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Effect of head orientation on gaze processing in fusiform gyrus and superior temporal sulcus

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Abstract

We used functional MRI with an event-related design to dissociate the brain activation in the fusiform gyrus (FG) and posterior superior temporal sulcus (STS) for multiple face and gaze orientations. The event-related design allowed for concurrent behavioral analysis, which revealed a significant effect of both head and gaze orientation on the speed of gaze processing, with the face and gaze forward condition showing the fastest reaction times. In conjunction with this behavioral finding, the FG responded with the greatest activation to face and gaze forward, perhaps reflecting the unambiguous social salience of congruent face and gaze directed toward the viewer. Random effects analysis showed greater activation in both the FG and posterior STS when the subjects viewed a direct face compared to an angled face, regardless of gaze direction. Additionally, the FG showed greater activation for forward gaze compared to angled gaze, but only when the face was forward. Together, these findings suggest that head orientation has a significant effect on gaze processing and these effects are manifest not only in the STS, but also the FG.

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Introduction

Humans have the remarkable ability to extract information regarding mental state, direction of attention, and intentions from facial expression and direction of gaze. These abilities are critical components of normal human social interaction. The acquisition of information from faces presumably requires several hierarchical processing stages, including recognizing the constellation of facial features, identifying the face, determining facial expression and direction of gaze, and then placing this information into a social context (Bruce and Young, 1986; Halgren et al., 1994; Sergent, 1995).

Research on automatic processing of low-level facial

features has provided consistent evidence of the role of the fusiform gyrus (FG) in the representation of fixed facial features. This research was prompted by the discovery that prosopagnosic patients who display specific deficits in identifying faces almost always have lesions in the ventral temporal lobe (De Renzi et al., 1991; Meadows, 1974; Sergent and Signoret, 1992). Neuroimaging, surface and intracranial EEG, and MEG studies of face perception have provided supportive evidence of the role of the FG in face processing (Clark et al., 1996; Eimer and McCarthy, 1999; George et al., 1996; Halgren et al., 1994, 2000; Kanwisher et al., 1997; McCarthy et al., 1997, 1999; Puce et al., 1995; Sergent et al., 1992; Sergent and Signoret, 1992).

More recently, the posterior superior temporal sulcus (STS) also has been implicated in processing facial features, particularly the more changeable features like gaze direction. In the monkey, neurons have been found in the STS that respond selectively to face and gaze direction (Perrett et al., 1985). Neuroimaging studies have shown similar involvement of the STS in face processing in humans. Several

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Fig. 1. Examples of stimuli. The stimuli consisted of 60 unique, static pictures of faces with neutral expressions and one of four combinations of gaze and face orientation: (1) face and gaze directed forward; (2) face forward, gaze averted 45 degrees; (3) face averted 45 degrees, gaze forward; and (4) face averted 45 degrees, gaze averted 45 degrees.

studies have shown STS activation when viewing static faces (George et al., 2001; Halgren et al., 1999; Hoffman and Haxby, 2000; Kanwisher et al., 1997). STS activation also has been shown during perception of eye and mouth movement (Puce et al., 1998; Wicker et al., 1998).

The distinct roles of the FG and STS in face processing are not known. Hoffman and Haxby (2000) have attempted to differentiate the functions of these regions by looking at variations in task instructions. They found that subjects had greater activation in the FG when instructed to pay attention to the identity of the person and greater activation in the STS when instructed to attend to the direction of gaze (Hoffman and Haxby, 2000). The present study attempts to further elucidate the roles of the FG and STS by investigating activation in these regions in response to viewing multiple face and gaze orientations.

The effect of head and gaze orientation on brain activation is unclear from current literature. Monkey studies have indicated that there is a differential response in STS cells to different face and gaze orientations (Perrett et al., 1982, 1985). These monkey studies revealed that cells with preference for a specific face direction also prefer the corresponding gaze direction (i.e., cells that respond to face forward also show greatest response to direct gaze) (Perrett et al., 1985). Furthermore, Perrett et al. (1985) found that sensitivity to gaze direction could override sensitivity to

head orientation, which provided support for a model in which gaze direction could affect perception of head orientation, but not vice versa.

Only two studies with limited subject numbers ($N = 7$) have attempted to differentiate brain activation in humans for specific views of the face (George et al., 2001; Tong et al., 2000). George et al. (2001) used a block-design functional MRI (fMRI) study to investigate brain activation when subjects viewed varying face and gaze orientations (a 2×2 factorial design of head and gaze orientation). In the study, subjects were asked to determine the gender of the faces they viewed. Although both FG and STS activation was observed during the task, no difference in activation in either of these regions was revealed for the comparison of head orientation, regardless of gaze orientation. The only effect of head orientation was found in the posterior striate and extrastriate regions (V1/V2) and the left motor cortex, which showed greater activation when viewing frontal versus angled head orientations, regardless of gaze angle. Tong et al. (2000) used fMRI to look specifically at the fusiform face area and found no differences in activation for frontal versus profile view of the head, when subjects passively viewed the faces or performed a one-back matching task. However, the study revealed decreasing FG activation as the head orientation was rotated further away from view, with the least activation for a view of the back of the head.

Additional functional imaging studies have tried to differentiate the response to direct gaze versus averted gaze, but there is no evidence of a consistent distinct response to either of these gaze orientations. One study found greater activation in the right amygdala for direct gaze versus averted gaze in a gaze discrimination task (Kawashima et al., 1999). In a second study, subjects who passively viewed faces showed greater activation in the left STS and bilaterally in the intraparietal sulcus (IPS) to averted gaze in comparison to direct gaze (Hoffman and Haxby, 2000). A recent study showed greater activation in the FG, but not the STS, for forward gaze compared to averted gaze during a gender determination task (George et al., 2001).

To further investigate these inconsistencies of brain activation in response to variations in head and gaze orientation, especially with respect to activation in the FG and STS, we used event-related fMRI with a 2×2 factorial design of head and gaze orientation. Since there is clear evidence that the FG is involved in featural processing of the face, and since angled head orientation provide altered views of facial features, we hypothesized that FG activation would be modulated by variations in head orientation. Since the STS has recently been implicated in processing changeable aspects of the face such as gaze direction and since monkey studies revealed cells responsive to face and gaze direction, we hypothesized that STS activation would be modulated by variations in both head and gaze direction.

lution = $1.5 \times 0.9 \times 1.2$ mm. The images were reconstructed as a $124 \times 256 \times 256$ matrix with a $1.5 \times 0.9 \times 0.9$ -mm spatial resolution.

The task was programmed using PsyScope (Cohen et al., 1993) on a Macintosh (Cupertino, CA) notebook computer. Initiation of scan and task was synchronized using a TTL pulse delivered to the scanner timing microprocessor board from a “CMU Button Box” microprocessor (<http://poppy.psy.cmu.edu/psyscope>) connected to the Macintosh. Stimuli were presented visually at the center of a screen using a custom-built, magnet-compatible projection system (Resonance Technology, CA).

Image processing

Images were reconstructed, by inverse Fourier transform, for each of the 135 time points into $64 \times 64 \times 18$ image matrices (voxel size: $3.75 \times 3.75 \times 7$ mm). fMRI data were preprocessed using SPM99 (<http://www.fil.ion.ucl.ac.uk/spm>). Images were corrected for movement using least-square minimization without higher order corrections for spin history, and normalized to stereotaxic Talairach coordinates (Talairach and Tournoux, 1988). Images were then resampled every 2 mm using sinc interpolation and smoothed with a 4-mm Gaussian kernel to decrease spatial noise.

fMRI data analysis

Statistical analysis was performed on individual and group data using the general linear model and the theory of Gaussian random fields as implemented in SPM99 (Friston et al., 1995). This method takes advantage of multivariate regression analysis and corrects for temporal and spatial autocorrelations in the fMRI data. Activation foci were superposed on high resolution T1-weighted images and their locations interpreted using known neuroanatomical landmarks (Duvernoy and Bourgouin, 1999; Mai et al., 1997).

A within-subjects procedure was used to model all the effects of interest for each subject. Individual subject models were identical across subjects (i.e., a balanced design was used). Confounding effects of fluctuations in global mean were removed by proportional scaling where, for each time point, each voxel was scaled by the global mean at that time point. Low frequency noise was removed with a high pass filter (0.5 cycles/min) applied to the fMRI time series at each voxel. We then defined the effects of interest for each subject with the relevant contrasts of the parameter estimates.

Group analysis was performed using a random effects model that incorporated a two-stage hierarchical procedure. This model estimates the error variance for each condition of interest across subjects, rather than across scans (Holmes and Friston, 1998) and therefore provides a stronger generalization to the population from which data are acquired.

This analysis proceeded in two steps. In the first step, contrast images for each subject and each effect of interest were generated as described above. In the second step, these contrast images were analyzed using a general linear model to determine voxelwise *t* statistics. One contrast image was generated per subject for the face-minus-scrambled-image contrast. A two-way *t* test was then used to determine group activation for each effect. Finally, the *t* statistics were normalized to *Z* scores, and significant clusters of activation were determined using the joint expected probability distribution of height and extent of *Z* scores (Poline et al., 1997), with height ($Z > 2.33$; $P < 0.01$) and extent thresholds ($P < 0.05$).

Functional ROI analysis

Structural regions of interest (ROI) were drawn for each individual subject on spatially normalized high resolution structural images. For each subject, activation in the FG and posterior STS was identified using the structural ROI and the fMRI data from the blocked study. This activation constituted a subject-specific functional ROI, which was used for the event-related study. A repeated-measures ANOVA was used to analyze the difference in percent activated voxels ($Z > 1.67$) for each of the four face and gaze angle conditions. The following definitions were used to determine the boundaries of each structural ROI (drawn on consecutive coronal slices):

Fusiform gyrus

The anterior slice of the FG is defined as the slice on which white matter of the anterior commissure is thickest across the midline. The lateral border of the FG is defined by the lateral occipitotemporal sulcus. The inferior border is delineated by following the inferior surface of the cortical matter. The medial border of the FG is defined as the collateral sulcus. The posterior border of the FG is determined in two steps. First, the sagittal plane tangent to the lateral border of the amygdala is identified. Second, in the previously identified sagittal slice, the coronal plane crossing at the level of the posterior transverse collateral sulcus delineates the most posterior slice of the FG.

Posterior superior temporal sulcus

Allison et al. (2000) identified an extended region around the posterior STS that may be involved in processing changeable aspects of the face. For this study, the STS structural ROI includes the STS, middle temporal gyrus (MTG), and superior temporal gyrus (STG). The combined STG/MTG is measured in the coronal plane in images that have been positionally normalized and aligned to Talairach stereotaxic space. The boundaries of the STG/MTG are defined laterally by the cortical surface, and medially by a line connecting the deepest extension of the middle temporal sulcus to the furthest extent of the inferior ramus of the sylvian fissure. The most anterior slice of the STG/MTG

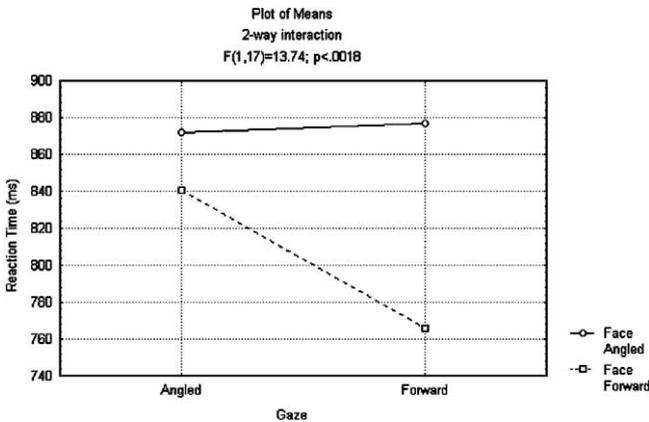


Fig. 2. Mean reaction times for each condition. The fastest reaction times were observed for the face forward, gaze forward condition.

coincides with the coronal slice in which gray matter of the temporal lobe first appears. The most posterior slice of the STG coincides with the slice containing the branch point of the sylvian fissure (into superior and inferior limbs) or simply the end of the sylvian fissure if no branch point exists. The MTG continues to extend posteriorly after the disappearance of the STG. The most posterior slice of the MTG coincides with the disappearance of the inferior temporal sulcus into the superior temporal, occipitotemporal, or intraparietal sulcus (Ono et al., 1990). The total MTG, STG, STS region is divided into an anterior, middle, and posterior third. Recent research has shown STS activation in response to face and gaze to be located in the posterior STS region (Allison et al., 2000) and the block study results identified a region of the activation in the posterior STS region, so the posterior third of the designated region was used for the ROI analysis.

A repeated-measures ANOVA of percent activation within the ROIs was performed with the ROI (FG vs. posterior STS) as the first within-subjects factor, head orientation (angled face vs. forward face) as the second within-subjects factor, gaze direction (angled gaze vs. forward gaze) as the third within-subjects factor, and hemisphere (right vs. left) as the fourth within-subjects factor.

Results

Task performance

Accuracy for all four experimental conditions was high ($99 \pm 4\%$) and repeated-measures ANOVA revealed no significant difference in the accuracy for any of the four conditions. Repeated-measures ANOVA demonstrated a significant effect on RT of both head orientation [$F(1,17) = 54.27, P < 0.0001$] and gaze direction [$F(1,17) = 10.04, P < 0.006$] (mean AA reaction time, 872 ms; mean AF reaction time, 877 ms; mean FA reaction time, 841 ms; mean FF

reaction time, 766 ms). There also was a significant interaction between head orientation and gaze direction [$F(1,17) = 13.74, P < 0.002$], with subjects demonstrating the fastest RT for the face forward, gaze forward condition (Table 1, Fig. 2).

Brain activation

Block design—faces versus scrambled condition

In the block design task, group activation for the experimental versus scrambled condition was observed bilaterally in the FG and lingual gyrus. Right hemisphere activation was observed in the middle temporal gyrus, superior temporal sulcus, lateral occipitotemporal sulcus, cingulate gyrus, cuneus, calcarine sulcus, and cerebellum. Left hemisphere activation was found in the inferior occipital gyrus, middle occipital gyrus, lateral occipital sulcus, and parahippocampal gyrus, extending into the brainstem (Table 2, Fig. 3).

Main effect of head orientation

Face forward minus face angled. To elucidate the main effect of head orientation on brain activation, we examined the comparisons of the two face forward conditions (FF and FA) minus the two face averted conditions (AF and AA) and vice versa. The face forward minus face averted comparison [(FF + FA) – (AF + AA)] demonstrated signifi-

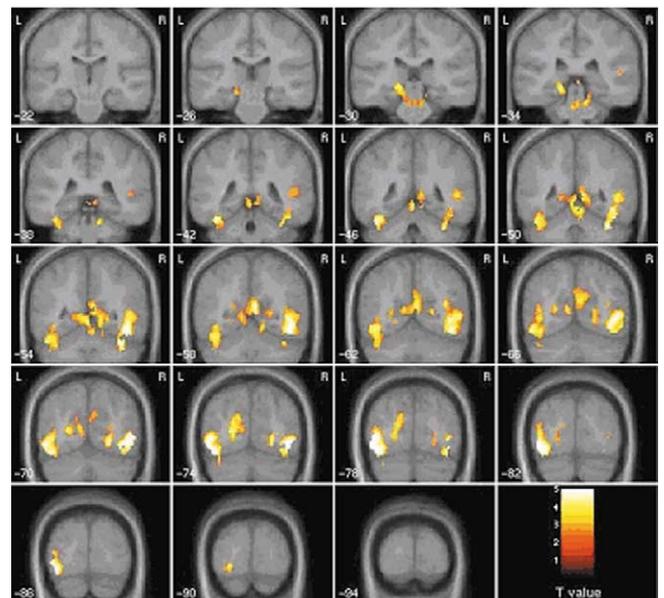


Fig. 3. Brain activation in the block design study for the experimental vs. scrambled condition. Average activation during the face-processing task is shown as a montage of successive 2.4-mm-thick coronal slices, superimposed on corresponding average structural images. The y-axis coordinates are presented as Montreal Neurological Institute (MNI) values. Left parahippocampal activation is apparent in the first row. The activation in the right superior temporal sulcus and fusiform becomes visible in the second row. The pattern of fusiform, as well as inferior occipitotemporal activation, continues through the bottom three rows.

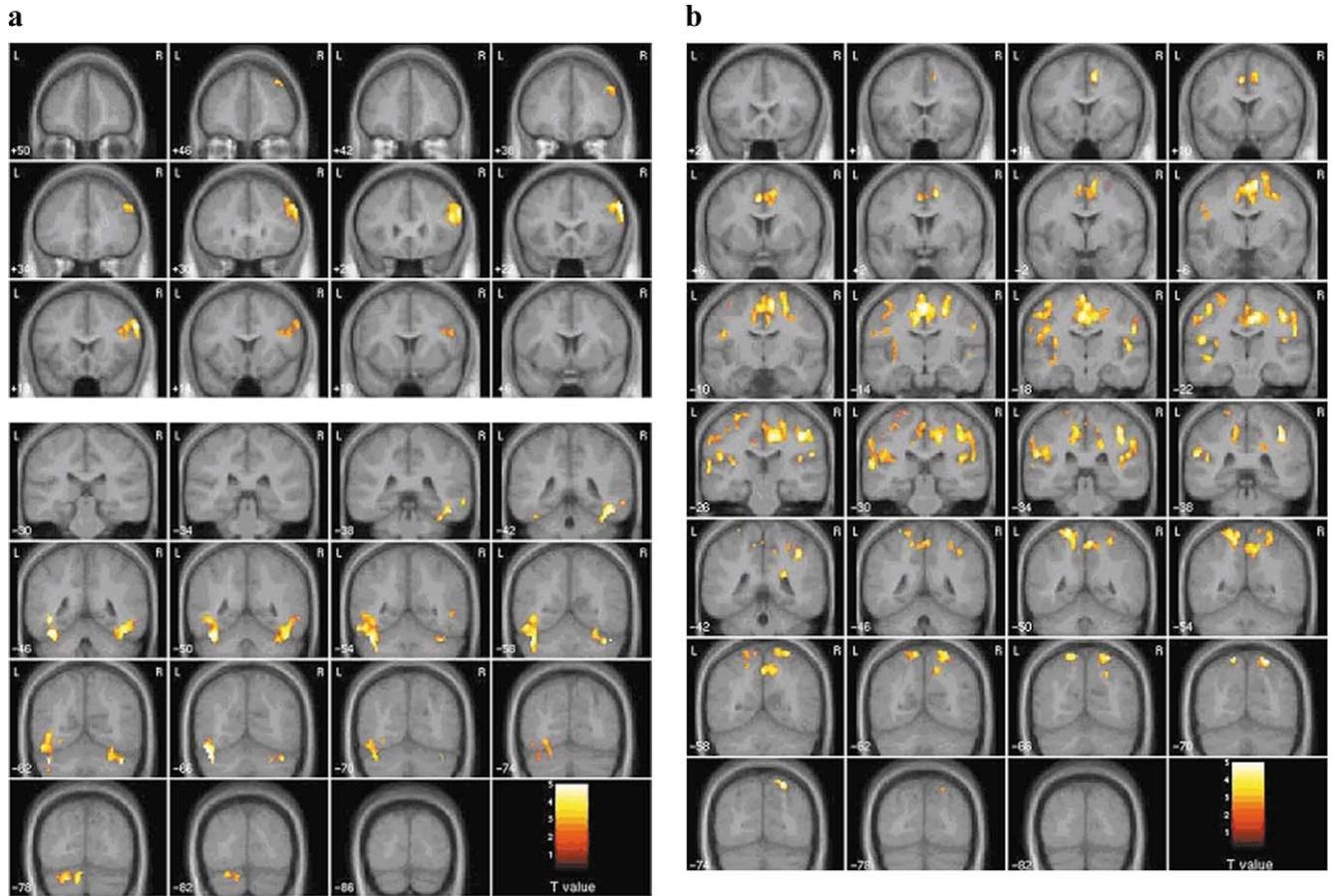


Fig. 4. (a) Brain activation for the forward face minus angled face contrast [(FF + FA) - (AF + AA)]. Average activation for the forward face minus angled face contrast is shown as a montage of successive 2.4-mm-thick coronal slices, superimposed on corresponding average structural images. The y-axis coordinates are presented as MNI values. Right inferior frontal activation is apparent in the top three rows. The pattern of fusiform, inferior occipitotemporal, and cerebellar activation can be seen in the bottom four rows. (b) Brain activation for the angled face minus forward face contrast [(AF + AA) - (FF + FA)]. Average activation for the angled face minus forward face contrast is shown as a montage of successive 2.4-mm-thick coronal slices, superimposed on corresponding average structural images. The y-axis coordinates are presented as MNI values. Anterior cingulate activation is apparent in the first row. The cingulate activation, as well as superior frontal activation can be seen in the second row. Activation in the inferior parietal gyrus, cingulate, and intraparietal sulci can be seen in the next two rows. The pattern of superior parietal and posterior cingulate activation can be seen extending through the bottom three rows.

cant differential activation bilaterally in the FG, lateral occipitotemporal sulcus, and cerebellum. Significant clusters also were found in the right middle frontal gyrus and left inferior occipital sulcus and gyrus (Table 3, Fig. 4a).

Face angled minus face forward. The face averted minus face forward comparison [(AF + AA) - (FF + FA)] revealed significant clusters of activation bilaterally in the cingulate gyrus, intraparietal sulcus, and inferior parietal gyrus. Additional activation was found in the right superior frontal sulcus, central sulcus, postcentral sulcus, superior temporal gyrus and in the left superior parietal gyrus, supramarginal gyrus, and parietal operculum (Table 3, Fig. 4b).

Main effect of gaze direction

To determine the main effect of gaze direction on brain activation, we looked at the comparison of the two direct

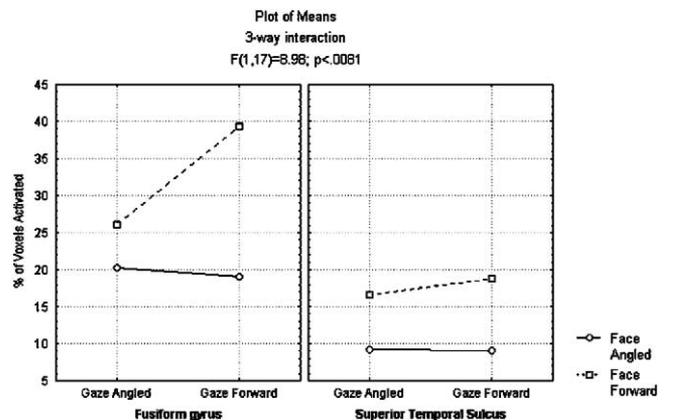


Fig. 5. Mean activation in the fusiform gyrus and superior temporal sulcus for each condition. The greatest activation in both the superior temporal sulcus (STS) and fusiform gyrus (FG) was observed for the face forward, gaze forward condition. For both the STS and FG, there was significantly greater activation for the face forward conditions than the face angled conditions.

Table 1
Repeated-measures ANOVA of reaction times revealed a significant effect of both head orientation and gaze direction

Within-subjects factor	df effect	MS effect	df error	MS error	F	P level
Face	1	90895.20	17	1674.80	54.27	0.001
Gaze	1	22045.67	17	2196.57	10.04	0.006
Face × gaze	1	28170.55	17	2050.27	13.74	0.002

gaze conditions (FF and AF) minus the two averted gaze conditions (FA and AA) and vice versa. No significant activation was seen in either of these comparisons.

Functional ROI analysis—FG and posterior STS

To further dissociate the effect of face and gaze orientation on activation in the FG and posterior STS, we conducted an analysis using ROIs derived from activation data in the block gaze experiment. Repeated-measures ANOVA was conducted with the two ROIs (FG and posterior STS) as the first factor, the two head orientations (face angled and face forward) as the second factor, the two gaze orientations (gaze angled, gaze forward) as the third factor, and the two hemispheres as the fourth factor (Table 4, Fig. 5). The analysis revealed a significant interaction between ROI, head orientation, and gaze direction [$F(1,17) = 8.98, P < 0.008$].

To further investigate this interaction, repeated-measures ANOVA was conducted independently for the FG and posterior STS. The two head orientations (face angled and face forward) were used for the first within-subjects factor; the two gaze orientations (gaze angled and gaze forward) were used for the second factor; and the two hemispheres were used as the third factor. The analysis of the FG revealed a significant effect of head orientation [$F(1,17) = 20.30, P < 0.000$] as well as an interaction between head and gaze orientation [$F(1,17) = 9.31, P < 0.007$] (Table 5a). The effect of gaze direction on FG activation was nearly significant [$F(1,17) = 3.65, P < 0.073$]. In contrast, the analysis of the posterior STS revealed only a significant effect of

head orientation on activation [$F(1,17) = 13.36, P < 0.002$] (Table 5b).

Because of the possible complex social interpretation of the various face and gaze combinations, we further investigated the effect of gaze orientation with a simplistic comparison of the face forward, gaze forward (FF) condition with the face forward, gaze angled (FA) condition conducted independently for FG and posterior STS. In the repeated-measures ANOVA, the two gaze orientations served as the first within-subjects factor and the two hemispheres served as the second within-subjects factor. Significantly greater activation for the gaze forward condition was found in the FG [$F(1,17) = 7.91, P < 0.012$], but not in the STS [$F(1,17) = 0.42, P < 0.527$].

Discussion

To our knowledge, this is the first study to use an event-related design to investigate FG and posterior STS activation during gaze processing. This study provides evidence that both head and gaze orientation significantly affect gaze processing. The 2×2 factorial design, with head orientation (face forward vs. face angled) as one factor and gaze orientation (gaze forward vs. gaze angled) as a second factor, allowed investigation of effects of both head and gaze orientation on gaze processing. The behavioral analysis revealed a significant effect of both head and gaze orientation on the speed of gaze processing, with the face and gaze forward (FF) condition showing the fastest reaction times. In conjunction with this behavioral finding, analysis of regional activation revealed that the FG responded with the greatest activation to face and gaze forward (FF), perhaps reflecting the unambiguous social salience of congruent face and gaze directed toward the viewer. The ROI analysis showed significantly greater activation in both the FG and posterior STS for face forward (FF + FA) compared to face angled (AF + AA) conditions. These results suggest a more significant effect of head orientation on perception of gaze direction than has been suggested by

Table 2
Brain activation in the block design study during experimental conditions contrasted with control activation*

Activated regions in cluster	No. of voxels	Cluster <i>P</i> value (corrected)	Z max (primary peak)	Primary peak location	Brodmann's area (peak)
Left inferior occipital gyrus, middle occipital gyrus, fusiform gyrus, lateral occipital sulcus	1894	0.001	4.88	-44, -80, -6	19
Right cerebellum, fusiform gyrus, middle temporal gyrus, superior temporal sulcus, lateral occipitotemporal sulcus	1839	0.001	4.62	34, -52, -21	37
Right cingulate, cuneus, calcarine sulcus; bilateral lingual gyrus	2056	0.001	3.98	2, -55, 18	23
Left parahippocampal gyrus, brainstem	309	0.031	3.84	-18, -32, -8	35

* Areas of activation include bilateral fusiform gyrus (FG) and left superior temporal sulcus (STS).

Table 3
Brain activation for face angle comparisons*

Activated regions in cluster	No. of voxels	Cluster <i>P</i> value (corrected)	Z max (primary peak)	Primary peak location	Brodmann's area (peak)
(a) Forward face – angled face [(FF + FA) – (AF + AA)]					
Right middle frontal gyrus	787	0.001	4.69	56, 20, 32	9
Left fusiform gyrus, lateral occipitotemporal sulcus, cerebellum, inferior occipital sulcus & gyrus	1305	0.001	4.50	–50, –65, –10	37
Right fusiform gyrus, lateral occipitotemporal sulcus, cerebellum	703	0.001	3.99	44, –39, –11	37
(b) Angled face – forward face [(AF + AA) – (FF + FA)]					
Bilateral cingulate sulcus & gyrus; right superior frontal sulcus, central sulcus, postcentral sulcus; left superior parietal gyrus	4242	0.001	4.83	20, –67, 56	7
Right inferior parietal gyrus, adjacent superior temporal gyrus, intraparietal sulcus	1089	0.001	4.53	42, –23, 42	2
Left intraparietal sulcus, inferior parietal gyrus, supramarginal gyrus, parietal operculum	1455	0.001	3.93	–57, –34, 24	40

* Areas of activation for the face forward minus face angled conditions include bilateral fusiform gyrus (FG).

previous models. Additionally, the FG showed increased activation for forward gaze (FF) compared to angled gaze (FA), but only when the face was directed toward the viewer. These findings suggest that, while the posterior STS is equally activated by direct and averted gaze for a given head orientation, activation in the FG is modulated by an interaction between head and gaze direction. In addition to these findings in the FG and STS, our study also implicates the involvement of other regions, such as the intraparietal sulcus (IPS) and cingulate gyrus, in a broader distributed network responsible for face and gaze processing.

The event-related design of this study provided a unique opportunity to concurrently investigate behavioral findings that could shed light on the significance of differences in brain activation. There are limited behavioral studies that investigate effects of head and gaze orientation on the processing of gaze direction, and no other imaging studies of gaze processing have provided a behavioral analysis in conjunction with their imaging findings. In this study, accuracy in determining gaze direction was similar for all the head and gaze orientations. However, both gaze direction and head orientation significantly affected reaction times,

Table 4

Repeated-measures ANOVA of activation in the fusiform gyrus and STS revealed a significant 3-way (ROI {fusiform gyrus, STS} × head orientation {face angled, face forward} × gaze direction {gaze angled, gaze forward}) interaction

Within-subjects factor	<i>df</i> effect	MS effect	<i>df</i> error	MS error	<i>F</i>	<i>P</i> level
ROI	1	11745.84	17	1047.37	11.21	0.004
Face	1	8438.38	17	340.91	24.75	0.001
Gaze	1	880.49	17	427.95	2.057	0.170
Hemisphere	1	1676.19	17	559.61	3.00	0.102
ROI × face	1	365.66	17	160.59	2.28	0.150
ROI × gaze	1	431.86	17	157.67	2.73	0.116
Face × gaze	1	1261.31	17	200.74	6.28	0.023
ROI × hemisphere	1	149.54	17	330.71	0.45	0.510
Face × hemisphere	1	29.23	17	113.51	0.26	0.618
Gaze × hemisphere	1	211.30	17	100.03	2.11	0.164
ROI × face × gaze	1	646.30	17	71.94	8.98	0.008
ROI × face × hemisphere	1	108.95	17	86.60	1.26	0.278
ROI × gaze × hemisphere	1	14.03	17	43.78	0.32	0.579
Face × gaze × hemisphere	1	293.30	17	160.49	1.83	0.194
ROI × face × gaze × hemisphere	1	108.77	17	156.65	0.69	0.416

Table 5
Repeated-measures ANOVA of activation in the FG and in the STS

Within-subjects factor	<i>df</i> effect	MS effect	<i>df</i> error	MS error	<i>F</i>	<i>P</i> level
(a) Fusiform gyrus activation						
Face	1	6158.60	17	303.46	20.30	0.001
Gaze	1	1272.81	17	349.06	3.65	0.073
Hemisphere	1	1413.52	17	616.24	2.29	0.148
Face × gaze	1	1856.69	17	199.46	9.31	0.007
Face × hemisphere	1	12.66	17	77.83	0.16	0.692
Gaze × hemisphere	1	167.12	17	86.44	1.93	0.182
Face × gaze × hemisphere	1	379.65	17	102.52	3.70	0.071
(b) Superior temporal sulcus activation						
Face	1	2645.44	17	198.04	13.36	0.002
Gaze	1	39.53	17	236.57	0.167	0.688
Hemisphere	1	412.21	17	274.08	1.50	0.237
Face × gaze	1	50.93	17	73.22	0.70	0.416
Face × hemisphere	1	125.53	17	122.28	1.03	0.325
Gaze × hemisphere	1	58.21	17	57.37	1.01	0.328
Face × gaze × hemisphere	1	22.42	17	214.61	0.10	0.750

with fastest reaction times for the face forward, gaze forward (FF) condition. The analysis also revealed a significant interaction of face and gaze orientation. These findings are consistent with recent studies that suggest that gaze processing is mediated by both head and gaze orientation. Langton (2000) used a Stroop-like interference paradigm in which head orientation and gaze direction conflicted. The study revealed that incongruent gaze direction slowed reaction times to head orientation, and similarly incongruent head orientation slowed response to gaze direction. These results are consistent with our findings, although our results suggest that the effect of gaze angle on reaction time is most significant when the face is forward. In another recent study, subjects were shown a face with varying head and gaze orientations. After the face stimulus, an asterisk was shown to either the left or right of a central fixation point. Subjects were instructed to press the left or right response key as soon as possible after seeing the asterisk (Hietanen, 1999). Hietanen (1999) found that incongruent head and gaze orientations affected reaction times more than congruent head and gaze orientations. When the face was forward and the gaze was angled in the direction of the asterisk, the response times were faster than for any of the conditions in which the face and gaze were aligned. When the face was forward, and the gaze was angled in the opposite direction of the asterisk, the response time was slower than for the conditions in which the face and gaze were aligned. Although the Hietanen (1999) study did not focus on the gaze direction, their results nevertheless are consistent with our findings of significant interaction between gaze and head orientation. The implication of these studies is that both head and gaze orientation affect how we determine another person's gaze direction. More specifically, these results suggest that head orientation affects the perception of gaze direction, which contrasts a previous model proposed by Perrett et al. (1992) in which gaze direction could affect perception of head

orientation but not vice versa. The results of the current study in conjunction with the Langton (2000) study indicate that the Perrett et al. (1992) model needs to be extended to allow for effects of head orientation on gaze processing.

Consistent with previous studies, we observed activation in both fusiform gyrus and STS during gaze processing. FG activity during face processing has been shown in several ERP (McCarthy et al., 1999; Taylor et al., 1999), MEG (Halgren et al., 2000), PET (Kuskowski and Pardo, 1999; Sergent et al., 1992; Sergent and Signoret, 1992), and fMRI (Clark et al., 1996; Puce et al., 1995) studies. Additionally, the STS has recently been implicated as an ancillary region involved in face processing, specifically in processing changeable aspects of the face including gaze direction (George et al., 2001; Halgren et al., 1999; Hoffman and Haxby, 2000; Kanwisher et al., 1997; Puce et al., 1998; Wicker et al., 1998).

In congruence with the behavioral findings discussed above, the ROI analysis revealed that the FG activation (Fig. 6) followed an inverse pattern compared to the reaction times for each condition (Fig. 2). In other words, face and gaze conditions that had the fastest reaction times also showed the greatest activation in the FG. Furthermore, the greatest activation in both the FG and posterior STS region was observed for the face forward, gaze forward condition. This result corresponds with the shortest reaction times for the face forward, gaze forward condition. The increased activation in the FG and posterior STS in the face and gaze forward condition can thus be interpreted in terms of more efficient face processing and determination of gaze direction for this condition. Findings by Perrett et al. (1985) that specific cells in monkey STS show greatest activation for congruent face and gaze orientation (i.e., face forward, gaze forward) may provide explanation for increase efficiency in processing these congruent orientations. It is possible that

cells in human FG and STS have an analogous preference for congruent face and gaze orientation.

The ROI analysis illuminates the complex interaction of face and gaze orientation and its effect on FG and posterior STS activation during gaze processing. Repeated-measures ANOVA revealed a significant three-way interaction between region, head orientation, and gaze direction. Both the FG and posterior STS showed significantly greater activation for face forward (FF + FA) compared to face angled (AF + AA). This finding was supported by the voxel-by-voxel, whole brain comparison of face forward orientation versus face angled orientations irrespective of gaze direction [(FF + FA) – (AF + AA)], which revealed significant differential activation bilaterally in the FG and posterior STS. Neither the ROI nor the whole brain analysis revealed significant effect of gaze alone in either the FG or posterior STS. However, in the FG, but not the posterior STS, a significant interaction of face and gaze direction was detected. In other words, there are gaze effects in the FG that are dependent on the face being directed toward the viewer. When the face was directed toward the viewer, the FG showed greater activation in response to forward gaze compared to averted gaze. This finding was further supported by the independent analysis of the gaze orientation for the two face forward conditions, which revealed significantly greater activation in the FG when gaze was forward.

Since the FG and posterior STS are both involved in featural processing of the face, increased activation in both of these regions when viewing a forward face is likely due to the ability of subjects to more effectively detect and recognize distinct facial features compared to an averted facial view. Work by Perrett et al. in single temporal cells in monkey supports the finding of differential sensitivity to dissimilar face orientation (Perrett et al., 1982, 1985). However, ours is the first human imaging study to show significant differential activation in key face-processing brain regions for direct versus averted faces. In contrast to our findings, two recent fMRI studies found no significant differences in activation in the FG when viewing a frontal versus angled view of the face. The first study found no significant differences in activation for a frontal versus a profile view of the face (Tong et al., 2000), while the second study found no differential activation in the FG when a frontal facial view was compared to an angled view (George et al., 2001).

The lack of significant findings for the front versus angled view of the face in these two studies may, in part, be secondary to small subject numbers [$N = 5$ (Tong et al., 2000) and $N = 7$ (George et al., 2001)], compared to the present study ($N = 18$). The study by Tong et al. (2000) provided evidence of decreased FG activation as head orientation was rotated past the profile view away from the viewer. It is possible that a larger number of study participants in that study would have revealed differential activation for smaller changes in head orientation, as was shown in our study. In addition, both previous studies used block

designs, as opposed to the event-related design in this study. Subjects in the previous studies were not exposed to varying head and gaze orientations within a block, and thus did not need to explicitly determine gaze direction for each face, which may have led to reduced capability of the studies to discriminate the differential neural components of face and gaze processing. Also, each of the previous studies utilized behavioral tasks that were different from that used in the present study. In the study by George et al. (2001), subjects were asked to determine gender; in the study by Tong et al. (2000), subjects were asked either to passively view the stimuli or to perform a one-back matching task. This is in contrast to the present study where subjects were asked to explicitly determine gaze direction. Recently, Hoffman and Haxby (2000) found that brain activation during face processing is affected by the task instructions. Specifically, they found that FG activation was greater when subjects tried to identify the face compared to trying to determine gaze direction, while STS activation is greater when subjects were asked to determine gaze direction (Hoffman and Haxby, 2000). It is possible that the task context and instructions may similarly affect differential brain activation in response to variations in head and gaze orientation. Further studies should investigate activation in the FG and STS in the context of different task requirements, such as determining the identity of the face or determining head orientation. Furthermore, our results underscore the importance of investigating brain activation and also providing parallel information on the behavioral effects with specific task instructions.

The finding that gaze direction does not modulate activation in the posterior STS is not necessarily inconsistent with the hypothesis that the STS is involved in gaze processing. The fMRI results support the role of the STS in processing gaze direction, but suggest that when subjects are asked to pay attention to gaze direction, the composite activation in the posterior STS is invariant for different gaze directions. Studies by Perrett et al. (1982, 1985) identified subsets of STS cells that are selective for direct or averted gaze. Analogous subregions of the STS in humans that may be activated by distinct gaze directions could be difficult to detect by the present ROI analysis. Our whole brain, voxel-by-voxel analysis also did not reveal these subregions, but there remains the possibility that the spatial resolution was not sufficient to detect these effects.

Although the focus of this study was on the roles of the FG and posterior STS, there is clearly a broader distributed network involved in gaze and attention processing. Depending on the context of the task requirements, other regions may be involved in the integration and processing of information from the face and gaze. In the present study, the comparison of angled face versus a frontal face view [(AF + AA) – (FF + FA)] indicated that compared to a frontal face view, an angled face may cause stronger activation in brain regions involved in spatial processing and attention. Specifically, the activation in the parietal lobe and cingulate

gyrus in that comparison may be related to processing visuospatial information related to head and gaze orientation. There is evidence that the IPS is normally activated during tasks that involve determining another person's direction of attention and shifting one's own attention accordingly (Corbetta, 1998; Corbetta et al., 2000; George et al., 2001; Hoffman and Haxby, 2000; Nobre et al., 1997). Recent evidence also suggests that both the anterior and posterior cingulate gyri are involved in processing spatial information (Mesulam et al., 2001; Nobre et al., 1997; Vanderberghe et al., 2001). Monkey studies have revealed interconnections of the posterior parietal cortex (including the IPS) with premotor cortex, frontal eye fields, and the cingulate gyrus (Mesulam et al., 1977; Pandya et al., 1981). Anatomic studies in monkeys have also demonstrated projections from the upper bank of the STS to the inferior IPS (Harries and Perrett, 1991). These connections may represent a pathway by which information about face and gaze orientation is transferred to regions involved in spatial processing as part of the overall network responsible for determining another person's direction of attention.

Although we did not identify amygdala activation in this study, it is possible that the scanning parameters for this study did not allow for sufficient resolution to fully characterize the response in the amygdala. Several studies have identified amygdala involvement in face and gaze perception with affect neutral faces (Aylward et al., 1999; Courchesne, 1997; Kawashima et al., 1999; Leonard et al., 1985), and further studies are necessary to fully investigate its role in the broad network involved in face and gaze processing.

A thorough understanding of the neural networks involved in processing face and gaze angle may have great significance in social and clinical research. The importance of face and gaze processing in social interactions is well recognized in the psychological literature. An accurate model of the neural processes involved in determining another person's direction of attention may advance our understanding of disorders such as fragile X syndrome (Baumgardner et al., 1995) and autism (Pierce et al., 2001), in which patients show significant dysfunction in reading social cues from face and gaze.

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