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Asymmetric modulation of human visual cortex activity during 10° lateral gaze (fMRI study)

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We used BOLD fMRI to study the differential effects of the direction of gaze on the visual and the ocular motor systems. Fixation of a target straight ahead was compared to fixation of a target 10° to the right and 10° to the left from gaze straight ahead, and to eyes open in complete darkness in thirteen healthy volunteers. While retinotopic coordinates remained the same in all fixation conditions, the fixation target shifted with respect to a head-centered frame of reference. During lateral fixation, deactivations in higher-order visual areas (one ventral cluster in the lingual and fusiform gyri and one dorsal cluster in the postero-superior cuneus) and, as a trend, activations in early visual cortical areas were found predominantly in the hemisphere contralateral to the fixation target. We propose that visual processing is performed predominantly in the hemisphere contralateral to gaze direction, even during small gaze shifts into one visual hemifield. The excitability of visual neurons may be modulated depending on eye position to construct a head-centered frame of reference from a retinotopic input, thus allowing perceptual stability of space during eye movements. A further finding was that BOLD signal increases in fronto-parietal ocular motor and attentional structures were more pronounced during lateral than central fixation.

Keywords: Eccentric fixation; Lateral gaze; fMRI; Attention; Visuospatial perception; Laterality; Perceptual stability

Introduction

Fixation is an active ocular motor stabilization process, by which a target's image is held steady on the fovea, the area on the retina with highest visual acuity. Cortical areas in the parietal and frontal lobe as well as subcortical areas are part of the fixation system. Electrophysiological non-human primate studies found neurons that exhibit increased activity during fixation in the frontal eye field (FEF; Bizzi, 1968; Bruce and Goldberg, 1985), supplementary eye field (SEF; Schlag and Schlag-Rey, 1987), prefrontal cortex (Suzuki and Azuma, 1977), area 7a of the parietal lobe (Sakata et al., 1980), substantia nigra pars compacta (Hikosaka and Wurtz, 1983), and in the rostral pole of the superior colliculus (Munoz and Wurtz, 1993). Clinico-pathological studies suggest the existence of a fronto-parietal fixation system also in humans. Impaired fixation was observed in patients with bilateral parieto-occipital lesions (Balint, 1909); spasm of fixation was attributed to bilateral frontal lobe damage (Holmes, 1938), and locking of fixation was seen in patients with parietal lesions (Pierrot-Deseilligny et al., 1986). Patients with impaired fixation often also show attentional deficits, such as peripheral visual attention disorder in Balint's syndrome and foveally restricted attention occurring with locked fixation. Thus, a strong interdependence of fixational and attentional systems has been proposed. Electrophysiological findings have largely been confirmed by PET studies that demonstrated activations in parietal and frontal cortical areas [FEF, SEF, intraparietal sulcus (IPS), precuneus, dorsolateral prefrontal cortex (DLPFC)] during steady fixation of targets straight ahead. These brain activation studies were performed in darkness, and fixation was compared to different baseline conditions, such as eyes open with gaze straight ahead (Petit et al., 1995; Petit et al., 1999), saccades (Anderson et al., 1994; Sweeney et al., 1996), or suppression of saccades (Law et al., 1997).

To localize objects in space and to establish a stable external coordinate system, the brain needs to combine information about the position of the stimulus in retinotopic coordinates with information about the position of the eyes in their orbits. Visual spatial information is conveyed to the primary visual cortex in retinotopic coordinates. This sensory frame of reference is transformed into a frame appropriate for selected body parts, such as eye and head. Cortical neural processes for encoding information of the 3D position of a target in space start as early as in area V1 in

Abbreviations: FEF, frontal eye field; PEF, parietal eye field; SEF, supplementary eye field; DLPFC, dorsolateral prefrontal cortex; SMA, supplementary motor area.

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non-human primates (Weyand and Malpeli, 1993; Guo and Li, 1997; Trotter and Celebrini, 1999). These processes are commonly interpreted as forming a distributed representation of space in head-centered coordinates, thereby contributing to the stability of visuospatial perception during combined eye and head movements as well as to planning and coordinating movements. To our knowledge, no brain activation studies have yet been conducted during lateral fixation.

The goal of our functional magnetic resonance (fMRI) study was to determine, whether gaze-dependent differential effects can be detected in ocular motor and visual structures during the fixation of retinotopically identical targets presented 10° to the right or left as compared to gaze straight ahead. We especially focused on the question of whether the shift of the target in head coordinates is reflected by asymmetries in visual cortex blood oxygen level-dependent (BOLD) signal responses.

Methods

Subjects

Thirteen healthy volunteers (eight females, five males; 24 to 38 years of age, mean age 29 years) without any history of CNS, visual, or vestibular disorders participated in the study. All subjects gave their informed written consent before the fMRI experiment. The study was approved by the local Ethics Committee of the Ludwig-Maximilians University.

Experimental procedure

Subjects lay supine in the MRI scanner in a completely darkened room. Three red LEDs were placed at the end of the MRI bore above the subject's head at a distance of about 1.25 m from the subject's eyes, into which a mirror attached to the head coil reflected the light of the LED. Subjects were instructed to relax, to direct their gaze straight ahead, to avoid any eye movements, and to fixate the single LED, as soon as it appeared.

Four conditions were applied in randomized order: *central fixation*: LED appeared at primary eye position; *fixation right*: LED appeared 10° to the right of primary eye position (directions given from the volunteer's point of view); *fixation left*: LED appeared 10° to the left of primary eye position; *rest*: subjects lay still with the eyes open in total darkness and gazed straight ahead, without LED. Each condition lasted 22.5 s. Each scanning session consisted of two successive runs. Fixation tasks were presented 22–24 times per session. Each fixation task was followed by rest. During the scanning procedure, horizontal eye movements were recorded using MRI-compatible infrared oculography (Kimmig et al., 1999). Eye movement recordings showed that subjects were able to maintain fixation on the presented target during the scanning periods. With eyes open in darkness (*rest*), subjects performed a few small-amplitude saccades.

Data acquisition

Functional images were acquired on a 1.5-T standard clinical MRI scanner (Siemens Vision, Erlangen, Germany) using echo-planar imaging (EPI) with a T2*-weighted gradient-echo multislice sequence (TE = 60 ms, voxel size: 3.75 × 3.75 × 3.75 mm^3, matrix: 64 × 64, interscan interval: 4.5 s). Thirty-two transversal slices covering the whole cerebrum and most parts of the cerebellum were acquired.

Data analysis

Data processing was performed on UltraSPARC workstations (Sun Microsystems) using SPM99 implemented in MATLAB (Mathworks, Sherborn, MA; http://www.fil.ion.ucl.ac.uk/spm). The first five images of each imaging series were discarded to eliminate spin saturation effects. Motion correction was performed by realigning each volume to the first one of each scanning session. Volumes were spatially normalized to the template space defined by the Montreal Neurological Institute (MNI) template and resampled to a resolution of 2 × 2 × 2 mm^3 (Friston et al., 1995a). Data sets were smoothed with a 12-mm Gaussian isotropic kernel. Group analysis was performed by collapsing repeated measures within subjects and experimental runs. To allow inference to the general population, the resulting condition images were compared among subjects, yielding a random effects model. The following types of comparisons were performed: First, fixation tasks were compared to *rest* (eyes open in darkness). Subtracting *rest* from a fixation task (fixation task − *rest*) shows task-specific BOLD activations, i.e., increases in the neuronal firing rate; subtracting fixation tasks from *rest* (*rest* − fixation task) shows task-specific BOLD deactivations. Second, fixation tasks were compared with each other; e.g., subtracting fixation left from fixation right (fixation right − fixation left) shows all brain areas with higher intensity of BOLD-weighted fMRI signals during fixation right than during fixation left. This includes areas with stronger activation and areas with absent or weaker deactivation during fixation right than fixation left. SPMs were generated using the general linear model and the theory of the Gaussian fields (Friston et al., 1995b). Activations exceeding a significance threshold of $P < 0.001$ (group analysis) were considered significant. In addition, activations that correspond best to ocular motor structures and exceeded a significance threshold of $P < 0.01$ are reported for the group analyses fixation right − central fixation and fixation left − central fixation.

Results

Activations during central and lateral fixation compared to eyes open in darkness

During central fixation − rest, activations were seen bilaterally in occipital visual cortex areas (BA 17–BA 19; middle and inferior occcipital gyri, posterior fusiform gyri) and in the middle occipital gyri extending into the middle temporal gyri (BA 19/37; MT/V5) (group analysis, $P < 0.001$, Fig. 1, Table 1). Further clusters were seen bilaterally in the lateral geniculate nuclei (LGN). No relevant fronto-parietal activations were seen that could correspond to ocular motor structures.

During fixation right − rest, activations in visual cortex areas (BA 17–BA 19, BA 19/37) were more pronounced in the left hemisphere and extended bilaterally into MT/V5. A small cluster corresponded to the right LGN. Two small fronto-parietal clusters were seen (right inferior parietal lobule and right precentral gyrus).

During fixation left − rest, activations in visual cortex areas (BA 17–BA 19, BA 19/37) also included MT/V5 bilaterally. There

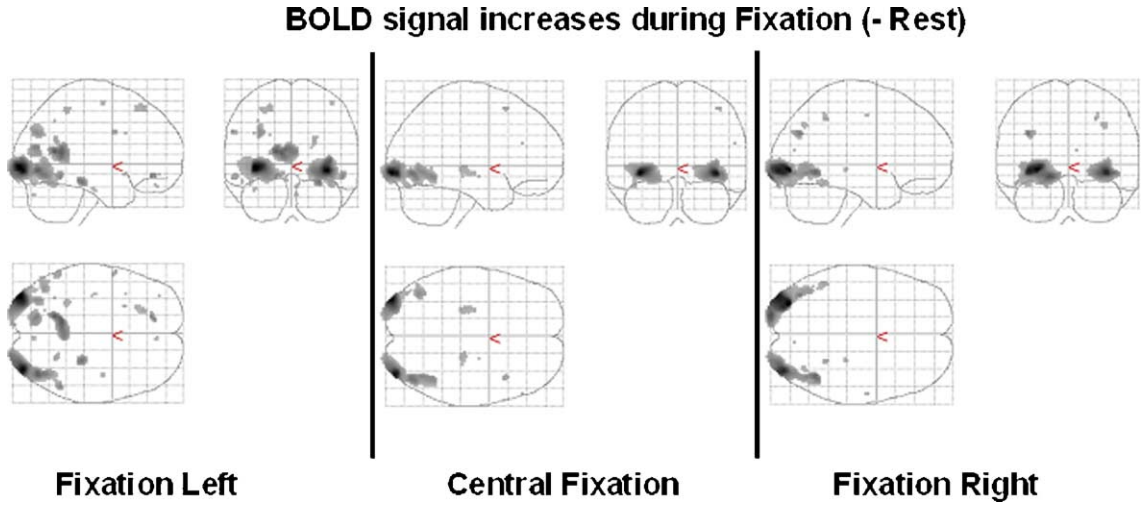

Fig. 1. BOLD signal increases obtained by statistical group analysis for the comparisons fixation left − rest (left), central fixation − rest (middle), and fixation right − rest (right) (group analysis; $n = 13$; $P < 0.001$; glass brain view). The clusters in occipital visual cortical areas extend into MT/V5 bilaterally. Activations in ocular motor structures, such as the dorsolateral prefrontal cortex, frontal eye field, parietal eye field, and supplementary eye fields, are absent during central fixation and minimal during fixation right or left.

were three frontal clusters and one parietal activation, close to the left IPS.

Deactivations during central and lateral fixation compared to eyes open in darkness

During central fixation − rest, BOLD signal decreases were found in dorsal and ventral medial occipital visual areas. Bilateral clusters were seen in the superior occipital gyri/superior cunei (BA 19), extending to the medial parieto-occipital sulcus, as well as in the lingual gyri, extending into the fusiform gyri (more pronounced in the right hemisphere, number of deactivated voxels, right: 578, left: 30) (group analysis, $P < 0.001$, Fig. 2, upper row, Table 2). Further deactivations were found in the right posterior insula, which correspond to the parieto-insular vestibular cortex, and in the left superior temporal gyrus (BA 22), bilaterally including Heschl's gyri.

Table 1
BOLD signal increases during fixation versus rest (group analysis; $n = 13$; $P < 0.001$)

Brain area	BA	Central fixation − rest			Fixation right − rest			Fixation left − rest		
		MNI coordinates	*t* value	Voxels	MNI coordinates	*t* value	Voxels	MNI coordinates	*t* value	Voxels
GOi/GOm/GF	18/19/17	−36,−94,−6	13.25	502	−30,−84,−4	10.53	1125*	−36,−94,−4	11.10	774
GOi/GOm/GF	18/19/17	38,−92,−6	11.94	813*	36,−88,−8	9.14	688*	36,−90,−6	10.82	1050*
GOm/GTm	19/37	42,−76,−6	7.19	813*	40,−58,−6	6.64	688*	40,−74,−6	7.20	1050*
GOm/GTm	19/37	−40,−68,−4	5.93	110	−42,−66,−2	4.97	1125*	−44,−68,−4	5.03	169
GF	37				−50,−50,−18	4.57	18	−50,−66,−18	4.23	5
GOm/GOs/	19				−38,−72,30	6.02	33	−32,−76,30	5.48	89
GOs	19				36,−68,38	4.21	10			
Cu	18							−14,−78,16	5.98	146
GH	35							28,−30,−18	6.32	48
PCu	31							24,−56,22	4.60	18
LGN/Hi		18,−24,−2	4.62	27	26,−30,−4	4.34	4			
LGN		−26,−28,−4	4.60	38						
GTm/GTi	37							−56,−56,−12	4.79	20
GFs/GFm	8							−22,32,54	4.61	42
GFm	6	40,16,56	4.76	6						
GPrC	4				58,−8,48	4.21	2	−60,4,32	5.07	8
GPrC	4							40,−10,60	4.34	7
LPi	40				26,−48,44	4.63	10	−30,−44,52	4.36	15
GC post	30							−16,−58,12	7.38	426

Brodmann areas (BA), Montreal Neurological Institute (MNI) coordinates, cluster sizes, and *t* values for voxels showing maximum significance are listed. Positive *x*, *y*, and *z* coordinates indicate locations right, anterior, and superior to the middle of the anterior commissure, respectively.
G, gyrus; F, frontal; O, occipital; T, temporal; LP, parietal lobule; GC, cingulate gyrus; s, superior; m, middle; i, inferior; ant, anterior; post, posterior; Ins, insula; PCu, precuneus; GH, parahippocampal gyrus; GPrC, precentral gyrus; IPS, intraparietal sulcus; LPc, paracentral gyrus; GPoC, postcentral gyrus; SMA, supplementary motor area; GF, fusiform gyrus; GL, lingual gyrus; Ga, angular gyrus; calc S, calcarine sulcus; Cu, cuneus; CC, corpus callosum; LGN, lateral geniculate nucleus; Hi, hippocampus; PEF, parietal eye field; DLPFC, dorsolateral prefrontal cortex; NC, caudate nucleus; Pu, putamen.
* This subcluster is confluent with another listed subcluster. The voxel number represents the total cluster size.

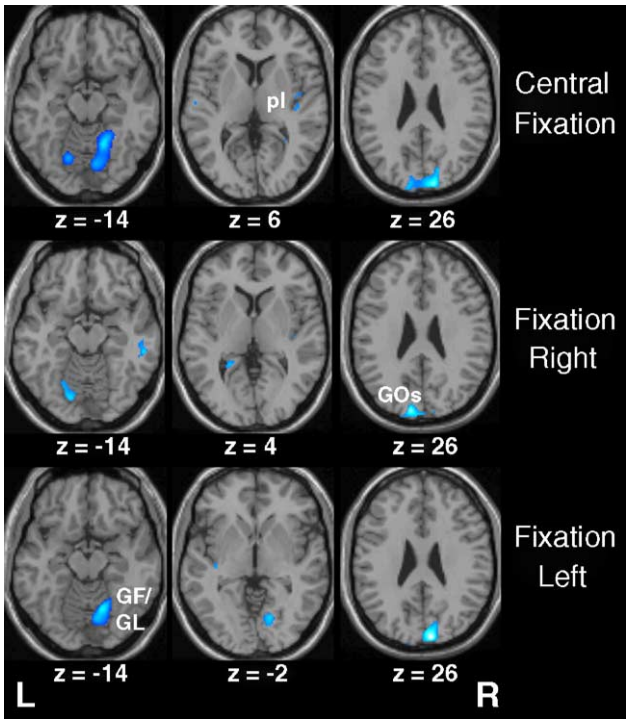

Fig. 2. BOLD signal decreases obtained by statistical group analysis for the comparisons central fixation − rest (top), fixation right − rest (middle), and fixation left − rest (bottom) ($n = 13$; $P < 0.001$). Deactivations are projected onto the MNI standard brain template, and transverse sections are shown. BOLD signal decreases were found in ventral medial occipital areas (fusiform and lingual gyri, GF/GL), in the postero-superior occipital gyri (GOs), extending into the parieto-occipital fissure, and in the posterior insula (pI). Occipital deactivations showed hemispheric asymmetries during lateral gaze.

During fixation right − rest, medial occipital BOLD signal decreases appeared more pronounced in the left hemisphere (number of deactivated voxels, superior occipital gyri/superior cunei, right: 5, left: 258; fusiform and lingual gyri, right: 128, left: 174; Fig. 2, middle row, Table 2). A small cluster was seen in the right posterior insula, extending into Heschl's gyrus. Additional signal decreases were found in the posterior corpus callosum bilaterally.

During fixation left − rest, medial occipital BOLD signal decreases were more pronounced in the right hemisphere (number of deactivated voxels, superior occipital gyri/superior cunei, extending to the medial parieto-occipital fissure, right: 424, left: 56; lingual gyrus, extending into the fusiform gyrus, right: 574 voxels, left: no voxel; Fig. 2, lower row, Table 2). A small cluster was seen in the left posterior insula. A further signal decrease was found in the right posterior corpus callosum.

Lateral fixation compared to central fixation

In the comparison fixation right − central fixation, BOLD signal increases were found bilaterally in occipital visual areas, i.e., in the right cuneus, right superior occipital gyrus, and in the right lingual gyrus extending into the fusiform and parahippocampal gyri, as well as in the left calcarine sulcus (group analysis, $P < 0.001$, Table 3). The right-hemispheric occipital signal increases (superior occipital gyrus, superior cuneus; lingual and fusiform gyri) largely overlap with deactivations during central fixation − rest (Fig. 2). Three clusters were seen in frontal cortical areas. The most prominent one was located in the right middle frontal gyrus (BA 46; Fig. 3, upper panel, $z = 24$). Two small clusters were found in the left precentral gyrus, which correspond best to the left FEF. One small cluster appeared in the left superior parietal lobule, adjacent to the paracentral gyrus (BA 7). A cluster in the left middle temporal gyrus (BA 39/22) was located slightly anterior to MT/V5. At a lower significance threshold ($P < 0.01$, Fig. 3, upper panel, Table 4), further clusters were seen bilaterally in the superior precentral gyrus at the junction with the superior frontal gyrus (corresponding best to the superior saccade-related subregion of the FEF; Berman et al., 1999; Fig. 3, $z = 60$), in the left IPS (corresponding to the left PEF; Fig. 3, $z = 50$), right precentral gyrus (3 voxels only), right precuneus (extending into

Table 2
BOLD signal decreases during fixation versus rest (group analysis; $n = 13$; $P < 0.001$)

Brain area	BA	Rest − central fixation			Rest − fixation right			Rest − fixation left		
		MNI coordinates	*t* value	Voxels	MNI coordinates	*t* value	Voxels	MNI coordinates	*t* value	Voxels
Cu	19	14,−90,26	7.55	627*	14,−92,24	4.18	5	10,−90,24	10.06	424
Cu	19	−16,−98,24	5.45	627*	−8,−90,28	8.10	258	−16,−98,24	5.44	56
GL/GF	18/19	18,−56,−14	6.03	578	22,−70,−8	6.51	128	16,−64,−8	7.56	574
GL/GF	18/19	−16,−68,−16	4.85	30	−14,−78,−14	5.75	174			
GFm/GFs	9/6	28,40,32	6.45	92						
GPrC	6	54,0,12	5.96	36*						
GPrC/GPoC	3/4	16,−32,72	4.95	34						
Ins post		44,−8,6	4.32	36*	42,−18,4	4.15	4	−36,−20,−2	4.73	15
Ins post		42,−20,4	5.30	29						
GTs	22	−58,−14,8	4.91	39						
GTs	38				38,0,−16	4.99	61			
GTm	21				56,−30,−16	6.03	107			
LPs	7	−20,−52,72	5.15	80						
CC					−12,−38,14	8.51	230			
CC					22,−40,16	5.47	213	16,−36,20	4.90	78
GC ant	32				−10,18,38	5.31	6			

* This subcluster is confluent with another listed subcluster. The voxel number represents the total cluster size.

Table 3
Lateral fixation versus central fixation (group analysis; $n = 13$; $P < 0.001$)

Brain area	BA	Fixation right − central fixation			Fixation left − central fixation		
		MNI coordinates	*t* value	Voxels	MNI coordinates	*t* value	Voxels
Cu/GF/GL	17–19				−14,−64,0	7.70	703
Cu	17/18	24,−68,16	5.65	88	22,−64,14	4.44	12
Cu/GOs	19				−16,−88,26	4.38	16
Cu/GOs	18	10,−96,16	4.20	8	−24,−94,10	4.20	13
calc S	18	−12,−100,−12	3.96	1	34,−90,−6	4.81	68
GL/GF/GH	19/37	12,−68,−4	4.32	29	36,−26,−24	6.14	54
GL/GF	19/37	30,−54,−4	4.31	5	−40,−34,−26	5.03	7
GF/GH	36/37				−14,−46,−18	4.33	12
GH/GF	35	22,2,−32	5.78	20	24,−28,−18	4.44	13
PCu	7				−12,−84,40	5.12	81
GOm/GTm	19/37				−52,−76,6	4.60	4
GTm/GTs	39/22	−38,−48,10	5.02	13			
GTm/GTi	37/21				−60,−52,−12	4.42	5
GTs	42				58,−28,16	4.51	23
GPrC/GFs/SMA	4/8				−16,−2,68	7.67	425*
GPrC/GFs	4/8				14,−6,70	5.63	263*
GFm/GPrC	6/4				−30,−14,68	6.94	425*
GFm/GPrC	6/4				18,−2,62	5.64	263*
GFm	46	42,48,22	6.42	53	−30,56,14	4.66	3
GPrC	4	−34,−16,44	4.02	5			
GPrC	4	−44,−2,16	4.26	4	14,−28,68	5.29	68
IPS	7				−26,−64,46	4.10	2
LPs/LPc	7	−16,−42,54	4.97	24	−12,−44,56	5.08	20
GPoC/LPi	2/40				−38,−26,36	4.82	14
LPs/GPoC	7/5				−24,−40,72	4.81	18

* This subcluster is confluent with another listed subcluster. The voxel number represents the total cluster size.

the medial parieto-occipital sulcus; Fig. 3, $z = 50$), and in the left supplementary motor area (SMA).

In the comparison fixation left − central fixation, BOLD signal increases in visual occipital areas were seen in the left superior occipital gyrus, cunei (more pronounced on the left side), fusiform gyri extending into the lingual and parahippocampal gyri (more pronounced on the left side), and in the right calcarine sulcus (group analysis, $P < 0.001$, Table 3). The cluster in the left superior cuneus extended to the medial parieto-occipital fissure. The predominantly left-hemispheric occipital signal increases (superior occipital gyri, superior cunei; lingual and fusiform gyri) largely overlap with deactivations during central fixation − rest (Fig. 2). A small cluster in the left middle temporal and middle occipital gyri corresponded best to left MT/V5 (Fig. 3, lower panel, $z = 0$). Signal increases were also seen in the left precuneus (Fig. 3, $z = 38$), left middle frontal gyrus (BA 46; Fig. 3, $z = 12$), left superior parietal lobule (adjacent to the paracentral gyrus, BA 7; Fig. 3, $z = 54$), left IPS (corresponding to the left PEF; Fig. 3, $z = 46$), and bilaterally in the superior precentral gyrus at the junction with the superior frontal gyrus (including the superior subregion of the FEF bilaterally and the left SMA; $z = 64$). At a lower significance threshold ($P < 0.01$, Fig. 3, lower panel, Table 4), clusters were also seen bilaterally in the precentral gyri (corresponding to the FEF; Fig. 3, $z = 32$, $z = 38$), and in the right SMA (Fig. 3, $z = 64$).

In the comparison central fixation − fixation right, three clusters were found (group analysis, $P < 0.001$). Bilateral clusters were seen in the LGN, extending into the hippocampus, and one cluster was found in the right cuneus (16 voxels). In the comparison central fixation − fixation left (group analysis, $P < 0.001$), no signal changes were seen.

Fixation right compared to fixation left

The comparison fixation right − fixation left showed BOLD signal increases in the right superior cuneus and right precuneus, both of which were located close to the medial parieto-occipital fissure, and in the right lingual gyrus (group analysis, Fig. 4, Table 5). These clusters reflect right-hemispheric medial occipital signal decreases found in the comparison fixation left − rest.

The comparison fixation left − fixation right showed confluent signal increases in the left lingual gyrus, left cuneus, and left superior occipital gyrus, extending to the medial parieto-occipital fissure (group analysis, Fig. 4, Table 5); they correspond to left-hemispheric medial occipital signal decreases found in the comparison fixation right − rest. Additional clusters were seen in the left inferior frontal gyrus, extending into the precentral gyrus, in the left IPS, corresponding best to the left PEF, and bilaterally in the SMA (Table 5).

Discussion

Visual perception entails both perception of an image and the establishment of its spatial coordinates. In order to maintain stability of visuospatial perception during independent eye and head movements, the visual system has to correct for shifts of the visual target in

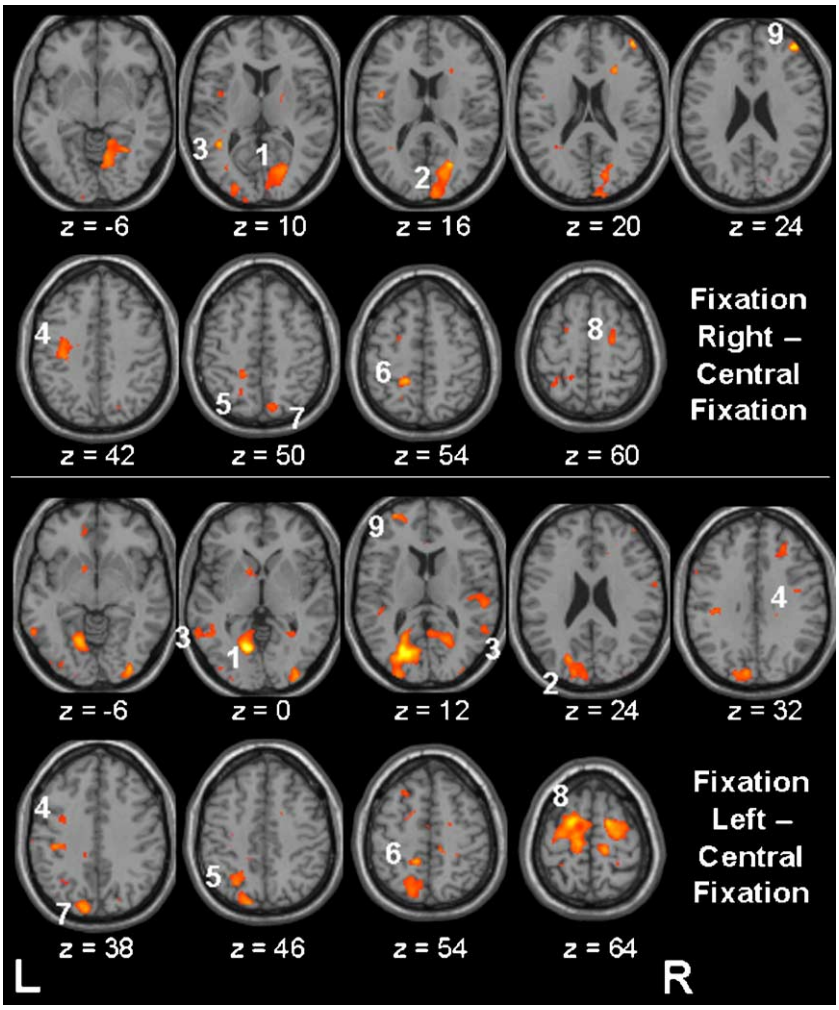

Fig. 3. BOLD signal increases obtained by statistical group analysis for the comparisons fixation right − central fixation (top) and fixation left − central fixation (bottom) ($n = 13$; $P < 0.01$). Activations are projected onto the MNI standard brain template, and transverse sections are shown. Signal increases were seen in the lingual/fusiform gyri (1), superior occipital gyrus (2), middle temporal gyrus (3), precentral gyrus (frontal eye field, 4), parietal eye field (5), superior parietal lobule (6), precuneus (7), middle and superior frontal gyri (8), and in the dorsolateral prefrontal cortex (9). BOLD signal changes in the medial occipital cortex (lingual, fusiform, superior occipital gyri) in the hemisphere ipsilateral to the fixation target and in the superior temporal gyrus bordering the posterior insula are interpreted as less deactivation of these areas during lateral than during central fixation (see Fig. 2).

retinotopic and head coordinates by integrating retinal and motor system signals.

Lateral gaze modulates human visual cortex activity with preference of the hemisphere contralateral to gaze direction

Asymmetric activations and deactivations in the visual cortex during lateral fixation of an LED presented in complete darkness only 10° to the right or left from straight ahead are the most interesting findings of our study. The translation of a fixation target, accompanied by a small shift of gaze, leads to a shift of the target in a head-centered frame of reference, while retinotopic coordinates remain the same. We found that modulations of the amplitude of the BOLD signal correlate with gaze direction and show preference for the hemisphere contralateral to gaze direction. This is schematically depicted in Fig. 5, which shows BOLD signal increases (primary visual areas; calcarine sulcus) and decreases (ventral and dorsal visual stream areas: lingual/fusiform gyri and superior occipital gyrus/cuneus) predominantly in the hemisphere contralateral to gaze direction. During gaze straight ahead, these areas show largely symmetrical BOLD signal changes.

Activations

During lateral fixation versus rest, as a trend, BOLD activations in the striate visual cortex showed asymmetries in favor of the hemisphere contralateral to gaze direction: First, when fixation right (or left) was compared to rest, the largest visual cortex activation cluster that includes the early visual cortex was located in the hemisphere contralateral to the fixation target (Table 1). Second, in the comparison fixation right (or left) − central fixation, there were activations in the calcarine sulcus of the hemisphere contralateral to the lateral fixation target (Table 3). The number of activated voxels in occipital visual areas was larger during lateral than during central fixation, which may be caused by an increase in visuospatial attention during lateral fixation.

Deactivations

FMRI studies measure BOLD signal increases (activations) and decreases (deactivations), relative to a chosen rest condition, that

Table 4
Lateral fixation versus central fixation: activations in ocular motor structures (group analysis; $n = 13$; $P < 0.01$)

Brain area	BA	Fixation right − central fixation			Fixation left − central fixation		
		MNI coordinates	*t* value	Voxels	MNI coordinates	*t* value	Voxels
GPrC	4	58,−8,48	3.28	3	40,−4,32	3.37	22
GPrC	4	−34,−16,44	4.02	257	64,−2,24	3.06	15
GPrC	4				−30,−18,48	3.16	17
GPrC	4				−32,−2,38	3.03	48
GPrC	4				−58,16,30	3.39	12
GPrC/GFs	4/8	−22,0,58	3.32	46			
GPrC/GFs	4/8	24,−10,62	3.67	182*	14,−6,70	5.63	1126*
GPrC/GFs	4/8	22,−4,72	4.31	182*			
SMA	6				8,4,58	2.76	1
SMA	6	−6,−18,72	3.09	51	−16,−2,68	7.67	1466*
IPS	7/40	−34,−52,66	3.91	319	−26,−64,46	4.10	3917*
GFm	46	42,48,22	6.42	141	−30,56,14	4.66	129
PCu	7	12,−72,48	3.59	95	−12,−84,40	5.12	3917*

* This subcluster is confluent with another subcluster. The voxel number represents the total cluster size.

derive from changes in neuronal activity driven by sensory stimulation, motor or cognitive tasks. It has been proposed that BOLD deactivations in the visual cortex reflect functional alterations, e.g., BOLD signal decreases of motion sensitive visual areas are associated with impaired visual motion perception (Brandt et al., 2003). Deactivations during fixation were seen in higher-order ventral and dorsal stream areas and showed striking asymmetries during lateral fixation (Figs. 2–4).

During central fixation, deactivations in ventral stream visual areas (lingual and fusiform gyri) were found bilaterally, slightly more pronounced in the right hemisphere. During fixation right, they were found predominantly in the left hemisphere, and during fixation left, they appeared in the right hemisphere only. The functions of the lingual and fusiform gyri are related to recognition, storage, and retrieval of complex visual patterns with right-hemispheric dominance (Roland and Gulyas, 1995; Menon et al., 2000), as well as to color analysis (Lee et al., 2000). These functions, however, were not required in our simple paradigm of fixation of a single LED. One may speculate that deactivations in these areas may correspond to a mismatch between expected and actual visual stimulation. Indeed, using unimodal vestibular (Wenzel et al., 1996) or unimodal visual motion stimulation (Brandt et al., 1998), we found an inhibitory visuo-vestibular interaction, which can also be explained by a mismatch between expected and actual input to the particular sensory modality (Brandt et al., 2002).

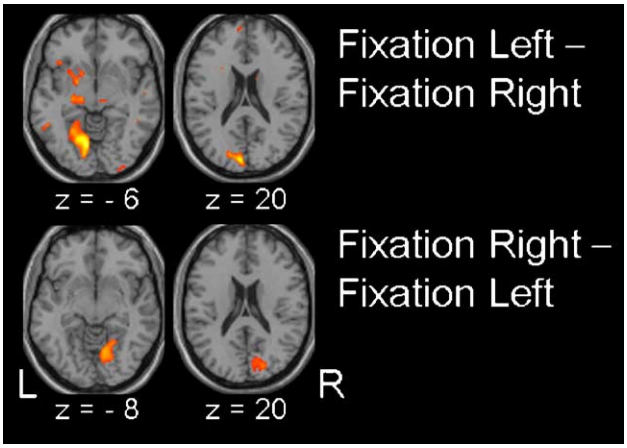

Fig. 4. BOLD signal increases obtained by statistical group analysis for the comparison fixation right versus fixation left ($n = 13$; $P < 0.01$). Activations are projected onto the MNI standard brain template, and transverse sections are shown. Relative BOLD signal increases in the visual cortex ipsilateral to the fixation target reflect missing ipsilateral deactivation in these brain areas (superior occipital, fusiform, and lingual gyri) during lateral fixation (see Fig. 2).

Deactivations in dorsal stream visual areas in the postero-superior cuneus, extending to the parieto-occipital fissure during central fixation and fixation left, showed similar asymmetries. They were found bilaterally during central fixation and predominantly in the hemisphere contralateral to the fixation target during lateral fixation. They may correspond to the parieto-occipital area PO (V6) or be located slightly postero-inferior. The receptive fields of PO (V6) are located predominantly in the peripheral visual field, where no stimulus appeared in our study. It was repeatedly demonstrated that PO (V6) processes visually induced apparent self-motion (vection) (Brandt et al., 1998; Kleinschmidt et al., 2002; Deutschländer et al., 2004). PO (V6) is thought to be involved in the construction of an internal map of the extrapersonal visual environment by encoding spatial locations in the field of view in a head frame of reference, thereby allowing stability of visual perception despite eye movements (Colby et al., 1988). In monkeys, it contains neurons that are sensitive to eye positions, also in complete darkness (Galletti et al., 1995). In humans, lesions of putative PO produced deficits in visual target localization, and electrical stimulation of the medial parieto-occipital fissure evoked visual motion phenomena in epileptic patients (Richer et al., 1991).

When two fixation tasks were compared to each other (Figs. 3 and 4), the above-described deactivations in the lingual and fusiform gyri (ventral cluster) and in the medial superior occipital gyrus/cunei (dorsal cluster) largely appeared as relative BOLD signal increases in the hemisphere ipsilateral to the fixation target due to the missing ipsilateral deactivation.

Eye position exerts an influence on the excitability of neurons in widespread visual areas, as demonstrated by electrophysiological recordings in monkeys and cats. Retinal and eye position signals have been shown to interact in higher visual areas, both of the dorsal stream, such as the posterior parietal cortex (Andersen and Mountcastle, 1983), area VIP (Duhamel et al., 1997), area PO (Galletti et al., 1995), MT/MST (Bremmer et al., 1997), area V3A (Galletti and Battaglini, 1989), and of the ventral stream (areas V2 and V4; Rosenbluth and Allman, 2002), as well as in the earliest

Table 5
Fixation right versus fixation left (group analysis; $n = 13$; $P < 0.001$)

Brain area	BA	Fixation right − fixation left			Fixation left − fixation right		
		MNI coordinates	*t* value	Voxels	MNI coordinates	*t* value	Voxels
GL	19	12,−70,−6	4.95	113			
GL/Cu/GOs	18/19				−12,−68,−2	9.82	1083
Cu	19	10,−82,30	4.40	18			
PCu/LPs	7	14,−70,48	5.04	15			
IPS	7/40				−26,−64,42	4.74	9
GFi/GPrC	44/6				−32,6,32	5.16	25
GFs	9				−24,32,32	5.41	43
SMA	6				12,6,60	5.14	15
SMA	6				−6,22,56	4.20	2
Ga	39				36,−58,30	5.90	13
GTm/GTi	21/20				54,−18,−18	4.75	79
GTs	38				−36,6,−22	4.34	17
Hi					−14,−18,−8	5.65	38
NC		12,22,−2	4.11	3			
Pu					−24,14,−10	7.12	112

stages of cortical and subcortical visual processing (Lal and Friedlander, 1990; Weyand and Malpeli, 1993; Guo and Li, 1997; Trotter and Celebrini, 1999). Electrophysiological recordings in cat striate cortex showed a slight tendency for neurons to respond best when gaze was directed into the visual hemifield contralateral to the hemisphere from which neuronal responses were recorded (Weyand and Malpeli, 1993). This preference for contralateral gaze was also reported in monkey striate cortex (Guo and Li, 1997) and area V3A (Galletti and Battaglini, 1989).

Ocular motor activity during central and lateral fixation

During lateral as well as central fixation versus eyes open in darkness, activations in fronto-parietal ocular motor structures, such as the FEF, PEF, SEF, and the DLPFC, were largely absent, although the fixation tasks involved ocular motor activity and attention (Table 1, Fig. 1). This finding can be explained by assuming that ocular motor and attentional structures already show BOLD activations during eyes open in darkness (Marx et al., 2003; Deutschländer et al., 2003; Marx et al., 2004). Small activations in fronto-parietal structures that can be attributed to the ocular motor system were, however, seen in the comparisons fixation right − central fixation and fixation left − central fixation, i.e., in the FEF, PEF, DLPFC, and SMA (Fig. 3, Tables 3 and 4). One small fronto-parietal cluster was seen during fixation left, close to the left IPS; it corresponds best to the PEF. This finding reflects an increase in ocular motor activity during eccentric compared to central fixation. This increase, however, may be caused not only by eye position effects, but also by voluntary overt shifts of visuospatial attention or suppression of contraversive eye movements back to primary position. Covert and overt shifts of visuospatial attention induce responses in the FEF and IPS with right-hemispheric dominance (Corbetta et al., 1993, 1995; Nobre et al., 2000; Beauchamp et al., 2000). Sheliga et al. (1997) proposed that active inhibition of reflexive eye movements during fixation is mediated by ocular motor structures (FEF, IPS, superior colliculus; "suppression hypothesis"). The DLPFC controls suppression of reflexive or inappropriate saccades during voluntary fixation (Funahashi et al., 1989; Milea et al., 2003; Pierrot-Deseilligny et al., 2003) and is considered part of the anterior attentional network (Nobre et al., 1997).

In the comparison fixation right versus fixation left, activations that correspond best to ocular motor structures were seen in the right precuneus (fixation right − fixation left) as well as in the left PEF, left FEF, bilaterally in the SMA, and left superior frontal gyrus (fixation left − fixation right; Table 5). Putaminal activation may reflect a part of the ocular motor loop described by Alexander et al. (1986).

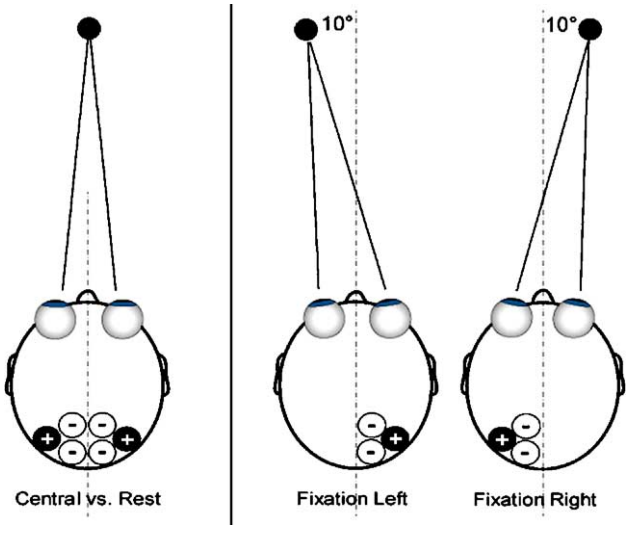

Fig. 5. Schematic representation of visual activations (calcarine sulcus) and deactivations (one ventral cluster in the fusiform and lingual gyri; one dorsal cluster in the postero-superior cuneus) during central fixation − eye open (left) and during lateral fixation 10° to the right or left versus central fixation (right). During 10° lateral gaze relative to head coordinates, the hemisphere contralateral to gaze direction predominantly mediates visual processing.

Activation in MT/V5

The motion-sensitive area MT/V5 showed bilateral activations during central and lateral fixation versus rest, which may be the cortical correlate of illusory motion of the visual target, i.e., the autokinetic phenomenon (Royce et al., 1966; Levy, 1972). Some

subjects reported illusory motion of the stationary visual target during central and lateral fixation in darkness. Indeed, other forms of illusory motion have been reported to activate MT/V5 (PET: Zeki et al., 1993; fMRI: Muckli et al., 2002). This agrees with findings of Kaneoke et al. (1996), who found responses in MT/V5, while recording magnetic fields with a biomagnetometer during apparent motion.

Cross-modality inhibition

When fixational tasks were compared to eyes open in darkness, we found BOLD signal decreases in the posterior insula and superior temporal gyrus, bilaterally including Heschl's gyri, i.e., in areas that contain neurons, that respond to vestibular and acoustic stimuli. This finding confirms the concept of cross-modality inhibition between the visual and the vestibular systems as proposed by Brandt et al. (1998). Using PET, Petit et al. (1999) also demonstrated deactivations in acoustic cortical areas, including Heschl's gyri, during fixation.

Conclusions

Neurons in widespread visual areas combine information about the position of the eye in the orbit with that of the position of a stimulus on the retina, thus encoding spatial locations of the field of view in a head-centered frame of reference. Thus, an internal map of the visual environment is constructed, in which the topographical positions of objects reflect their objective position in space instead of the retinotopic position of their images. Such an objective map of the visual world might allow the stability of visual perception during eye movements.

We hypothesize that both hemispheres contribute equally to visual processing during fixation straight ahead; with a shift of gaze direction into the right or left visual hemifield, the hemisphere contralateral to gaze direction predominantly mediates visual processing, due to eye-position-dependent modulation of neuronal activity in the visual cortex. Thus, the left hemisphere will gain a greater "sensorial weight", when gaze is directed to the right, and the right hemisphere will gain more "sensorial weight", when gaze is directed to the left. It is remarkable that hemispheric asymmetries were significant even with small gaze shifts of 10° to the right or left from straight ahead. This is the first study in humans that shows eye position effects in early as well as in ventral and dorsal higher-order visual areas with preference for the contralateral field of view. Further investigations are required with larger gaze shifts, various gaze directions, and complex visual tasks, which include pattern recognition and large-field visual stimulation.

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