Current Biology 17, 1568–1573, September 18, 2007 DOI 10.1016/j.cub.2007.07.063

Report

TMS Evidence for the Involvement of the Right Occipital Face Area in Early Face Processing

David Pitcher,[1,*] Vincent Walsh,[1] Galit Yovel,[2] and Bradley Duchaine[1]
[1]Institute of Cognitive Neuroscience
Department of Psychology
University College London
Alexandra House
17 Queen Square
London WC1N 3AR
United Kingdom
[2]Department of Psychology
Tel Aviv University
Tel Aviv 69978
Israel

Summary

Extensive research has demonstrated that several specialized cortical regions respond preferentially to faces [1–6]. One such region, located in the inferior occipital gyrus, has been dubbed the occipital face area (OFA) [7]. The OFA is the first stage in two influential face-processing models [8, 9], both of which suggest that it constructs an initial representation of a face, but how and when it does so remains unclear. The present study revealed that repetitive transcranial magnetic stimulation (rTMS) targeted at the right OFA (rOFA) disrupted accurate discrimination of face parts but had no effect on the discrimination of spacing between these parts. rTMS to left OFA had no effect. A matched part and spacing discrimination task that used house stimuli showed no impairment. In a second experiment, rTMS to rOFA replicated the face-part impairment but did not produce the same effect in an adjacent area, the lateral occipital cortex. A third experiment delivered double pulses of TMS separated by 40 ms at six periods after stimulus presentation during face-part discrimination. Accuracy dropped when pulses were delivered at 60 and 100 ms only. These findings indicate that the rOFA processes face-part information at an early stage in the face-processing stream.

Results

To examine whether the occipital face area (OFA) is especially critical for face processing, repetitive transcranial magnetic stimulation (rTMS) was targeted at the OFA in each cerebral hemisphere during a delayed match-to-sample task requiring discrimination of matched faces and houses. The faces and houses varied either in the parts or the spacing between parts (see Figure 1). Face and house stimuli were blocked, but within blocks the parts and spacing trials were randomly interleaved. These stimuli were used previously in a functional magnetic imaging resonance (fMRI) study of face processing and were behaviorally matched for accuracy (for details, see [10]). To control for site specificity of TMS effects, vertex was also stimulated and a no TMS condition was included for comparison.

Analysis of mean accuracy scores in experiment 1 showed that rTMS delivered at the right OFA (rOFA) impaired the discrimination of faces but not houses (see Figures 2A and 2B). Further analysis showed that rTMS at rOFA produced a selective impairment in discrimination of face parts but not face spacing. Face and house discrimination were unaffected by rTMS delivered at the left OFA (lOFA) and vertex. A repeated-measures ANOVA of the face results showed a main effect of TMS site ($F = 4.1$, $df = 3,33$, $p = 0.014$) but not of part v. spacing ($F = 4.4$, $df = 1,11$, $p = 0.06$). TMS site and part v. spacing combined in a significant two-way interaction ($F = 4.4$, $df = 3,33$, $p = 0.011$). Bonferroni corrected post hoc comparisons revealed a significant difference between discrimination of parts and spacing when stimulating rOFA ($p < 0.001$). For face-part discriminations, there were significant accuracy differences between the rOFA and vertex ($p = 0.004$) and rOFA and no TMS conditions ($p < 0.001$). No further post hoc tests approached significance. There were no significant results for the response time (RT) data. An ANOVA performed on the accuracy and RT data for the house discriminations showed no significant differences.

In experiment 2, the spatial specificity of the TMS-induced face-part impairment at rOFA was further assessed. In experiment 1, the rOFA was localized with the mean Talairach coordinates from an fMRI study of face processing [11], and its location does vary among participants (see also [10, 12]). The same face and house discrimination task was repeated, this time during TMS stimulation of rOFA and an adjacent area, the lateral occipital cortex (LO) (see Figure S1 in the Supplemental Data available online). Although the two sites are very close (within 2 cm when marked on the heads of all participants), each demonstrates a functionally different response in brain imaging studies. The rOFA responds preferentially to faces [7, 11] and the LO to objects [13, 14].

rTMS delivered at the rOFA again impaired the discrimination of faces parts but not face spacing, house parts, or house spacing (see Figure 2C and Figure S2). However, rTMS delivered at LO produced no part- or spacing-discrimination impairments to either faces or houses. A repeated-measures ANOVA of the face data showed a main effect of TMS site ($F = 3.1$, $df = 3,27$, $p = 0.043$) but not of part v. spacing ($F = 1.1$, $df = 1,9$, $p = 0.279$). TMS site and part v. spacing combined in a significant two-way interaction ($F = 8.4$, $df = 3,27$, $p = 0.001$). For face-part discriminations, there were significant accuracy differences between the rOFA and LO ($p = 0.034$), the rOFA and vertex ($p = 0.001$), and the rOFA and no TMS condition ($p = 0.011$). No further post hoc tests were significant. There were no significant results for the RT data. An ANOVA performed on the accuracy

*Correspondence: d.pitcher@ucl.ac.uk

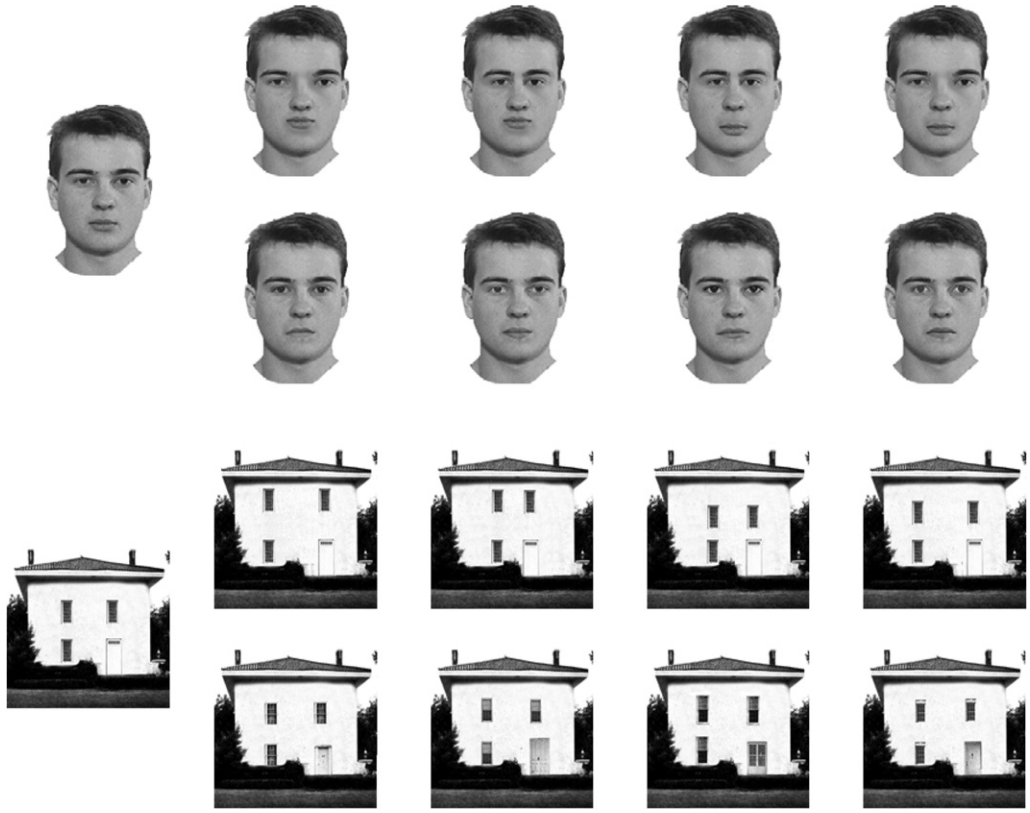

Figure 1. Examples of the Closely Matched Face and House Stimuli

Faces: Two sets of stimuli were generated from an image of a male face. For the spacing set, four faces were constructed by varying the distance between the two eyes and between the mouth and the nose (see Figure 4). For the part set, the two eyes and the mouth were replaced in each of the four faces by eyes and mouths from different faces.

Houses: House stimuli were created with a method similar to that used for the face stimuli. For the spacing set, four houses were constructed by manipulating the location of the windows and the door. For the part set, the windows and the door were replaced by windows and a door with the same shape but different internal features.

and RT data for the house discriminations showed no significant differences.

In experiment 3, the timing of rOFA's contribution to face-part processing was assessed by delivering double-pulse TMS separated by 40 ms at different time points. Double-pulse TMS allows exploitation of the temporal resolution of TMS by targeting short time periods while benefiting from the summation effects of two pulses [15]. Six timing conditions between 20 and 250 ms after stimulus onset were chosen. Time windows were specifically targeted to affect the periods contributing to the face-specific M100 and M170 components reported by MEG studies [16–19], which are believed to correspond with face-specific activity.

Double-pulse TMS to rOFA at 60 and 100 ms impaired accurate discrimination of face parts, but no other TMS timings affected performance (see Figure 2D). A repeated-measures ANOVA revealed a significant two-way interaction of timing and TMS site ($F = 4.2$, $df = 1,60$, $p = 0.002$) but no main effect of timing ($F = 1.7$, $df = 1,60$, $p = 0.141$) or of TMS site ($F = 1.7$, $df = 1,60$, $p = 0.219$). Bonferroni corrected comparisons revealed a highly significant difference between the accuracy scores in the 60–100 ms time window between rOFA and vertex ($p = 0.001$). No other comparisons approached significance. The RT data showed a main effect of TMS site ($F = 5.023$, $df = 1,60$, $p = 0.045$), with participants responding more slowly during rOFA stimulation (see Figure S3). rOFA mean RT across all six TMS conditions was 670 ms (SE = 44 ms), and vertex mean RT across all six TMS conditions was 629 ms (SE = 43 ms). The main effect of timing and the interaction were not significant for RT.

Discussion

The results demonstrate that the rOFA plays an important role in facial discrimination and furthermore that its contribution occurs at an early stage of the face-processing stream. Such a conclusion is in keeping with two influential models of the face-processing network [8, 9] that claim that the OFA generates an initial representation of a face before subsequent processing of other features such as identity and emotional expression. Evidence for these models comes from two principal sources: brain imaging studies and neuropsychological patient data.

A recent fMRI study demonstrated that the OFA shows release from adaptation when the physical appearance of a face is varied, even when that change does not lead observers to perceive a different identity [20]. In contrast, the fusiform gyrus (an area that shows

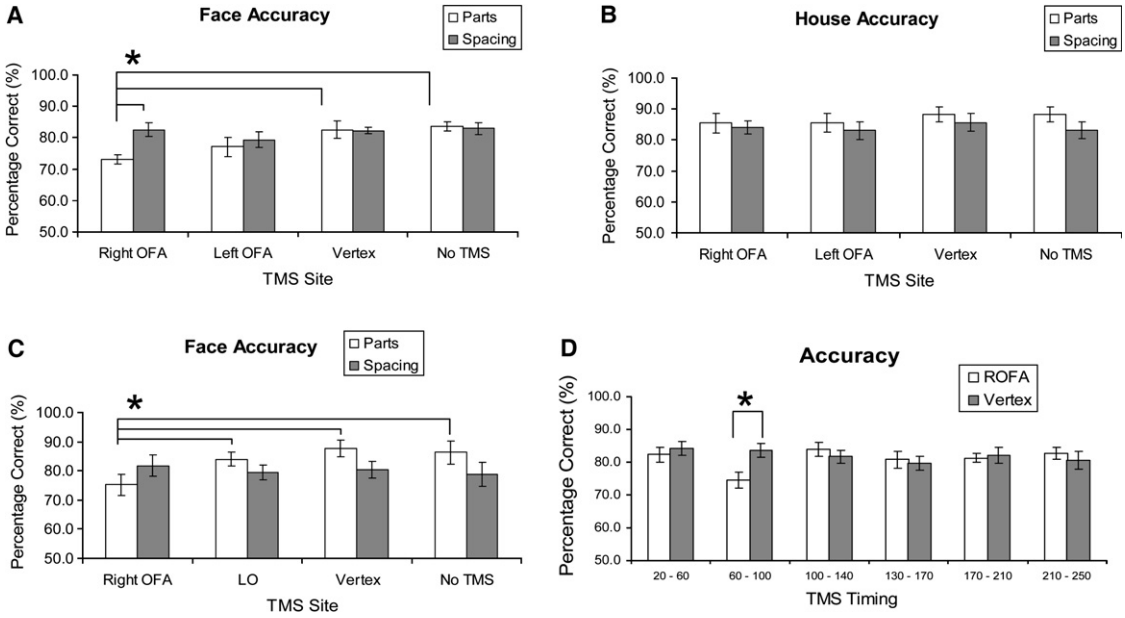

Figure 2. Graphs Illustrating the Results from Experiments 1, 2, and 3

(A) Mean accuracy scores for faces in experiment 1. Asterisk denotes a significant difference between face parts and face spacing ($p < 0.001$) at rOFA, and between face-part discrimination at rOFA and vertex ($p = 0.004$) and rOFA and no TMS ($p < 0.001$).

(B) Mean accuracy scores for the house stimuli in experiment 1.

(C) Mean accuracy scores for faces in experiment 2. Asterisk denotes a significant difference for face-part discrimination between the right OFA and LO ($p = 0.034$), the right OFA and vertex ($p = 0.001$), and the right OFA and no TMS condition ($p = 0.011$).

(D) Mean accuracy scores for face parts in experiment 3. Double-pulse TMS to rOFA significantly affected discrimination only when delivered at 60 and 100 ms after stimulus presentation (asterisk denotes the significant difference between rOFA and vertex when double-pulse TMS was delivered 60 and 100 ms from stimulus, $p = 0.001$).

Error bars denote standard errors.

greater activation during facial identification) showed release from adaptation only when the face changes caused viewers to perceive a different identity.

Lesion analysis in prosopagnosics has revealed the critical role played by the rOFA. A meta-analysis of neuropsychological patients found the majority of those with face-processing impairments exhibited lesions encompassing the rOFA as defined by anatomical coordinates [21]. By comparison, neurological damage in the fusiform gyrus across the group was less common. Likewise, two detailed case studies of acquired prosopagnosia appear to result from damage to the cortical region usually encompassing the rOFA [11, 22, 23]. The present finding complements and strengthens these lesion studies because the temporary impairment induced by TMS was specific to the rOFA, whereas neuropsychological patients frequently exhibit cortical damage extending to other visual areas (see [21]). Furthermore, the transient interference of TMS precludes any account of the rOFA effect based on compensatory neural reorganization [24, 25].

In experiment 1, rTMS delivered at the rOFA selectively impaired face-part but not face-spacing discrimination. A possible explanation for this dissociation is suggested by an fMRI study that assessed repetition suppression for faces composed of either low or high spatial frequencies (SF) [26]. The study found the right inferior occipital gyrus (the area containing the OFA) showed suppression for high SF faces but not low SF faces [27, 28]. Although the relationship between spacing/part discrimination and low/high SFs is not straightforward [29], a study showed that discrimination of face parts relied more heavily on high SFs than face spacing, and so our part task was more likely to be disrupted by TMS to rOFA than our spacing task (see also [30]).

rTMS delivered at the lOFA in experiment 1 did not lead to significant impairments in face discrimination. This difference between rOFA and lOFA is in keeping with the many lines of evidence demonstrating that faces are preferentially processed in the right hemisphere [3, 10, 31–34], particularly fMRI results that have shown that rOFA is more consistently detected than lOFA [7, 11]. It is also possible that the comparatively deeper cortical location of lOFA made it more difficult to impair with TMS.

Magnetoencephalography (MEG) studies of face processing report a face-specific response approximately 100 ms after stimulus onset (the M100 component), which is generated bilaterally in occipitotemporal regions [16, 17]. Experiment 3 demonstrated that the time period affected by two TMS pulses at 60 and 100 ms was the only one that resulted in significant performance degradation. This temporal correspondence between the M100 and the TMS effects suggest that the rOFA and the right lateralized M100 may be produced by the same cortical activity. Given that no further dips were observed from 20 to 250 ms, rOFA appears to make a relatively early and discrete contribution to face processing.

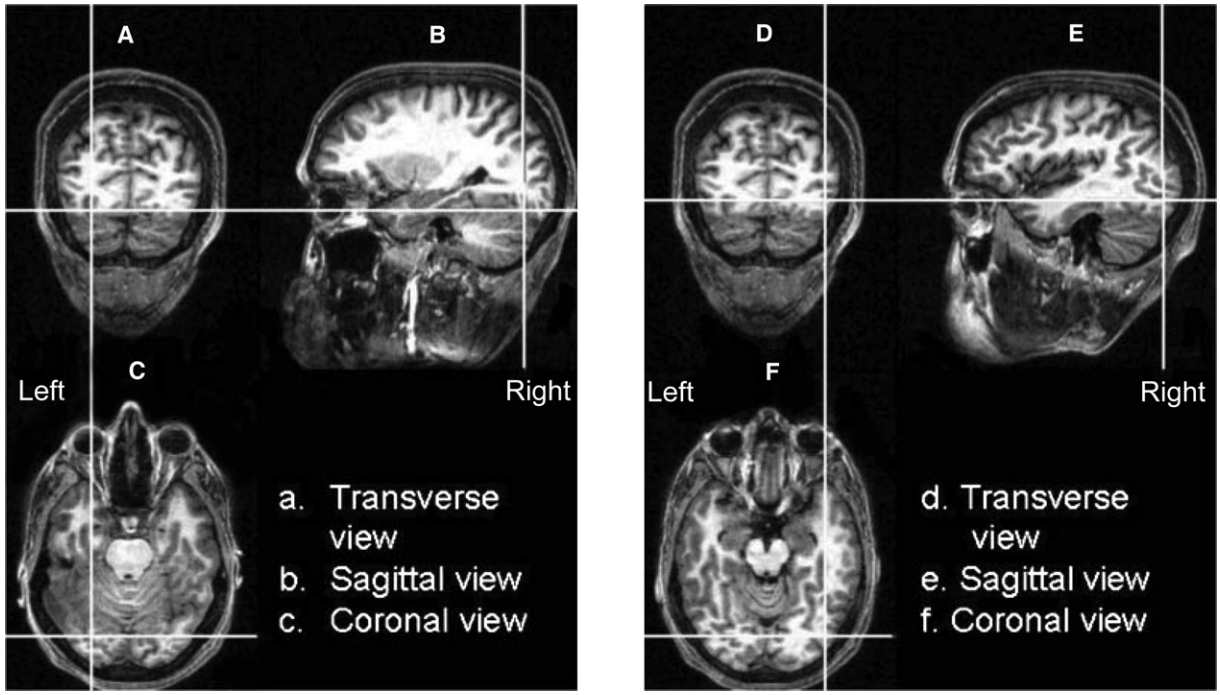

Figure 3. Diagram Showing the Location of the Left OFA and Right OFA in One Subject

Left: Normalized location of the left OFA (lOFA) in one subject. Based on Talairach coordinates −34, −81, 14.
Right: Normalized location of the right OFA (rOFA) in one subject. Based on Talairach coordinates 38, −80, −7.

In summary, experiment 1 demonstrated that rTMS delivered at the rOFA selectively disrupted discrimination of face parts while leaving discrimination of face spacing and both types of house discriminations unaffected. In contrast, rTMS targeted at lOFA and vertex had no effect. The face-part discrimination impairment at rOFA was replicated in experiment 2. More importantly, it also demonstrated the spatial specificity of the TMS-induced effect by failing to produce an impairment in an adjacent area of the occipital cortex, the LO. Finally, in experiment 3, paired TMS pulses delivered at 60 and 100 ms after stimulus onset to rOFA affected face-part discrimination whereas pairs delivered at other times had no effect. This study is the first to apply TMS to the rOFA and demonstrates that rOFA is involved at an early and important stage in the face-processing stream. We expect that future TMS studies will further refine the understanding of how face information is represented in the posterior visual cortex.

Experimental Procedures

Participants

Twenty-five right-handed healthy volunteers (11 males and 14 females, aged 19 to 33) gave informed consent in accordance with the ethics committee of University College London. Twelve participants took part in experiment 1, ten in experiment 2, and thirteen in experiment 3. Three took part in all three experiments, two in experiments 1 and 2, and two in experiments 2 and 3. One participant was removed from analysis in experiment 1 for performing at chance in all house-spacing conditions. Across all experiments, three participants withdrew during testing because of discomfort with TMS stimulation.

Apparatus and Materials

Stimuli were presented centrally on an SVGA 17-inch monitor set at 1024 by 768 resolution and refresh rate of 100 Hz. Experimental stimuli were grayscale images of faces and houses that were 300 × 300 pixels. See Figure 1 for details.

TMS Stimulation and Site Localization for Experiment 1 and Experiment 2

A Magstim Super Rapid Stimulator (Magstim, UK) was used to deliver the TMS via a figure-of-eight coil with a diameter of 70 mm. TMS was delivered at 10 Hz and 60% of maximal stimulator output, with the coil handle pointing upwards and parallel to the midsagittal plane. A single intensity was used for all subjects on the basis of several previous studies [15, 35–37]. On blocks of trials with TMS, test stimuli were presented during 500 ms rTMS with onset concurrent with the onset of the target visual stimulus. FSL software (FMRIB, Oxford) was used to transform coordinates for the lOFA, rOFA, and LO individually for each subject. Each subject's MRI scan was normalized against a standard template, and each transformation was used to convert the appropriate Talairach coordinates to the untransformed (structural) space coordinates, yielding subject-specific localization of the sites. The Talairach coordinates for the lOFA (−34, −81, −14) and rOFA (38, −80, −7) were taken from an fMRI study of face processing [11] (see Figure 3). The LO coordinates (46, −71, −4) were taken from an fMRI study of object and motion processing [14]. TMS sites were located by Brainsight TMS-MRI coregistration system (Rogue Research, Montreal, Canada), utilizing individual high-resolution MRI scans for each subject. The relevant target area was localized by the individual transformed coordinates and then marked on each participant's head. The vertex, a point at the center of the top of the head, was defined as a point midway between the inion and the nasion and equidistant from the left and right intertragal notches.

Procedure for Experiment 1 and Experiment 2

The trial procedure is illustrated in Figure 4. Subjects were seated with their heads stabilized on a chinrest 57 cm from the computer screen. Face and house stimuli were blocked. Within each block,

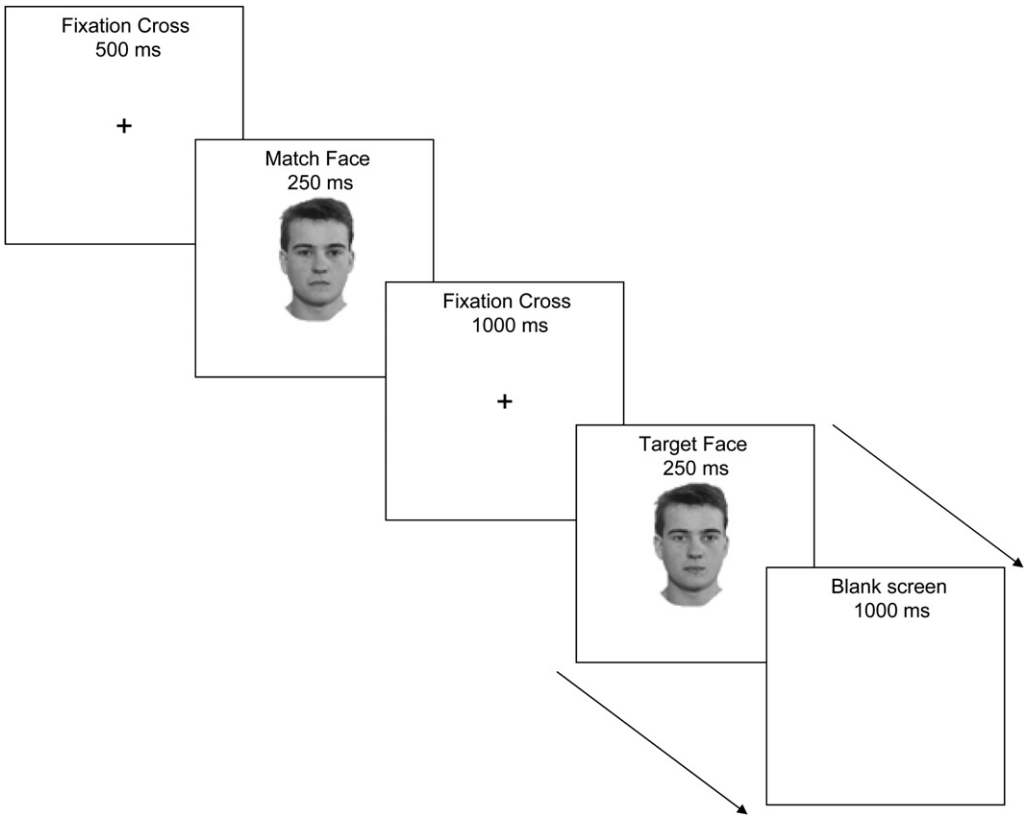

Figure 4. Trial Procedure for Experiments 1, 2, and 3

Timeline of the experimental procedure for experiment 1, experiment 2, and experiment 3 (an example of face-part stimuli is shown). TMS protocol for experiments 1 and 2: 10 Hz for 500 ms; TMS protocol for experiment 3: double-pulse TMS, 40 ms apart delivered at 20 and 60 ms, 60 and 100 ms, 100 and 140 ms, 130 and 170 ms, 170 and 210 ms, 210 and 250 ms.

the part images (40 trials) and the spacing images (40 trials) were randomly interleaved. Block order (houses or faces) was balanced between participants. In experiment 1, TMS was delivered at three locations in different blocks; rOFA, lOFA, and vertex. In experiment 2, TMS was delivered at rOFA, LO, and vertex. The order of TMS stimulation site was balanced between participants. Participants were instructed to indicate whether the target face was the same or different by means of a keyboard response with the right hand and were instructed to try to respond as accurately and as quickly as possible.

TMS Stimulation and Procedure for Experiment 3

All aspects of the TMS protocol were identical to experiment 1 except the timing of the TMS delivery and the sites stimulated. Double-pulse TMS was delivered at rOFA and vertex with 40 ms between pulses at six different times from stimulus onset: 20 and 60 ms, 60 and 100 ms, 100 and 140 ms, 130 and 170 ms, 170 and 210 ms, and 210 and 250 ms.

Pairs of faces that differed in parts were shown in random order in blocks of 40 trials. The order of the six double-pulse TMS timing blocks was balanced among participants and stimulation site, rOFA, and vertex. Trial procedure was as in experiment 1.

Supplemental Data

Three figures are available at http://www.current-biology.com/cgi/content/full/17/18/1568/DC1/.

Acknowledgments

Thanks to N. Muggleton and S. Rizzo for advice, support, and technical assistance. This work was partly supported by ESRC grant (RES-061-23-0400) to B.D. and a Royal Society URF to V.W.

Received: June 12, 2007
Revised: July 9, 2007
Accepted: July 30, 2007
Published online: August 30, 2007

References

1. Bodamer, J. (1947). Die Prosop-Agnosie. Arch. Psychiatr. Nervenkr. *179*, 6–53.
2. Bentin, S., Allison, T., Puce, A., Perez, E., and McCarthy, G. (1996). Electrophysiological studies of face perception in humans. J. Cogn. Neurosci. *8*, 551–565.
3. Kanwisher, N., McDermott, J., and Chun, M.M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. J. Neurosci. *17*, 4302–4311.
4. Moscovitch, M., Winocur, G., and Behrmann, M. (1997). What is special about face recognition? Nineteen experiments on a person with visual object agnosia and dyslexia but normal face recognition. J. Cogn. Neurosci. *9*, 555–604.
5. Winston, J., Henson, R., Fine-Goulden, M., and Dolan, R. (2004). fMRI-adaptation reveals dissociable neural representations of identity and expression in face perception. J. Neurophysiol. *92*, 1830–1839.
6. Kanwisher, N., and Yovel, G. (2006). The fusiform face area: a cortical region specialized for the perception of faces. Philos. Trans. R. Soc. Lond. B Biol. Sci. *361*, 2109–2128.
7. Gauthier, I., Tarr, M.J., Moylan, J., Skudlarski, P., Gore, J.C., and Anderson, A.W. (2000). The fusiform "face area" is part of a network that processes faces at the individual level. J. Cogn. Neurosci. *12*, 495–504.
8. Haxby, J.V., Hoffman, E.A., and Gobbini, M.I. (2000). The distributed human neural system for face perception. Trends Cogn. Sci. *4*, 223–233.

9. Calder, A.J., and Young, A.W. (2005). Understanding the recognition of facial identity and facial expression. Nat. Neurosci. *6*, 641–651.
10. Yovel, G., and Kanwisher, N. (2004). Face perception: domain specific, not process specific. Neuron *44*, 889–898.
11. Rossion, B., Caldara, R., Seghier, M., Schuller, A.M., Lazeyras, F., and 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.
12. Yovel, G., and Kanwisher, N. (2005). The neural basis of the behavioral face-inversion effect. Curr. Biol. *15*, 2256–2262.
13. Malach, R., Reppas, J., Benson, R., Kwong, K., Jiang, H., Kennedy, W., Ledden, P., Brady, T., Rosen, B., and Tootell, R. (1995). Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. Proc. Natl. Acad. Sci. USA *9*, 8135–8139.
14. Downing, P.E., Wiggett, A.J., and Peelen, M.V. (2007). Functional magnetic resonance imaging investigation of overlapping lateral occipitotemporal activations using multi-voxel pattern analysis. J. Neurosci. *27*, 226–233.
15. O'Shea, J., Muggleton, N.G., Cowey, A., and Walsh, V. (2004). Timing of target discrimination in human frontal eye fields. J. Cogn. Neurosci. *16*, 1060–1067.
16. Liu, J., Harris, A., and Kanwisher, N. (2002). Stages of processing in face perception: an MEG study. Nat. Neurosci. *5*, 910–916.
17. Itier, R.J., Herdman, A.T., George, N., Cheyne, D., and Taylor, M.J. (2006). Inversion and contrast-reversal effects on face processing assessed by MEG. Brain Res. *1115*, 108–120.
18. Tanskanen, T., Nasanen, R., Montez, T., Paallysaho, J., and Hari, R. (2005). Face recognition and cortical responses show similar sensitivity to noise spatial frequency. Cereb. Cortex *15*, 526–534.
19. Xu, Y., Liu, J., and Kanwisher, N. (2005). The M170 is selective for faces, not for expertise. Neuropsychologia *43*, 588–597.
20. Rotshtein, P., Henson, R.N., Treves, A., Driver, J., and Dolan, R.J. (2005). Morphing Marilyn into Maggie dissociates physical and identity face representations in the brain. Nat. Neurosci. *8*, 107–113.
21. Bouvier, S.E., and Engel, S.A. (2006). Behavioral deficits and cortical damage loci in cerebral achromatopsia. Cereb. Cortex *16*, 183–191.
22. Schiltz, C., Sorger, B., Caldara, R., Ahmed, F., Mayer, E., and Goebel, R. (2006). Impaired face discrimination in acquired prosopagnosia is associated with abnormal response to individual faces in the right middle fusiform gyrus. Cereb. Cortex *16*, 574–586.
23. Steeves, J.K., Culham, J.C., Duchaine, B.C., Pratesi, C.C., Valyear, K.F., and Schindler, I. (2006). The fusiform face area is not sufficient for face recognition: evidence from a patient with dense prosopagnosia and no occipital face area. Neuropsychologia *44*, 594–609.
24. Walsh, V., and Cowey, A. (1998). Magnetic stimulation studies of visual cognition. Trends Cogn. Sci. *2*, 103–109.
25. Walsh, V., and Pascual-Leone, A. (2003). Transcranial Magnetic Stimulation: A Neurochromometrics of Mind (Cambridge, MA: MIT Press).
26. Rotshtein, P., Vuilleumier, P., Winston, J., Driver, J., and Dolan, R. (2007). Distinct and convergent visual processing of high and low spatial frequency information in faces. Cereb. Cortex, in press. Published online February 5, 2007. 10.1093/cercor/bhl180.
27. Eger, E., Schyns, P.G., and Kleinschmidt, A. (2004). Scale invariant adaptation in fusiform face-responsive regions. Neuroimage *22*, 232–242.
28. Vuilleumier, P., Armony, J.L., Driver, J., and Dolan, R.J. (2003). Distinct spatial frequency sensitivities for processing faces and emotional expressions. Nat. Neurosci. *6*, 624–631.
29. Boutet, I., Collin, C., and Faubert, J. (2003). Configural face encoding and spatial frequency information. Percept. Psychophys. *65*, 1078–1093.
30. Goffaux, V., Hault, B., Michel, C., Vuongô, Q., and Rossion, R. (2005). The respective role of low and high spatial frequencies in supporting configural and featural processing of faces. Perception *34*, 77–86.
31. Barton, J.J., Press, D.Z., Keenan, J.P., and O'Connor, M. (2002). Lesions of the fusiform face area impair perception of facial configuration in prosopagnosia. Neurology *58*, 71–78.
32. Landis, T., Cummings, J.L., Christen, L., Bogen, J.E., and Imhof, H.G. (1986). Are unilateral right posterior cerebral lesions sufficient to cause prosopagnosia? Clinical and radiological findings in six additional patients. Cortex *22*, 243–252.
33. Yovel, G., Levy, J., Grabowecky, M., and Paller, K.A. (2003). Neural correlates of the left-visual-field superiority in face perception appear at multiple stages of face perception. J. Cogn. Neurosci. *15*, 462–474.
34. Young, A.W., Hay, D.C., McWeeny, K.H., Ellis, A.W., and Barry, C. (1985). Familiarity decisions for faces presented to the left and right cerebral hemispheres. Brain Cogn. *4*, 439–450.
35. Beck, D., Muggleton, N., Walsh, V., and Lavie, N. (2006). The right parietal cortex plays a critical role in change blindness. Cereb. Cortex *16*, 712–717.
36. Muggleton, N.G., Postma, P., Moutsopoulou, K., Nimmo-Smith, I., Marcel, A., and Walsh, V. (2006). TMS over right posterior parietal cortex induces neglect in a scene-based frame of reference. Neuropsychologia *44*, 1222–1229.
37. Silvanto, J., Lavie, N., and Walsh, V. (2005). Double dissociation of V1 and V5/MT activity in visual awareness. Cereb. Cortex *15*, 1736–1741.