightLO compared with vertex (baseline), whereas stimulation of leftOFA did not affect performance. In Experiment 1b, TMS over rightLO and leftOFA significantly impaired shape detection compared with vertex stimulation, whereas rightOFA TMS did not.

OFA but not over LO should affect face discrimination based on featural differences (cf. Pitcher et al., 2007, 2011). The stimulation sites were rightOFA, rightLO, and vertex (baseline).

Stimuli. Stimuli were taken from the Jane faces task set (Mondloch et al., 2002) and consisted of five grayscale images (picture size: 9.7 × 14.4 degrees of visual angle) of a Caucasian female face (called "Jane") and of its four featural variants ("Jane's sisters"; (Fig. 2*D*). Specifically, featural variants were obtained by replacing the original Jane's eyes and mouth with matching features from different female faces (for a detailed stimulus description, see Mondloch et al., 2002). The mean luminance of the stimuli was 97.32 cd/m^2 and the background luminance was 32.56 cd/m^2.

Procedure. Procedure was similar to that used in a previous TMS study using the Jane faces task (Renzi et al., 2013). Each trial started with a black fixation cross appearing in the middle of the screen for 1000 ms, followed by a blank screen (500 ms), and the presentation of the first face appearing on the screen for 200 ms. A blank screen was then presented for 300 ms, followed by a second face that remained visible on the screen until participants' response. Participants were required to indicate, with a button press, whether the two faces were identical or different. On each trial, the TMS pulse train began simultaneously with the onset of the second face (Renzi et al., 2013). Stimulation site and parameters were the same as in Experiment 2a. Participants were instructed to respond as accurately and as quickly as possible. The experiment consisted of three blocks, one for each stimulation site (rightOFA, rightLO, and vertex). Each block consisted of 40 face pairs (20 "different" trials and 20 "same" trials) randomly presented. The order of the TMS blocks was randomized across subjects. Before the experiment, participants performed a short no-TMS practice consisting of 20 trials (10 "different" trials and 10 "same" trials).

Results

Overall performance level was high in all experiments (mean accuracy = 96%, SD = 2.08 in Experiment 1a; mean = 87%, SD = 6.41 in Experiment 1b; mean = 86%, SD = 4.48 in Experiment 2a; and mean = 91%, SD = 5.85 in Experiment 2b). Statistical analyses were performed on mean response latencies adjusted for level of accuracy (i.e., inverse efficiency = mean RT/proportion of correct responses) to account for possible speed/accuracy trade-off effects (Brozzoli et al., 2008; Pasalar et al., 2010; Bardi et al., 2013; Bona et al., 2014).

Experiment 1a: symmetry detection in dot patterns

Figure 4*A* shows the mean ($n = 14$) inverse efficiency for each TMS condition. A repeated-measures ANOVA with TMS site (rightLO, rightOFA, leftOFA, and vertex) as within-subjects variable revealed a significant effect of TMS ($F_{(3,39)} = 7.46$, $p < .001$; $\eta_p^2 = 0.36$). *Post hoc t* tests (Bonferroni–Holm correction applied) showed that, relative to the baseline (vertex), performance was impaired when TMS was applied over rightOFA ($t_{(13)} = 4.15$, $p = 0.007$), and rightLO ($t_{(13)} = 3.57$, $p = 0.014$). TMS over the leftOFA had no effect relative to vertex ($t_{(13)} < 1$, $p = 0.92$). LeftOFA and rightOFA did not significantly differ from each other ($t_{(13)} = 3.22$, $p = 0.19$).

In summary, results of Experiment 1a reveal that both rightLO and rightOFA are causally involved in symmetry detection in dot patterns.

Experiment 1b: detection of shapes defined by collinear Gabor patches

Figure 4*B* shows the mean ($n = 14$) inverse efficiency for each TMS condition. A repeated-measures ANOVA with TMS site (rightLO, rightOFA, leftOFA, and vertex) as within-subjects variable revealed a significant effect of TMS ($F_{(3,39)} = 6.18$, $p = 0.002$; $\eta_p^2 = 0.32$). *Post hoc t* tests (Bonferroni–Holm correction applied) showed that compared with vertex (baseline), performance was impaired by leftOFA TMS ($t_{(13)} = 3.25$, $p = 0.031$) and by rightLO TMS ($t_{(13)} = 3.46$, $p = 0.026$), but not by rightOFA TMS ($t_{(13)} = 1.73$, $p = 0.33$). LeftOFA and rightOFA did not significantly differ from each other ($t_{(13)} = 2.29$, $p = 0.12$).

The results of Experiment 1b are consistent with previous data (Pitcher et al., 2007; Solomon-Harris et al., 2013) indicating that LO but not rightOFA plays a causal role in detection of shapes. The results of Experiments 1a and 1b indicate that rightOFA plays a role in figure-ground segregation based on symmetry detection, but not based on collinearity.

Experiment 2a: symmetry detection in faces

Figure 5*A* shows the mean ($n = 14$) inverse efficiency for each TMS condition. A repeated-measure ANOVA with TMS site

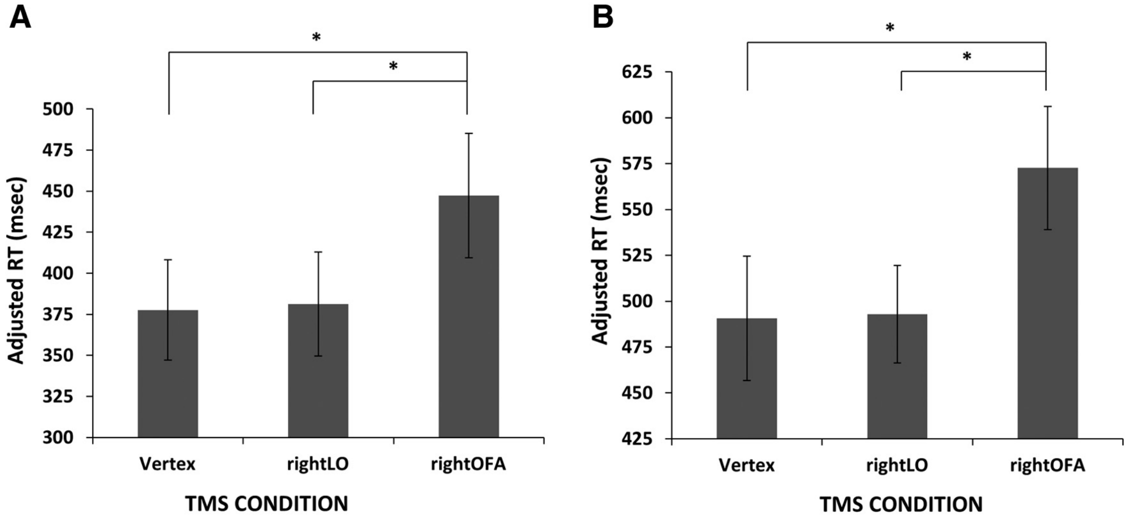

Figure 5. The mean ($n = 14$) inverse efficiency (i.e., RT/accuracy) for each TMS condition in Experiment 2a (***A***), which assessed symmetry detection in faces, and Experiment 2b (***B***), which assessed face discrimination. The asterisks indicate significant pairwise comparisons (Bonferroni–Holm corrected). Error bars represent ± 1 SEM. In Experiment 2a, TMS significantly impaired symmetry detection in faces when applied over rightOFA compared with vertex (baseline), whereas stimulation of rightLO did not. Similarly, in Experiment 2b, TMS over rightOFA affected face discrimination, whereas TMS over rightLO did not.

(rightLO, rightOFA, and vertex) as within-subjects variable on adjusted RT showed a significant effect of TMS ($F_{(2,26)} = 7.38$, $p = 0.003$; $\eta_p^2 = 0.36$). *Post hoc t* tests (Bonferroni–Holm corrected) showed a significant impairment of performance when TMS was applied over rightOFA compared with vertex ($t_{(13)} = 3.15$, $p = 0.015$), but not when it was applied over rightLO ($t_{(13)} < 1$, $p = 0.79$), compared with vertex. RightLO and rightOFA significantly differed from each other ($t_{(13)} = 3.69$, $p = 0.008$).

In summary, results of Experiment 2a demonstrate that rightOFA but not rightLO is involved in discriminating facial symmetry.

Experiment 2b: facial feature discrimination (Jane faces task). Figure 5*B* shows the mean ($n = 14$) inverse efficiency for each TMS condition. A repeated-measure ANOVA with TMS site (rightLO, rightOFA, and vertex) as within-subjects variable on adjusted RT showed a significant effect of TMS ($F_{(2,26)} = 8.09$, $p = 0.002$; $\eta_p^2 = 0.38$). *Post hoc t test*s (Bonferroni–Holm corrected) showed a significant impairment in performance following stimulation of rightOFA compared with vertex ($t_{(13)} = 2.88$, $p = 0.026$), whereas rightLO TMS did not affect performance compared with vertex stimulation ($t_{(13)} < 1$, $p = 0.92$). RightLO and rightOFA significantly differed from each other ($t_{(13)} = 4.37$, $p = 0.002$).

Results of Experiment 2b are therefore consistent with previous studies showing that rightOFA but not rightLO is involved in discrimination of facial features (Pitcher et al., 2007, 2011), confirming that these regions were correctly localized and that, despite of their cortical proximity, these regions can be selectively affected by TMS.

Discussion

The aim of our study was to shed light on the roles of rightOFA and rightLO in symmetry detection both in low-level stimuli (dot configurations) and in faces, where the features (e.g., ears, eyes) are normally somewhat symmetric, but not fully so. In the first experiment (Experiment 1a), we showed that interfering with rightOFA or rightLO activity with TMS impaired participants' performance in detecting symmetry in dot patterns, whereas TMS over the homolog of OFA in the left hemisphere (leftOFA; used here as a control site as in Pitcher et al., 2007) had no effect. In the second experiment we showed that TMS over rightOFA but not over rightLO affected participants' ability in deciding whether a face was perfectly symmetric or not (Experiment 2a). Our findings cannot be explained in terms of poor localization of rightOFA, as in two control experiments we showed a double dissociation for the effects of TMS on rightLO and rightOFA, confirming that these two sites can be selectively affected by TMS (Pitcher et al., 2007). Specifically, TMS over rightLO but not over rightOFA impaired detection of shapes defined by collinearity of Gabor patches (Experiment 1b); conversely TMS over rightOFA but not rightLO impaired face discrimination (Experiment 2b) based on featural aspects (the Jane faces task; Mondloch et al., 2002; for a similar result see Pitcher et al., 2007).

Although the literature on rightOFA tends to focus on face processing (Haxby et al., 2000; Pitcher et al., 2007, 2009, 2011; Kadosh et al., 2011; Solomon-Harris et al., 2013; Zhao et al., 2014), there is evidence for its involvement in processing of nonface stimuli (Gilaie-Dotan et al., 2008; Haist et al., 2010; Silvanto et al., 2010; Slotnick and White, 2013). For example, Haist et al. (2010) showed that OFA is equally activated by faces and objects when participants are required to process objects at an individual level (i.e., to discriminate between individual exemplars). Furthermore, a prior TMS study (Silvanto et al., 2010) has implicated the rightOFA in the processing of 2D shapes. It is interesting to note that in that study, the stimuli were symmetric; it may be that OFA can be involved in the encoding of shapes if these contain attributes (such as symmetry) that are strongly characteristic of faces. In fact, prior TMS studies have found no evidence for the involvement of OFA in processing of houses or meaningless objects (where symmetry was not a salient feature) (Pitcher et al., 2007, 2009). Our results are consistent with this literature, as TMS over rightOFA did not impair detection of nonsymmetric shapes, whereas TMS over rightLO did so (Experiment 1b). Symmetry may be a special case for rightOFA's involvement in the encoding of nonface stimuli.

In a further experiment (Experiment 2a), we investigated whether rightOFA and rightLO are causally involved in detection of facial symmetry. TMS over rightOFA impaired performance whereas stimulation of rightLO had no significant effect. Our results show that whereas symmetry in dot configurations involves both rightOFA and rightLO, facial symmetry detection (discriminating perfectly symmetric relative to "normal" faces, which are always somewhat asymmetric) relies only on the former. These findings can be reconciled by the coexistence of low-level/general and high-level/face-specific symmetry encoding mechanisms. On one hand, symmetry is a low-level visual feature detected by mechanisms operating on simple image properties and independently of object identity and acts as a basic Gestalt principle of perceptual organization (Wagemans, 1995; Koning and Wagemans, 2009; Machilsen et al., 2009; Treder, 2010). On the other hand, facial symmetry detection may rely on more specialized or higher level mechanisms, functionally different from those involved in other lower level forms of symmetry processing (Rhodes et al., 2005, 2007). For example, facial symmetry is more easily detected in upright than in inverted faces, although inversion does not affect low-level properties of faces (Rhodes et al., 2005, 2007). The level of symmetry in faces may also affect its perceived attractiveness, the evaluation of which involves OFA (Iaria et al., 2008). Our results indicate that symmetry as a low-level stimulus property (as in dot configurations) recruits both rightLO and rightOFA. In contrast, the detection of facial symmetry selectively relies on rightOFA (with no causal involvement of rightLO), consistently with the existence of face-specific symmetry mechanisms. Whether these processes share a common basis is unknown. It is possible that generic symmetry detection mechanisms might become tuned to facial symmetry detection because of high exposure to human faces (Rhodes et al., 2005).

Overall, our data shed new light on the functional role of rightOFA. Although this area is widely considered to be a critical node in face processing (Haxby et al., 2000; Rossion et al., 2003; Kadosh et al., 2011; Pitcher et al., 2011), the specific types of face information encoded by this region are still under debate (Rossion et al., 2003). For example, OFA role in face detection is controversial (Rossion et al., 2003; Nestor et al., 2008; Renzi et al., 2014). Other studies indicate that the OFA is involved in face recognition via its sensitivity to spatial arrangement of facial elements (Kovács et al., 2008; Jones et al., 2012). There is much support for the role of OFA in face discrimination (Pitcher et al., 2007; Kadosh et al., 2011; Solomon-Harris et al., 2013). Our results extend the range of visual processes in which OFA is involved to include symmetry processing.

In Experiment 1b, TMS affected shape detection based on collinearity of Gabor patches both when delivered over rightLO and over leftOFA, the homolog of OFA in the left hemisphere. The causal involvement of rightLO in shape detection replicates our previous findings using the same task (Bona et al., 2014) and is consistent with numerous TMS studies highlighting the critical role of this region in object/shape processing (Altmann et al., 2004; Ellison and Cowey, 2009; Mullin and Steeves, 2011; Ales et al., 2013). The effect observed with TMS over the leftOFA may be due to the stimulation actually affecting the leftLO. This is because the leftOFA is not a robust region in terms of fMRI localization; in almost half of our participants there was no face-selective response in this area, consistent with prior reports (Rossion et al., 2003; Haist et al., 2010). Furthermore, leftOFA does not seem to play a causal role in face processing (Rossion et al., 2003; Pitcher et al., 2007); thus it may be that the functional role of this region in the left hemisphere relates to object processing. While the precise role of leftOFA is unclear, the key issue for the conclusions of our study is that the rightOFA and rightLO could be accurately localized. This is shown by the findings that TMS over rightOFA but not over rightLO affected the face discrimination task (Jane task, Experiment 2b, replicating findings by Pitcher et al., 2007), and TMS over rightLO but not over rightOFA affected shape detection (Experiment 1b). This double dissociation in the effects of rightOFA and rightLO in the processing of faces and objects indicates that TMS could selectively and differentially target these two sites.

Overall, our results demonstrate that the rightOFA is causally involved in detection of symmetry, also for nonface dot configurations. In contrast, the rightLO is involved in detection of symmetry in dot configurations but not in faces.

References

Ales JM, Appelbaum LG, Cottereau BR, Norcia AM (2013) The time course of shape discrimination in the human brain. Neuroimage 67:77–88. CrossRef Medline

Altmann CF, Deubelius A, Kourtzi Z (2004) Shape saliency modulates contextual processing in the human lateral occipital complex. J Cogn Neurosci 16:794–804. CrossRef Medline

Anderson ND, Gleddie C (2013) Comparing sensitivity to facial asymmetry and facial identity. Iperception 4:396–406. CrossRef Medline

Atkinson AP, Adolphs R (2011) The neuropsychology of face perception: beyond simple dissociations and functional selectivity. Philos Trans R Soc Lond B Biol Sci 366:1726–1738. CrossRef Medline

Azañón E, Longo MR, Soto-Faraco S, Haggard P (2010) The posterior parietal cortex remaps touch into external space. Curr Biol 20:1304–1309. CrossRef Medline

Bardi L, Kanai R, Mapelli D, Walsh V (2013) Direct current stimulation (tDCS) reveals parietal asymmetry in local/global and salience-based selection. Cortex 49:850–860. CrossRef Medline

Bauer C, Yazzolino L, Hirsch G, Cattaneo Z, Vecchi T, Merabet LB (2014) Neural correlates associated with superior tactile symmetry perception in the early blind. Cortex 63C:104–117. CrossRef Medline

Bona S, Herbert A, Toneatto C, Silvanto J, Cattaneo Z (2014) The causal role of the lateral occipital complex in visual mirror symmetry detection and grouping: an fMRI-guided TMS study. Cortex 51:46–55. CrossRef Medline

Brozzoli C, Ishihara M, Göbel SM, Salemme R, Rossetti Y, Farnè A (2008) Touch perception reveals the dominance of spatial over digital representation of numbers. Proc Natl Acad Sci U S A 105:5644–5648. CrossRef Medline

Cattaneo Z, Mattavelli G, Papagno C, Herbert A, Silvanto J (2011) The role of the human extrastriate visual cortex in mirror symmetry discrimination: a TMS-adaptation study. Brain Cogn 77:120–127. CrossRef Medline

Chen CC, Kao KL, Tyler CW (2007) Face configuration processing in the human brain: the role of symmetry. Cereb Cortex 17:1423–1432. CrossRef Medline

Dilks DD, Julian JB, Paunov AM, Kanwisher N (2013) The occipital place area is causally and selectively involved in scene perception. J Neurosci 33:1331–1336a. CrossRef Medline

Ellison A, Cowey A (2009) Differential and co-involvement of areas of the temporal and parietal streams in visual tasks. Neuropsychologia 47:1609–1614. CrossRef Medline

Friston KJ, Ashburner JT, Kiebel SJ, Nichols TE, Penny WD (2007) Statistical parametric mapping: the analysis of functional brain images. London: Academic.

Ganaden RE, Mullin CR, Steeves JK (2013) Transcranial magnetic stimulation to the transverse occipital sulcus affects scene but not object processing. J Cogn Neurosci 25:961–968. CrossRef Medline

Gilaie-Dotan S, Nir Y, Malach R (2008) Regionally-specific adaptation dynamics in human object areas. Neuroimage 39:1926–1937. CrossRef Medline

Gilaie-Dotan S, Silvanto J, Schwarzkopf DS, Rees G (2010) Investigating representations of facial identity in human ventral visual cortex with transcranial magnetic stimulation. Front Hum Neurosci 4:50. CrossRef Medline

Haist F, Lee K, Stiles J (2010) Individuating faces and common objects produces equal responses in putative face-processing areas in the ventral occipitotemporal cortex. Front Hum Neurosci 4:181. CrossRef Medline

Haxby JV, Hoffman EA, Gobbini MI (2000) The distributed human neural system for face perception. Trends Cogn Sci 4:223–233. CrossRef Medline

Iaria G, Fox CJ, Waite CT, Aharon I, Barton JJ (2008) The contribution of the fusiform gyrus and superior temporal sulcus in processing facial attractiveness: neuropsychological and neuroimaging evidence. Neuroscience 155:409–422. CrossRef Medline

Jones RM, Victor JD, Conte MM (2012) Detecting symmetry and faces: separating the tasks and identifying their interactions. Atten Percept Psychophys 74:988–1000. CrossRef Medline

Kadosh KC, Walsh V, Kadosh RC (2011) Investigating face-property specific processing in the right OFA. Soc Cogn Affect Neurosci 6:58–65. CrossRef Medline

Koning A, Wagemans J (2009) Detection of symmetry and repetition in one and two objects. Structures versus strategies. Exp Psychol 56:5–17. CrossRef Medline

Kourtzi Z, Betts LR, Sarkheil P, Welchman AE (2005) Distributed neural plasticity for shape learning in the human visual cortex. PLoS Biol 3:e204. CrossRef Medline

Kovács G, Cziraki C, Vidnyánszky Z, Schweinberger SR, Greenlee MW (2008) Position-specific and position-invariant face aftereffects reflect the adaptation of different cortical areas. Neuroimage 43:156–164. CrossRef Medline

Landis T, Regard M, Bliestle A, Kleihues P (1988) Prosopagnosia and agnosia for noncanonical views. An autopsied case. Brain 111:1287–1297. CrossRef Medline

Machilsen B, Pauwels M, Wagemans J (2009) The role of vertical mirror symmetry in visual shape detection. J Vis 9(12):11.1–11. CrossRef Medline

Mondloch CJ, Le Grand R, Maurer D (2002) Configural face processing develops more slowly than featural face processing. Perception 31:553–566. CrossRef Medline

Mullin CR, Steeves JK (2011) TMS to the lateral occipital cortex disrupts object processing but facilitates scene processing. J Cogn Neurosci 23:4174–4184. CrossRef Medline

Nagy K, Greenlee MW, Kovács G (2012) The lateral occipital cortex in the face perception network: an effective connectivity study. Front Psychol 3:141. CrossRef Medline

Nestor A, Vettel JM, Tarr MJ (2008) Task-specific codes for face recognition: how they shape the neural representation of features for detection and individuation. PLoS One 3:e3978. CrossRef Medline

Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9:97–113. CrossRef Medline

Pasalar S, Ro T, Beauchamp MS (2010) TMS of posterior parietal cortex disrupts visual tactile multisensory integration. Eur J Neurosci 31:1783–1790. CrossRef Medline

Pascual-Leone A, Walsh V, Rothwell J (2000) Transcranial magnetic stimulation in cognitive neuroscience–virtual lesion, chronometry, and functional connectivity. Curr Opin Neurobiol 10:232–237. CrossRef Medline

Pitcher D, Walsh V, Yovel G, Duchaine B (2007) TMS evidence for the involvement of the right occipital face area in early face processing. Curr Biol 17:1568–1573. CrossRef Medline

Pitcher D, Charles L, Devlin JT, Walsh V, Duchaine B (2009) Triple dissociation of faces, bodies, and objects in extrastriate cortex. Curr Biol 19:319–324. CrossRef Medline

Pitcher D, Walsh V, Duchaine B (2011) The role of the occipital face area in the cortical face perception network. Exp Brain Res 209:481–493. CrossRef Medline

Pitcher D, Goldhaber T, Duchaine B, Walsh V, Kanwisher N (2012) Two critical and functionally distinct stages of face and body perception. J Neurosci 32:15877–15885. CrossRef Medline

Renzi C, Schiavi S, Carbon CC, Vecchi T, Silvanto J, Cattaneo Z (2013) Processing of featural and configural aspects of faces is lateralized in dorsolateral prefrontal cortex: a TMS study. Neuroimage 74:45–51. CrossRef Medline

Renzi, C, Ferrari C, Schiavi S, Pisoni A, Papagno C, Vecchi T, Antal A, Cattaneo Z (2014) The role of the occipital face area in holistic processing involved in face detection and discrimination: a tDCS study. Neuropsychology. Advance online publication. doi: 10.1037/neu0000127. Medline

Rhodes G, Proffitt F, Grady JM, Sumich A (1998) Facial symmetry and the perception of beauty. Psychon Bull Rev 5:659–669. CrossRef

Rhodes G, Peters M, Lee K, Morrone MC, Burr D (2005) Higher-level mechanisms detect facial symmetry. Proc Biol Sci 272:1379–1384. CrossRef Medline

Rhodes G, Peters M, Ewing LA (2007) Specialised higher-level mechanisms for facial-symmetry perception: evidence from orientation-tuning functions. Perception 36:1804–1812. CrossRef Medline

Rossion B, Caldara R, Seghier M, Schuller AM, Lazeyras F, Mayer E (2003) A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. Brain 126:2381–2395. CrossRef Medline

Sack AT, Cohen Kadosh R, Schuhmann T, Moerel M, Walsh V, Goebel R (2009) Optimizing functional accuracy of TMS in cognitive studies: a comparison of methods. J Cogn Neurosci 21:207–221. CrossRef Medline

Säisänen L, Pirinen E, Teitti S, Könönen M, Julkunen P, Määttä S, Karhu J (2008) Factors influencing cortical silent period: optimized stimulus location, intensity and muscle contraction. J Neurosci Methods 169:231–238. CrossRef Medline

Sandrini M, Umiltà C, Rusconi E (2011) The use of transcranial magnetic stimulation in cognitive neuroscience: a new synthesis of methodological issues. Neurosci Biobehav Rev 35:516–536. CrossRef Medline

Sasaki Y, Vanduffel W, Knutsen T, Tyler C, Tootell R (2005) Symmetry activates extrastriate visual cortex in human and nonhuman primates. Proc Natl Acad Sci U S A 102:3159–3163. CrossRef Medline

Schwarzkopf DS, Silvanto J, Gilaie-Dotan S, Rees G (2010) Investigating object representations during change detection in human extrastriate cortex. Eur J Neurosci 32:1780–1787. CrossRef Medline

Silvanto J, Schwarzkopf DS, Gilaie-Dotan S, Rees G (2010) Differing causal roles for lateral occipital cortex and occipital face area in invariant shape recognition. Eur J Neurosci 32:165–171. CrossRef Medline

Simmons LW, Rhodes G, Peters M, Koehler N (2004) Are human preferences for facial symmetry focused on signals of developmental instability? Behav Ecol 15:864–871. CrossRef

Slotnick SD, White RC (2013) The fusiform face area responds equivalently to faces and abstract shapes in the left and central visual fields. Neuroimage 83:408–417. CrossRef Medline

Solomon-Harris LM, Mullin CR, Steeves JK (2013) TMS to the "occipital face area" affects recognition but not categorization of faces. Brain Cogn 83:245–251. CrossRef Medline

Treder MS (2010) Behind the looking-glass: a review on human symmetry perception. Symmetry 2:1510–1543. CrossRef

Tyler CW, Baseler HA, Kontsevich LL, Likova LT, Wade AR, Wandell BA (2005) Predominantly extra-retinotopic cortical response to pattern symmetry. Neuroimage 24:306–314. CrossRef Medline

Uttner I, Bliem H, Danek A (2002) Prosopagnosia after unilateral right cerebral infarction. J Neurol 249:933–935. Medline

Wada Y, Yamamoto T (2001) Selective impairment of facial recognition due to a haematoma restricted to the right fusiform and lateral occipital region. J Neurol Neurosurg Psychiatry 71:254–257. CrossRef Medline

Wagemans J (1995) Detection of visual symmetries. Spat Vis 9:9–32. CrossRef Medline

Walsh V, Cowey A (2000) Transcranial magnetic stimulation and cognitive neuroscience. Nat Rev Neurosci 1:73–79. CrossRef Medline

Zhao M, Cheung SH, Wong AC, Rhodes G, Chan EK, Chan WW, Hayward WG (2014) Processing of configural and componential information in face-selective cortical areas. Cogn Neurosci 2:1–8. CrossRef Medline