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Horizontal or vertical optokinetic stimulation activates visual motion-sensitive, ocular motor and vestibular cortex areas with right hemispheric dominance

An fMRI study

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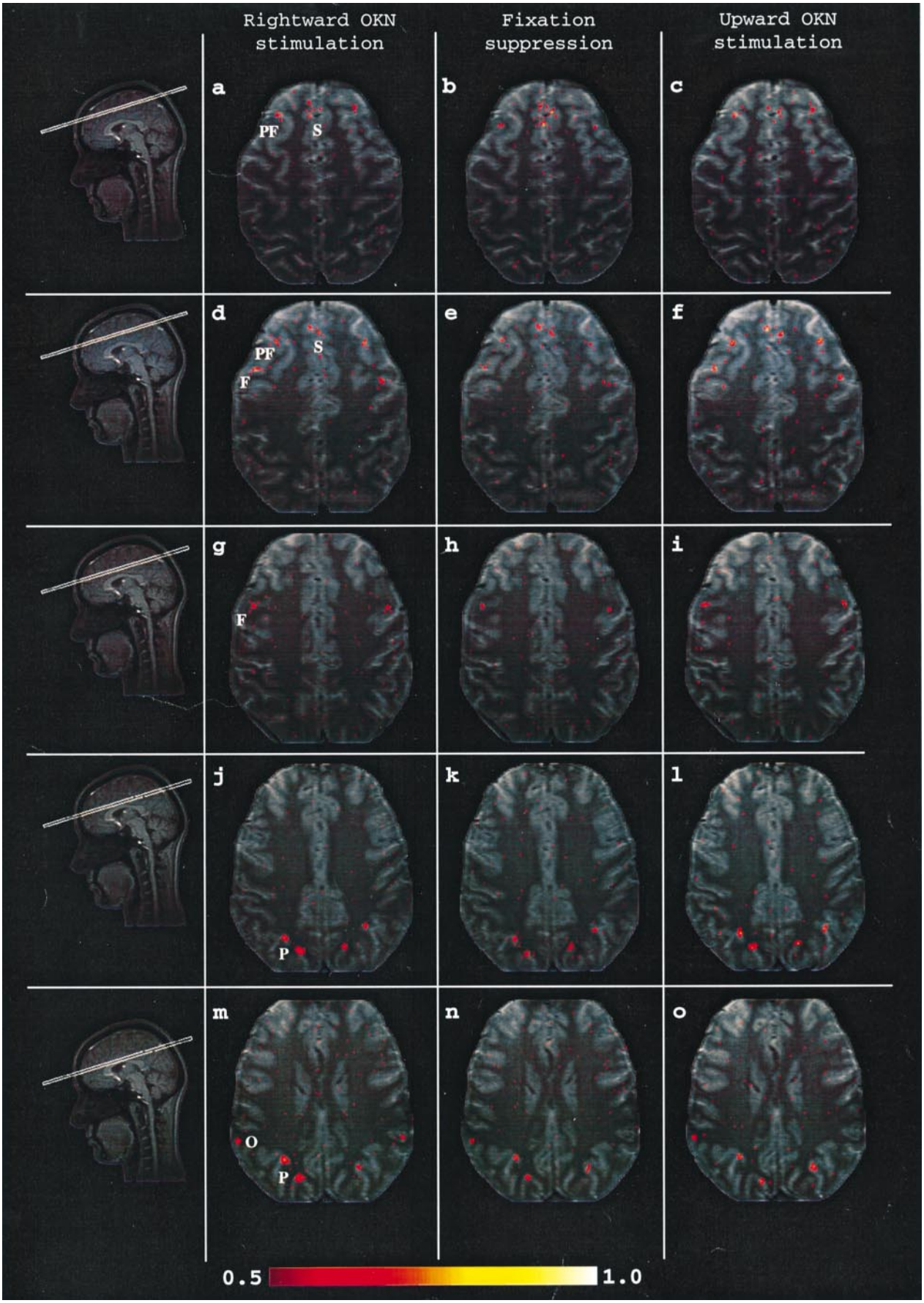
Summary

The differential effects of optokinetic stimulation with and without fixation suppression were analysed in an fMRI study in 10 right-handed healthy subjects. Horizontal and vertical small-field optokinetic stimulation activated the same multiple visual, ocular motor and vestibular cortical and subcortical areas in both hemispheres. The extent of activation in each hemisphere was independent of the stimulus direction. All activated areas representing cortical (occipitotemporal cortex, posterior parietal cortex, precentral and posterior median frontal gyrus, prefrontal cortex, medial part of the superior frontal gyrus) and subcortical (caudate nucleus, putamen, globus pallidus and paramedian thalamus) ocular motor structures were activated during optokinetic stimulation as well as during fixation suppression of optokinetic nystagmus. However, the activation was significantly stronger with optokinetc nystagmus compared with fixation suppression. The only relatively increased activity during fixation suppression was seen in the medial part of the superior frontal gyrus (supplementary eye field) and the anterior cingulate gyrus. The anterior insula and the posterior insula (human homologue of the parieto-insular vestibular cortex) were activated during optokinetic nystagmus but not during fixation suppression. A significant right hemispheric predominance (regardless of stimulus direction) was found under both conditions in the visual motion-sensitive and ocular motor areas of the cortex, except the supplementary eye field and anterior cingulate gyrus. This was most prominent in the occipitotemporal cortex, but did not occur in the primary visual cortex and in subcortical ocular motor structures (putamen, globus pallidus and caudate nucleus). Thus, cortical and subcortical activation patterns did not differ for horizontal and vertical optokinetic stimulation, and there was distinct right-hemisphere dominance for visual motion-sensitive and cortical ocular motor areas and the thalamus. Fixation suppression of optokinetic nystagmus yielded four different results: (i) increased activation in the supplementary eye field and anterior cingulate gyrus; (ii) unchanged activation in the visual cortex; (iii) decreased activation in most of the ocular motor areas; and (iv) suppressed activation in the anterior and posterior insula and the thalamus. Activation of the parieto-insular vestibular cortex may be related to ocular motor function rather than self-motion perception.

Keywords: vestibular system; optokinetic stimulation; visual cortex; hemispheric dominance; fMRI; activation study

Abbreviations: BA = Brodmann area; fMRI = functional MRI; OKN = optokinetic nystagmus; PEF = parietal eye field; PFC = prefrontal cortex; PPC = posterior parietal cortex


Rightward OKN stimulation
Fixation suppression
Upward OKN stimulation
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Introduction

Voluntary eye movements, saccades and pursuit activate different cortical structures depending on the particular experimental paradigm (saccades: Pierrot-Deseilligny *et al.*, 1995; Sweeney *et al.*, 1996; Bodis-Wollner *et al.*, 1997; visual motion perception without pursuit eye movements: Tootell *et al.*, 1995; McCarthy *et al.*, 1996; motion perception with pursuit: Barton *et al.*, 1996*a*). In an earlier functional MRI (fMRI) study during small-field optokinetic stimulation (which involves the pursuit and optokinetic systems) the following cortical and subcortical areas were activated bilaterally: the primary visual areas [Brodmann area (BA) 17], the motion-sensitive areas in the occipitotemporal cortex (middle temporal area and medial superior temporal area) and different cortical ocular motor centres for the control of saccades, including the parietal eye field, the frontal eye field, the prefrontal cortex and the supplementary eye field (Bucher *et al.*, 1997). These areas can be attributed to three aspects of the optokinetic and pursuit systems: the sensory visual evaluation of motion, the cortical initiation of eye movements, and the efferent pathways to the common supranuclear integration centres for eye movements in the pontine brainstem and the nucleus of the optic tract. Moreover, unexpectedly distinct, activated areas (not yet included in this concept) were located separately in the anterior and posterior parts of the insula. These findings raised the question of how activations of the anterior and posterior insula can be integrated in the concept of optokinetic nystagmus (OKN), particularly the processes of generating eye movements or mediating self-motion or object-motion perception. The latter is important, since OKN allows two perceptual interpretations: surround-motion, relative to a stationary observer, and self-motion, relative to a stationary surrounding (or a combination of both).

In continuation of our previous study, first the experimental paradigm of optokinetic stimulation eliciting OKN in fMRI was modified so that OKN was suppressed by fixation of a stationary target during visual motion stimulation (i.e. fixation suppression of OKN). The different effects of OKN with and without fixation suppression should be suitable for determining the differential effects of eye movements on the activation of the cortical ocular motor and vestibular system. Secondly, the effects of horizontal optokinetic stimulation were compared with those of vertical optokinetic stimulation. Thirdly, hemispheric differences were analysed for all activated areas separately. This procedure was suggested by the occasional observation in the previous study of asymmetrical activation of certain cortical ocular motor, insular and thalamic areas, with a predominance in the right hemisphere.

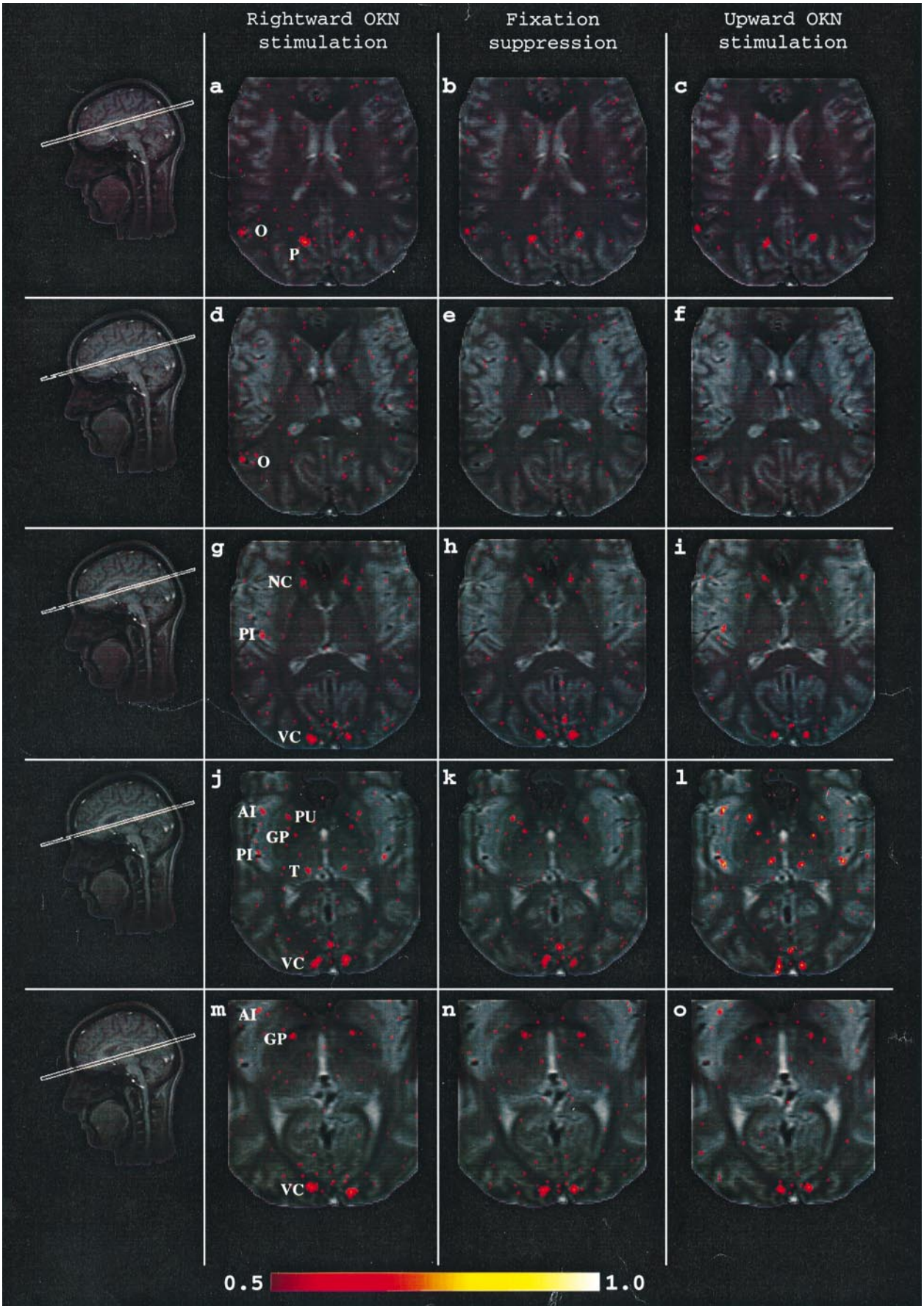
Method

MRI acquisition

Ten right-handed healthy volunteers (six women and four men), aged 25–31 years (mean ± SD 28.7 ± 2.4 years), were examined with a 1.5 T standard clinical scanner (Siemens Vision, Erlangen, Germany) using a circularly polarized head coil. The subjects gave their informed written consent before undergoing the MR scans, and the study was approved by the Ethics Committee of the Ludwig-Maximilians University. High-resolution coronal and transverse proton density (PD)- and T_2-weighted images were acquired ($TR/TE_{PD}/TE_2$ = 5400/14/99 ms, voxel size = 0.65 × 0.45 × 3 mm) to allow later anatomical correlation with the stimulation data. Single-slice flow-sensitized images (TR/TE = 75/8 ms, $\alpha = 60°$) delineated the macrovasculature so as to exclude large vessels as a source of activation. Functional images were acquired during two recording sessions from 10 oblique transverse slices covering the cortex, the basal ganglia and the thalamus with the same orientation of the anatomical images, using a radio frequency-spoiled single-slice FLASH (fast low-angle shot) pulse sequence with first-order motion compensation (TR/TE = 63/30 ms, voxel size = 0.78 × 0.78 × 4 mm, flip angle = 10°, bandwidth = 32 Hz/pixel), as described in a previous paper (Bucher *et al.*, 1997)]. The oblique coronal-to-axial slices were oriented according to the intercommissural [AC–PC (anterior commissure–posterior commissure)] line that was determined on a midsagittal MRI slice. The lowest acquired plane was ~5 mm below the AC–PC line; the highest was 40 mm above the AC–PC line, as indicated by the anatomical scouts in Figs 1 and 2. Single-slice recordings that were contaminated with motion were not analysed; new recordings of these slices were made. Subjects who could not suppress motion were not included in the study. The different activated brain structures were then identified by tracing the gyri and sulci on the transverse and sagittal anatomic images.

Additionally, we examined four subjects with whole-brain fMRI using a blipped T_2*-weighted gradient-echo multislice

Fig. 1 T_2*-weighted coronal MR images of five cortical sections with superimposed activation map associated with optokinetic nystagmus induced by right (**a**, **d**, **g**, **j**, **m**) and top (**c**, **f**, **i**, **l**, **o**) rotation of a drum and by fixation suppression (**b**, **e**, **h**, **k**, **n**) of rightward OKN in a 32-year-old control subject (TR/TE = 63/30 ms, $\alpha = 10^o$). The colour-coded correlation coefficient scale ranges from 0.5 (red) to a maximum of 1.0 (yellow). During horizontal and vertical OKN, the bilaterally activated areas are the medial part of the superior frontal gyrus/anterior cingulate gyrus (supplementary eye field; S; **a**–**f**), the prefrontal cortex (PF; **a**–**f**), the precentral and posterior median frontal gyrus (frontal eye fields; F; **d**–**i**) and parts of the parietal cortex including the parietal eye field (P; **j**–**o**). The lateral occipitotemporal cortex (O; **m**–**o**) shows a strong asymmetric activity, mainly in the right hemisphere. Note that there is no difference in the anatomical location and extent of activation for both horizontal and vertical OKN and fixation suppression of OKN.


Rightward OKN stimulation
Fixation suppression
Upward OKN stimulation
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echoplanar pulse sequence (EPI; TE = 40 ms, TR = 2000 ms, FOV = 250 mm, matrix size = 128 × 128, slice thickness = 5 mm, 17 slices/volume, 50–100 consecutive serial scans, 5 s interscan interval).

Recording procedure

Subjects lay supine wearing prism glasses, which allowed visual stimulation from outside the scanner. A rotating drum (diameter 0.4 m; constant rotation velocity 6–8°/s) covered with coloured objects was placed in front of the MR scanner bore to elicit horizontal OKN. The stimulated field was limited by the prism glasses and subtended 20° in the horizontal and 15° in the vertical direction (small-field stimulus).

The small-field stimulation was due to methodological geometric limitations of the scanner. In a strict sense, this small-field stimulus, which in the following is called optokinetic stimulation, activates both the optokinetic and the pursuit systems, predominantly the pursuit system (direct OKN component; Kjallman and Frisén, 1986). The generation of the slow nystagmus phase is based on the direct OKN component and an indirect OKN component ('velocity-storage mechanism' due to visual–vestibular convergence) (Waespe and Henn, 1987). The latter is elicited only by full-field stimulation, which induces apparent self-motion (vection; Brandt *et al.*, 1973). Pattern movement did not induce vection in our study. Thus, in our stimulation condition the indirect OKN component was less relevant.

Subjects had to fixate the drum throughout the whole fMRI acquisition. All control subjects were scanned during horizontal rotation of the drum to the right (i). The second condition was scanning during fixation suppression of the horizontal OKN to the right (ii). Fixation suppression was accomplished by placing a red ball in front of the rotating drum for foveal target fixation. We did not examine the effects of horizontal rotation to the left, since in the previous study (Bucher *et al.*, 1997) there was no significant difference in the anatomical location and extent of activation for rightward or leftward drum rotation. Therefore, in this series we did not alternate the horizontal direction of object motion. Instead we introduced vertical drum rotation as an additional stimulus. Three of the 10 subjects were tested in a series with vertical optokinetic stimulation (upward drum rotation) during vertical OKN and fixation suppression of vertical OKN (iii).

Thirty-two serial images were continuously acquired at the same slice for drum rotation rightward, upward and for suppression of OKN separately over 7 min. Eight initial images at rest (with fixation of the stationary OKN pattern) were followed by eight images during drum rotation, followed again by a period of rest and rotation, resulting in a total of 32 serial images. The acquisition of one slice lasted 12.2 s. The different paradigms were chosen in a random manner. A rest period of 2 min was inserted between each experimental run. Activations during optokinetic stimulation and activation during fixation suppression of OKN were determined separately in comparison with the rest condition. This appeared to be necessary, since a direct comparison of both activated conditions would not be conclusive about the question whether certain insular areas are activated in one or both conditions. Activations in some areas could cancel each other. A simultaneous analysis of the three conditions was not possible because of software limitations (at the time of data recording statistical parametric mapping software was not yet available; we later added the EPI scans of four subjects which were analysed with SPM96 for better comparison by means of Talairach coordinates).

Series of 50–100 consecutive brain EPI scans were acquired at each of the 17 slice locations during 10–20 alternating cycles of rest and horizontal rightward optokinetic stimulation. Each cycle consisted of five images (25 s).

An EOG recorded the OKN of both eyes during fMRI acquisition. Ag/AgCl electrodes were placed at the external canthi to monitor task performance. EOG recording has been explained in detail in a previous paper (Bucher *et al.*, 1997). We recorded 146 ± 15 beats/min (range: 121–172 beats/min) during the optokinetic stimulation task and 4 ± 2 beats/min (range: 1–8 beats/min) during the fixation suppression of OKN. During the rest condition (fixation of the stationary OKN pattern) the beat frequency ranged between 0 and 2/min. The EOG recording thus demonstrated that the subjects were able to maintain fixation during the suppression task. The efficiency of OKN fixation suppression was 97.3% (absence of OKN or saccades during this paradigm). Slow-phase velocity was 6–8°/s during optokinetic stimulation conditions (i.e. a gain of 1 due to slow-velocity drum rotation). The amplitude of the OKN recorded varied from 1.7° to 11.2° between and within individuals.

Data analysis

Functional activation maps were created on a pixel-by-pixel basis by correlating the time courses of the signal intensities with the stimulus protocol (Bandettini *et al.*, 1993) using our own specially developed software, described in detail in a previous publication (Bucher *et al.*, 1996). Red–yellow colour-coded quantitative maps were superimposed onto the

Fig. 2 Magnified cortical and subcortical activation maps superimposed on the corresponding coronal T_2*-weighted anatomical images of the lower five sections of the subject shown in Fig. 1. The activation maps demonstrate significant bilateral activity in the lateral occipitotemporal cortex (O; **a**–**f**), in parts of the parietal cortex (P, **a**–**c**), in the anterior part (AI; **j**–**o**) and posterior part (PI; **g**–**l**) of the insula, the caudate nucleus (NC, **g**–**i**), the putamen (PU; **j**–**l**), the globus pallidus (GP; **j**–**o**), the paramedian thalamus (T; **j**–**l**) and the visual cortex (VC; **g**–**o**).

corresponding first anatomical image of the functional data set to enhance visualization and to localize activation in relation to cerebral anatomy.

As described in a previous study (Bucher *et al.*, 1996, 1997), the evaluation of our functional data refers only to the anatomical location and the extent of activation (number of activated voxels), because of the large interindividual variety in signal intensity changes. We used a region of interest analysis to calculate the numbers of activated voxels. In order to test whether the activation condition is a significant factor, the number of activated voxels was subjected to a repeated measures ANOVA (analysis of variance) for all regions of interest. The stimulus tasks (rightward OKN, fixation suppression of rightward OKN; upward OKN, fixation suppression of upward OKN), the hemispheric preponderance (right and left hemisphere) and the direction of drum rotation (rightward, upward) were the confounding variables. The extent of activation (number of activated voxels) was the dependent variable. The extent of activated areas was then compared between the left and right hemispheres using Student's *t* test after checking for Gaussian distribution. Gaussian distribution was examined using the David, Pearson and Stephens test (Ramm and Hofmann, 1986). The calculated a values are given in Table 1 for all brain structures. According to this test, the measured number of activated voxels is considered to follow a Gaussian distribution if the a value at an α level of 1% falls within a range of 2.51–3.87 for 10 measurements and within a range of 1.71–2.0 for three measurements. Additionally, we compared the number of activated voxels during drum rotation with and without fixation suppression. We also compared the extent of activation between horizontal OKN to the right and vertical upward OKN. The *post hoc t* tests were used with a significant threshold set at a Bonferroni-adjusted α level of $P < 0.01$ following correction for multiple, non-independent comparisons (equivalent to $P < 0.001$). Single activated voxels that were not activated in a cluster (more than two activated voxels) were considered to represent false-positive activation.

The additional EPI whole-brain scans were analysed using the SPM96 software package (Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, UK) on a Sun UltraSPARC computer (Sun Microsystems, Mountain View, Calif., USA). The scans from each of the four subjects were realigned and corrected for subject movement (maximum 1.4 mm and 1.7°) using the first image as a reference and using non-linear minimization and a computationally efficient cubic algorithm (Friston *et al.*, 1995). The scans were then stereotactically transformed to a standard template in the Talairach space (Talairach coordinates corresponding to the stereotactic conventions of the atlas of Talairach and Tournoux, 1988). The upper level of the search volume was at $z = 54$ mm and the lower level at $z = 28$ mm. Images were smoothed with a Gaussian kernel of $5 \times 5 \times 10$ mm^3. Data were analysed using a delayed box-car reference waveform and a high-pass filter of 50 s. After specifying the appropriate design matrix, the condition and covariate effects were estimated according to the general linear model at each voxel (Friston *et al.*, 1994). The design matrix included global activity as a confounding covariate. To test the hypothesis about regionally specific condition effects, the estimates were compared using linear contrasts. The resulting set of voxel values for each contrast constituted a statistical parametric map of the *t* statistic (SPM{*t*}). The SPM{*t*} values were thresholded at $P < 0.001$ uncorrected and at $P < 0.05$ after correction for multiple comparisons.

Results

All 10 subjects revealed cortical and subcortical activation associated with OKN and the fixation suppression of OKN. The percentage of signal changes within the activated areas during OKN or OKN fixation suppression ranged from 2.4 to 10.5% among individuals. Repeated measurements of the same subject showed a consistent extent of activation. We found a maximum individual standard deviation in the area of the intraparietal sulcus of 14.2 activated voxels (13.5%). The mean false-positive activation of the 10 subjects at a significance level of at least $P < 0.005$ and for 32 images was 20.1%. Activation was centred almost exclusively over the grey matter and small draining vessels. Flow-sensitized images excluded large vessels as a source of activation. We detected a significant difference in the number of all activated voxels between the OKN condition and the fixation suppression condition ($P < 0.001$). Additionally, ANOVA for repeated measurements revealed a significant difference in the number of all activated voxels between the right and the left hemispheres ($P < 0.001$). In contrast, there was no significant difference in the number of activated voxels between rightward OKN and upward OKN for both the OKN condition and the fixation suppression condition ($P > 0.5$).

The horizontal and vertical OKN were associated with activity in the precentral and posterior median frontal gyrus (Talairach coordinates $x, y, z = 40, 22, 36$; BA 8 and 9; Fig. 1, d–i), the prefrontal cortex (BA 46; Fig. 1, a–f), the medial part of the superior frontal gyrus (26, 40, 28; BA 9 and 10; Fig. 1, a–f), the anterior cingulate cortex (BA 24; Fig. 1, a–f), in the area of the (posterior) parietal cortex (20, –56, 52 and 42, –38, 32; Fig. 1, j–o; Fig. 2, a–c), in the lateral occipitotemporal cortex (42, –66, 4; Fig. 1, m–o; Fig. 2, a–f) and in the visual cortex (20, –90, –2; BA 17 and 18; Fig. 2, g–o). The anatomical localization of occipitotemporal activity ranged from F-d-6 to G-d-10 (BA 22 and 40), using the Talairach three-dimensional proportional grid system for referential orientation (Talairach and Tournoux, 1993). Activation of the posterior parietal cortex was located deep in the intraparietal sulcus, near the border between the angular gyrus and the supramarginal gyrus (BA 39 and 40). The posterior parietal cortex revealed the strongest response (130.2 ± 11.0 voxels; Table 1). We found insular activation during both horizontal and vertical OKN in two spatially separate areas: the anterior part of the insula (38, 8, 4) and

Table 1 *Number of activated voxels associated with rightward optokinetic stimulation and fixation suppression of OKN*

Hemisphere	Paradigm	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Mean ± SD	a*	*t* Value OKN vs Fix. Sup.	*t* Value Right vs left hemisphere
Precentral and posterior median frontal gyrus															
Right	OKN	37	32	31	34	36	30	31	29	36	36	33.4 ± 2.9	2.72	–	7.38 S
	Fix. Sup.	18	17	15	15	18	20	19	18	16	13	16.9 ± 2.1	3.28	12.13 S	7.89 S
Left	OKN	32	25	27	26	30	28	21	22	30	24	26.5 ± 3.6	3.06	–	–
	Fix. Sup.	15	10	12	10	9	11	10	13	10	9	10.8 ± 1.9	3.14	12.95 S	–
Prefrontal cortex															
Right	OKN	50	44	46	45	43	46	46	42	49	52	46.2 ± 3.2	3.16	–	7.80 S
	Fix. Sup.	37	38	40	41	40	42	37	33	42	44	39.4 ± 3.1	3.43	7.28 S	7.72 S
Left	OKN	37	38	34	38	41	36	32	33	35	38	36.2 ± 2.7	3.28	–	–
	Fix. Sup.	32	35	29	32	32	33	28	29	33	30	31.3 ± 2.1	3.16	6.94 S	–
Median part of superior frontal gyrus/anterior cingulate cortex															
Right	OKN	12	14	10	15	11	16	14	0	13	12	11.7 ± 4.5	3.56	–	5.52
	Fix. Sup.	20	22	19	21	21	24	23	0	21	20	19.1 ± 6.9	3.49	8.37 S	6.71
Left	OKN	9	6	9	8	6	9	8	0	9	7	7.1 ± 2.8	3.25	–	–
	Fix. Sup.	14	16	17	15	13	17	15	0	14	15	13.6 ± 4.9	3.44	7.56 S	–
Anterior part of the insula															
Right	OKN	18	16	18	15	12	14	13	13	11	17	14.7 ± 2.6	2.80	–	5.06
	Fix. Sup.	0	0	0	3	0	0	5	0	3	0	1.1 ± 1.9	2.70	12.17 S	1.76
	Fix. Sup.	0	0	0	2	0	0	3	0	0	0	0.5 ± 1.1	2.78	6.69 S	–
Posterior part of the insula															
Right	OKN	29	36	34	29	36	34	35	0	25	34	29.2 ± 10.9	3.31	–	7.53 S
	Fix. Sup.	0	0	0	0	2	0	3	0	5	0	1.0 ± 1.8	2.83	8.17 S	1.86
Left	OKN	16	21	19	21	19	20	18	0	15	20	16.9 ± 6.3	3.35	–	–
	Fix. Sup.	0	0	0	0	0	0	2	0	3	0	0.5 ± 1.1	2.78	8.08 S	–
Posterior parietal cortex															
Right	OKN	136	133	135	134	114	138	131	106	138	137	130.2 ± 11.0	2.90	–	8.06 S
	Fix. Sup.	83	74	76	80	89	79	65	83	92	90	81.1 ± 8.2	3.28	10.68 S	7.18 S
Left	OKN	96	112	102	106	109	97	99	87	98	96	100.2 ± 7.3	3.42	–	–
	Fix. Sup.	74	60	63	62	68	60	65	66	74	67	65.9 ± 5.1	2.76	10.59 S	–
Occipitotemporal cortex															
Right	OKN	57	42	51	40	39	50	54	0	58	44	43.5 ± 16.8	3.46	–	7.81 S
	Fix. Sup.	38	30	35	29	27	34	36	0	34	32	29.5 ± 10.9	3.49	6.94 S	7.63 S
Left	OKN	16	14	0	5	0	0	6	0	24	0	6.5 ± 8.6	2.79	–	–
	Fix. Sup.	0	11	0	2	2	0	3	0	10	0	2.1 ± 4.2	2.61	1.89	–
Visual cortex															
Right	OKN	99	130	121	106	117	118	110	137	128	125	119.1 ± 11.6	3.26	–	1.71
	Fix. Sup.	106	133	129	100	114	115	124	130	125	133	120.9 ± 11.6	2.85	0.82	3.80
Left	OKN	104	127	136	112	107	95	91	131	110	105	111.8 ± 15.0	2.99	–	–
	Fix. Sup.	91	124	118	98	108	107	98	128	117	101	109.0 ± 12.3	3.00	0.89	–
Caudate nucleus															
Right	OKN	14	12	13	0	9	0	11	9	16	13	9.7 ± 5.5	2.89	–	2.08
	Fix. Sup.	8	5	6	0	7	0	7	4	10	8	5.5 ± 3.3	2.99	4.99	3.36
Left	OKN	12	0	8	0	5	8	4	7	11	8	6.3 ± 4.1	2.94	–	–
	Fix. Sup.	6	0	6	0	3	0	4	3	4	6	3.2 ± 2.5	2.41	3.27	–
Putamen															
Right	OKN	35	30	34	32	36	28	34	32	38	26	32.5 ± 3.7	3.25	–	0.89
	Fix. Sup.	24	22	22	23	27	23	21	25	23	19	22.9 ± 2.2	3.66	7.43 S	0.92
Left	OKN	39	33	31	26	37	32	28	0	36	32	29.4 ± 11.1	3.53	–	–
	Fix. Sup.	25	21	24	16	27	21	18	0	27	24	20.3 ± 8.0	3.37	7.66 S	–

Table 1 *Cont.*

Hemisphere	Paradigm	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Mean ± SD	a*	*t* Value OKN vs Fix. Sup.	*t* Value Right vs left hemisphere
Globus pallidus															
Right	OKN	19	18	14	13	17	23	20	0	22	16	16.2 ± 6.5	3.52	–	1.21
	Fix. Sup.	11	12	8	7	10	13	12	0	12	10	9.5 ± 3.8	3.39	7.49 S	3.07
Left	OKN	20	19	13	15	12	13	20	0	17	18	14.7 ± 6.0	3.35	–	–
	Fix. Sup.	14	13	9	12	11	12	14	0	14	12	11.1 ± 4.2	3.33	4.81	–
Thalamus															
Right	OKN	29	20	23	25	21	17	22	25	29	22	23.3 ± 3.8	3.16	–	8.32 S
	Fix. Sup.	0	0	0	2	4	7	0	0	2	8	2.3 ± 3.1	2.62	11.92 S	1.34
Left	OKN	7	13	10	11	7	11	10	14	9	10	10.2 ± 2.3	3.11	–	–
	Fix. Sup.	0	0	0	5	3	0	0	0	4	2	1.5 ± 2.0	2.56	9.24 S	–

Significant *t* values are marked with the letter S. Fix. Sup. = fixation suppression of rightward OKN; SD = standard deviation; a* = values to test for Gaussian distribution according to David, Pearson and Stephens (Ramm and Hofmann, 1986) are tabulated.

the posterior part of the insula (36, –30, 18). In the three-dimensional proportional grid system (Talairach and Tournoux, 1993) the activation of the anterior insula ranged from C-c-10 to D-c-11 (Fig. 2, j, l, m, o) and that of the posterior insula from E-c-10 to E-c-11 (Fig. 2, g, i, j, l). The extent of activation was significantly higher ($P < 0.001$) in the posterior part of the insula (29.2 ± 10.9 voxels) than in the anterior part (14.7 ± 2.6 voxels) for both horizontal and vertical OKN conditions. Subcortical activation included the nucleus caudatus (D-a-8 to D-a-9; Fig. 2, g–i), the putamen (Fig. 2, j–l), the globus pallidus (Fig. 2, j–o) and the paramedian thalamus (10, –10, 4; Fig. 2, j–l). The anatomical localization of the thalamic activation ranged from E2-a-9 to E3-a-9 and from E3-a-7 to F-b-7 with the corresponding thalamic subnuclei nucleus ventralis lateralis, nucleus dorsomedialis and nucleus pulvinaris.

Suppression of OKN

Suppression of the OKN by fixation of a target in front of the rotating drum was associated with activation of the same loci as in the OKN paradigm, such as the precentral and posterior median frontal gyrus (BA 9 and 10; Fig. 1, e, h), the prefrontal cortex (BA 46; Fig. 1, b, e), the medial part of the superior frontal gyrus (BA 9 and 10; Fig. 1, b, e) and the anterior cingulate gyrus (BA 24; Fig. 1, b, e), the posterior parietal cortex (BA 39 and 40; Fig. 1, k, n; Fig. 2, b), the lateral occipitotemporal cortex (BA 22 and 40; Fig. 1, n; Fig. 2, b), the visual cortex (BA 17 and 18; Fig. 2, h, k, n), the nucleus caudatus (Fig. 2, h), the putamen (Fig. 2, k) and the globus pallidus (Fig. 2, k, n). However, the number of activated voxels was significantly higher ($P < 0.005$) in the medial part of the superior frontal gyrus and the anterior cingulate gyrus during suppression of OKN (19.1 ± 6.9 voxels) than under the OKN condition (11.7 ± 4.5 voxels). In contrast, the extent of activation was significantly smaller during fixation suppression of OKN than under the OKN condition in the prefrontal cortex, the precentral and posterior median frontal gyrus, the posterior parietal cortex, the lateral occipitotemporal cortex, the putamen and the globus pallidus (Table 1). There was no activation of the anterior and posterior insula and negligible activation of the thalamus (2.3 ± 3.1 voxels) during fixation suppression of OKN (Fig. 3). We did not detect any significant difference ($P > 0.1$) in the number of activated voxels in the visual cortex and the caudate nucleus during fixation suppression of OKN and the OKN condition itself (Table 1).

Vertical OKN

Comparison of vertical OKN with the condition of fixation suppression of vertical OKN yielded results similar to those for horizontal OKN (Table 2). The anterior part of the insula and the thalamus were not activated during fixation suppression of upward OKN. There was negligible activation in the posterior part of the insula (1.7 ± 1.5 voxels). There was a significant decrease in the prefrontal cortex, the precentral and posterior median frontal gyrus, the posterior parietal cortex, the lateral occipitotemporal cortex, the putamen and the globus pallidus ($P < 0.005$) (Table 2). The extent of activation remained unchanged in the visual cortex and the caudate nucleus ($P > 0.5$). Comparison of horizontal and vertical OKN for both the fixation suppression condition and the OKN condition itself revealed no significant difference in the anatomical location of activation or the number of activated voxels ($P > 0.5$).

Hemispheric dominance

The visual cortex, superior frontal gyrus/anterior cingulate gyrus, anterior part of the insula, caudate nucleus, putamen and globus pallidus showed symmetrical bilateral activation during rightward OKN (Table 1) without any hemispheric asymmetry ($P > 0.1$). All other cortical areas activated during OKN demonstrated lateralized activation, predominantly of the right hemisphere (Fig. 4). Hemispheric asymmetry was

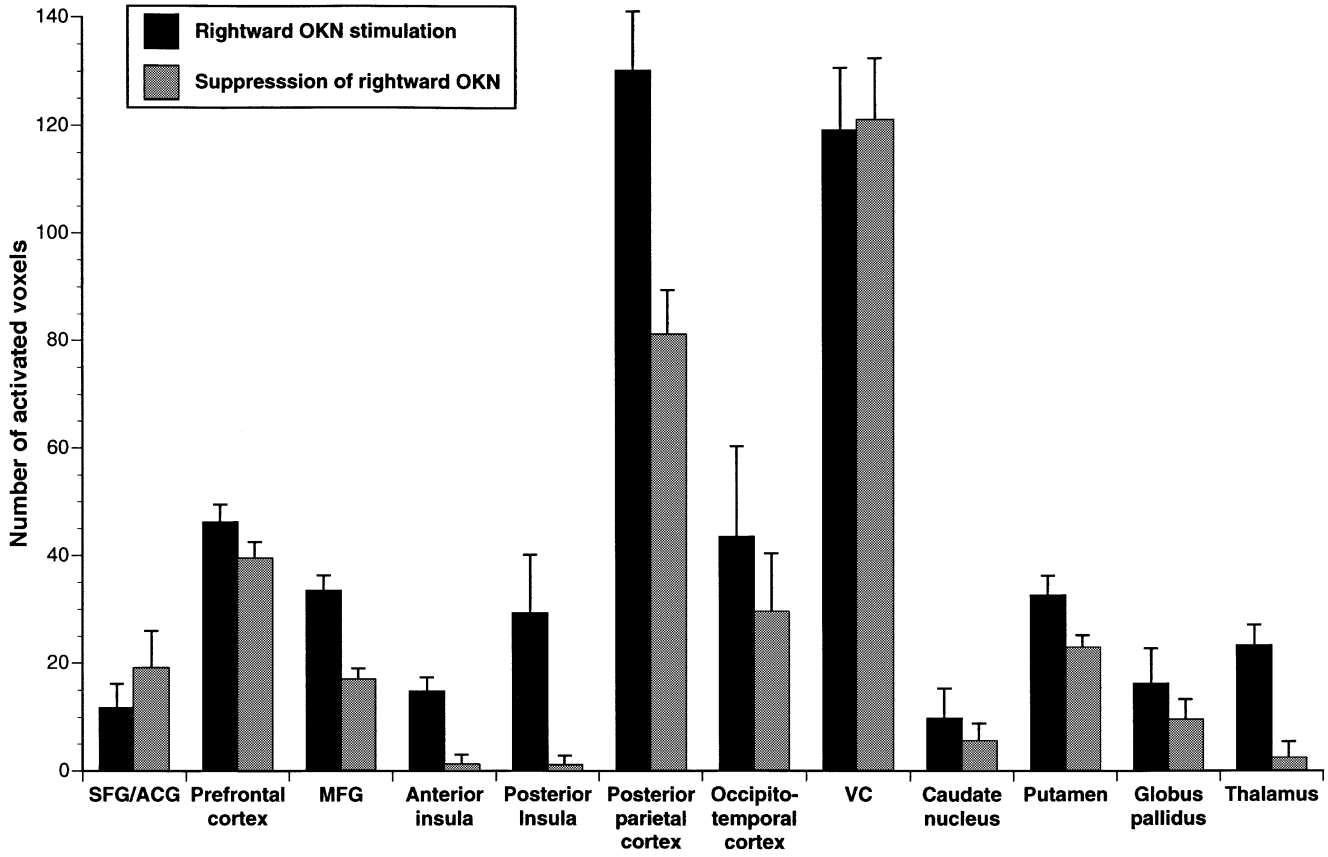

Fig. 3 Averaged values of the number of activated voxels in the right hemisphere during rightward optokinetic nystagmus (black columns) and during fixation suppression of rightward optokinetic nystagmus (grey columns). Mean and standard deviations (black bars) are shown for activation associated with object motion to the right. Note that there is no activation of the anterior and posterior insula and only slight activation of the thalamus during fixation suppression of OKN. ACG = anterior cingulate gyrus; MFG = precentral and posterior median frontal gyrus; SFG = superior frontal gyrus.

most prominent in the occipitotemporal cortex (BA 22 and 40; Fig. 4). Five of the 10 control subjects presented with a unilateral, right hemispheric activation of this area. The mean of activated voxels was 43.5 ± 16.8 voxels in the right hemisphere and 6.5 ± 8.6 voxels in the left hemisphere. There was also a preponderance of the right hemisphere ($P < 0.001$) for activation of the posterior parietal cortex (BA 39 and 40; Fig. 4); only 76% of voxels were activated on the left hemisphere compared with the right hemisphere. Additionally, a significantly right-lateralized response was found in the posterior insula (Table 1). We found 29.2 ± 10.9 activated voxels on the right and 16.9 ± 6.3 voxels on the left hemisphere during OKN. Compared with the right hemisphere, only 58% of the voxels on the left were activated in the posterior insula (E-c-10 to E-c-11). The precentral and posterior median frontal gyrus and the prefrontal cortex were also activated, accordingly with dominance of the right hemisphere (Table 1). Thalamic activation was highly lateralized ($P < 0.005$); the extent of activation was 56% greater in the right thalamic nuclei than in the left thalamic nuclei (Fig. 4). The preponderance of the right hemisphere was also present during fixation suppression of OKN in the precentral and posterior median frontal gyrus, the prefrontal cortex, the posterior parietal cortex and the lateral occipitotemporal cortex (Table 1). In contrast, hemispheric asymmetry of insular and thalamic areas was not found during fixation suppression of OKN, because the insula was not activated and the thalamus only negligibly activated.

Discussion

Horizontal and vertical small-field optokinetic stimulation activated the same multiple visual, ocular motor, and vestibular cortical and subcortical areas in both hemispheres. Their extent of activation was independent of the stimulus direction. All areas representing cortical (posterior parietal cortex, precentral and posterior median frontal gyrus, prefrontal cortex, medial part of the superior frontal gyrus, and occipitotemporal cortex) and subcortical (caudate nucleus, putamen and globus pallidus) ocular motor structures were activated during OKN as well as during fixation suppression of OKN. Significant right hemispheric dominance was observed in the motion-sensitive and ocular motor cortex

Table 2 *Number of activated voxels associated with upward OKN and fixation suppression of upward OKN*

Upward OKN stimulation			Fixation suppression of upward OKN			OKN vs fixation suppression of OKN	
Right hemisphere	Left hemisphere	Right vs left hemisphere	Right hemisphere	Left hemisphere	Right vs left hemisphere	Right hemisphere	Left hemisphere
Precentral and posterior median frontal gyrus							
31.7 ± 2.5	25.7 ± 4.2	$t = 3.93$; $P > 0.05$	15.3 ± 1.5	9.7 ± 2.5	$t = 4.25$; $P > 0.05$	$t = 24.51$; $P < 0.005$	$t = 16.00$; $P < 0.005$
Prefrontal cortex							
44.7 ± 2.5	34.0 ± 3.0	$t = 32.04$; $P < 0.001$	39.3 ± 2.6	29.3 ± 4.2	$t = 13.02$; $P < 0.01$	$t = 16.00$; $P < 0.005$	$t = 5.29$; $P > 0.01$
Median part of superior frontal gyrus/anterior cingulate cortex							
12.3 ± 2.5	7.0 ± 2.0	$t = 16.00$; $P < 0.005$	19.7 ± 2.5	13.0 ± 2.0	$t = 5.54$; $P > 0.01$	$t = 3.14$; $P > 0.1$	$t = 5.19$; $P > 0.05$
Anterior part of the insula							
12.7 ± 2.5	6.0 ± 5.7	$t = 1.60$; $P > 0.5$	Not activated	Not activated	–	–	–
Posterior part of the insula							
33.7 ± 3.1	17.3 ± 2.1	$t = 18.52$; $P < 0.005$	1.7 ± 1.5	Not activated	–	$t = 20.95$; $P < 0.005$	–
Posterior parietal cortex							
130.3 ± 7.0	100.0 ± 5.6	$t = 25.24$; $P < 0.005$	71.0 ± 3.0	60.3 ± 4.7	$t = 11.88$; $P < 0.01$	$t = 25.43$; $P < 0.005$	$t = 27.30$; $P < 0.005$
Occipitotemporal cortex							
41.7 ± 4.0	4.0 ± 6.9	$t = 18.58$; $P < 0.005$	31.0 ± 3.6	2.7 ± 4.6	$t = 32.13$; $P < 0.005$	$t = 32.00$; $P < 0.005$	$t = 1.00$; $P > 0.5$
Primary visual cortex							
123.7 ± 13.5	120.0 ± 17.3	$t = 0.68$; $P > 0.5$	117.7 ± 20.5	122.7 ± 19.2	$t = 4.33$; $P > 0.05$	$t = 1.33$; $P > 0.5$	$t = 0.58$; $P > 0.5$
Nucleus caudatus							
10.0 ± 2.6	4.0 ± 3.6	$t = 5.35$; $P > 0.01$	7.3 ± 1.5	7.0 ± 1.0	$t = 0.84$; $P > 0.5$	$t = 1.40$; $P > 0.5$	$t = 0.56$; $P > 0.5$
Putamen							
34.0 ± 4.0	31.3 ± 4.5	$t = 6.03$; $P > 0.01$	18.3 ± 2.5	18.7 ± 3.5	$t = 0.51$; $P > 0.5$	$t = 17.76$; $P < 0.005$	$t = 19.00$; $P < 0.005$
Globus pallidus							
19.0 ± 3.6	17.7 ± 4.0	$t = 4.00$; $P > 0.05$	9.7 ± 3.1	8.7 ± 3.2	$t = 1.01$; $P > 0.5$	$t = 28.00$; $P < 0.005$	$t = 5.79$; $P > 0.05$
Thalamus							
23.7 ± 3.1	9.3 ± 2.1	$t = 16.25$; $P < 0.005$	Not activated	Not activated	–	–	–

Analysis of the number of activated voxels during optokinetic nystagmus (OKN) induced by a drum rotating upward and fixation suppression of OKN. The *t* values and significance levels for task and hemisphere comparisons are also tabulated (corrected for multiple non-independent comparisons). The a values to test for Gaussian distribution at an alpha level of 1% according to David, Pearson and Stephens (Ramm and Hofmann, 1986) ranged between 1.73 and 2.00.

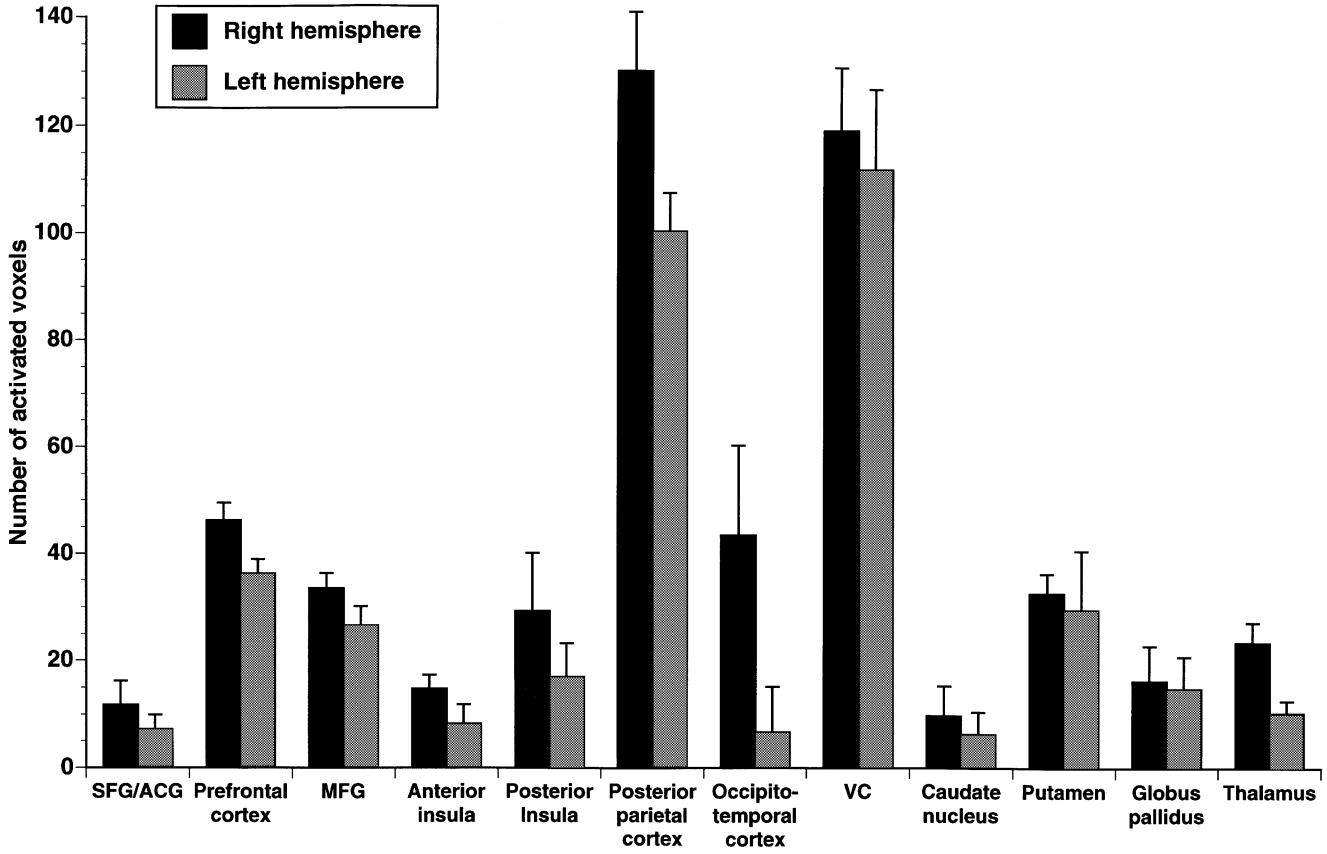

Fig. 4 Averaged values of the number of activated voxels in the right hemisphere (black columns) and left hemisphere (grey columns) during rightward optokinetic nystagmus. Mean and standard deviations (black bars) are shown for activation during object motion to the right. ACG = anterior cingulate gyrus; MFG = precentral and posterior median frontal gyrus; SFG = superior frontal gyrus.

areas and in the thalamus (except for the supplementary eye field and anterior cingulate gyrus) under both conditions.

Differential effects of suppression of OKN by fixation of a stationary target

Fixation suppression of eye movements during optokinetic stimulation yielded four different results: (i) increased activation; (ii) unchanged activation; (iii) decreased activation; and (iv) suppressed activation. Cortical and subcortical activation patterns were the same for horizontal and vertical optokinetic stimulation regardless of the stimulus direction. The small-field optokinetic stimulation elicited a regular eye movement pattern without apparent self-motion (vection). This kind of stimulation activates both the pursuit and the optokinetic system (Tusa and Zee, 1989). It occurs frequently under natural conditions, e.g. when a stationary observer (a pedestrian) watches the street traffic.

(i) The only areas with increased activation were in the medial part of the superior frontal gyrus, where the supplementary eye field is located, and the anterior cingulate cortex. The supplementary eye field is anatomically close to the anterior cingulate cortex and could not be separated from it in our study. Previous PET studies of visually guided (Fox *et al.*, 1985) and non-visually guided self-paced saccades (Petit *et al.*, 1993; Anderson *et al.*, 1994) have also reported activation of the supplementary motor area. The supplementary eye field is located in the medial anterior part of the supplementary motor area. In contrast to the study of Fox *et al.* (1985), who described activation of the supplementary motor area during visually guided saccades, other authors found no supplementary motor area activation during visually guided reflexive saccades but found it instead during memory-guided saccades and antisaccades (Anderson *et al.*, 1994; Sweeney *et al.*, 1996). Our data may explain this divergence in findings. A small increase in neuronal activity in the supplementary motor area can be seen during reflexive saccades (some studies could not detect this due to relatively low rates of saccades), whereas a significant increase is seen in tasks requiring voluntary behaviour and preparatory activity (Sweeney *et al.*, 1996). Fixation suppression of OKN requires motivation and voluntary behaviour consistent with the increased supplementary motor area activity (in contrast to the lower activity during OKN). The site of the latter activation agrees with findings of microstimulation studies in monkeys, which elicited contraversive saccades by stimulating the supplementary eye field in an area in the superior medial frontal lobe immediately rostral to the

supplementary motor area (Schlag and Schlag-Rey, 1987). These findings closely parallel those of human stimulation studies, in which electrical stimulation of the anterior supplementary motor area evoked contraversive eye movements (Fried *et al.*, 1991).

On the other hand, previous PET studies have shown activation of the anterior cingulate cortex during ocular motor paradigms (rostral part of the anterior cingulate cortex during visually guided saccades: Fox *et al.*, 1985; Paus *et al.*, 1993; remembered saccades: Petit *et al.*, 1993; Anderson *et al.*, 1994; Sweeney *et al.*, 1996), intentional movements (Colebatch *et al.*, 1991) and tasks with special (divided visual) attention and motivation (Corbetta *et al.*, 1991). Activation of the anterior cingulate cortex due to special attention to the fixation suppression during OKN could also explain our findings. Thus, activation of the supplementary eye field or the anterior cingulate cortex cannot be differentiated by anatomical activation data or functional considerations.

(ii) Activation of the visual cortex remained unchanged. This result was expected, since these areas reflect the purely visual evaluation of motion stimulation independently of the simultaneous ocular motor response. Activation in the caudate nucleus also seemed unchanged, but this was probably due to the small extent and the large variance of activation in this brain area.

(iii) Decreased activity was seen in the cortical and subcortical ocular motor areas, the precentral and posterior median frontal gyrus, where the frontal eye field is located, the prefrontal cortex, and the posterior parietal cortex, where it has to be assumed that the parietal eye field is located, and the lateral occipitotemporal cortex, which corresponds best with the human homologue of the motion-sensitive middle temporal and medial superior temporal areas as well as in the putamen, globus pallidum and paramedian thalamus. This finding of decreased activation reflects the different levels of activity of the ocular motor system, which subserves either OKN or fixation of a stationary target. Fixation of a target involves mechanisms different from those involved in eye movements. It is striking that the quantitative difference is most pronounced in the paramedian thalamus (nuclei ventralis lateralis, dorsomedialis and pulvinaris), where there is very little activation during fixation suppression. This is in agreement with electrophysiological findings in animal experiments, which showed increased activity in neurons of the nucleus pulvinaris during and after saccades (Robinson and McClurkin, 1989). As distinct from the putamen, the pallidus and the caudate nucleus, which can be interpreted as parts of the efferent ocular motor pathways (the basal ganglia–thalamocortical motor loop proposed by Alexander *et al.*, 1986), the thalamus is considered a more complex ocular motor relay station.

(iv) Fixation completely suppressed the activation of the anterior and posterior insula. These two areas most probably represent completely different functions and therefore must be discussed separately. The activated area in the posterior insula may be the homologue of the multisensory parieto-insular vestibular cortex and/or the adjacent visual temporal sylvian area complex, described by Grüsser and colleagues in the monkey (Grüsser *et* al.,1982, 1990*a*, *b*; Guldin and Grüsser, 1996).

Activation of the posterior insula during optokinetic stimulation

At first glance, it seems surprising that visual motion stimulation due to OKN activated the posterior insula, probably a homologue of the parieto-insular vestibular cortex, but the animal experiments of Grüsser and colleagues (Grüsser *et* al.,1982, 1990*a*, *b*; Guldin and Grüsser, 1996) confirm this finding. They found multisensory neurons that responded to vestibular, somatosensory and optokinetic stimuli in the parieto-insular vestibular cortex and neurons that especially responded to visual stimuli in the visual temporal sylvian area.

The question arises whether this activation is related to eye movements or the perception of self-motion, or both. Complete suppression of this activation by fixation suppression of OKN strongly supports the view that it is related to eye movements. On the other hand, this does not exclude the involvement of sensory vestibular functions such as spatial orientation (awareness of subjective straight ahead) during eye movements. It is necessary under moving eye conditions to keep control of the direction during locomotion and grasping movements. This so-called ‘vestibular cortex’ is not a primary cortex, but a multisensory integration centre for spatial orientation and self-motion perception.

A human lesion study showed that the area in the posterior insula also corresponds with the central overlapping area in patients with middle cerebral artery infarctions who presented with significant disturbances of the perception of verticality, i.e. disturbance of vestibular (otolith) input (Brandt *et al.*, 1994, 1995). Infarctions of this region may cause transient rotational vertigo in exceptional cases (Brandt *et al.*, 1995). Moreover, the same area in the posterior insula was activated in PET studies during caloric vestibular stimulation in humans (Bottini *et al.*, 1994; Dieterich *et al.*, 1996). This strongly suggests that multisensory neurons in the posterior insula receive vestibular input in human and non-human primates. The significant visual–vestibular convergence in these neurons seems a precondition for the activation of this area by optokinetic stimulation in the otherwise stationary subjects of our study. It seems unlikely that the functional correlate of this convergence is related to the decision-making process of whether OKN is secondary to self-motion or object-motion stimulation, since fixation suppression abolished activation.

In previous activation studies during ocular motor tasks the possible involvement of the posterior insula remained unclear. An fMRI study of the lateral occipitotemporal cortex leads one to speculate that activity, although not mentioned, seemed to appear in the right posterior insula during ocular

pursuit of a small dot but not during viewing of a moving grating (Barton *et al*., 1996*a*). Some PET studies on saccadic eye movements reported a unilateral or bilateral insula cortical activation in general terms as a finding outside the area of interest of these studies (Petit *et al*., 1993; Anderson *et al*., 1994). A precise anatomical localization of this activation in the anterior, middle or posterior part of the insula is difficult because of the limited spatial resolution of PET (if present, then the more anterior part of the insula is likely). Most earlier PET studies suffered from limited spatial resolution, which does not permit detailed description of the anatomical extent of activation. This limited not only the exact attribution to anatomical structures but also the spatial extent and separation of neighbouring areas. The latter is very relevant for the present discussion, since only the posterior insula is related to the vestibular system. Our data now allow the clear distinction of both areas in the anterior and posterior parts activated during OKN.

Activation of the anterior insula during optokinetic stimulation

Activation of the anterior insula has to be differentiated from that of the posterior insula. Animal studies failed to demonstrate a vestibular input to this area. The posterior insula may represent the 'sensory' part of visual–vestibular interaction for spatial orientation, whereas the anterior insula in cooperation with the saccadic and pursuit centres may be involved in the generation and control of eye movements, especially of spatially oriented eye movements and their temporal structuring. There is substantial evidence for this point of view. An animal study by Emmans *et al*. (1988) proved that anterior insular neurons are connected with the orbital and infralimbic cortex. The strongest afferents were thalamo-insular projections from the intralaminar nuclei, the ventromedial posterior nucleus, the mediodorsal nucleus and the claustrum (Brockhaus, 1940; Guldin and Markowitsch, 1984; Guldin *et al.*, 1986); the strongest efferents included projections to the suprasylvian sulcal area, the prefrontal cortex, the cingulate and claustral areas, and auditory and sensorimotor areas (Emmans *et al.*, 1988). There was a strong similarity in the connectivity patterns and the cytoarchitecture of the anterior insular and prefrontal cortices of different species. Both the temporal pole and the premotor cortex receive direct input from geniculate visual sources as well as from the anterior insula (Emmans *et al.*, 1988). The similarities in cytoarchitecture in the lateral orbitofrontal cortex, the temporal polar cortex and the anterior insula were interpreted to constitute a 'family of related paralimbic structures' (Mesulam and Mufson, 1982*a*, *b*; Emmans *et al.*, 1988).

Electrical stimulation of the contralateral insula in monkeys induced motor activity. Stimulation of the posterior half of the insula, the adjacent frontoparietal operculum (Sugar *et al.*, 1948), and, to a minor degree, the neighbouring anterior parts of the insula (Showers and Lauer, 1961) elicited movements of the face, hand and foot with a roughly somatotopic arrangement. Stimulation of the anterior half of the insula mainly caused respiratory slowing, movements of the vocal cords, and vegetative symptoms. Eye movements were induced only from a small anterior–superior part of the insula near the infrafrontal plane (Sugar *et al.*, 1948).

PET activation studies reported that 'bilateral insula cortical activation' occurs during remembered saccades as opposed to reflexive saccades (Anderson *et al.*, 1994). Statistical parametric maps in three projections of the bilateral insular activation during these remembered saccades clearly show activity in the anterior part of the insula but no activity in the posterior insula regardless of the experimental paradigm (see fig. 3 in Anderson *et al.*, 1994). Right (anterior) insula activation was also seen in PET studies during the performance of large-amplitude, self-paced saccades in the dark (Petit *et al.*, 1993). Furthermore, PET activation has also been reported at the floor of the left insular cortex near the claustrum during voluntary arm and hand movements in normal subjects (Colebatch *et al.*, 1991) and in intermediate or anterior parts of the insula bilaterally (not in the posterior insula) during voluntary limb movements of the recovered hand after a first hemiplegic stroke (Chollet *et al.*, 1991). Some authors have concluded from all these features that the anterior parts of the insula are a secondary motor area, which is activated in paced, stereotyped tasks (Anderson *et al.*, 1994).

Thus, the cytoanatomical data and the non-activation of the anterior insula during fixation suppression of OKN (Fig. 2, k, n) in our study suggest that the anterior insula is part of the neural network for spatially oriented (eye) movements, and is not necessarily involved in the fixation of a stationary target. This view is further supported by early studies in monkeys which showed an extensive efferent pathway from the anterior insula directly across the external capsules into the putamen and the globus pallidus (Showers and Lauer, 1961). These are subcortical stations of the efferent ocular motor pathway, which were also activated in our OKN paradigm. The anterior insula could possibly be a relay station between the cortical motor (saccadic and pursuit) centres in the frontal and prefrontal cortex, on the one hand, and the efferent subcortical ocular motor pathways (with the neighbouring putamen, globus pallidus and caudate nucleus), on the other. These suggestions are in parallel with the symmetrical bilateral activation of both the anterior insula and the efferent ocular motor centres (caudate nucleus, putamen, pallidus), which did not exhibit activation with right-hemispheric dominance, as did the cortical ocular motor areas, the thalamus and the posterior insula. This relay station is important for the co-ordination of ocular motor activities with respect to spatial orientation and temporal structuring. The findings of PET activation in the anterior insula during large-amplitude, self-paced saccades in the dark (Petit *et al.*, 1993) and during remembered saccades to locations of recent target appearance (Anderson *et al.*, 1994) are in agreement

with this concept, i.e. activation with eye movements under conditions that require spatial orientation in head-fixed coordinates.

Cortical activation is largely independent of the direction of horizontal or vertical optokinetic stimulation

Activation patterns of both hemispheres (including right hemispheric predominance) were independent of the direction of optokinetic stimulation. This held for horizontal (rightward versus leftward; Bucher *et al.*, 1997) and vertical optokinetic stimulation. In view of the fact that unilateral hemispheric lesions can cause transient or persistent asymmetrical or unidirectional ocular motor disturbances for both smooth pursuit and saccades (Thurston *et al.*, 1988; Ventre *et al.*, 1992; Heide *et al.*, 1995, 1996; Israël *et al.*, 1995; Lekwuwa and Barnes, 1996), this independence of stimulus direction was not expected, and it requires further explanation.

The data on directional preference in area V5 are mixed. Dubner and Zeki (1971) found a preference for centrifugal motion, but subsequent single-cell recordings suggest that all directions are well represented (Maunsell and van Essen, 1983; Albright *et al.*, 1984), and a recent fMRI study did not find a centrifugal bias in the human middle temporal area (Tootell *et al.*, 1995). Another fMRI study of the lateral occipitotemporal cortex during pursuit and motion perception also found no significant difference between passive viewing of unidirectional or bidirectional grating motion, or sinusoidal spot motion (Barton *et al.*, 1996*a*). On the other hand, directional pursuit deficits were seen, e.g. in terms of lower pursuit velocities with ipsiversive target motion, in patients with unilateral cortical lesions (Thurston *et al.*, 1988; Morrow and Sharpe, 1990; Heide *et al.*, 1996). This occurred more frequently in patients with frontal eye field lesions (in each of four cases) than in patients with posterior parietal cortex lesions (in four of 13 cases with foveal and in eight of 13 cases with optokinetic stimulation) and was more pronounced with predictable than with step-ramp stimuli (Heide *et al.*, 1996). Similar predominantly ipsilesional pursuit deficits were found in a long band of lesion overlap areas that ran from the V5 occipitotemporal areas posteriorly, through the internal sagittal stratum, the posterior limb and anterior limb of the internal capsule with adjacent striatum, to the dorsomedial frontal cortex anteriorly. In contrast, a bidirectional deficit with no significant asymmetries was noted in patients with lesions of the frontal eye field (Lekwuwa and Barnes, 1996). In view of other contradictory findings (Morrow and Sharpe, 1990, 1995; Rivaud *et al.*, 1994), ipsidirectional or bidirectional pursuit deficits from unilateral frontal eye field lesions will remain a matter of debate.

The topic of direction-specific deficits of saccades in patients with unilateral cortex lesions is also controversial. Areas in the frontal and parietal cortex of both hemispheres are involved in the generation of saccades in all directions; however, there is often a preference for the contralateral side. Focal unilateral lesions cause deficits that can often only be seen when special parameters of a saccade are investigated in complex experimental paradigms. Unilateral posterior parietal lesions induced prolonged latency and hypometry bilaterally in visually guided saccades under special (e.g. overlap) paradigm conditions. This was more pronounced in the contralateral visual hemifield and in right hemisphere localization (Pierrot-Deseilligny *et al.*, 1995). When 'double-step' stimuli were applied, unilateral frontal lesions sometimes impaired temporal properties, whereas parietal lesions caused spatial dysmetria or failure of ipsiversive second saccades after contraversive first saccades (Heide *et al.*, 1995). For other special saccade paradigms, such as memory-guided saccades with a vestibular input, direction-specific deficits were found in patients with lesions of (i) the right frontal eye field (only slightly for ipsilateral timing parameters and contralateral direction errors), (ii) the right posterior parietal cortex (deficient only in ipsilateral saccade reaction time anticipation), and (iii) the right parietotemporal cortex, i.e. the vestibular cortex (deficient in contralateral spatial parameters), but not in patients with lesions of the supplementary eye field, prefrontal cortex and parietal eye field (Israël *et al.*, 1995). All lesion studies are limited by their use of data obtained only after the loss of a circumscribed cortical area, when other areas of the affected and the unaffected sides have compensated for the deficit. This makes it difficult to evaluate these findings in the light of our fMRI data on right hemisphere dominance. Comparable cerebral activation studies that focus on this topic are rare. The direction of attention affected occipital and frontal PET activity (right occipital and left lateral frontal activity were higher with attention to the left, whereas right lateral frontal activity was higher with attention to the right), but not that of the parietal, premotor and anterior cingulate cortex (Vandenberghe *et al.*, 1997). Other studies of lateralized attention have not revealed parietal differences depending on changing the direction of attention (Heinze *et al.*, 1994; Woldorff *et al.*, 1995).

Thus, the lateralization of hemispheric activation seems possible, and it appears to be dependent on task-dependent variables such as attention and the complexity of stimulus paradigms. These variables were less relevant in our simple small-field optokinetic stimulation paradigm performed in the centre of the visual field (without a significant deviation of the beating field of nystagmus, *Schlagfeldverlagerung*). Deviation of the beating field towards the quick nystagmus phase, as it occurs with full-field OKN, will shift the attention and thus ocular motor activities towards one hemifield of the extrapersonal space.

Right hemisphere dominance for cortical motion-sensitive, ocular motor and vestibular structures

There was a significant dominance of activated cortical areas in the right hemisphere for motion-sensitive and ocular motor

structures and, in the OKN paradigm only, for the posterior (vestibular) insula. It was most prominent in the occipitotemporal cortex. The only significant subcortical difference was seen in the thalamus, but not along the efferent ocular motor structures (putamen, globus pallidus and caudate nucleus) and the anterior insula. Our findings for the right hemisphere predominance of activation support the PET indicate that the right hemisphere is dominant for visuospatial orientation (Nobre *et al.*, 1997). Right hemisphere predominance was also observed in previous activation studies, in a PET study on voluntary saccadic eye movements for the frontal eye field and the supplementary motor area during memory-guided saccades after a delay period (Sweeney *et al.*, 1996), in an fMRI study on visually guided saccades for the parietal eye field (Müri *et al.*, 1996), and in an fMRI study on a spatial working memory task for the middle frontal gyrus, corresponding to BA 46 (McCarthy *et al.*, 1996). Similarly, PET activation in the anterior temporal lobe (midway along the superior temporal sulcus) was clearly stronger on the right side for selective attention during visual discrimination of shape, but not of speed and colour (Corbetta *et al.*, 1991). Similar right/left asymmetries have been found in the inferotemporal cortex during several object recognition tasks (Corbetta *et al.*, 1990). Another PET study on attention showed activated areas in the prefrontal and superior parietal cortex, also primarily in the right hemisphere, independent of the laterality and modality of the sensory input (Pardo *et al.*, 1991). Furthermore, strong right lateralization in the mid-dorsolateral frontal cortex (BA 46) was reported by Petrides *et al.* (1993) in an experiment that required subjects to point to designs arranged in spatial locations. This asymmetry presumably reflects the role of the right hemisphere in processing non-verbal spatial material.

Furthermore, the right hemisphere predominance is evident for parietal lesions (where the asymmetry of fMRI activity was strongest in our study), causing visuospatial hemineglect in humans (Vallar and Perani, 1986), a finding that has not yet been described in monkeys. A study on directional defects in pursuit and motion perception in patients with unilateral cerebral lesions (Barton *et al.*, 1996*b*) reported that two of three patients with left hemisphere lesions had bidirectional defects in motion discrimination, but none of the 21 patients with right-sided lesions had bidirectional deficits. Although Vaina (1989) in parallel found right hemisphere predominance for perceiving motion-defined form in humans, this could not be confirmed later (Regan *et al.*, 1992). However, the hemispheric asymmetry of the parieto-occipital cortex and the frontal eye field in our OKN study closely paralleled that of significantly more severe smooth pursuit impairments in patients with lesions involving the right posterior parietal cortex and/or the right dorsolateral frontal cortex than in their left-sided counterparts (Lekwuwa and Barnes, 1996). Moreover, right-sided lesions in the corticolimbic-reticular formation loop for directed attention produced a significantly more profound deficit in smooth pursuit eye movements than equivalent lesions in the left hemisphere. Subcortical lesions that did not affect the attention network produced similar degrees of deficit in left- and right-hemisphere lesions (Lekwuwa and Barnes, 1996). Our data with the strongest predominance in the right occipitotemporal cortex suggest that the right hemisphere dominance in oculomotor performance may be closely related to its dominance in spatially selective visual attention.

In conclusion, the functional interpretation of a network of multiple visual, ocular motor and vestibular areas activated with a comparatively simple mode of small-field optokinetic stimulation deserves further study. Circumscribed cerebral pathology in patients with infarctions should prove helpful for correlating the particular functional deficit with changes in activation patterns.

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