Supporting Information

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SI Methods

Subjects. Twenty-one (eight females, mean age = 21.8 y, range = 19-29 y) and nine (two females, mean age = 25.1 y, range = 19-41 y) healthy subjects participated in the functional MRI (fMRI) and transcranial magnetic stimulation (TMS)/fMRI experiments, respectively. It was possible to define, with the functional localizer, the extrastriate body area (EBA), parahippocampal place area (PPA), and fusiform face area (FFA) in at least one hemisphere for 20, 19, and 16 subjects, respectively, in experiment 1 and in 9, 9, and 8 subjects, respectively, in experiment 2. All subjects were right-handed with normal or corrected-to-normal vision and gave written informed consent for the procedure in accordance with protocols approved by the Central Oxford Research Ethics Committee.

Stimuli. A total of 72 unique photographs of body parts, houses, and faces were taken by the experimenters or obtained from the Internet. The images were converted to grayscale and centered on a white box scaled to 400×400 pixels.

Attentional Tasks. The subjects' task was to judge whether images presented at the start of each trial were either present (match) or absent (nonmatch) in an array of three stimuli presented several seconds later. A trial began with the sequential presentation of two stimuli, each for 0.95 s (Fig. 1A). The fixation cross appeared in the center of the screen for a variable time (4-8 s), followed by the appearance of a number cue or an exclamation mark cue (0.5 s). A number (1 or 2) cue instructed subjects to focus on either the first or second image (selective attention), and the exclamation mark (!) cue instructed them to remember both images (nonselective attention). After a variable interval (1.5-2.5 s), an array of three images was presented for 1 s. Subjects responded by pushing one of two buttons with the right-hand index (match) or middle finger (nonmatch), as quickly and accurately as possible. The target was followed by an inter-trial interval (ITI) (4 s). Experiment 1 consisted of 144 trials comprising pseudorandomly interleaved match (50%) and nonmatch (50%) trials. Number cue (50%) and exclamation mark cue (50%) trials were also randomly interleaved. Within the selective condition, one-third of the trials required subjects to attend to body parts (BA condition), one-third required attention to face (FA condition), and one-third required attention to houses (HA). At the same time, a third of each of the selective trials entailed ignoring body part (BI), face (FI), or house (HI) when those stimuli were presented in the nonattended list position. Half of the HA trials entailed BI and half FI, half of the FA trials entailed BI and HI, and half of the FA trials entailed HI and half BI. The task for experiment 2 was modified to consist of 120 trials in which only the selective (number cue) trials were presented. All tasks were programmed and presented with the Presentation software package (Neurobehavioral Systems).

Localizer Task. A separate localizer task was performed to define regions responsive to body parts, houses, and faces (EBA, PPA, and FFA, respectively) in each subject. Subjects were shown pairs of body parts, houses, or faces in a sequence. Each block contained 10 images all drawn from the same category, and subjects indicated with a speeded-choice response whether the presented stimulus was the same or different to the previously presented one. Stimuli were presented for 1 s, followed by the appearance of a fixation cross for a 1-s period in which the response had to be made. In total, 12 blocks were separated by 6-s intervals and

presented in a randomized order. The localizer scans were carried out after the scan for the main attentional task in experiment 1 and after the two fMRI sessions in experiment 2.

fMRI Data Acquisition. MRI data were acquired on a 3T Siemens MRI scanner with maximum gradient strength 40 mT·m⁻¹ at the Oxford Centre for Clinical Magnetic Resonance Imaging. Blood oxygen level–dependent (BOLD) T2-weighted MRI images were obtained by using echoplanar images (25×5 -mm-thick axial slices positioned from the top of the brain; repetition time, 3.0 s; echo time, 30 ms; matrix, 64×64 voxels; field of view, 192×192 mm). A T1-weighted FLASH image was acquired for each subject (repetition time, 3 ms; echo time, 4.71 ms; flip angle, 87° ; giving a voxel size, $1 \times 1 \times 1$ mm). The first three image sets were collected in the absence of any task to allow the signal to reach the equilibrium state, and they were excluded for the following processing and analysis.

TMS/fMRI Experiments. TMS was applied with a 70-mm figure-ofeight coil and Magstim2000 (The Magstim Company Ltd.) magnetic stimulators. First, the TMS sites were verified anatomically with Brainsight frameless stereotaxy (Rogue Research). Each subject's brain was coregistered with their anatomical MRI in native space, and a trajectory was plotted from each scalp location at which TMS was applied onto the cortical surface by using Brainsight software. TMS was applied over the most superficial part of the activated frontal region identified in experiment 1 so that the mean Montreal Neurological Institute (MNI) coordinate location of TMS was -55, 24, -3 (Fig. 4B). Next, to determine the TMS intensity, we searched the scalp location in the left motor cortex where TMS stimulation caused the largest contraction of the first dorsal interosseous muscle of the right hand. Approximately 90% of the active motor threshold at this point was then used for repetitive TMS over the inferior frontal cortex (1, 2). Subjects underwent two fMRI sessions (18-20 min each) on the same day, one of which was preceded by a 1-Hz TMS for 15 min. The coil was replaced after 7.5 min to avoid overheating. Approximately 30 s elapsed during changeover of the coil. Scan order was counterbalanced so that approximately half of the subjects (4/9) participated in the post-TMS session before the pre-TMS sessions. After TMS application, subjects were moved to the immediately adjacent MRI scanner room and were scanned. No more than 5 min elapsed between the end of TMS and the start of fMRI data acquisition.

fMRI Data Analysis. fMRI analysis was carried out with tools from the software library of the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB). Using MELODIC, we first performed probabilistic independent components analysis to identify and remove large motion artifacts. The data were then corrected for motion (3), and the data in each volume were spatially smoothed with a 5-mm full width at half maximum Gaussian kernel. We applied a high-pass temporal filter to the data to remove low-frequency noise that may have arisen from scanner drift. Local autocorrelation correction (4) was used instead of low-pass filtering.

The resulting denoised time series data were analyzed by using a general linear model approach. The model included explanatory variables for all phases of a trial, which were convolved with the hemodynamic response function (HRF). The onsets for the following events were entered into the model. For the main attentional task, 17 regressors were created: BA cues, HA cues, FA cues, BI cues, HI cues, FI cues, nonselective cues, initial body stimuli, initial house stimuli, initial face stimuli, target array, and six motion regressors produced during realignment. For localizer tasks, three regressors, presentation of body stimuli, house stimuli, and face stimuli, were included.

For group analyses, images were skull-stripped (5) and then coregistered with FMRIB's linear registration tool, with each subject's echoplanar images being registered with their high-resolution structural image and transformed into MNI space performed by using affine transformations (3). We then fit a general linear model to estimate the group mean effects for the regressors described above. FMRIB's Local Analysis of Mixed Effects (FLAME) was used to perform a mixed-effects group analysis that modeled both fixed-effects variance and random-effects variance (6). Group Z (Gaussianized T) statistics images were thresholded by using clusters determined by Z > 2.3 and a corrected cluster significance threshold of P < 0.05.

For region-of-interest analyses, a sphere of 6-mm radius was centered over the EBA, PPA, and FFA location peak derived from the localizer scans. Parameter estimates were averaged over all voxels within the region of interest for each subject.

Psychophysiological interaction (PPI) analysis was used to test whether the frontal operculum (fO) showed functional in-

- O'Shea J, Johansen-Berg H, Trief D, Göbel S, Rushworth MF (2007) Functionally specific reorganization in human premotor cortex. *Neuron* 54:479–490.
- Jenkinson M, Bannister P, Brady M, Smith S (2002) Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage* 17:825–841.

teraction with the EBA, PPA, and FFA, in a task-dependent manner. First, we defined volumes of interest corresponding to the focus of activation of the left and right fO in each functional data from individual subject. We extracted the time course of activity from each voxel of interest, corrected for effects of interest. These time courses were deconvolved to remove the effects of the HRF, multiplied with the psychological regressor of interest, and reconvolved with the canonical HRF. The PPI regressors, together with the fO time series and psychological regressor, were then entered into the general linear model as confound regressors. The parameter estimates were extracted for each subject and region of interest.

For the time-course analyses (Fig. 3 G-I), each subject's BOLD time series was divided into trials, which were resampled to a duration of 20 s, such that the first stimulus on each trial was presented at 0 s and cues were presented at 8 s (averaged) because these were the mean timings for each event across trials and subjects. The resampling resolution was 0.1 s. A general linear model was then fit across trials at every time point in each subject independently. We then calculated group average effect size at each time point and their SEs.

- Woolrich MW, Ripley BD, Brady M, Smith SM (2001) Temporal autocorrelation in univariate linear modeling of FMRI data. *Neuroimage* 14:1370–1386.
- Smith SM (2002) Fast robust automated brain extraction. Hum Brain Mapp 17: 143–155.
- Woolrich MW, Behrens TE, Beckmann CF, Jenkinson M, Smith SM (2004) Multilevel linear modelling for FMRI group analysis using Bayesian inference. *Neuroimage* 21: 1732–1747.





Fig. S1. Accuracy in six conditions in which subjects indicated body (BA), face (FA), and house (HA) stimuli were present under selective and nonselective conditions.

Rossini PM, et al. (1994) Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: Basic principles and procedures for routine clinical application. Report of an IFCN committee. *Electroencephalogr Clin Neurophysiol* 91:79–92.



Fig. S2. Cue-locked activation of the intraparietal sulcus. This region was more active in the nonselective than in the selective condition at a cluster-corrected threshold of P < 0.05, Z > 2.3 shown on the group average MRI scan. Table S1 lists brain areas activated by the nonselective attention > selective attention contrast. Z scores represent peak voxels from a whole-brain random-effects analysis thresholded at 2.3 using a corrected cluster extent significance threshold of P = 0.05.



Fig. S3. fO activation proceeded suppression in the three occipitotemporal regions when subjects were selectively ignoring those stimuli. Time courses for the regressor coefficients relating the FO and the PPA BOLD signal to the HI condition (A), the FO and EBA BOLD signal to the BI condition (B), and the fO and FFA BOLD signal to the FI condition (C) throughout the duration of the trial, respectively. There is an initial peak in the effect size in each occipitotemporal area at the time of initial stimulus presentation, but, unlike the otherwise similar HA, BA, and FA conditions (Fig. 3 G-L), the relationship between the BOLD signal becomes negative at the time of presentation of the match array. The negative trough in the occipitotemporal effect size is consistently preceded by an fO peak in the HA (A), BA (B), and FA (C) conditions.



Fig. S4. Changes in occipitotemporal attentional modulation were not proportional to TMS intensity. Attentional modulation is shown on the abscissas. For example, in the *Upper Left*, the activity in the left EBA that was associated with the BA – BI difference in the pre-TMS and post-TMS stages is compared. The TMS intensity, which varied with each subject's threshold, is shown on the ordinate.

Area	Cluster extent (voxels)	x	У	Ζ	Peak (Z)
Occipito-temporal cortex	852	-48	-74	0	4.11
Occipito-temporal cortex	570	48	-64	-6	4.05
Posterior intraparietal sulcus	366	30	-70	46	3.41
Pontine nucleus	281	8	-22	-42	3.3
Precentral cortex	95	-46	-10	34	3.2
Transverse occipital sulcus	92	-24	-82	8	3.11

Table S1. Regions activated by the nonselective attention > selective attention contrast