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Guided Saccades Modulate Object and Face-Specific Activity in the Fusiform Gyrus

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Abstract: We investigated the influence of saccadic eye movements on the magnitude of functional MRI (fMRI) activation in brain regions known to participate in object and face perception. In separate runs, subjects viewed a static image of a uniform gray field, a face, or a flower. Every 500 ms a small fixation cross made a discrete jump within the image and subjects were required to make a saccade and fixate the cross at its new location. Each run consisted of alternating blocks in which the subject was guided to make small and large saccades. A comparison of large vs. small saccade blocks revealed robust activity in the oculomotor system, particularly within the frontal eye fields (FEF), intraparietal sulcus (IPS), and superior colliculi regardless of the background image. Activity within portions of the ventral occipitotemporal cortex (VOTC) including the lingual and fusiform gyri was also modulated by saccades, but here saccade-related activity was strongly influenced by the background image. Activity within the VOTC was strongest when large saccadic eye movements were made over an image of a face or a flower compared to a uniform gray image. Of most interest was activity in the functionally predefined face-specific region of the fusiform gyrus, where large saccades made over a face increased activity, but where similar large saccades made over a flower or a uniform gray field did not increase activity. These results demonstrate the potentially confounding influence of uncontrolled eye movements for neuroimaging studies of face and object perception. *Hum Brain Mapp 28:691–702, 2007.*

Key words: face processing; fusiform gyrus; fMRI

INTRODUCTION

An extensive literature derived from several experimental modalities has implicated regions of the ventral occipitotemporal cortex (VOTC), including the fusiform gyrus, in face and object processing. For example, subdural electrophysiological recordings [Allison et al., 1994, 1999; McCarthy et al., 1999; Puce et al., 1999], direct cortical stimulation [Allison et al., 1994; Puce et al., 1999], positron emission tomographic (PET) imaging [Haxby et al., 1994; Sergent et al., 1992], and functional MRI (fMRI) [Kanwisher et al., 1997; McCarthy et al., 1997; Puce et al., 1995] studies in humans have identified a discrete region of the fusiform gyrus (FFG) that responds robustly for faces but not for other objects. Neuroimaging studies have also implicated other regions of the VOTC in nonface object processing [Malach

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et al., 1995] and in the processing of higher-order constructs such as place [Epstein et al., 1999].

There is inconsistency in the literature regarding the functional role of the FFG in face processing. Subdural electrophysiological studies have shown that the initial face-specific response in the FFG occurs at ~200 ms and is relatively insensitive to attention, emotional context, familiarity, priming, or memory [McCarthy et al., 1999; Puce et al., 1999]. This pattern suggests that this initial electrophysiological response may reflect an early structural encoding process for faces [McCarthy, 1999]. However, the FFG activations measured in PET and fMRI neuroimaging studies are strongly influenced by top-down processes including attention [Clark et al., 1996; Haxby et al., 1994; Wojciulik et al., 1998], emotional content [Vuilleumier et al., 2001], and familiarity [Henson et al., 2000]. Because these neuroimaging methods have relatively poor temporal resolution and can integrate neural activity over many seconds, it is possible that some variation in VOTC activity evoked by faces and objects may be due to later top-down or recurrent processing [Puce et al., 1999]. Top-down processing may also influence the manner in which a subject scans a face or object with eye movements, and thus uncontrolled and potentially systematic differences in subjects' patterns of eye saccades and fixations, or scanpaths, could account for some variation in FFG activity evoked by faces and objects.

Here we directly tested our thesis in normal adults by guiding subjects' saccades with a crosshair while subjects viewed a static background picture of a face, a flower, or a uniform gray field. In successive blocks subjects alternated between making small or large saccades to fixate the crosshair as it made discrete jumps over the picture, and we determined whether these differences in saccade patterns modulated activity in VOTC. Critically, we tested whether differences in saccades and fixations made over a background picture of a face differentially modulated activity in face-specific regions of the FFG when compared to the same pattern of saccades and fixations made over a background picture of a flower or over a uniform gray field. In a separate study, we tested whether activity in these same FFG regions was influenced when subjects switched between making saccades over pictures of a face and flower that were simultaneously present in the same background image.

MATERIALS AND METHODS

Subjects

We report here the results of an eye-tracking experiment conducted outside of the scanner and two fMRI experiments. These three experiments were conducted separately and with different groups of subjects. Each experiment was approved by the Duke University Institutional Review Board and all subjects provided informed consent. All subjects had normal or corrected-to-normal vision and all were screened against neurological and psychiatric illnesses.

Eight subjects (ages 19–27; four female, four male) participated in the eye-tracking study. Twelve subjects (ages 19–34 years; eight female, four male) participated in fMRI Study I. Eight subjects (ages 19–28 years; four female, four male) participated in fMRI Study II.

Experimental Design

Eye-tracking study

Eye-tracking data were collected on a Tobii 1750 eye-tracker with 50 Hz sampling. Subjects were seated with their head fixed in a chin and forehead rest and with their eyes positioned 50 cm from the center of the monitor. The purpose of the eye-tracking study was to determine whether subjects could accurately fixate a small cross as it made discrete jumps in location over different background images.

Each subject participated in a single experimental session in which eye fixation data were acquired for three experimental conditions. On each run the subject viewed a single image that remained unchanged while a small fixation cross superimposed on the image made discrete jumps every 500 ms to a different location on the image. The subject was required to make a saccade and fixate the cross at each new location. The run was divided into 10 alterations of a 12-s block in which subjects made large saccades to widely separated locations on the background image, followed by a 12-s block in which subjects made small saccades localized in the center of the image. Figure 1 illustrates the experimental design for the Face background condition. The Flower and Gray Field conditions were identical to the Face condition, with only the background image differing.

The order of background image was counterbalanced across subjects and the eye-tracker was calibrated before each experimental run. Each run started and ended with a blinking central fixation cross that persisted for 5 s and to which subjects were required to fixate and which was used as an internal calibration to rule out changes in the accuracy of eye-tracking over the duration of the run.

The three different background images were a single human face, a flower, and a uniform gray field. The uniform gray field subtended a visual angle of 14° wide and 23° high. Both the flower and face background images subtended a visual angle of 13° wide and 15.5° high and each was superimposed on the same uniform gray field described above. The average Euclidean distance of a fixation cross jump for the large saccade condition was 5.30°, while the average Euclidean distance of a fixation cross jump during the small saccade condition was 1.70°.

Prior research has indicated that faces are scanned in a stereotypical fashion in which most fixations are made on the core features, with ~70% of all fixations made to the eyes [Klin et al., 2002; Luria and Strauss, 1978; Pelphrey et al., 2002; Walker-Smith et al., 1977]. To avoid confound-

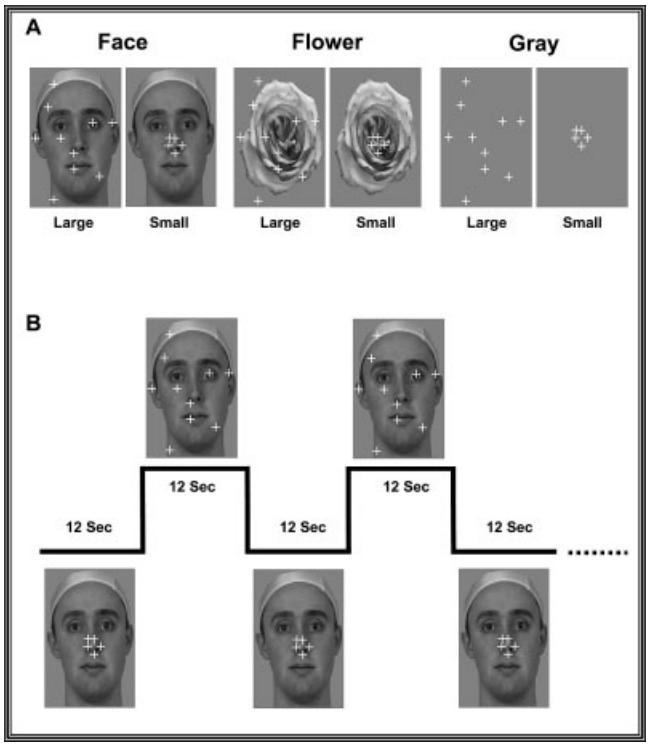

Figure 1.

Experimental design. **A:** The different types of background images: face, flower, and gray field along with all possible locations of the fixation cross for both large and small saccade conditions. In each run subjects alternated between making large and small saccadic eye movements in order to track a yellow fixation cross over one of these three background images. The sequence of crosshair jumps on each block was different. **B:** The design for one run in the experiment. In this run the face background is present throughout the entire duration of the run. The run was divided into 10 alterations of a 12-s block in which subjects made small saccades localized in the center of the image, followed by a 12-s block in which subjects made large saccades to widely separated locations on the face. (Note that the fixation cross is shown here in white for visual clarity.)

ing the influence of relative eye movements on activity in face- and object-processing regions of the brain with fixations on the eye, the fixation cross jumps landed on the eyes on only 20% of jumps in the large saccade blocks of the Face condition. For the small saccade blocks in the Face condition the fixation cross jumps were centered on the tip of the nose.

fMRI Study I

The main experimental task used a design similar to that employed in the eye-tracking study with changes made to accommodate the dimensions of the visual display system. There were six runs consisting of the Face, Flower, and Gray Field conditions, with the order of runs counterbalanced across subjects. The uniform gray field subtended a visual angle of 14° wide and 25° high. Both the flower and face background images subtended a visual angle of 10.35° wide and 17.5° high, and each image was superimposed on the same uniform gray field described above. The average Euclidean distance of a fixation jump for the large saccade condition was 6.25°. During the small saccade blocks the fixation cross made a maximum excursion of 1.2° in the X dimension and 1.88° in the Y dimension. The average distance of a fixation jump for the small saccade condition was 0.75°. The fixation jumps in the large saccade condition were constrained to an invisible central rectangle 10.9° wide and 22.4° high, and thus could land anywhere within or slightly outside of the background image. The small saccades were restricted to an invisible central rectangle 1.2° wide and 1.88° high.

In addition to these six experimental runs we collected two runs of a face-localization task to independently identify face-selective voxels in the VOTC. Each localizer run consisted of 10 alternations of a 12-s block of faces (24 different faces per block or 2 faces/s) followed by a 12-s block of flowers (24 different flowers per block).

fMRI Study II

As a follow-on to the main fMRI experiment, a second fMRI study was conducted in which the background image contained a face on one side and a flower on the other side of a narrow black central strip. The face and flower images switched sides between runs. As before, a small fixation cross made discrete jumps in location every 500 ms. Each run consisted of three repeating blocks, each block having a 12-s duration. In the first block, subjects fixated the cross as it made large jumps restricted to the face. In the second block, subjects fixated the cross as it made small jumps restricted to the center of the black strip. In the third block, subjects fixated the cross as it made large jumps restricted to the flower. The order of the face and flower blocks was reversed for half of the runs. The instruction to fixate was reinforced by requiring subjects to indicate via button press whenever the cross momentarily changed to 75% of its normal size, which occurred at random six times throughout each of the six experimental blocks. Pilot testing indicated that this was a difficult detection task that required subjects to attend to the cross.

The entire display subtended a visual angle of 27.5° wide by 19.1° high. Both the face and flower images subtended a visual angle of 12.11° wide by 19.1° high, while the central black field subtended a visual angle of 3.53° wide by 19.1° high. The average Euclidean distance of a fixation jump in the large saccade condition was 2.35° wide by 3.54° high, while the average Euclidean distance of a fixation jump in the small saccade condition was 0.91° wide by 0.78° high.

Imaging

Scanning was performed on a General Electric 4T LX NVi MRI scanner system equipped with 41 mT/m gradients (GE, Waukesha, WI). A quadrature birdcage radiofrequency (RF) head coil was used for transmit and receive. The subject's head was immobilized using a vacuum cushion and tape. Sixty-eight high resolution images were acquired using a 3D fast Spoiled-Grass (SPGR) pulse sequence (TR = 500 ms; TE = 20 ms; FOV = 24 cm; image matrix = 256^2; voxel size = 0.9375 × 0.9375 × 1.9 mm) and used for coregistration with the functional data. These structural images were aligned in a near axial plane defined by the anterior and posterior commissures. Whole-brain functional images were acquired using a gradient-recalled inward spiral pulse sequence [Glover and Law, 2001; Guo and Song, 2003] sensitive to blood oxygenation level-dependent (BOLD) contrast (TR, 1500 ms; TE, 35 ms; FOV, 24 cm; image matrix, 642; $\alpha = 62^\circ$; voxel size, 3.75 × 3.75 × 3.8 mm; 34 axial slices). The functional images were aligned similar to the structural images. A semiautomated high-order shimming program ensured global field homogeneity.

Data Analysis

Eye-tracking study

The accuracy of the eye tracker was rated by the manufacturer as 0.5–1°. A fixation was defined as an interval of at least 160 ms in which the eye position remained within the confines of a circle with a ~1° radius. An accurate fixation was defined as a fixation that occurred with within ~2° of the center of the cross.

fMRI Study I

Image preprocessing was performed with custom programs and SPM modules (Wellcome Department of Cognitive Neurology, UK). Head motion was detected by center of mass measurements. No subject had greater than a 3-mm deviation in the center-of-mass in any dimension. Images were time-adjusted to compensate for the interleaved slice acquisition and then motion-corrected to compensate for small head movements.

Our primary analysis employed a functional region of interest (ROI) approach in which the ROIs were defined for each individual by the results of his or her functional localizer runs. In the localizers, face-specific activity was identified by measuring the *t*-difference in activation for faces and flowers in the localizer task. Each subject's time-adjusted functional data was plotted on his or her anatomy and face-related activity was defined as activity in the VOTC where faces evoked significantly more activity than flowers ($P < 0.01$). Activity within these face-specific regions was then measured for large and small saccade blocks when the background image was a face, a flower, or a uniform gray field. These functional ROI analyses comprised the primary method for evaluating the influence of saccades on face-specific brain regions in VOTC.

Our secondary analysis employed a voxel-based analytical approach. These additional voxel-based analyses were performed as a check to confirm the individual ROI analysis and to search in an exploratory manner for other brain regions in which the activation evoked by saccades was modulated by the background image. The realigned and motion-corrected images used for the ROI analysis described above were first normalized to the Montreal Neurological Institute (MNI) template found in SPM 99. These normalized functional data were then high-pass filtered and spatially smoothed with an 8 mm isotropic Gaussian kernel prior to statistical analysis. These normalized and smoothed data were used in the remaining analyses described below. The purpose of these voxel-based analyses was to identify all brain regions differentially activated by large vs. small saccades, and to identify all voxels in the brain for which differences in saccade activation could be attributed to the content of the background image.

A random-effects assessment of the differences among the three conditions (face, flower, and gray field) at the peak of the hemodynamic response (HDR) was performed. This analysis consisted of the following steps: 1) The epoch of image volumes beginning two images before (–3.0 s) and 16 images after (27 s) the onset of each large saccade block was excised from the continuous time series of volumes, allowing us to visualize an entire cycle of large and small saccade blocks. 2) The average intensity of the HDR peak (6–18 s) was computed. A *t*-statistic was then computed at each voxel within the brain to quantify the HDR differences among the three conditions. This process was performed separately for each subject. 3) The individual t-maps created in the preceding step were then subjected to a random-effects analysis that assessed the significance of differences across subjects.

To reduce the number of statistical comparisons, the results of the random-effects analyses computed above were then restricted to only those voxels in which a significant HDR was evoked by any of the three different conditions. For this analysis we thresholded our activation at a false discovery rate (FDR) [Genovese et al., 2002] of 0.001 ($t(11) > 5.81$). The voxels with significant HDRs were identified in the following steps: 4) The single trial epochs for each subject were averaged separately for each of the three conditions and the average BOLD-intensity signal values for each voxel within the averaged epochs were converted to percent signal change relative to the prestimulus baseline. 5) The time waveforms for each voxel were correlated with a canonical reference waveform and *t*-statistics were calculated for the correlation coefficients for each voxel. This procedure provided a whole-brain t-map in MNI space for each of the three conditions. 6) The t-maps for each subject and for each condition were used to calculate an average t-map for the union of all three trial types across subjects. We then identified active voxels as those that surpassed the FDR threshold. 7) The difference t-map computed in Step 3

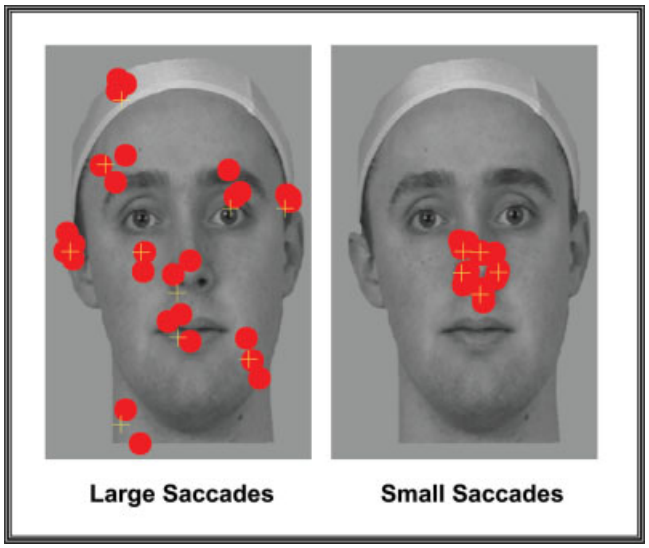

Figure 2.
Eye-tracking results. The results from one representative subject demonstrating relative difference in the amount of eye movements made in the large saccade vs. small saccade condition. Each red sphere reflects a fixation made by the subject while the yellow crosshairs indicate locations to where the fixation cross jumped during the run.

above was then masked by the results of Step 6. Thus, the differences in HDR amplitude between conditions were only evaluated for those voxels in which at least one condition evoked a significant HDR as defined above. The threshold for significance in the HDR peak was set at $P < 0.01$ (two-tailed, uncorrected) and a minimal spatial extent of 12 uninterpolated voxels.

fMRI Study II

The analysis procedures were similar to fMRI Study I described above. Each subject's time-adjusted and motion-corrected functional images were analyzed for the ROIs defined by the results of each subject's functional localizer runs. In the localizers, face-specific activity was identified by measuring the *t*-difference in activation for faces and flowers in the localizer task. Each subject's time-adjusted functional data was plotted on his or her anatomy and face-related activity was defined as activity in the VOTC where faces evoked significantly more activity than flowers ($P < 0.01$). Activity within these face-specific regions was then measured for large saccades made over either a face or flower, and small saccades made with the central black strip. These functional ROI analyses comprised the only method for evaluating the influence of saccades on face-specific and face-nonspecific brain regions in VOTC, as separate voxel-based analyses were not employed for this experiment.

RESULTS

Eye-Tracking Study

Subjects achieved a high level of accuracy by acquiring 93% of all targets across the three experimental conditions. A within-subjects analysis of variance showed no main effect of background picture on accuracy. Figure 2 plots the average fixations for both small and large saccade condi-

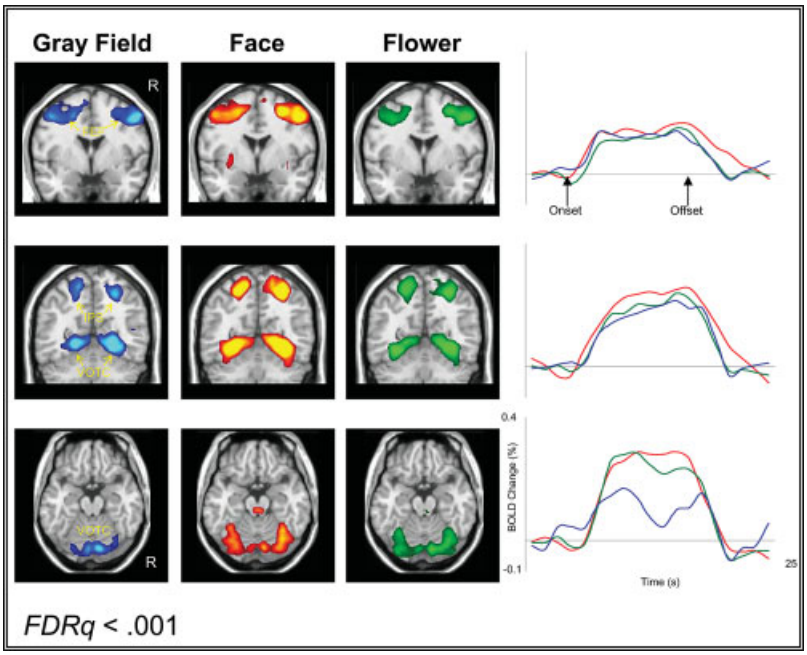

Figure 3.
Active regions. Grand-average *t*-maps plotted on a template brain. The *t*-maps were thresholded at an FDR of $P < 0.001$ ($t > 5.25$), based on the union of the three experimental conditions. The plots reflect activation evoked by large saccades collapsed across each background condition at this threshold. The waveform plots reflect the average evoked response for the onset of large saccade blocks from voxels that were identified on the basis of the FDR analysis. The top panel shows activity, measured in percent change in BOLD signal, from voxels in the frontal eye fields, the middle panel shows activity from the intraparietal sulcus, and the bottom panel shows activity from the ventral occipitotemporal cortex.

tions for one representative subject taken from the face background condition.

fMRI Study I

Brain regions in which differences between large and small saccades evoked a significant HDR

Each of the three conditions evoked significant activation in regions previously identified as participating in the oculomotor system. The overlays in Figure 3 depict regions in which we found a significant difference across subjects ($t_{(11)} = 5.25$, $P < 0.001$) between the large and small saccade blocks for the Face, Flower, and Gray Field background conditions. Large saccades evoked significant activity in bilateral frontal eye fields (FEF) (top panel, Talairach coordinates: X = 42, Y = –2, Z = 47; X = –26, –4, 48), IPS (middle panel, Talairach coordinates: X = 30, Y = –66, Z = 48; X = –20, –58, 51), and VOTC (bottom panel, Talairach coordinates: X = 30, Y = –54, Z = –9; X = –34, –58, –9). As can be appreciated from the waveform plots, activation evoked by large saccades in the FEF and IPS was roughly equivalent for each of the three background images. This was also true for the superior colliculi (not shown). However, the saccade-evoked VOTC activation had a much larger spatial extent for the Face and Flower conditions compared to the Gray Field condition.

Ventral occipitotemporal cortex (VOTC)

In VOTC, large saccades evoked greater activity than small saccades when made over each of the three background pictures. Figure 4A displays two different random-effects contrasts. First, the red overlay indicates regions of the VOTC where activity evoked by large saccades during the Face condition was greater than that evoked by large saccades during the Gray Field condition ($P < 0.01$). The green overlay indicates regions of the VOTC where activity evoked by large saccades during the Flower condition was greater than that evoked by large saccades during the Gray Field condition ($P < 0.01$). Figure 4B represents the pattern of activation at peak for both the left and right VOTC. Activity evoked during the large saccade blocks was clearly influenced by the presence of a face or flower background compared to a uniform field.

Fusiform gyrus

The measurement of saccade-related activity in each subject's face area as defined by the results of his or her individual face localizer task was used to test our main hypothesis that fusiform face activity is influenced by the pattern of saccades made over a face picture. Figure 5A displays the average amplitude and time course of activation evoked in each individual's face area for the transition from flowers to faces in the functional localizer task (black line), and for the transition from small to large saccades with Face, Flower, and Gray Field background images (red, green, and blue lines, respectively). Figure 5B repeats the saccade task data in Figure 5A on a more sensitive scale. As is evident in this figure, the transition from small to large saccades over a face background image evokes considerable and significant amplitude variability in the face-specific area. Indeed, the amplitude variation due to saccades is roughly one-seventh that observed in the face localizer task. In striking contrast, saccades made over flower and gray field backgrounds evoked little or no variation in the activation in the face region.

We confirmed these individual subject analyses with a voxel-based analysis of normalized data and identified regions where the large saccade blocks evoked greater activity for face backgrounds than gray fields (blue overlay of Fig. 5C) and where the large saccade blocks evoked greater activity for face backgrounds than flower backgrounds (red overlay). The focal region indicated in red for this group analysis corresponds to the modal location of each individual's face-specific region as determined by the face-localizer task. Finally, a conjunction analysis revealed a large region of VOTC where the large saccade blocks evoked greater activity for both face and flower backgrounds when compared with activity evoked by large saccades made over a gray background. Within these voxels a small subset of voxels evoked significantly more activity for large saccades made over a face background relative to large saccades made over the flower background. The location of these voxels corresponded to the functional ROI defined in the primary analysis and thus confirmed the results of the localizer-based analysis.

As described in Materials and Methods, we also used a voxel-based analysis in an exploratory manner to search for other brain regions in which saccade-related activity was modulated by the background image. The only significant cluster occurred in the right postcentral gyrus and extended posteriorly into the superior parietal lobule (Talairach coordinates: 35, –48, 62) where large saccades over the face image evoked twice the HDR amplitude than did large saccades over the flower or the gray field, which did not differ from each other. Interestingly, this area was not activated in the face localizer task.

fMRI Study II

Subjects accurately detected the small and brief changes in the size of the fixation cross on 86.4% of occurrences. There was no significant difference in detection during saccades made during face or flower saccade conditions ($P > 0.05$). The results from each subject's independent face localizer runs defined two distinct regions within the VOTC. The average spatial location for these regions is plotted on a template brain in Figure 6. The red color map in Figure 6A is the grand-average t-map evoked by the block presentation of faces ($t > 6$), while the green color map in Figure 6B shows the grand-average t-map evoked by the presentation of flowers ($t > 6$). Figure 6A displays the average amplitude and time course of activation evoked in each individual's face area for the transition from large saccades made over

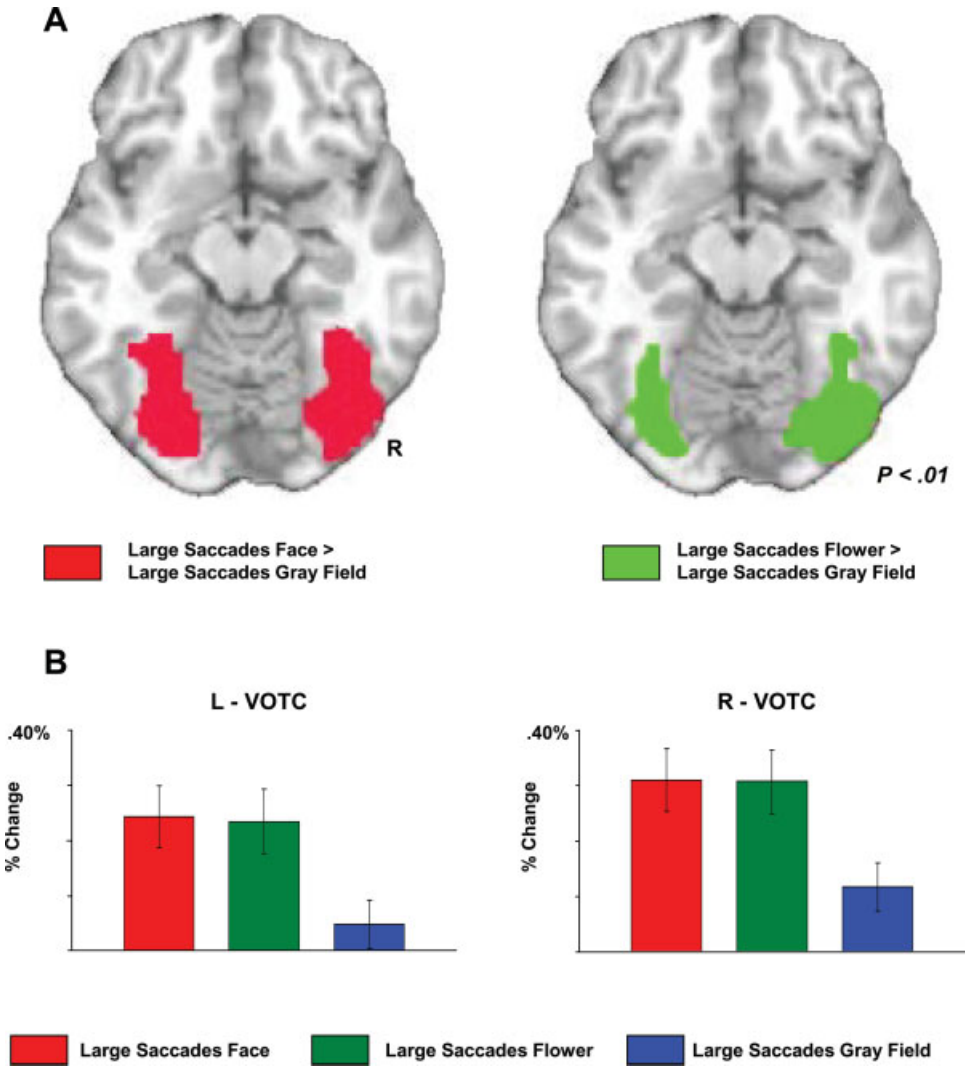

Figure 4.

Ventral occipitotemporal activation. **A:** Regions that displayed significant random-effects contrasts in the VOTC. The red color map represents voxels that responded stronger for large saccadic eye movements made over a face when compared to the same movements made over a uniform gray screen ($P < 0.01$). The green color map represents voxels that responded stronger for large saccadic eye movements made over a flower when compared to the same movements made over a uniform gray screen ($P < 0.01$). **B:** Peak activation in the left and right VOTC for each of the three experimental conditions.

faces to small saccades made in the central portion of the image, followed by large saccades made over the flower and back to small fixation saccades to close out one experimental cycle. Figure 6B displays the average amplitude and time course of activation evoked in each subject's functionally defined flower area for one experimental cycle. The interaction of anatomy (Face or Flower ROI) by background picture over which saccades were made (Face or Flower picture) was significant, $F_{(1,7)} = 72.52$, $P < 0.0001$. While large saccades made over the face picture evoked significant activation in the localizer derived face ROI, large saccades made over the picture of a flower evoked little or no activity ($t_{(7)} = 5.8$, $P < 0.001$). Within the localizer-derived flower ROI, large saccades made over the face picture evoked significantly less activity than that evoked when large saccades were made over the flower picture ($t_{(7)} = 4.09$, $P < 0.01$).

DISCUSSION

The results from our eye-tracking study revealed that subjects can accurately perform the large and small saccade task over different background pictures. Although no eye-tracking was performed in the magnet, these results strongly suggest

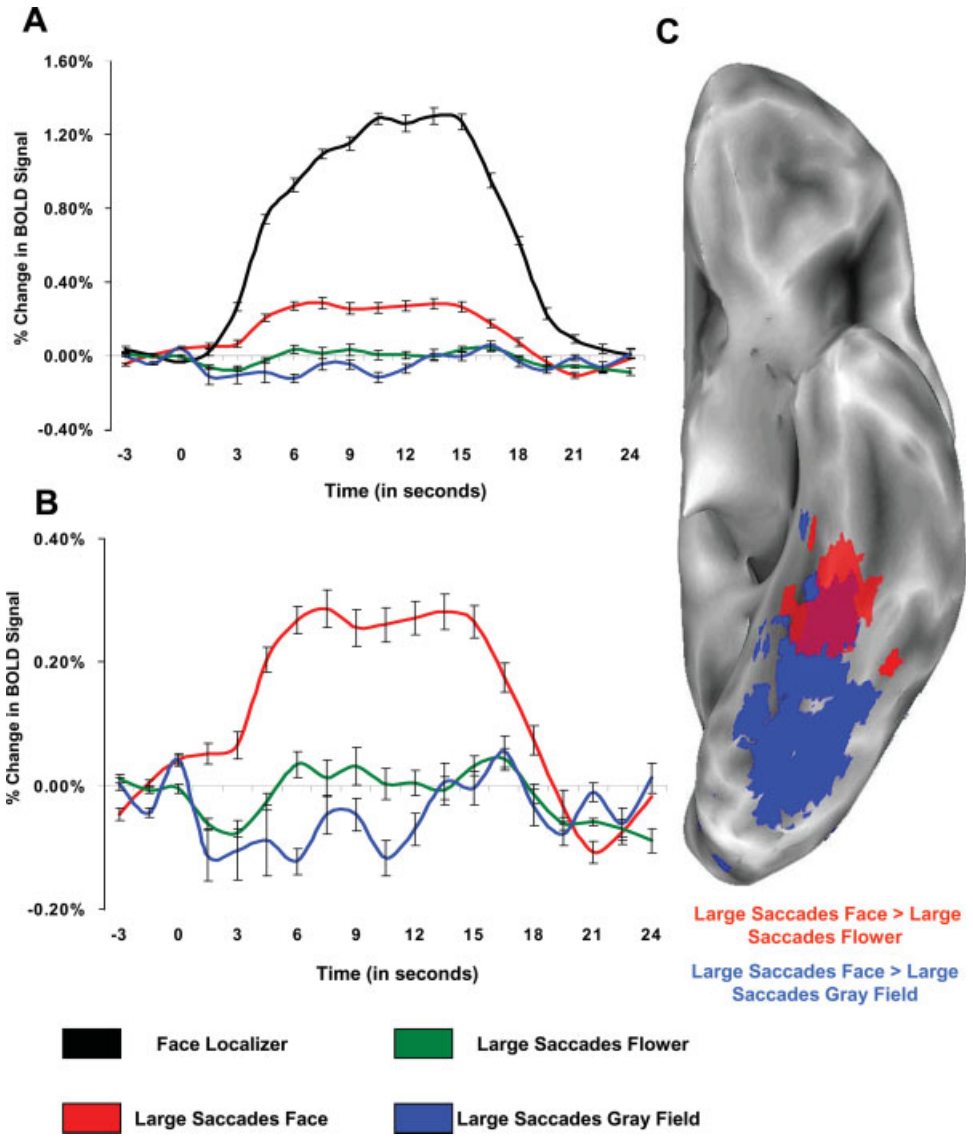

Figure 5.

Face-related activity in the VOTC. A,B: The results of a functional ROI analysis conducted on individual subjects. The face-specific region of the VOTC was identified for each subject based on the results of a localizer scan. We then quantified activity in this region for large saccadic eye movements made over each of our three different backgrounds. **A:** The response to faces in the localizer task; **B:** excludes this response. **C:** The results of random-effects analysis where peak amplitude varied across condition. The blue color map represents a region of the VOTC where large saccades made over a face were greater than those made over a uniform gray screen ($P < 0.01$). The red color map represents a region of the VOTC where large saccades made over a face were greater than those made over a flower.

that subjects in the fMRI tasks should have been able to perform similarly. The results of the main fMRI experiment demonstrate that systematic differences in scanpaths—here operationalized as differences between small and large guided saccades—cause systematic differences in the amplitude of the BOLD hemodynamic response in VOTC. Furthermore, these saccade-dependent differences depend on the nature of the stimulus over which the saccades were made. Guided saccades over a uniform gray field evoked the least activation within VOTC and this activation occurred primarily within the posterior lingual gyrus. Guided saccades over a background picture of a flower or face evoked stronger and more spatially extensive activation that included much of the lingual and fusiform gyri. Of critical importance, guided saccades over an image of a face evoked significant variation in the activation obtained within the functionally defined face

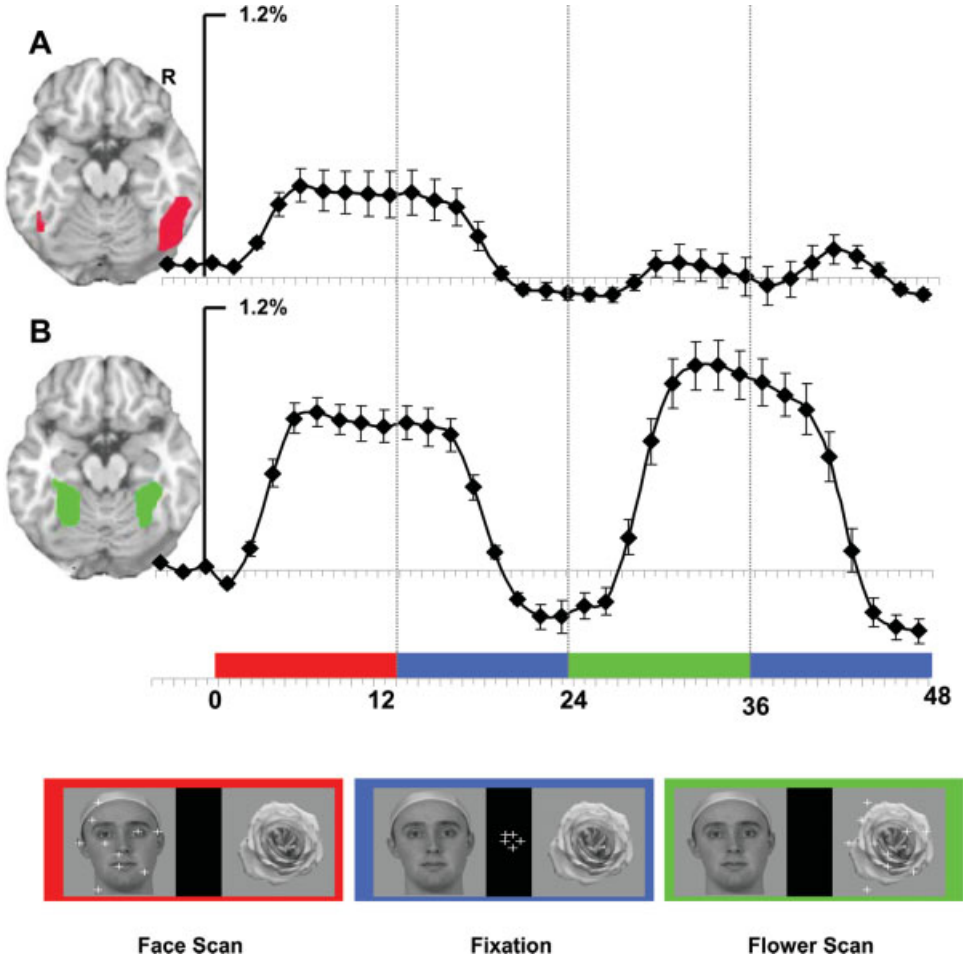

Figure 6.

Face and flower related activity in the VOTC. **A:** The results of the functional ROI analysis. The face and flower specific region of the VOTC was identified for each subject based on the results of a localizer scan. The red color map in **A** represents the average face area calculated across subjects and plotted on a template brain. The green color map in **B** represents the average flower area calculated across subjects and plotted on a template brain. **A:** The average amplitude and time course of activation evoked in each subject's predefined face area across an entire experimental cycle. In this ROI, large saccades made over the face picture evoked significant activation, while large saccades made over the flower image evoked little or no activation. **B:** The average amplitude and time course of activation evoked in each subject's predefined flower area across an entire experimental cycle. Within this ROI, large saccades made over the face evoked significantly less activity than that evoked when making large saccades over the flower. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

area in the right fusiform gyrus. Similar saccades over an image of a flower or uniform gray field evoked no variation in the activation of the face area.

The second fMRI study extends the results of the first by demonstrating that within a multiobject scene, activation within the predefined face and flower regions is strongly influenced by the object (face or flower) over which the subject is currently making saccades and fixations. By introducing a task in which subjects had to detect a brief and subtle change in the size of the fixation cross, we further strengthened our experimental control of eye movements. As the detection task was demanding of attention, it further deemphasized the relevance of the background picture. Nevertheless, the ~0.3% increase in amplitude of the HDR from the functionally localized face area due to large saccades was the same as in the first fMRI study. Although not the focus of the present study, it is notable that there was virtually no activity in the functionally localized face area when the subject made saccades over the flower.

The results of both fMRI tasks raise theoretical questions and practical concerns. With respect to the former, the mechanism by which the guided saccades modulate VOTC activity is undetermined. We purposefully used a single static face and a single static flower throughout the session

to minimize novelty. In addition, each run started with a 6-s free viewing period to further encourage stimulus habituation. Our background pictures were similar in visual angle to those used in other studies of face and object perception (for example, Kanwisher et al. [1997] used faces that subtended ~15° in their initial fMRI study). Attention was drawn to the jumping fixation cross (reinforced by task demands in fMRI Study II) and not to the background pictures that were never relevant to the subject's task. Our working hypothesis is that the large saccades caused subjects to reexperience the sensory and featural details of the object. This may have enabled the subject to extract more information from the picture and/or refresh a degrading percept. In the case of our guided saccade manipulation, these perceptual gains would be incidental. However, we believe that nontask-guided saccades may have a similar perceptual and information gathering purpose.

The practical concerns raised by these results are obvious—uncontrolled but systematic differences in scanpaths can lead to differences in activation that are misattributed to other task manipulations. Many manipulations influence scanpaths. For example, face familiarity has been shown to systematically influence scanpaths in both humans [Rizzo et al., 1987] and nonhuman primates [Gothard et al., 2004]; thus, it is possible that these differences in scanpaths can account for significant variation in FFG activation. Indeed, prior neuroimaging studies have demonstrated that FFG activation evoked by faces is modulated by face familiarity, although the nature of the modulation is controversial. Some studies have reported a stronger response to familiar faces [Eger et al., 2005; Henson et al., 2000; Leveroni et al., 2000], while others have reported hypoactivation of the FFG for familiar faces [Dubois et al., 1999; Rossion et al., 2001, 2003].

Perhaps more pertinent are recent neuroimaging studies that have investigated the neural basis of social perception in typical adults and those with autism or other disorders. Atypical scanning of faces has been reported in autism [Klin et al., 2002; Pelphrey et al., 2002], schizophrenia [Loughland et al., 2002a,b; Manor et al., 1999], and social phobia [Horley et al., 2003, 2004]. While several studies have shown that faces evoke less FFG activation in individuals with autism than in typically developing individuals [Critchley et al., 2000; Pierce et al., 2004; Schultz et al., 2000], a recent study using an eye-tracking system in the scanner found that activation in the FFG and amygdala in autistic subjects was strongly correlated with the amount of time spent as the autistics fixated the eyes of the face stimulus [Dalton et al., 2005]. This correlation suggests that FFG hypoactivation to faces in individuals with autism might reflect systematic differences in scanpaths when compared to controls rather than fundamental dysfunction in the FFG face area. The study by Dalton et al. [2005] thus raises the bar for experimental control in this important area of research. Eye-tracking in the fMRI environment has become less expensive and more reliable, but it still represents a technical challenge. As an alternative approach, Beauchamp [2003] has introduced a method for direct measurement of eye movements in the scanner by measuring changes in the MR time series from the vitreous of the eye.

It is noteworthy that while the right posterior superior temporal sulcus (pSTS) showed strong activation in the face localizer task, it showed little or no saccade-related signal variation. Prior studies from our laboratory [Pelphrey et al., 2003a,b, 2005; Puce et al., 1998] and others [Beauchamp et al., 2003; Bonda et al., 1996; Grossman et al., 2000; Grossman and Blake, 2002] have shown that the pSTS is involved in the perception of biological motion—such as gaze shifts and mouth movements. It is also noteworthy that several brain areas that were strongly influenced by eye movements, such as the FEF, IPS, and superior colliculi, showed no differences related to the background image over which the saccades were made.

Our saccade manipulation was artificial and not comparable to the kind of saccades made in normal perception. We accept this criticism, but as we have diminished the task-relevance and novelty of the face and flower pictures, we believe it unlikely that the unguided inspection of novel images by eye movements in normal perception would yield less activation variation than that observed here. Thus, our results raise cautions for studies using scenes with multiple objects and faces. Indeed, Hasson et al. [2004] demonstrated functional selectivity for preferred objects in face and object processing regions during free-viewing. Activation evoked in these areas was greatest for frames focused exclusively on the region's preferred stimulus.

The flower picture background had strong symmetry, and so the large differences in activation evoked during small and large saccade blocks could be reasonably attributed to the magnitude of the saccades. This is less certain for the face background, as faces have core features such as eyes and mouths that may be more important for activation of face processing regions than other features such as the nose or chin. Thus, it may be possible to construct qualitatively different scanpaths of the face that involve saccades of identical visual angle that nevertheless land near different face features and evoke different levels of activation. We are currently investigating this possibility. However, such a result would neither diminish nor invalidate the methodological importance of the present findings.

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