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RESEARCH ARTICLE

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Motion-responsive regions of the human brain

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Abstract Functional magnetic resonance imaging was used to map motion responsive regions of the human brain by contrasting passive viewing of moving and stationary randomly textured patterns. Regions were retained as motion responsive if they reached significance either in the group analysis or in the majority of hemispheres in single-subject analysis. They include well-known regions, such as V1, hMT/V5+, and hV3A, but also several occipito-temporal, occipito-parietal, parietal, and frontal regions. The time course of the activation was similar in most of these regions. Motion responses were nearly identical for binocular and monocular presentations. Flicker-induced-activation introduced a dichotomy amongst these motion responsive regions. Early occipital and occipito-temporal regions responded well to flicker, while flicker responses gradually vanished as one moved to occipito-parietal and then parietal regions. Finally, over a more than four-fold range, stimulus diameter had little effect on the motion activations, except in V1.

Key words Visual cortex · Motion · Functional imaging · Human · Flicker

Introduction

There is considerable agreement that a region in the ascending limb of the inferior temporal sulcus of the human brain responds well to moving in contrast to static patterns (Zeki et al. 1991; Watson et al. 1993; Dupont et al. 1994, 1997; Cheng et al. 1995; McCarthy et al. 1995; Tootell et al. 1995; Beauchamp et al. 1997; O'Craven et al. 1997; Van Oostende et al. 1997; Cornette et al. 1998b; Goebel et al. 1998; Smith et al. 1998; Culham et al. 1999). This region was initially labeled the homologue of monkey MT/V5 (Zeki et al. 1991), but, more recently, it has been considered to include the homologue of MT/V5 satellites and is referred to as hMT/V5+. In our earlier positron emission tomography (PET) studies, however, we have repeatedly reported that many regions in the human brain respond to moving in contrast to stationary patterns (Dupont et al. 1994, 1997; Cornette et al. 1998a). These additional regions were located in the parietal cortex, in the posterior insula, but also in the more ventral, occipito-temporal cortex and in the frontal cortex. This is in agreement with data obtained in the monkey, indicating that direction selectivity, often considered an a hallmark of motion-processing regions, is a property shared by neurons in many visual areas (for a review, see Orban 1998). Yet functional magnetic resonance imaging (fMRI) studies have concentrated on early motion-responsive regions, in particular MT/V5 and retinotopically organized regions (Tootell et al. 1995, 1997; O'Craven et al. 1997; Smith et al. 1998), although activation of parietal regions by motion has been mentioned (Tootell et al. 1995; Beauchamp et al. 1997; Goebel et al. 1998). The main purpose of the present fMRI study was to describe the additional motion-responsive regions in detail.

It has been repeatedly suggested that V1 neurons are simple spatio-temporal filters (Movshon et al. 1978; Adelson and Bergen 1985; McLean and Palmer 1989). Such neurons respond to the motion energy present in motion displays, but also in flickering displays, and thus confuse temporal and spatio-temporal correlation in the stimulus. Indeed, even direction-selective V1 neurons respond relatively well to flicker (Qian and Andersen 1994). It has been reported that MT/V5 neurons respond less to flicker than V1 neurons, and this has been related to suppression between neurons tuned to different directions in MT/V5 (Qian and Andersen 1994). Since neurons at the next stage, in MST, respond even less to flicker than MT/V5 neurons (Lagae et al. 1994), flicker responses seem to be gradually rejected in the motion-processing pathway of the monkey. In human, it has

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been reported that hMT/V5+ is also responsive to flicker (Tootell et al. 1995), but less so than V1 (Goebel et al. 1998). The question thus arises whether motion and flicker are distinguished by the motion-responsive regions at later stages of visual processing in the human brain, e.g., in parietal regions. Addressing this question was the second purpose of the present study.

In most imaging studies of the human brain, V1 has been reported to respond to motion (Zeki et al. 1991; Watson et al. 1993; Tootell et al. 1995; McKeefry et al. 1997; Goebel et al. 1998; Smith et al. 1998). Yet, in our studies using both PET (Dupont et al. 1994, 1997) and fMRI (Van Oostende et al. 1997), this activation is usually weak or insignificant. One constant feature of our stimuli is their small size: we typically use diameters of 3–4° compared with 30–40° in most other studies. Thus, it may well be that stimulus size interacts with motion responses in human V1. We cannot a priori exclude the possibility that stimulus size also affects motion responses in higher order visual regions. Indeed, in monkey MT/V5 and MST, there are units displaying strong spatial summation (Saito et al. 1986; Tanaka et al. 1986; Lagae et al. 1994), while others show reduced responses to large stimuli due to the antagonistic surroundings in their receptive fields (Allman et al. 1985; Tanaka et al. 1986; Raiguel et al. 1995). Since the relative proportions of these two types of neurons are unknown in the human motion-responsive regions and most of these regions fall outside the early retinotopically organized cortical areas (Sereno et al. 1995; DeYoe et al. 1996; Engel et al. 1997), it is difficult to predict whether or not activation of motion-responsive regions will depend on stimulus size. Therefore, studying the interaction of stimulus size with stimulus type (moving/stationary) was the third objective of the present study.

Materials and methods

Subjects

Thirteen subjects (8M and 5F) participated in the present study. Their age ranged from 20 to 29 years. They had normal or corrected to normal vision and no history of neurological or psychiatric disease. All were right handed as assessed by the Edinburgh inventory (Oldfield 1971), with an average laterality quotient of 0.83. They gave their informed consent in accordance with the declaration of Helsinki, and the study was approved by the ethical committee of the KU Leuven Medical School. All subjects were immobilized using a bite bar. They were instructed to maintain fixation on a small red target in the center of the screen and to perform no task other than the fixation, while passively viewing the stimuli. Subjects were familiarized with this task during an initial training session. Subjects viewed the stimuli binocularly except in experiment 2, in which monocular and binocular viewing were compared. Fixation was controlled using an MR-compatible infrared eye-movement tracking device (Ober2, Permobil MeditechAB, Sweden) in experiments one and two. Eye-movement traces, plotting horizontal and vertical eye positions as a function of time, were inspected for changes in amplitude to detect saccades and blinks. As shown in Fig. 1A–C these two types of motor events can be readily distinguished. Figure 1D and E show that the susceptibility artifact of the Ober2 in the anterior frontal lobe was reduced by using only a single goggle and by additional shimming of the magnetic field. In half of the subjects, the goggle was positioned over the left eye, in the other half over the right eye.

Stimuli and conditions

Stimuli were projected by means of a LCD projector (Sharp GX-3800E, 640×480 pixels and 60 Hz refresh rate) onto a translucent screen positioned in the bore of the magnet at 30 cm from the subjects' eyes. Stimuli were generated with a PC using a Tiga-diamond (Salient AT3000) graphics card. Circular random textured patterns (RTPS) consisting of 50% white dots (5 minarc pixelsize) on a black background were used as stimuli. The mean luminance was 79.4 cd/m^2 and the contrast 0.97. The stimulus diameter was 7°, except in experiment 3, where different values were tested. All stimuli were presented centrally in the visual field.

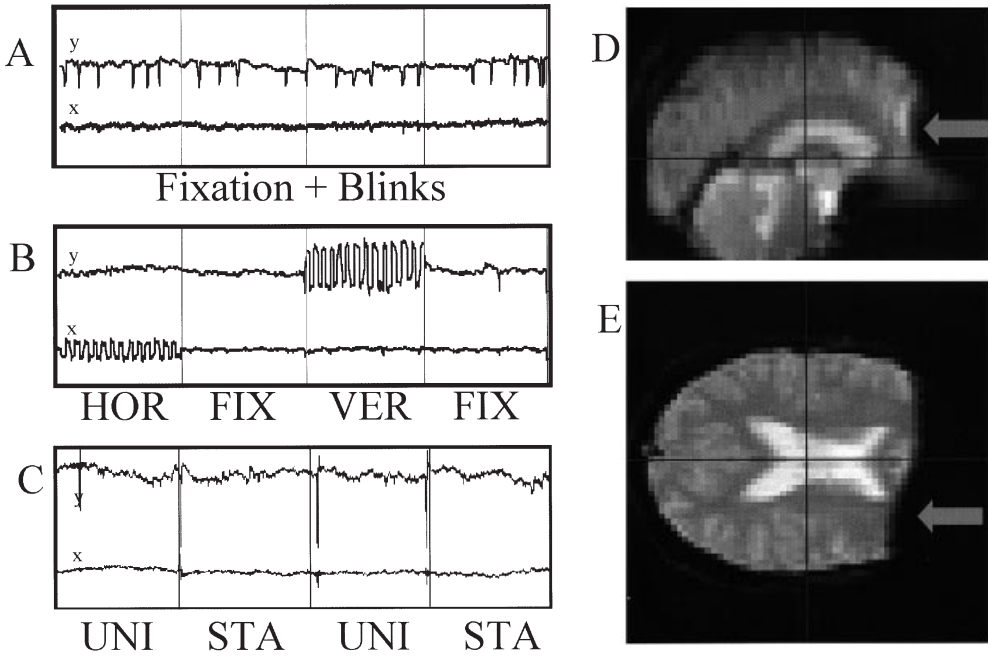

Fig. 1A–E Eye-movement recording using the Ober2 eye-movement tracking device. **A–C** Vertical (*y*) and horizontal (*x*) eye position plotted as a function of time in a pilot subject making blinks (**A**) or horizontal (*HOR*; 5° amplitude) and vertical (*VER*; 5° amplitude) saccades alternating with fixation (*FIX*) (**B**), and in one of the subjects during alterations between moving (*UNI*) and stationary (*STA*) random textured patterns (**C**). **D, E** Sagittal and transverse sections of T2-weighted scans showing the susceptibility artifact (*arrow*) in the frontal cortex induced by the goggle

Three modes of stimulation were used. The RTP remained stationary in a first condition (STA). In a second condition (UNI), the RTP moved coherently at 6°/s. The direction of motion reversed every 427 ms, while a new axis of motion was randomly selected every 854 ms. In a third condition (FLI), the RTP remained stationary, but a new pattern was presented every 10 or 4 frames, yielding an RTP flickering at 6 or 15 Hz. These conditions are the same as some of those used by Van Oostende et al. (1997). Hence, for consistency, we have retained the same labels.

fMRI measurements

A functional time series consisted of 120 gradient-echo (GE) echoplanar imaging (EPI) whole-brain scans (Siemens Vision 1.5T), acquired every 3.6 s (TR/TE=3600/40 ms, field of view: 200×200 mm, 64×64 matrix, 4 mm slice thickness, 1 mm gap, 32 transversal slices). In experiment 3, carried out earlier, only 20 slices were acquired every 3 s. A time series included alternations of 2, 4, or 6 conditions, depending on the number of conditions to be compared directly. The number of time series acquired was adjusted such that, for each condition, 120 images of each slice were taken. In experiment 1, the UNI and STA conditions alternated and two time series were acquired. Experiment 2 included UNI and STA as well as FLI at 6 and 15 Hz. Time series with these four conditions were alternatively tested with binocular and monocular viewing. Thus, eight time series were acquired in each subject. In experiment 3, a factorial design was used with stimulus size (three levels: 3, 7, and 14°) and type (two levels: UNI and STA) as factors, yielding six conditions. Consequently, six time series were acquired in each subject.

Sagittal anatomical images were acquired before the functional scanning in each session (3D MPRAGE, TR/TE=11.4/4.4 ms, TI=300 ms, field of view: 256×256 mm, matrix 256×256, 160 mm slab thickness, 128 sagittal partitions).

Analysis

Both a group and a single-subject analysis were carried out. The functional volumes acquired in each subject were realigned using the MIRIT algorithm (Maes et al. 1997), normalized to the stereotactic space of Talairach and Tournoux and smoothed spatially (Gaussian kemel with 6 and 10 mm full width at half maximum for single and group analysis respectively) using SPM 96 (Friston et al. 1991, 1995).

Global changes in BOLD signal were removed by proportional scaling (Holmes et al. 1997), and the values were mean adjusted. After the appropriate design matrix was specified, the covariates of interest were estimated according to the general linear model at each and every voxel, and low frequency fluctuations were modeled as covariates of no interest. The best least-square fit of the adjusted data to the modeled experimental conditions represents the parameter estimates. To test the hypothesis about regional condition specific effects, the estimates were compared using linear contrasts.

Significant hemodynamic changes for each contrast were assessed using Z statistical parametric maps (SPMs). We report activations above a threshold corresponding to $P<0.05$ corrected for muItiple comparisons. In the group analysis the main effect of condition over subjects was masked with all subject-specific contrasts (at a threshold of $P<0.05$). The resulting SPM indicates the voxels at which all subjects significantly activated (Friston, personal communication). The smoothness of the SPMs (full width at half maximum) was 8 mm in all directions for the single-subject and 15 mm in all directions for the group analyses. If one accepts that two local SPM maxima indicate different activation sites when the intervening activity decreases to at least 50% of their maximum, this smoothness indicates the minimum distance between two resolvable sites.

To identify motion-responsive regions (experiment 1), we used the contrast UNI minus STA. In the second experiment UNI was compared to STA and to FLI 15 Hz, as well as FLI 15 Hz to STA. In the third experiment, we computed both the main effects and their interactions. The main effect of size was tested by contrasting 14 to 3° diameter and the main effect of stimulus type by comparing UNI to STA.

Results

Motion-responsive regions: eye movements

The six subjects maintained fixation well during experiment one. Three subjects made very few saccades per functional time series (0–3 saccades), and the incidence was the same in the UNI and STA conditions. The three remaining subjects made slightly more saccades (4–6/time series) with 1 or 2 saccades more during UNI than during STA.

Motion-responsive regions: group analysis

Passive viewing of moving compared with stationary RTPs yielded a number of differentially active regions in the group of six subjects (Fig. 2). The most significant activation was observed in the left and right temporo-parieto-occipital cortex, in the location corresponding to hMT/V5+ according to earlier studies (Watson et al. 1993; Tootell et al. 1995; Van Oostende et al. 1997). In left occipital cortex, significant activation was observed in three sites, two of which correspond to regions implicated earlier in motion processing: hV3A (Tootell et al. 1997; Van Oostende et al. 1997; Goebel et al. 1998) and the lingual region, which has been shown to be involved in direction and speed discrimination (Cornette et al. 1998b; Orban et al. 1998b). The third site, located in the lateral occipital sulcus, seems too anterior to correspond to region KO (Orban et al. 1995; Dupont et al. 1997; Van Oostende et al. 1997). Therefore, we have labeled it LOS/KO. These three occipital regions were also activated in the right hemisphere, but somewhat less so than on the left. In the left hemisphere, three additional regions of significant activation included an anterior parietal region at the junction of intraparietal and postcentral sulcus, a region in the occipital ventral end of the intraparietal sulcus, and a fusiform region. Finally, a frontal region at the junction of the superior frontal sulcus with the precentral sulcus was activated bilaterally.

It should be noted that all these regions are separated by at least 15 mm. Hence, given the resolution of our measurements, they most likely represent distinct functional regions, corresponding to representations of central vision in different cortical areas. The only exception is LOS/KO, the most significant voxel of which is only 11–12 mm from that of the hV3A activation in the two hemispheres (Table 1). This is in agreement with our earlier study (Van Oostende et al. 1997), in which we showed that hV3A and KO are distinct, but abutting, with KO slightly more ventral and anterior than hV3A.

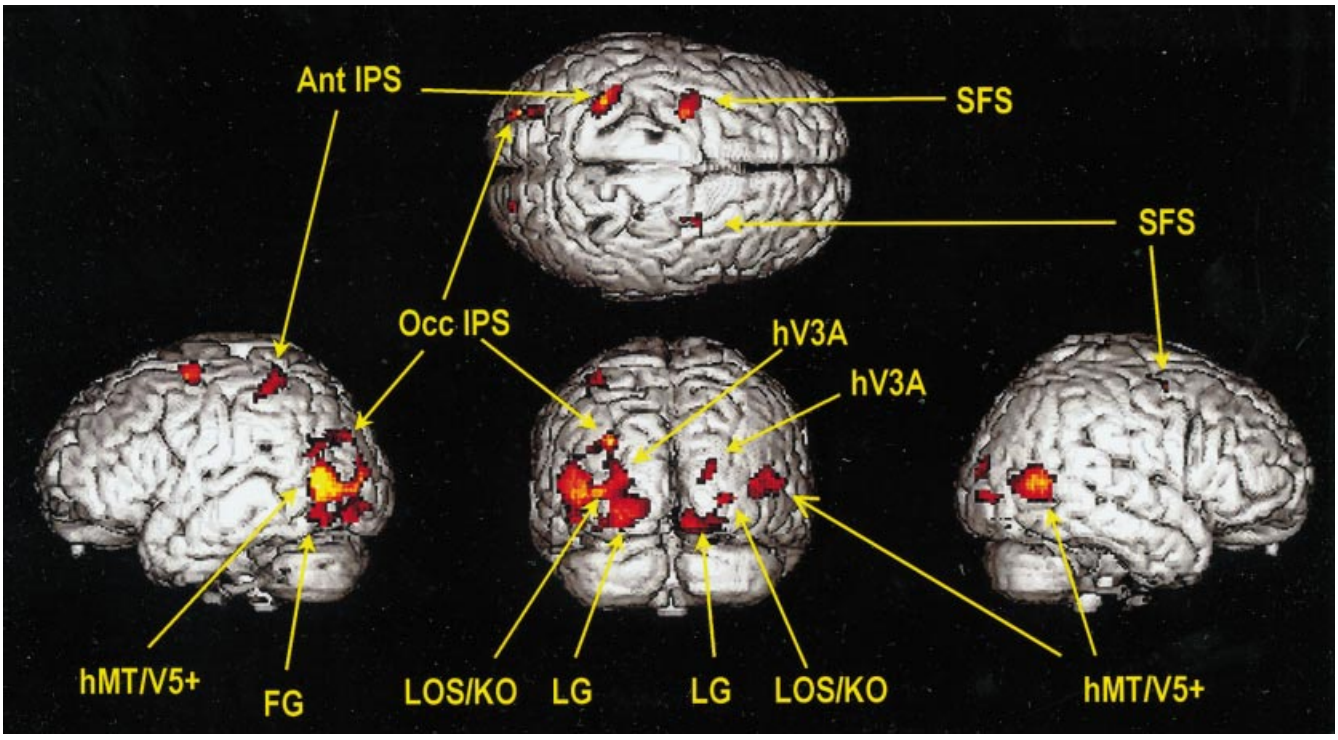

Fig. 2 Group (n=6) statistical parametric map indicating the voxels in which the hemodynamic changes were larger in the moving (UNI) than in the stationary (STA) conditions. The SPM is thresholded at P<0.05, corrected, and superimposed onto a three-dimensional surface reconstruction of the SPM 96 template (top, lateral, and posterior views). The significance increases are indicated as color changes from *deep red* to *light yellow*. The functional regions are indicated using the labels of Table 1

Table 1 Group analysis: activation sites in left and right hemispheres. *LG* Lingual gyrus, *antIPS* anterior intraparietal sulcus, *occIPS* occipital intraparietal sulcus, *FG* fusiform gyrus, *SFS* superior frontal sulcus

Left hemisphere						Right hemisphere				
Activation site	x	y	z	Z-score	Corrected *P*-value	x	y	z	Z-score	Corrected *P*-value
hMT/V5	–42	–66	2	9.34	<0.0001	42	–62	6	9.46	<0.0001
hV3A	–24	–84	10	8.69	<0.0001	22	–90	10	8.04	0.044
LOS/KO	–34	–80	4	8.78	<0.0001	28	–86	2	7.91	0.048
LG	–20	–80	–8	8.78	<0.0001	14	–76	–10	8.37	<0.0001
antIPS	–30	–44	52	8.15	<0.0001					
occIPS	–26	–76	26	8.55	<0.0001					
FG	–40	–64	–12	7.93	<0.0001					
SFS	–28	–6	56	7.74	0.002	28	–6	60	7.73	0.037

Motion-responsive regions: single-subject analysis

In the single-subject analysis, we used the local maxima provided by the SPM analysis and considered them as separate regions, depending on a number of criteria. Obviously, the distance between the local maxima (more or less than 12 mm) and the significance levels in the bridges between the maxima (Z score more or less than 3.09) were taken into account. The presence of only one of two neighboring regions in some subjects was an additional indication that the regions were distinct. The location with respect to sulci was a final major criterion: whether the regions were located along the same or a different sulcus. Since the cerebral sulci run in different directions, we found it useful to study the locations of the activation sites in multiplanar sections, as some distinctions were clearer in sagittal sections, others in coronal or transverse sections.

In all subjects, there was a motion activation on the ascending limb of the ITS, best viewed in sagittal sections. Figure 3 shows such sections from two different subjects. hMT/V5+ was a large activation located mainly in the lower bank of the sulcus, but extending to the other side (“1” in Fig. 3). In these sections, two other activation sites in the parieto-temporal-occipital junction occurred: one located in the banks of the superior temporal

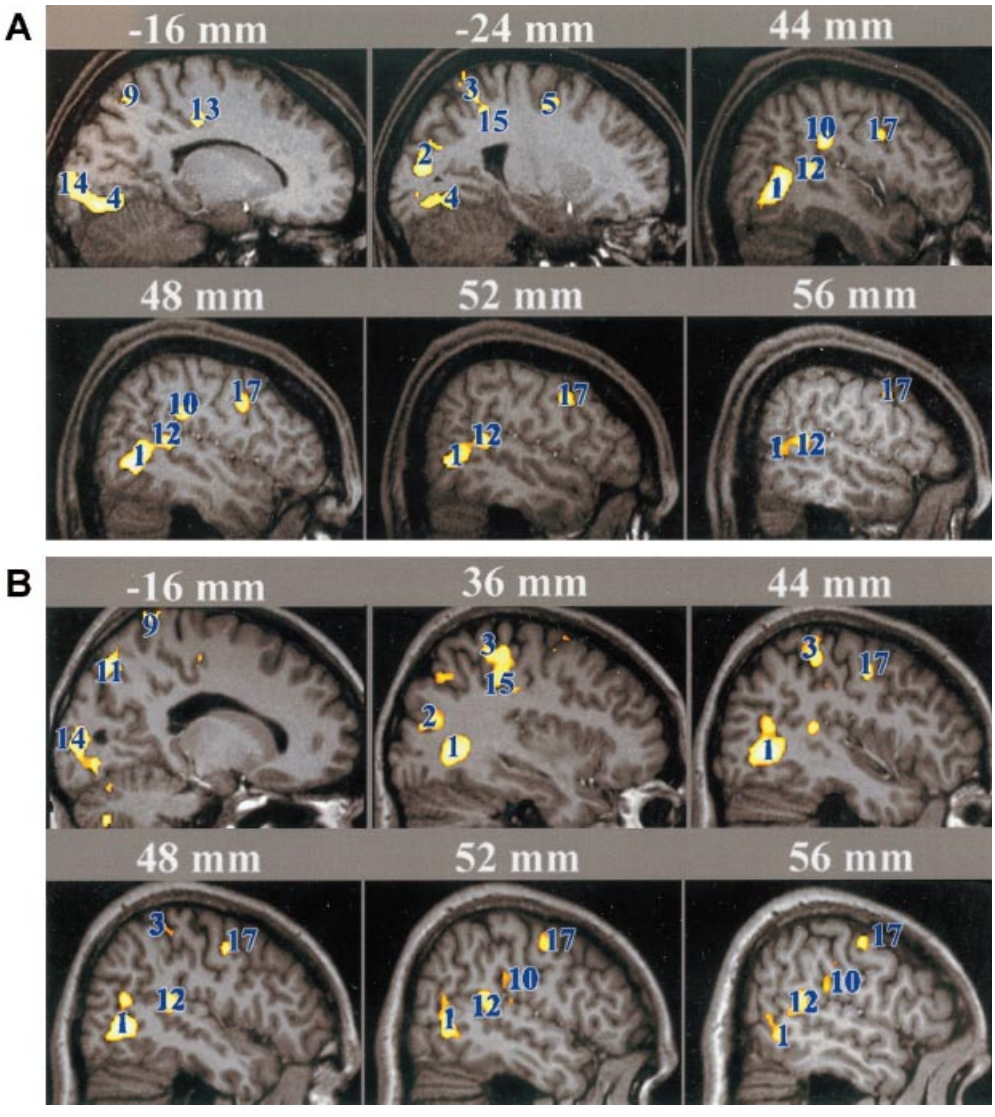

Fig. 3A, B Individual statistical parametric maps, corresponding to the contrast moving minus stationary (UNI-STA), superimposed onto selected sagittal sections through the brain of subjects 2 (**A**) and 3 (**B**). The distance from the AC-PC line is indicated on top of each section, negative values indicating left hemisphere. Threshold is $P<0.05$ corrected, and the *color* indicates significance level, with white most significant and red least significant. The *numbering* corresponds to that of Table 2

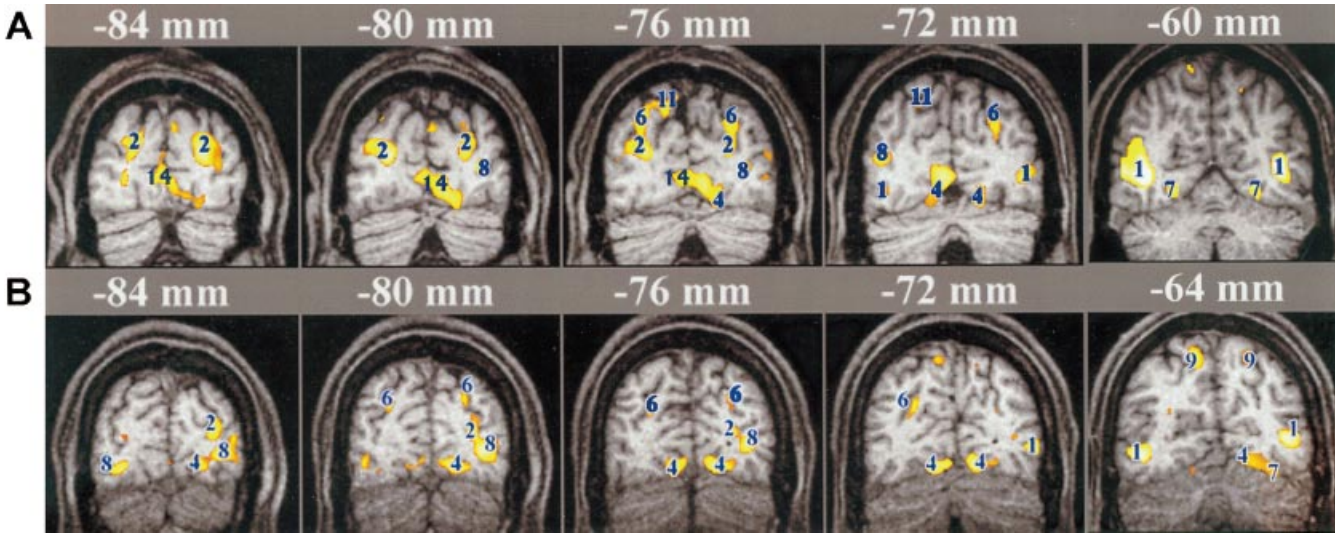

Fig. 4A, B Individual statistical parametric maps, corresponding to the contrast moving minus stationary (UNI-STA), superimposed onto selected coronal sections though the brain of subject 1 (**A**) and 2 (**B**). Same conventions as in Fig. 2, negative values indicate regions behind AC

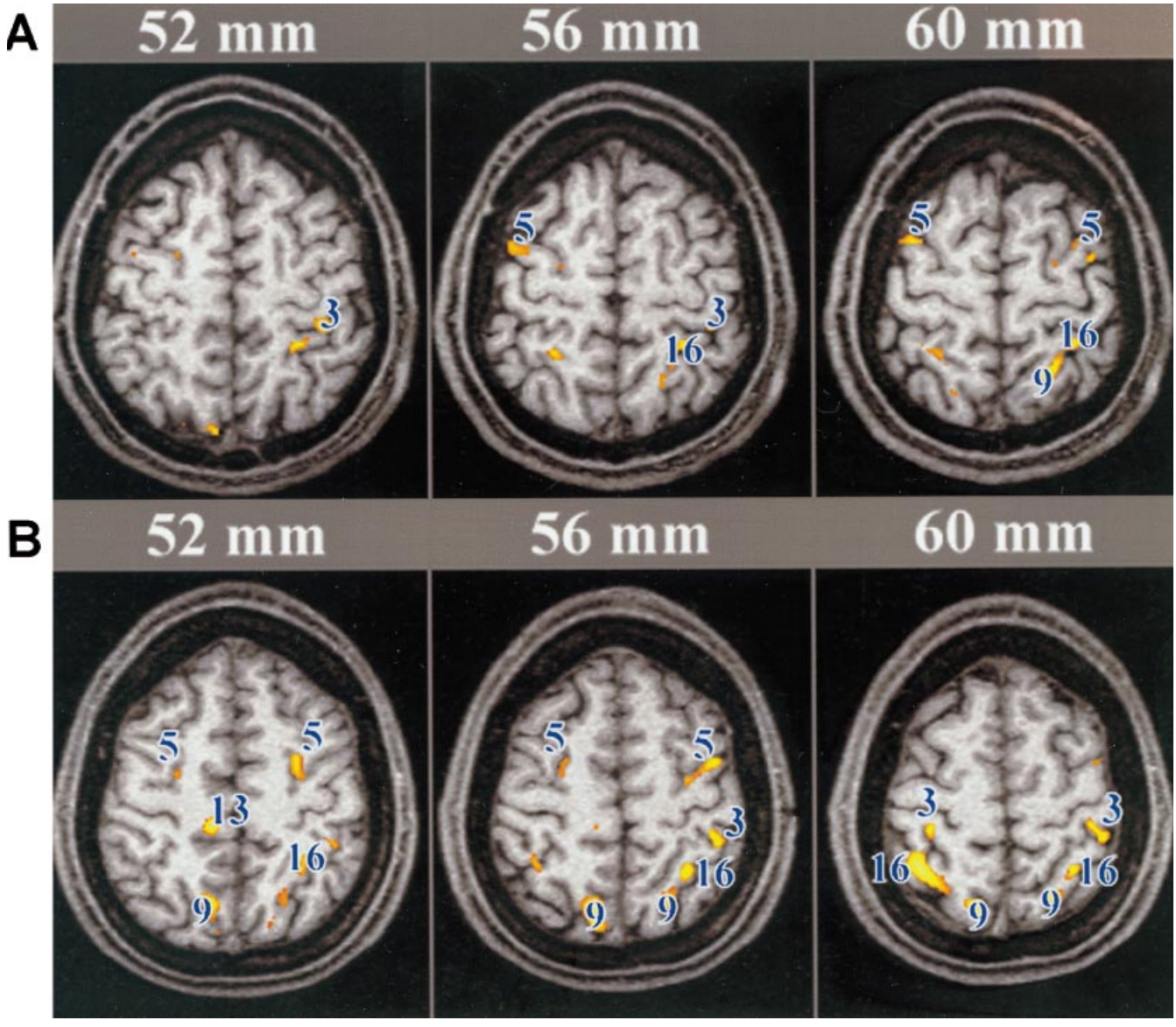

Fig. 5 Individual statistical parametric maps, corresponding to the contrast moving minus stationary (UNI-STA), superimposed onto selected transversal sections though the brain of subject 1 (**A**) and 2 (**B**). Same conventions as in Fig. 2, positive values indicate regions above AC

sulcus (STS, "12" in Fig. 3) and one even more anterior associated with the sylvian fissure ("10" in Fig. 3). The coordinates of this latter posterior insular cortical (PIC) region correspond to those of the region identified as PIVC in our earlier PET study (Dupont et al. 1994).

In the sagittal sections, one can also observe two activation sites more medially in the postcentral sulcus ("3" and "15" in Fig. 3) and a more lateral one in the precentral sulcus ("17" in Fig. 3). The more dorsal postcentral activation site ("3" in Fig. 3) corresponds to the region, observed in the group analysis, located at the junction of the intraparietal sulcus and the postcentral sulcus. Since this site was located anteriorly along the dorsal lip of the IPS and since we observed several activation sites along these lips (see Fig. 5), we have termed this region "the dorsal IPS anterior" region (DIPSA). The more ventral region in the postcentral sulcus ("15" in Fig. 3) is then simply referred to as the postcentral region. Similarly, the precentral activation ("17" in Fig. 3) is labeled the precentral region.

The activation sites in the occipital region are best described in the coronal planes (Fig. 4). Posteriorly, one can observe two motion-responsive regions: hV3A more dorsally ("2" in Fig. 4), associated with the transverse occipital sulcus as described by Tootell et al. (1997), and V1 located medially along the calcarine sulcus ("14" in Fig. 4). Just lateral and ventral from hV3A, one can observe a small activation site linked to the lateral occipital sulcus ("8" in Fig. 4): this site was apparently situated anterior to region KO, which, according to Van Oostende et al. (1997), is located on average 90 mm behind the anterior commissure. At somewhat more anterior levels,

Table 2 Single subject analysis: activation sites significant in at least five of 12 hemispheres. Abbreviations as in Table 1

Activation site		Frequency of occurrence	x[a]	y	z	Z-score[a]	%MR change[b]
1	hMT/V5	(12/12)	45 (43.5; 48)	–66 (–63.5; –68)	3 (0; 6.5)	8.7 (8.6; 9)	1.56
2	V3A	(11/12)	24 (19; 29)	–86 (–81; –93)	6 (4; 14)	8.2 (7.7; 8.4)	0.85
3	DIPSA	(10/12)	33 (29; 38)	–44 (–37.5; –44)	61 (58; 64)	7.3 (7; 8)	0.93
4	LG	(10/12)	18 (16; 25)	–81 (–74.5; –83.5)	–11 (–10; –17)	7.8 (7.5; 7.9)	1.17
5	SFS	(7/12)	38 (36; 40)	–4 (–2; –4)	58 (55; 61)	7.0 (5.8; 7.8)	0.64
6	VIPS	(5/12)	24 (24; 28)	–76 (–74; –78)	28 (28; 32)	7.7 (7.3; 8.5)	0.94
7	FG	(4/12)	27 (24.5; 31.5)	–63 (–59; –65)	–9 (–6.5; –10.5)	7.4 (7.5; 7.8)	0.92
8	LOS	(3/12)	36 (30; 38)	–82 (–68; –84)	6 (1; 12)	6.9 (6.4; 7)	1.03
9	DIPSM	(9/12)	18 (16;28)	–60 (–60; –66)	62 (60; 68)	6.7 (5.9; 7.7)	1.04
10	PIC	(8/12)	45 (43.5; 48.5)	–31 (–28; –34)	24 (19.5; 30)	7.2 (7.5; 7.6)	0.34
11	POIPS	(6/12)	16 (15; 19)	–77 (–73; –78)	44 (41; 49)	7.7 (6.8; 7.67)	1.13
12	STS	(6/12)	57 (53; 58)	–45 (–42; –48)	10 (10; 17)	8.7 (7.8; 8.7)	0.89
13	CG	(6/12)	14 (12.5; 14)	–22 (–22; –23.5)	46 (44; 46)	7.6 (6.1; 7.8)	0.33
14	V1	(6/12)	7 (2; 8)	–79 (–75; –88)	–8 (–2; –12)	7.9 (7.7; 7.9)	0.75
15	PostCS	(6/12)	31 (25.5; 32)	–39 (–31.5; –43.5)	46 (43; 46)	7.0 (7.8; 8.1)	0.62
16	DIPSL	(5/12)	25 (23; 30)	–54 (–50; –56)	62 (56; 66)	7.7 (7.2; 8.1)	0.46
17	PreCS	(5/12)	52 (48; 52)	0 (–4; 4)	42 (40; 44)	6.8 (7.0; 7.7)	0.82

[a] Median and quartiles in brackets
[b] Median value

two more motion-responsive regions were located dorsally. One was located near the bottom of the occipital end of the IPS ("6" in Fig. 4) and corresponds to the second, more ventral parietal activation observed in the group analysis (Table 1). Since this was the most ventral of the motion-responsive regions associated with IPS, we refer to it as the ventral IPS (VIPS) region. The distinction between V1PS and hV3A was not always obvious, but in some subjects (Fig. 4B) their separation was clear, and in some hemispheres one activation could be present without the other (left in Fig. 4B). The second motion region was located at the junction of IPS and parieto-occipital sulcus (POS), hence the label POIPS ("11" in Fig. 4). The distinction with VIPS was also not trivial, but VIPS was clearly located in the ventral third of the occipital part of IPS, while POIPS was at the angle where POS and IPS meet (seen better in sagittal section, see Fig. 3B). Again, one of the two activation sites could occur independently as VIPS in both hemispheres in Fig. 4B. At more anterior levels, one can also observe ventral activation sites. One was the lingual region ("4" in Fig. 4), also obtained in the group analysis, located on the medial bank of the collateral sulcus. Here, the distinction with V1 can be a problem, but there was a separate maximum along the collateral sulcus (Fig. 4A) and, in some hemispheres, the lingual activation occurred without significant V1 activation (Fig. 4B). More laterally and anteriorly, there was an additional region in fusiform cortex ("7" in Fig. 4), again corresponding to an activation in the group analysis. Although in the group analysis the hMT/V5+ and FG activations were separated by only 15 mm, they appeared as clearly distinct in single subjects (Fig. 4).

The different regions along the dorsal lip of IPS can be best observed in transverse sections (Fig. 5). Three motion-responsive sites were located along this dorsal IPS. The most anterior was DIPSA ("3" in Fig. 5), already described. The two more posterior ones sometimes seemed clearly distinct, as in the right hemispheres of Fig. 5. Therefore, we describe them as two regions and refer to the more medial and posterior region as DIPSM ("9" in Fig. 5) and the more lateral and anterior one as DIPSL ("16" in Fig. 5), respectively. This distinction is only tentative, but is supported by the observation that DIPSL was significantly more activated by viewing 3D shapes than 2D shapes (Orban et al. 1998a). In Fig. 5 one can also observe two more anterior activation sites: one in the posterior cingulate ("13" in Fig. 5) and one at the junction of superior frontal sulcus (SFS) and precentral sulcus ("5" in Fig. 5), corresponding to the SFS activation of the group analysis.

Human MT/V5+ was the only motion-responsive region reaching significance in all 12 hemispheres (Table 2). Two of the three occipital regions activated in the group were also significantly activated in a large proportion of single subjects. The exception was region LOS, suggesting that other factors, probably the variability in anatomical location, determine the significance of the group result in addition to the strength of activation in the individuals of the group. In general, there was a good correspondence between the location of the group activation and the median of the individual activation sites. The few exceptions (SFS and fusiforrn region) were those in which the number of significant activations in single subjects was small.

A number of motion-responsive regions reached significance in more than half of the subjects, yet did not reach significance in the group analysis. These included DIPSM, PIC, POIPS, STS, the cingulate region, V1, and the postcentral region (Table 2). The two regions failing to reach significance in at least half the hemispheres were DIPSL and the precentral region. The median coordinates of these regions are listed in Table 2. Except for the lingual region and V1 and for DIPSM and DIPSL,

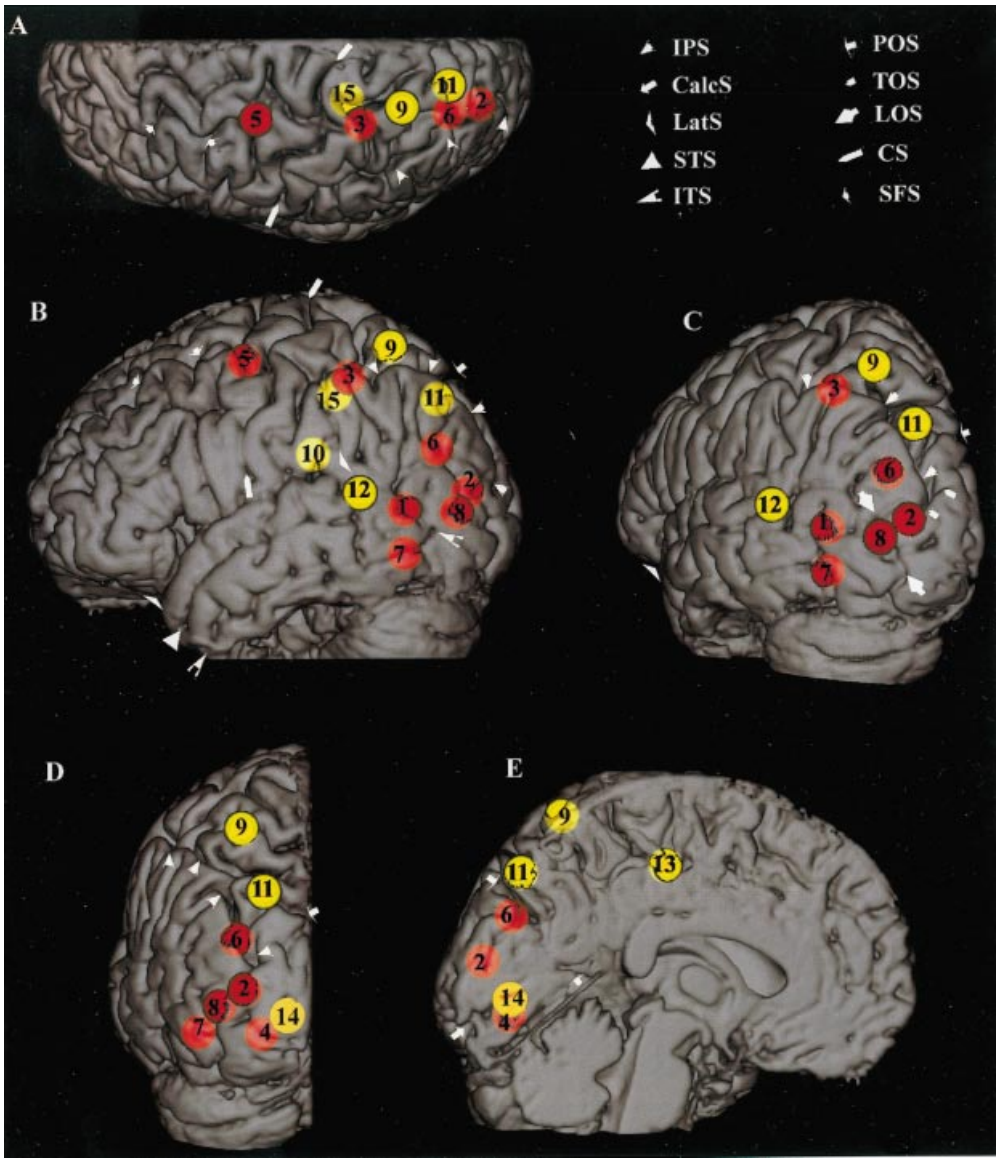

Fig. 6A–E Summary of the motion-responsive regions superimposed onto the brain of subject 1. The surface has been reconstructed at the level of the white and gray matter junction. The spheres are positioned at the median coordinates and labeled as indicated in Table 2. *Red* indicates regions belonging to the core of motion-responsive regions, and *yellow* indicates regions observed in a majority of hemispheres. The different *arrow types* indicate major sulci: *IPS* intraparietal sulcus, *CalcS* calcarine sulcus, *LatS* lateral sulcus, *STS* superior temporal sulcus, *ITS* inferior temporal sulcus, *POS* parieto-occipital sulcus, *TOS* transverse occipital sulcus, *LOS* lateral occipital sulcus, *CS* central sulcus, *SFS* superior frontal sulcus

the average distance between all these regions exceeded 15 mm. Given the resolution of the SPMs (8 mm), this supports the view that most of these regions are functionally distinct. V1 and the lingual region are probably different functional regions. Since the sulci run longitudinally in this region, the cortical distance along the surface is in fact much larger than 15 mm. In this part of cortex, retinotopic stimulation has demonstrated the existence of several regions (Sereno et al. 1995; DeYoe et al. 1996; Engel et al. 1997). In addition, lingual activation was observed in a number of subjects without concomitant activation of V1. This was occasionally observed in experiment one (Fig. 4B), but occurred even more frequently when a smaller stimulus was used, as in experiment three or in the study of Cornette et al. (1998b). On the other hand, the distinction between DIPSL and DIPSM was indeed only tentative.

If we consider the group and single-subject analyses together, one can conclude that, in addition to a core network of eight motion-responsive regions, which proved significant in the group analysis, there are seven more motion-responsive regions observed in the majority of individual hemispheres (Fig. 6).

Time course of motion activation

For the most significant voxel of each region reaching significance in single subjects, we calculated the average time course of the MR signal. These time courses were then averaged over subjects. The average time course of the hMT/V5+ activation is shown in the top panels of Fig. 7, where it serves as reference. Three to four images after motion onset, the hMT/V5+ activation reached a plateau. Similarly, the response returned to baseline in 3–4 images following the end of motion. Thus, the hMT/V5+ activity was simply shifted by 10–15 s with respect to the stimulus sequence. This shift may seem large compared with the

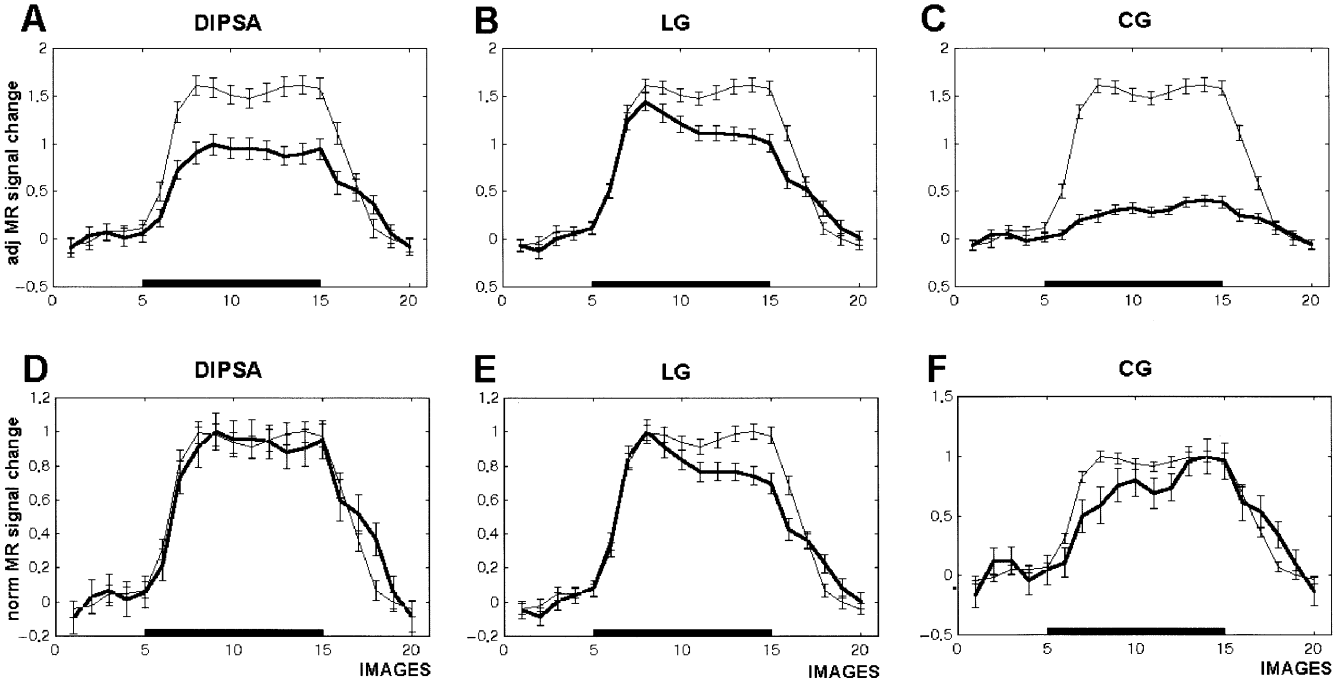

Fig. 7A–F Average time course of the adjusted magnetic-resonance signal, relative to the average value in the stationary (STA) condition, sampled in the most significant voxel of different regions (*dark curve*) compared with hMT/V5+ (*light curve*): DIPSA (**A** and **D**), LG (**B** and **E**), CG (**C** and **F**). The adjusted signals are plotted in **A–C**, and the normalized signals in **D–F**. *Vertical bars* indicate SEs. *Thick horizontal lines* indicate motion epochs

hemodynamic delay observed in event-related studies (Josephs et al. 1997). This might partially reflect the build up of the bold responses to a prolonged stimulation. Additionally, other factors, such as averaging over subjects, interleaved slice acquisition, and temporal high-pass filtering, may have contributed to the delay.

Most other motion-responsive regions had a similar time course. Once the difference in response level compared with MT/V5+ was removed by normalization, the time courses were very similar, as shown for DIPSA in Fig. 7D. The average time course differed significantly from that of hMT/V5+ in only two regions. This was tested by comparing the normalized signals of the other regions with those of hMT/V5+ at two time points: the 8th and the 15th image after motion onset. In one region, the lingual region, the MR response was more phasic and declined towards the end of the stimulus (Fig. 7). The normalized response at the 15th image was significantly (P<0.001) lower than that of hMT/V5+. The cingulate region exhibited the opposite behavior (Fig. 7). Its response was weak and gradually rose after motion onset: the normalized response at 8th image was significantly (P<0.01) lower than that of hMT/V5+.

Disentangling flicker and motion responses

In the second experiment, we compared passive viewing of moving and stationary RTP with the same pattern flickering at 15 and 6 Hz. Since more recent experiments (Orban et al. 1998a) have used monocular rather than binocular presentation of moving and stationary RTPS, we also compared binocular and monocular viewing in this experiment. The group analysis (n=3) for the binocular conditions is shown in Fig. 8. The contrast moving minus stationary RTP revealed, in addition to hMT/V5+ bilaterally, three occipital activation sites: the lingual region bilaterally and left hV3A, as well as four parietal activations: POIPS and DIPSA bilaterally. This latter activation was relatively extensive and probably also included the more posterior dorsal IPS regions. Contrasting moving with flickering (15 Hz) RTP only left the parietal regions active: DIPSA bilaterally and left POIPS. Conversely, contrasting flickering (15 Hz) with stationary RTPs revealed V1/V2 bilaterally, the lingual region bilaterally, and the right fusiform region. Thus, flicker nicely subdivides the motion-responsive regions. Some regions responded at least as well to flicker as to motion, this category included V1, lingual, and fusiform regions. Others responded to motion and little or none to flicker: this was the case for the parietal regions, with the early motion areas, such as hMT/V5+ and hV3A, lying in between.

The plots of the MR signal change for the different regions bear out this analysis. There was no significant difference between the monocular and binocular viewing conditions and, in fact, the MR signals for the different stimuli were very similar for the binocular and monocular viewing. Hence, we have averaged the MR signals for the two types of viewing in Fig. 9, using viewing of stationary RTP (STA) as a reference. The strength of the flicker response relative to stationary, compared with the motion response, nicely differentiated the elements of the motion network (Fig. 9). V1, in fact, responded more strongly to flicker than to motion. Responses of the lingual region

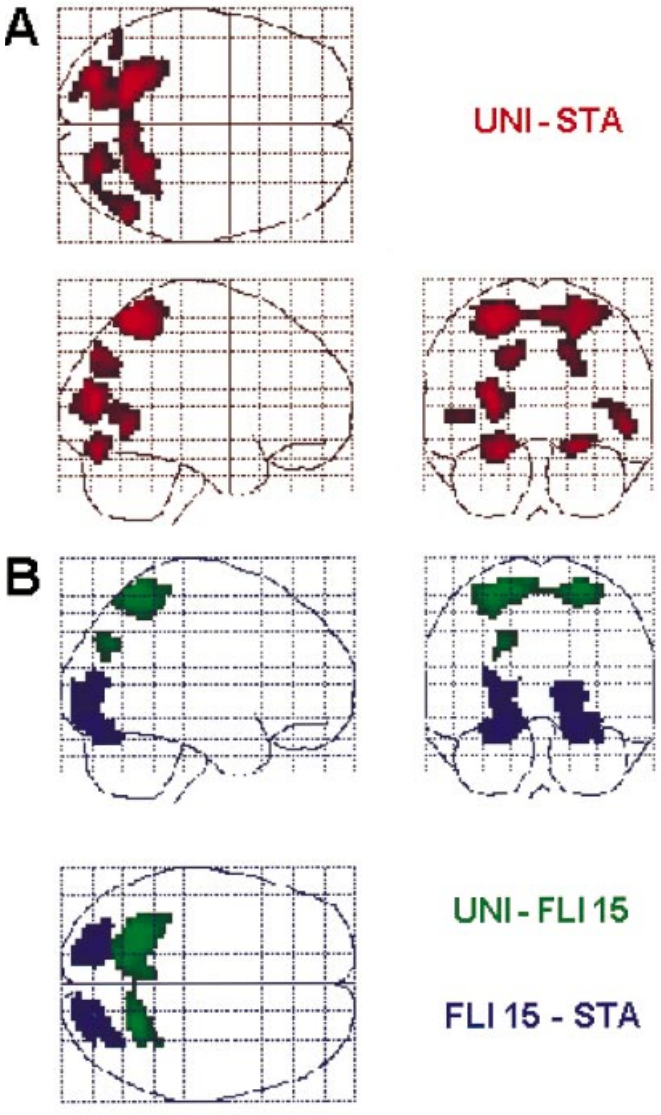

Fig. 8A, B Glass brain views of the group (n=3) statistical parametric maps, corresponding to the subtractions movement minus stationary (UNI-STA; **A**), and movement minus flicker (UNI-FLI 15) and flicker minus stationary (FLI 15-STA) (**B**) under binocular viewing. Threshold is P<0.05 corrected

were about equal for motion and flicker. Responses to flicker in hMT/V5+ and hV3A were smaller by a factor of 2–4 than those to motion. Their flicker responses were too small to be significant (P<0.05, corrected) in the subtraction FLI 15-STA. But they were large enough to prevent the difference between motion and flicker responses to be significant at P<0.05, corrected (Fig. 8). Finally, in DIPSA, the flicker response had almost vanished. Generally, the response to 15 and 6 Hz flicker was similar, with the slower rate slightly more effective outside V1.

Effects of stimulus size

In this experiment, we combined three stimulus sizes with stationary and moving RTP, but restricted our measurements to the lower part of the brain. Thus, we only have information for motion regions as far dorsal as POIPS, but not for the dorsal IPS regions. The group data (n=4) were analyzed according to the factorial design. The factor size (large compared with small) reached significance in the early retinotopic regions, including V1 and two regions identified tentatively as V2 ventral and dorsal. The factor motion compared with stationary reached significance in hMT/V5+, hV3A, and VIPS bilaterally, as well as in right POIPS, left STS, and left PIVC. The interaction term, in which the motion response was stronger for large than for small stimuli, reached significance only in V1. Even masking the interaction with the main factor motion did not reveal other regions of significant interaction. The opposite interaction, stronger motion response for small stimuli, showed only a weak non-significant tendency in PIC and STS. Figure 10 shows the activity profile of the V1 voxel with maximum interaction. This is strikingly different from the profile of the most significant hMT/V5+ voxel, which displayed only a main effect of motion (Fig. 10). Using the extent of the local maxima as the measure yielded an equally small effect of stimulus size on the hMT/V5+ activation.

Discussion

Our results show that there were many motion-responsive regions in the human brain, including not only occipital and occipito-parietal regions, but also occipito-temporal, temporal, parietal, and frontal regions. The comparison of motion and flicker response nicely differentiated amongst motion-responsive regions, and only parietal regions disentangle motion and flicker completely. Finally stimulus size, over the range explored, influenced motion responses little, with the exception of V1.

Technical issues

The subjects fixated well, as was confirmed by the eye movement recordings. Hence, it is unlikely that the differential activation during viewing of motion was due to the intrusion of eye movements. However, this still leaves open the possibility that the motion-related activations reflect the effort to maintain fixation rather than visual responses to the retinal motion. This is unlikely, since the structures involved in maintaining fixation are different from those observed in the present study. Both lesion (Paus et al. 1991) and PET (Anderson et al. 1994) indicate the involvement of prefrontal, and especially anterior cingulate, regions in maintenance of fixation. In an earlier study in which motion was much more predictable, since occurring on a single axis and, hence, required more effort to maintain fixation, we (Cornette et al. 1998a) indeed observed activation in BA-24/32, which is clearly distinct from the motion-responsive regions reported here.

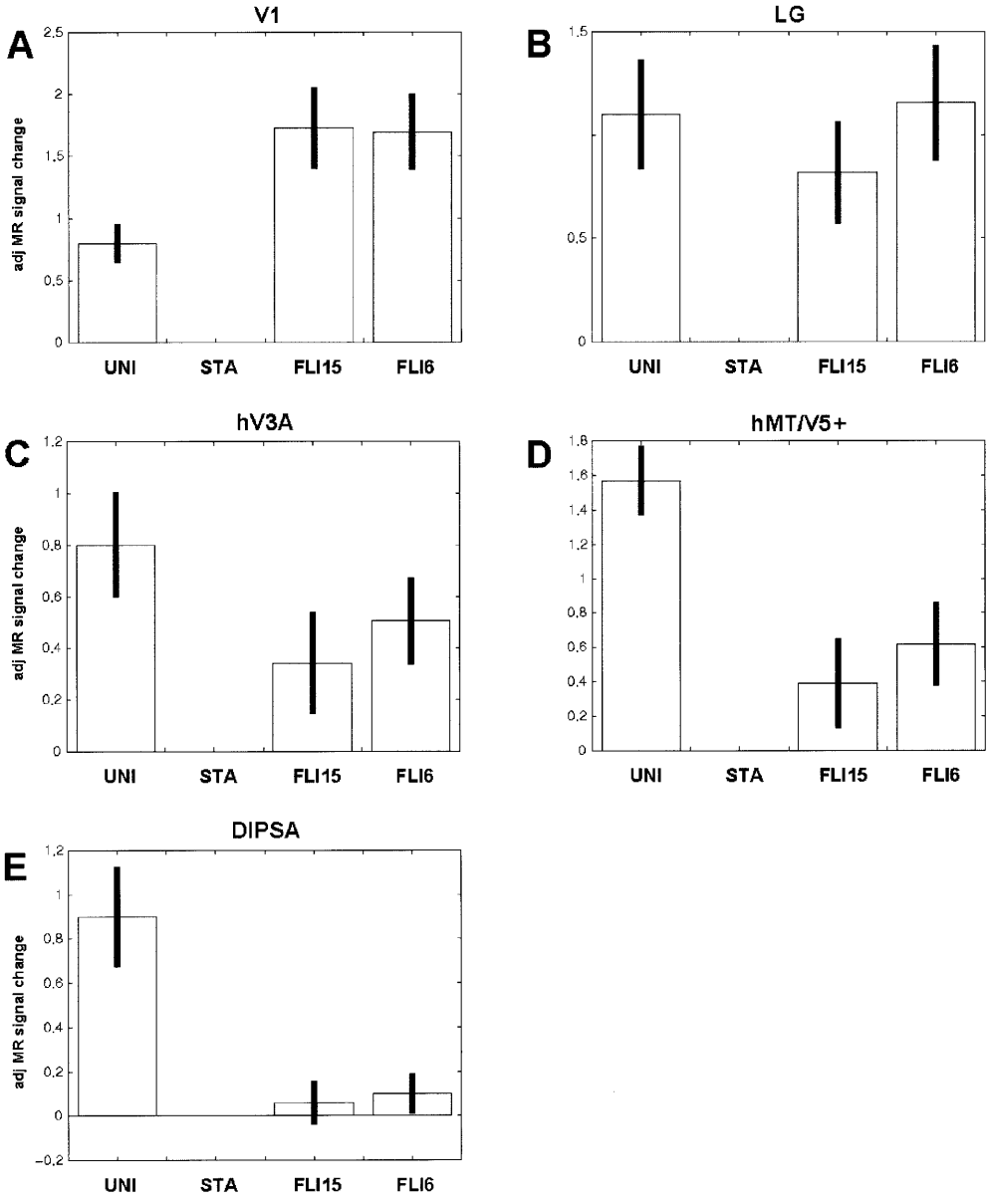

Fig. 9A–E Activity profile plotting the adjusted magnetic-resonance signal change (in percent), relative to stationary (*STA*), in conditions movement (*UNI*), STA, flicker at 15 Hz (*FLI 15*), and flicker at 6 Hz (*FLI 6*), for the most significant voxel of five regions: V1 (**A**), LG (**B**), hV3A (**C**), hMT/V5+ (**D**), and DIPSA (**E**). Values are averaged over binocular and monocular conditions and over subjects (n=3). *Vertical bars* indicate standard deviations

The Ober2 system used to monitor fixation produced a susceptibility artifact in anterior frontal cortex. This was reduced by using a single goggle, so that it is unlikely that the eye-movement recording would have caused us to miss an anterior frontal motion region.

The subjects remained passive with respect to stimuli. This is the paradigm which is routinely used in monkey studies of motion-responsive neurons. It has the drawback that we do not control the behavior of the subjects, although we did ask them not to engage in any cognitive interaction with the stimuli. On the other hand, we have observed that some motion-responsive regions become inactive during certain simple tasks (Cornette et al. 1998b). Thus, passive viewing has merit as an initial screening procedure (Zeki et al. 1991), but should be regarded as a preliminary screening tool for motion-responsive regions, as we ourselves have stressed the importance of a task in modulating activity in regions engaged by passive viewing of visual stimuli (Orban and Vogels 1998). Furthermore, analysis of retinal motion can serve many behavioral purposes (Nakayama et al. 1985), and we see it as a challenge for the near future to understand the relationship between the activity in the motion-responsive regions reported here and the several behavioral uses of motion information. For example, one of the motion responsive regions, region KO, has been implicated in the extraction of 2D shape from motion, i.e., kinetic shape (Orban et al. 1995; Dupont et al. 1997; Van Oostende et al. 1997).

In most cases, the motion-responsive regions were separated by more than 15 mm. In addition, their average Talairach coordinates were relatively similar in the group and single-subject analysis (compare Tables 1, 2). Given the resolution of the measurements, especial-

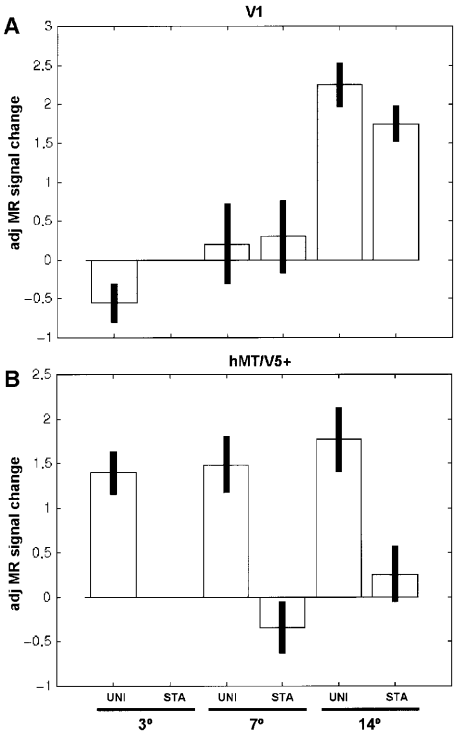

Fig. 10A, B Activity profile plotting the magnetic-resonance signal change (in percent), relative to stationary (*STA*) with 3° diameter, for movement (*UNI*) 3 deg, STA 3 deg, UNI 7 deg, STA 7 deg, UNI 14 deg, STA 14 deg in the most significant voxel of two regions: V1 (**A**) and hMT/V5+ (**B**). Average for four subjects. *Vertical bars* indicate standard deviations

ly those in single subjects (8 mm), these regions can tentatively be considered to be functionally distinct. Additional support comes from the observations that some regions could be present in some subjects, but not in others, and also that most regions were associated with different cerebral sulci. Only a few pairs of regions were located within 15 mm of each other: LOS and hV3A, V1 and the lingual region, and DIPSL and DIPSM. While the last distinction is only tentative, the other two pairs for which the distance between maxima exceeds 10 mm correspond in all likelihood to separate regions. Indeed a previous study, Van Oostende et al. (1997) demonstrated that KO and hV3A are distinct, but abutting regions, and the LOS activation is just anterior to region KO. Furthermore, hV3A is located along the transverse occipital sulcus, while region KO and LOS are located along the next sulcus, the lateral occipital sulcus. The lingual region is probably also distinct from V1, as it is again associated with different sulci: the collateral sulcus and the calcarine sulcus, respectively. Furthermore, in studies with small-motion stimuli (4° diameter), lingual activation was observed (Cornette et al. 1998b), but not V1 activation, in agreement with data of experiment 3. This lingual region, which is involved in processing both moving and static stimuli (Cornette et al. 1998b), seems to correspond to V8 of Hadjikhani et al. (1998) or V4 of Zeki et al. (1991). One must admit, however, that, even if the regions are functionally distinct, it can be difficult in a given subject to distinguish two neighboring regions, especially when they are located along the same sulcus, such as, e.g., VIPS and POIPS.

Comparison with previous studies

Our results are in good agreement with the many earlier studies reporting motion responses in human V1 and MT/V5+ (Zeki et al. 1991; Watson et al. 1993; Dupont et al. 1994, 1997; Tootell et al. 1995; Dieterich et al. 1998; Goebel et al. 1998; Smith et al. 1998). In all these studies, the hMT/V5+ activation was the only or at least the most significant activation in the contrast moving minus stationary pattern. This fits well with our observation that only hMT/V5+ reached significance in the 12 hemispheres examined. The second most frequently observed motion activation was located in the cuneus and, given its location close to the transverse occipital sulcus, seems to correspond to the human homologue of V3A, identified by Tootell et al. (1997) as a motion-responsive area. Activation in a similar location was observed in several other studies (Table 3), including those of Dupont et al. (1994), de Jong et al. (1994), Van Oostende et al. (1997), Goebel et al. (1998), and Smith et al. (1998).

In fact, most other motion-responsive regions reported here were observed in one or another of the earlier studies (Table 3). The motion activation in the lateral occipital sulcus (LOS) seems to be located at a level somewhat too anterior to correspond to the region KO described by Dupont et al. (1997) and Van Oostende et al. (1997). Activation in LOS has been observed in a recent PET study using different orders of motion stimuli (Dupont et al. 1998) and in an FMRI study of 3D extraction from motion (Orban et al. 1998a). Motion responses in lingual and fusiform cortex correspond to those reported by de Jong et al. (1994), Dupont et al. (1994, 1997), and Shipp et al. (1994) (Table 3). The PIC region corresponds to the motion-responsive region described by Dupont et al. (1994) as the human homologue of the parietoinsular vestibular cortex (PIVC). These authors based their tentative identification on the visual motion responses of PIVC neurons described by Grüsser et al. (1990). This identification was supported by the proximity of the vestibular activation (–36, –24, 16) reported by Bottini et al. (1994), taking into account the coarse resolution of PET measurements. More recently, Lobel et al. (1998) reinvestigated the cortical vestibular projections using fMRI. The region they identify tentatively as hPIVC is located more laterally (64, –36, 20) than our motion-responsive region. This suggests that PIC and hPIVC, rather than being identical, are distinct but neighboring regions and that, as originally suggested by Grüsser (personal communication), PIC might be the homologue of VPS, which in the monkey neighbors PIVC and is less vestibular, but more optokinetic in character (Guldin and Grüsser 1998). Visual motion responses have also been observed in this parietoinsular region by Dupont et al. (1997), Cornette et al.

Table 3 Anatomical location of activation sites compared in present and previous studies. Abbreviations as in Table 1

	Present study	de Jong et al. (1994), Watson et al. (1993)[b], Shipp et al. (1994)[a]	Dupont et al. (1994)	Dupont et al. (1997), Puce et al. (1998)*	Cornette et al. (1998a)	Goebel et al. (1998)	Dieterich et al. (1998)
V1	7, –79, –8	2, –88, 0[b]	8, –90, 0	16, –93, –14		6, –86, –7	20, –90, –2
hMT/V5	45, –66, 3	42, –68, 0[b]	39, –73, 4	40, –67, 0		47, –58, 4	42, –66, 4
V3A	24, –86, 6	22, –86, 8	24, –74, 16		22, –90, 8	14, –91, 13	
LOS	36, –82, 6			31, –91, –2 (KO)			
LG	18, –81, –11	28, –80, –8		14, –84, –16			
FG	27, –63, –9	(26, –57, –13)[a]	40, –72, –12				
PIC	45, –31, 24		52, –38, 16	60, –34, 20	54, –38, 8		36, –30, 18
STS	57, –45, 10			48, –50, 3*			
VIPS	24, –76, 28	22, –78, 32	20, –74, 28				
POIPS	16, –77, 44	22, –72, 40				20, –76, 36	
DIPSA	33, –44, 61			34, –48, 40	28, –50, 48		
DIPSM	18, –60, 62			22, –60, 40			20, –56, 52
(DIPSL	15, –54, 62)					22, –54, 52	
PostC	31, –39, 46		48, –28, 36		44, –24, 36		42, –38, 32
CG	14, –22, 46				12, –28, 44		
SFS	38, –4, 58			24, –10, 48	38, –14, 52		
(PreC	52, 0, 42)				46, –6, 40		

(1998a), and Dieterich et al. (1998) (Table 3). The motion-responsive region in STS corresponds relatively well to that (48, –50, 3) reported to be responsive to face and mouth motion by Puce et al. (1998). In that study, this facial motion region was shown to respond poorly to the radial motion of a background pattern, but that pattern was much larger than that used in the present study, and we observed a trend towards less motion response in this region for large stimuli.

The parietal motion-responsive regions correspond relatively well to earlier reported regions, especially if one takes into account that more dorsal parietal regions were not included in the brain volume scanned in our previous PET studies using a 2D camera (Table 3). VIPS and POIPS correspond well to two activation sites reported by de Jong et al. (1994) in their optical flow study. VIPS matches a region observed by Dupont et al. (1994), and POIPS matches the lower parietal region reported by Goebel et al. (1998). The three dorsal IPS regions fit relatively well with regions reported to be activated by visual motion by Dupont et al. (1997), Cornette et al. (1998a), Dieterich et al. (1998), and Goebel et al. (1998). The only region for which no clear match was found in earlier studies is the postcentral region, although several candidate regions are listed in Table 3. It is worth mentioning that these six parietal regions are strikingly similar to those observed by Culham et al. (1998) to be activated during attentive tracking.

Finally, the cingulate and frontal motion responses have also been observed in earlier studies. The posterior cingulate region corresponds to an earlier observation of Cornette et al. (1998a). The two frontal sites correspond well to those observed by Dupont et al. (1997), Cornette et al. (1998a), and Goebel et al. (1998). It is noteworthy that in the present study, as in that of Cornette et al. (1998a), two neighboring activations were observed in the precentral sulcus, which may well correspond to the two subparts identified in the FEF by Petit et al. (1997).

Relationships with monkey studies

Our observations are in good agreement not only with human imaging data, but also with the monkey literature. It is well established that direction-selective neurons occur in sizable proportions in many visual cortical areas (for a review, see Orban 1998). However, simply contrasting moving with stationary patterns will not specifically isolate direction-selective responses. Indeed, metabolic studies in monkeys using double-label 2-deoxyglucose have shown that regions or layers containing few direction-selective neurons are differentially activated in the motion-stationary contrast (Orban et al. 1997). Thus, it is no surprise that so many regions are revealed by this relatively unspecific contrast. Attempting to establish the homology between the different visual cortical regions in the two species seems premature, except for the MT/V5, V3A, and, of course, V1. Even here caution is required, since what is referred to as hMT/V5+ may correspond not only to MT/V5 of the monkey, but may also include its satellites. In a similar vein, it is worth mentioning that, if hV3A has a retinotopic organization similar to that of monkey V3A, its functional properties seem quite different, as V3A neurons respond little or none to random dot motion in the monkey (Joris et al. 1997).

Even the differential activation by motion of regions outside the "classical" visual system (Van Essen et al. 1992) is in agreement with monkey data. The PIC activa-

tion by visual motion is in agreement with the single-cell studies of Grüsser et al. (1990). The STS activation may well correspond to the STPa region in monkeys. Neurons in this region respond to biological and to eye motion (Perrett et al. 1985; Oram and Perrett 1994). The posterior cingulate has been shown to respond to visual motion in monkeys (Olson et al. 1993) and in cats has been shown to be visually responsive (Vanduffel et al. 1995). Finally, the responses in the human FEF fit the anatomical study of Schall et al. (1995), describing direct projections from MT/V5 to the FEF.

Disentangling motion and flicker

Flickering RTPs were in fact a more potent stimuli for human V1 than moving RTPs. This is in agreement with the data of McKeefry et al. (1997), who reported an increase in the activation over V1/V2 in the comparison incoherent to coherent movement. In the monkey, very few studies have tested the effects of flickering RTPs on single V1 neurons. A notable exception are Qian and Andersen (1994), who reported that flicker responses of direction-selective V1 neurons amount to 60% of their motion response. Both on theoretical grounds and from the metabolic mapping data of Orban et al. (1997) (see above), one expects that the motion response measured over V1 is not restricted to direction-selective neurons. Hence, it is not completely surprising that the flicker response in fMRI exceeds that reported for the V1 direction-selective neurons. It is in line with the exquisite sensitivity of V1 neurons to rapid changes in luminance (Orban 1986; Richmond et al. 1990). Beyond V1, there is a sharp distinction between the occipito-temporal or ventral pathway (Ungerleider and Mishkin 1982) and the occipito-parietal or dorsal pathway. Occipito-temporal regions, such as the lingual region, continue to respond well to flicker. On the other hand, along the occipitoparietal pathway, flicker responses gradually decreased. In hMT/V5+, they were reduced to 20–50% and in DIPSA to less than 10% of the motion response. These results are in excellent agreement with an earlier PET study of Cheng et al. (1995). These human data mirror a similar decrease observed in single-cell studies as one moves from V1 to MT/V5 and then to MSTd (Lagae et al. 1994; Qian and Andersen 1994). In fact, the flicker response expressed as the percent of motion activation in hMT/V5+ (20–50%, depending on the frequency) compares well with the 40% reported for MT/V5 neurons tested at 9 Hz (Qian and Andersen 1994). This is not surprising since almost all MT/V5 neurons are direction selective and, hence, the single-cell figure is representative for the whole MT/V5 population. Thus, while motion itself does not really distinguish between dorsal and ventral pathways, the distinction between spatio-temporal (coherent motion) and temporal correlation (flicker) does. In the present experiments, we obtained no information regarding the response to flicker of some motion-responsive regions, such as FEF or STS. In related experiments using random line stimuli, we observed that human FEF also differentiates between motion and flicker (Orban et al. 1998a). This is not surprising given the strong projections from parietal cortex to FEF in the monkey (Schall et al. 1995).

Effects of stimulus size

Stimulus size had little effect outside the retinotopically organized regions, at least over the range explored in our experiments. The interaction between size and type (moving/stationary) was significant only in V1. This probably reflects the combination of retinotopic organization and change in speed sensitivity with eccentricity documented for V1 in the monkey. Most neurons with RFs close to the fixation point have low pass speed response curves (Orban et al. 1986) and, therefore, respond little to the relatively fast 6°/s motion compared with static stimuli, which, because of slow movements during fixation, correspond to very slow speeds in anesthetized animals (Orban 1994). In contrast, neurons with more peripheral RFs respond to a wider range of speeds and, therefore, will respond about equally to moving stimuli and static ones. Thus, the weakness of V1 activations in some of our earlier studies (Dupont et al. 1994, 1997), especially in comparison with other studies (Zeki et al. 1991; Tootell et al. 1995), was in all likelihood due to the size of our stimuli. On the other hand, in extrastriate regions, motion responses were similar at all sizes tested. One of the challenges for the future will be to unravel the contributions of these many regions to the different behavioral uses of motion processing.

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