Human Cortical Areas Involved in Sustaining Perceptual Stability During Smooth Pursuit Eye Movements

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Abstract: Because both, eye movements and object movements induce an image motion on the retina, eye movements must be compensated to allow a coherent and stable perception of our surroundings. The inferential theory of perception postulates that retinal image motion is compared with an internal reference signal related to eye movements. This mechanism allows to distinguish between the potential sources producing retinal image motion. Referring to this theory, we investigated referential calculation during smooth pursuit eye movements (SPEM) in humans using event-related functional magnetic resonance imaging (fMRI). The blood oxygenation level dependent (BOLD) response related to SPEM in front of a stable background was measured for different parametric steps of preceding motion stimuli and therefore assumed for different states of the referential system. To achieve optimally accurate anatomy and more detectable fMRI signal changes in group analysis, we applied cortex-based statistics both to all brain volumes and to defined regions of interest. Our analysis revealed that the activity in a temporal region as well as the posterior parietal cortex (PPC) depended on the velocity of the preceding stimuli. Previous single-cell recordings in monkeys demonstrated that the visual posterior sylvian area (VPS) is relevant for perceptual stability. The activation apparent in our study thus may represent a human analogue of this area. The PPC is known as being strongly related to goal-directed eye movements. In conclusion, temporal and parietal cortical areas may be involved in referential calculation and thereby in sustaining visual perceptual stability during eye movements. *Hum Brain Mapp* 29:300–311, 2008. ©2007 Wiley-Liss, Inc.

Key words: cortex-based; 'Filehne' illusion; functional magnetic resonance imaging; motion perception; PPC; reference signal; SPEM; VPS; VTS

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INTRODUCTION

There are two potential sources of retinal image motion, namely self-motion versus object motion. Often, we move our eyes and watch a moving object in our environment at the same time; in this situation both of these potential sources contribute to the retinal image motion. What is the mechanism allowing the perception of stable surroundings during eye movements? On the basis of the early ideas of von Helmholtz [1910], the two types of retinal image motion might be dissociated by comparing the retinal

signal with an internal signal encoding eye movements [Sperry, 1950; von Holst and Mittelstaedt, 1950; Wertheim, 1994]. The functional model of Wertheim [1994] goes beyond the traditional inferential theory expanding the concept of the internal reference signal. It incorporates the fact that not only eye movements but also head movements and vection resulting from optokinetic stimulation should generate a reference signal. In summary, the internal reference signal is described as a compound signal comprising an eye movement component, a vestibular component, and a visual component. Subtraction of the internal reference signal from the retinal signal allows to discriminate between self versus object movements. Any retinal image motion remaining after subtraction of this internal signal is experienced as being due to movements of the environment.

When this referential mechanism is disturbed, deficits in situations requiring the differentiation between self and object motion can occur. For example, patient R.W., who had bilateral extrastriate occipital and intraparietal cortical lesions [Haarmeier et al., 1997], suffered from vertigo and nausea whenever he tracked a moving object with his eyes or fixated a stationary object during translational self-motion. In these situations R.W. not only experienced difficulties in every day life but also showed deficits in psychophysical tests under laboratory conditions.

Similarly, Wilhelm Filehne [1922] found that slight imperfections in this referential mechanism result in an illusionary perception of object motion [Filehne, 1922; Freeman, 1999; Freeman and Banks, 1998; Mack and Herman, 1973]. For example, when tracking a target moving in front of a stationary structured background, an extraretinal signal overestimating the eye movement velocity (too large reference signal) enhances the perception of background motion in the same direction as the pursuit movement. Under identical circumstances an extraretinal signal underestimating the eye movement velocity (too small reference signal) enhances the perception of background motion in the opposite direction as the pursuit movement. This so called 'Filehne' illusion can be modified by presenting a central fixation point and a structured background pattern moving briefly in one direction at a defined velocity (conditioning stimulus) prior to the 'Filehne'-type stimulus [Haarmeier et al., 2001; Haarmeier and Thier, 1996]. Depending on the velocity and the direction of this background motion the point at which the background is experienced as stable is shifted, resulting in an illusionary background movement during the following smooth pursuit eye movement in front of a stationary background. The influence of the first stimulus is not only transient since the 'Filehne' illusion shows a tendency even to increase in time when it is studied at various interstimulus-intervals (0.5, 3.0, 6.0 s) [Haarmeier and Thier, 1996]. As examined by adaptive two-forced-choice method conditioning stimulus velocities of for example $-8^\circ/\text{s}$, $-16^\circ/\text{s}$, or $-24^\circ/\text{s}$ led to the subjective perception of about $-2^\circ/\text{s}$, $-4^\circ/\text{s}$, or $-6^\circ/\text{s}$ motion, respectively, of the non-moving

background during the subsequent 'Filehne'-type stimulus. The amount of physical motion at the point of subjective stability is a measure of the quantity of the 'Filehne' illusion.

To elucidate the neural mechanisms underlying the discrimination of self-motion versus environmental motion during smooth pursuit eye movements (SPEM), the role of early and late visual processing areas has been studied in nonhuman primate single-cell recordings. Neurons in the visual area V1 discharged invariably for self-induced versus externally induced slow retinal image slip [Ilg and Thier, 1996]. This finding stood in contrast to an early work of Galletti et al. [1984]. Whereas also neurons in the visual area V4 and the middle temporal (MT) motion processing area typically discharged invariably for both motion conditions a significant number of neurons in the medial superior temporal (MST) area, especially its dorsal region, responded preferentially to externally induced slow retinal image slip [Erickson and Thier, 1991]. At a later date a study of Thier et al. [2001] suggested that the visual posterior sylvian area (VPS), which is located near the dorsal end of the lateral sulcus might be relevant for perceptual stability during SPEM. How perceptual stability is instantiated in the human brain and which brain regions play a role in this process is still unclear. An electroencephalography (EEG) study [Haarmeier and Thier, 1998] and another study employing magneto-encephalography (MEG) [Tikhonov et al., 2004] techniques found evidence for a crucial role of the parieto-occipital cortex in the perception of self-induced motion.

On the basis of the theoretical framework of the inferential theory of perception the goal of the present study was to investigate where in the human brain referential calculation is accomplished and thereby perceptual stability during SPEM in humans is achieved. Therefore, we used event-related functional magnetic resonance imaging (fMRI) and a 'Filehne'-type stimulus preceded by a stimulus, whose background moved at different parametrically stepped velocities. On the basis of the results of previous primate and human studies, we expected temporal and parietal cortical regions to respond differently to the identical 'Filehne'-type stimulus depending on the velocity of the preceding stimulus, and hence, to underlie referential calculation during SPEM.

MATERIALS AND METHODS

Subjects

Six right-handed male students (mean age 25 years, range 20–30 years) were examined using functional magnetic resonance imaging (fMRI). Subjects reported normal visual acuity; none had a history of neurological or psychiatric dysfunction. Subjects were naive as to the purpose of the study and were paid for their participation. Written and informed consent was obtained from each participant prior to investigation according to the declaration of

Figure 1.

Temporal course of an experimental trial. Each trial consisted of a preceding stimulus (PS) requiring fixation of a red dot in the center of the screen while the background pattern moved to the left at one of three velocities ($-8^\circ/\text{s}$, $-16^\circ/\text{s}$, or $-24^\circ/\text{s}$) for 0.3 s. After an inter-stimulus-interval (ISI) of 6.6 s the critical stimulus

(CS) appeared requiring a smooth pursuit eye movement (SPEM) tracking of a red dot that moved from left to right at $11^\circ/\text{s}$ for 2 s with a stationary structured background pattern shown for 0.3 ms starting 0.85 s after begin of the SPEM.

Helsinki. The study was approved by the local ethics committee.

Stimuli and Experimental Design

During the fMRI session each subject underwent two event-related fMRI experiments and completed seven fMRI-runs: In experiment (I) each subject completed one fMRI-run consisting of 120 volume-scans, and in experiment (II) six fMRI-runs consisting of each 172 volume-scans. The first four scans of each run were discarded. In each condition of the two experiments 32 trials were presented.

Stimuli consisted of a red target dot (diameter 10 min arc) and a background pattern, which had an extension of $24^\circ \times 18^\circ$ and consisted of 350 light gray dots (each of diameter 15 min arc) randomly spread over the dark gray background area. Visual stimuli were projected onto a mirror mounted on the head-coil resulting in a viewing distance of ~ 22 cm. Average stimulus luminance was $22 \text{ cd}/\text{m}^2$.

In both experiments, (I) and (II), subjects were instructed to track the red target dot as accurately as possible and were trained outside the scanner at the beginning of each session.

In experiment (I), subjects performed smooth pursuit eye movements (SPEM). This experiment served to localize regions involved in performing eye movements (SPEM and saccades) for subsequent regions of interest (ROI) analysis.

SPEM stimuli: The target dot was presented for 0.5 s in the center of the screen. Next it jumped 11° to the left and from there moved to the right at a constant velocity of $11^\circ/\text{s}$, resulting in a stimulus duration of 2.5 s. Finally, the target dot jumped back to the center of the screen.

In experiment (II), different degrees of change in the reference signal were induced in a parametric design by preceding stimuli of three different velocities, which were designed according to Haarmeier et al. [1996]. An experimental trial consisted of one preceding stimulus (PS) and one critical stimulus (CS) presented at an interval of 6.6 s (cf. Fig. 1). The duration of one trial was 10.5 s. The interval between trials varied between 9.0–15.0 s (mean = 12.0 s).

Preceding stimuli (PS): The target dot was presented for 1.4 s in the center of the screen, after 1.1 s followed by a background pattern that was visible for 0.3 s. The pattern moved leftwards at one of three velocities (PS-8 = $-8^\circ/\text{s}$, PS-16 = $-16^\circ/\text{s}$, PS-24 = $-24^\circ/\text{s}$), while subjects fixated the target in the center of the screen. Dots reaching the border of the pattern area disappeared and were replaced by fresh dots appearing on the opposite side. According to our assumptions this stimulus served to modify parametrically the state of the referential system.

Critical stimuli (CS): The target dot was presented for 0.5 s in the center of the screen. Next it jumped 11° to the left and from there moved to the right at a constant velocity of $11^\circ/\text{s}$ for 2.0 s. After 0.85 s of this SPEM a stationary background pattern appeared for 0.3 s while subjects continued to perform SPEM. Although CS was physically identical they will be referred to as CS-8, CS-16, or CS-24 depending on the velocity of the PS.

Please note, that the background motion of the PS and the SPEM during the CS were in opposite direction. This should result in an enhanced relative opposite background motion effect of a stable background during the SPEM.

PS velocity was constant during the course of each fMRI run (either $-8^\circ/\text{s}$, or $-16^\circ/\text{s}$, or $-24^\circ/\text{s}$). There were two fMRI runs of either velocity; the sequence of runs was balanced across subjects. One of the six possible sequences of

conditions (1-2-3; 1-3-2; 2-1-3; 2-3-1; 3-1-2; 3-2-1) was assigned to each subject and repeated for that subject. In between stimulations a white fixation cross was shown in the center of the dark gray screen.

Eye movements were controlled by video-oculography (MEyeTrack™ System, SensoMotoric Instruments GmbH, Teltow, Germany). The system uses infrared cameras to capture the eye movements. Data were recorded at a sampling rate of 50 Hz. The system tracks corneal reflexes on the iris together with the pupil compensating shifts of the camera relative to the head. For calibration prior to experiment I subjects were asked to track nine predetermined calibration dots. Video-oculography data acquired in the scanner was used for qualitative analysis. Eye movements were displayed on a computer monitor so that the performance could be monitored continuously by the experimenter.

Data Acquisition fMRI

Imaging was performed on a 1.5-T Siemens Vision echo-planar system with a standard head coil. The subject's head was immobilized by a vacuum pad to minimize movement artifacts. Echo-planar imaging (EPI) scans were acquired in 16 slices covering the supratentorial parts of the brain in an oblique orientation ($\sim 25^\circ$ to the anterior commissure-posterior commissure (ACPC) plane). Functional runs consisted of 120 (experiment (I)) or 172 (experiment (II)) whole brain volume scans using a T2*-weighted free induction decay (FID) EPI sequence (repetition time (TR) = 2 s, echo time (TE) = 60 ms, flip angle = 90°). Slice thickness was 5 mm (skip 0.5) with a field of view of $256 \times 256 \text{ mm}^2$ and an imaging matrix of 64×64 resulting in a plane resolution of $4 \times 4 \text{ mm}^2$.

Data Acquisition MRI

Following each functional session we collected a high-resolution T1-weighted 3D-MP RAGE dataset (TR = 9.7 ms, TE = 4 ms, flip angle = 90° , field of view = $256 \times 256 \text{ mm}^2$, voxel size $1 \times 1 \times 1 \text{ mm}^3$, 190 slices) to transform the EPI data into three-dimensional space and to align functional data from different scanning sessions. For visual control of the spatial transformation process a 2D T1-weighted scan (TR = 900 ms, TE = 14 ms, voxel size $2 \times 2 \times 5 \text{ mm}^3$, 16 slices) in the same orientation as the EPI-slices complemented each experiment. For individual surface reconstruction and individual 3D intersession alignment a high resolution 3D-Flash dataset was collected for each subject during an additional session (TR = 20 ms, TE = 5 ms, flip angle = 30° , field of view = $256 \times 256 \text{ mm}^2$, voxel size $1 \times 1 \times 1 \text{ mm}^3$, 190 slices, 2 acquisitions).

fMRI Data Analysis

Data were preprocessed and analyzed using Brain Voyager QX software (Brain Innovation B.V., Maastricht,

Netherlands). Preprocessing of the fMRI data involved a 3D motion correction based on the estimates of three translation and three rotation parameters of rigid body transformation, a slice scan time correction and the removal of slow linear and non linear trends. No further temporal or spatial filtering was applied. The latter because of spatial smoothing may be critical when differences of cortical areas are examined that may be relatively small.

Cortex-based fMRI Data Analysis

Three-dimensional individual cortex reconstruction was achieved by segmenting and tessellating the gray-white matter boundary and by inflating the resulting surface mesh on the basis of the 3D-Flash data [Carman et al., 1995; Van Essen et al., 1998]. The resulting individual reconstructions were transferred into Talairach standard brain space and further morphed into spherical representations. The subjects' individual spherical representations were aligned with each other following a coarse-to-fine matching strategy of the cortical folding pattern. This is a moving-average, group-alignment version of the cortex-based alignment process that substantially improves spatial correspondence mapping between subjects' brains beyond Talairach space [Fischl et al., 1999; Van Atteveldt et al., 2004].

The fixed effects statistical group analysis was based on a general linear model (GLM) involving a correction for linear serial correlations. Predictor size was 2 s for the PS and 4 s for the CS. Individual time courses were convolved with a hemodynamic response function [Boynton et al., 1996]. Statistical maps were displayed on one individual reconstructed surface. Cortex-based statistical group analysis comprised three steps:

- a. First, in order to identify cortical regions that are activated during the condition that served to induce a 'Filehne' illusion, a GLM was run on the BOLD (blood oxygenation level dependent) response to the CS stimuli (CS-8, CS-16, CS-24) from experiment (II) contrasted against fixation baseline; resulting activations were displayed at a threshold criterion of P (Bonferroni corrected) < 0.0001 and a cluster size criterion of 50 mm^3 .
- b. Second, to functionally localize cortical regions that are activated during eye movements (SPEM and saccades) as ROIs, a GLM was run on the BOLD response to the SPEM stimuli from experiment (I) contrasted against fixation baseline. Cortex-defined ROIs were localized by analysis of the activation during the SPEM task displayed at a threshold criterion of q (FDR) < 0.05 (false discovery rate, FDR) [Benjamini and Hochberg, 1995; Genovese et al., 2002] and a cluster size criterion of 25 mm^3 , and were defined on the reconstructed surface. Bilateral early visual processing areas (VIS), putative visual posterior sylvian area (VPS), posterior parietal cortex (PPC), visual

TABLE I. Results from ROI analysis

		BOLD signal change for CS										
		Talairach coordinates			Factor effect		CS-16 vs. CS-8		CS-24 vs. CS-8		CS-24 vs. CS-16	
ROI	Number of voxels	<i>x</i>	<i>y</i>	<i>z</i>	<i>F</i>	<i>p</i>	<i>D</i>	<i>p</i>	<i>D</i>	<i>p</i>	<i>D</i>	<i>p</i>
RH												
VPS	1411	58	−25	22	1.44	0.70						
PPC	3767	34	−40	39	4.45	0.04*	−0.28	0.34	0.00	1.00	0.28	0.05*
STS	2945	55	−36	11	1.88	0.20						
MT+	4257	46	−55	−5	0.68	0.53						
Vis	15813	18	−65	−1	2.37	0.14						
LH												
FEF	224	−38	−17	51	3.95	0.07						
VPS	1629	−58	−42	23	7.05	0.01*	−0.27	0.50	0.25	0.48	0.52	<0.01*
PPC	1159	−28	−60	43	1.93	0.20						
STS	752	−56	−44	5	2.57	0.13						
MT+	1960	−44	−67	−1	2.30	0.15						
Vis	13241	−14	−78	2	2.61	0.12						

Anatomical properties of the chosen ROIs and the results of ROI analysis (ANOVA with repeated measures on predictor beta values from ROI GLM) are listed. Values significant after Bonferroni correction for multiple comparisons are linked by *; *D* is the mean difference between predictor beta weights.

motion complex (MT+), and the activated part of the superior temporal sulcus (STS) as well as the left frontal eye field (FEF) were defined as ROIs. The ROIs labeled as PPC (intraparietal sulcus), MT+, and FEF corresponded well to those defined in the human SPEM literature [Berman et al., 1999; Petit and Haxby, 1999; Petit et al., 1997]. The Talairach coordinates of VPS located at the superior temporal gyrus (RH: $x = 58$, $y = -25$, $z = 22$) almost matched to those given for the superior temporal gyrus activation to vestibular stimulation labeled as visual temporal sylvian area (VTS) (RH: $x = 66$, $y = -30$, $z = 14$) [Dieterich et al., 2003]. The STS activation in our study corresponds very well to STS defined as an area processing visual motion in humans [Noguchi et al., 2005]. Talairach coordinates of the cortex-defined ROIs are provided in Table I.

- c. Third, the BOLD response to CS stimuli was parametrically analyzed within the ROIs. On the basis of the

cortex-based alignment algorithm the individual anatomical equivalents of the ROIs in every subject could be included into the analysis. The predictor beta values resulting from the ROI-GLM were extracted for the three conditions of the PS and for the three conditions of the CS, and were fed into an analysis of variance (ANOVA) with repeated measures (using SPSS 13.0 software, SPSS, Chicago). Separate ROI ANOVAs with repeated measures on three-level factor 'CS' (CS-8, CS-16, or CS-24) and on three-level factor 'PS' (PS-8, PS-16, or PS-24) were run. In cases of a significant factorial main effect of 'CS' or 'PS', respectively, post-hoc contrasts with Bonferroni correction for multiple comparisons were calculated for the three parametric velocity conditions.

An additional parametric analysis was conducted to control for carry-over effects between the subsequent stimuli. Even ultra-short visual stimuli of 0.1 s elicit a BOLD

Figure 2.

BOLD responses to the critical stimulus (CS) and to the SPEM stimulus. (a) BOLD responses to the critical stimulus (CS), pooled over all three conditions, at a statistical level, Bonferroni corrected, of P (corrected) < 0.0001 from the cortex-based group analysis are displayed. Defined ROIs are named; ROIs have been defined by the response to the SPEM stimulus, which is shown in light blue, at a statistical level of q (FDR) < 0.05 . (b) The ROIs corresponding to VPS and PPC are zoomed. Labeling of gyri and sulci according to

Ono et al. (1990). AS, angular sulcus; AOS, anterior occipital sulcus; CINS, circular sulcus, insula; CS, central sulcus; FEF, frontal eye field; IFS, inferior frontal sulcus; IPS, intraparietal sulcus; ITS, inferior temporal sulcus; mfs, intermediate frontal sulcus; MT+, visual motion complex; POCS, postcentral sulcus; PPC, posterior parietal cortex; PRCS, precentral sulcus; SF, sylvian fissure; SFS, superior frontal sulcus; STS, superior temporal sulcus; VIS, early visual processing areas; VPS, putative visual posterior sylvian area.

Figure 2.

response lasting for about 6.0 s [Savoy et al., 1995]. Thus, the interstimulus-interval of 6.6 s in our study does not allow excluding an overlap between the BOLD-responses to the 0.3 s PS and the subsequent CS. To control for carry-over effects, which would include the risk of attributing PS effects to the CS, two different hemodynamic response functions (HRFs) (Boynton function [Boynton et al., 1996], 1. HRF: $\delta = 2.5$, $\tau = 1.25$, 2. HRF: $\delta = 2.5$, $\tau = 1.75$) were applied to the PS to modify the overlap between the GLM predictors of the two stimuli. The idea of that is that at a smaller overlap effects at the downward slope of the BOLD-response to the PS are less strongly modeled and would have more influence on the CS.

RESULTS

Figure 2 illustrates the BOLD-responses to the CS, irrespective of PS velocity, displayed on an inflated cortex (yellow patches). Group analysis revealed a significant increase of the BOLD signal in a distributed pattern of cortical areas involving bilateral occipital, superio-temporal, intraparietal, central, and precentral regions. Activation spots found for the SPEM task (light blue patches on the cortex in Fig. 2a and in volume plots shown in Fig. 3) were located at similar positions; all ROIs defined by SPEM corresponded to areas also responding to CS.

Grand-averaged event-related time courses from each ROI for both, the PS and the CS, are shown in Figures 3 and 4. Plots of the time courses differentiate between the activations caused by the three different PS velocities. It should be noted that in both instances, PS and CS, stimulation is very similar on the level of the retina. Real motion (for PS) and perceived motion (for CS) yielded an activation of up to 0.8% signal change found in the VIS for the highest velocities. The time courses show that the BOLD responses were stronger in left VPS and in right PPC for faster ($-24^\circ/\text{s}$) than for slower ($-16^\circ/\text{s}$) velocities of the stimulus in each subject (see Fig. 3). This is true for both, the PS and the CS.

ROI ANOVAs with repeated measures revealed a significant main effect of the three-level factor 'CS' on the BOLD response to CS in right-hemispheric PPC ($F(2,5) = 4.45$, $P = 0.04$) as well as in left-hemispheric VPS ($F(2,5) = 7.10$, $P = 0.01$). Post-hoc paired means comparison applying Bonferroni testing showed that this effect was due to a stronger BOLD-signal for CS that had been preceded by faster velocity PS (CS-24 vs. CS-16 comparison): in right PPC ($P = 0.05$) and in left VPS ($P < 0.01$). ROI ANOVAs with repeated measures did reveal an effect of the factor 'CS' but not of the factor 'PS' in right PPC and left VPS (right PPC: $F(2,5) = 2.20$, $P = 0.16$ and left VPS $F(2,5) = 3.30$, $P = 0.08$). Table I summarizes the results from ROI ANOVAs for the factor 'CS'.

To control for carry-over effects of the BOLD response between the narrowly spaced PS and CS stimuli the parametric analysis within ROIs was additionally modeled using a stronger overlap. With less overlap of the BOLD-

responses to the PS and the CS using a narrow HRF the effects in PPC and VPS were abolished or much reduced, respectively. Controlling PS effects stabilizes effects to the CS showing that these are not due to carry-over effects from the PS.

DISCUSSION

In the present study, we investigated the cortical basis of perceptual stability during SPEM in humans based on the theoretical framework of the inferential theory of perception. For that purpose, we used event-related fMRI and a 'Filehne'-type stimulus preceded by a stimulus, whose background moved at different parametrically stepped velocities. The background motion of the preceding stimulus and the subsequent SPEM during the 'Filehne'-type stimulus were in opposite direction, which should result in an enhanced relative opposite background motion effect of the stable background during the SPEM. We found that the cortical activity in two regions (left VPS and right PPC) covaried with the velocity of the preceding stimulus. Hence, higher velocities of background motion of the PS elicited a stronger response in these areas, most probably due to a larger shift of the 'point of stationarity' of the system that in turn induces a larger remaining motion signal during the CS.

The PPC activations to the SPEM stimulus were located in the ventral intraparietal sulcus (IPS), which is consistent with previous fMRI studies on SPEM [Berman et al., 1999; Petit and Haxby, 1999]. Also FEF and MT+ activations have been found in previous SPEM studies [Berman et al., 1999; Petit and Haxby, 1999; Petit et al., 1997]. Referring to the previous SPEM literature the activation spots in the superior temporal sulcus (labeled as STS) and in the superior temporal gyrus (labeled as VPS) to the SPEM stimulus were surprising to us. Human STS is known as an area processing second-order visual motion and biological motion [Noguchi et al., 2005; Servos et al., 2002]. VPS has been described as a polymodal area in the inferior parietal cortex of the squirrel monkey [Guldin and Grüsser, 1998] and corresponds to an area called the visual temporal sylvian area (VTS) [Guldin and Gruesser, 1996]. Although its main input is optokinetic, arriving from motion processing area MST, this area receives also vestibular afferences from the parieto-insular-vestibular cortex (PIVC) [Fasold et al., 2002; Gruesser et al., 1990a,b; Guldin and Grüsser, 1998]. In humans activation of the retroinsular cortex and the adjacent superior temporal gyrus or the transverse temporal gyrus probably best fit with the nonhuman VPS or VTS [Dieterich et al., 2003]. Thus VPS is located posterior to the putative human correspondent of PIVC in the posterior insula [Dieterich et al., 2003; Petit and Beauchamp, 2003]. The localization of the region of interest labeled VPS in our study according to its Talairach coordinates would allow an assignment to both, either to VPS or to PIVC. Although the immediate proximity of VPS and PIVC complicates their separation in human functional studies we

Figure 3.

BOLD responses in VPS and PPC covary with velocity of the preceding stimulus. Top: The ROIs corresponding to left VPS and right PPC are shown in a slice volume plot. Middle: Grand averages of the event-related time courses depending on the velocity of the PS are presented for two ROIs (left VPS and right PPC). Zero on the x-axis corresponds to the time when the critical stimulus (CS) is presented, -8 corresponds to the time when the preceding stimulus (PS) is presented. The baseline

for the time courses has been set to the time period from -8 to -7. The parametric variation is color coded (blue - PS/CS-8, green - CS/PS-16, red - CS/PS-24). Bottom: The diagram gives the differences between the beta values from the two parametric conditions that differ significantly (CS-24 and CS-16) in each single subject. Additionally the mean effect with its standard deviation is shown. PPC, posterior parietal cortex; PS, preceding stimulus; VPS, putative visual posterior sylvian area.

Figure 4.

Time courses from ROIs with no significant parametric effects. Grand averages of the event-related time courses depending on the velocity of the PS are presented for all ROIs. Zero on the x-axis corresponds to the time when the critical stimulus (CS) is presented, -8 corresponds to the time when the preceding stimulus is (PS) is presented. The baseline for the time courses

has been set to the time period from -8 to -7. The parametric variation is color coded (blue – PS/CS-8, green – CS/PS-16, red – CS/PS-24). FEF, frontal eye field; MT+, visual motion complex; PPC, posterior parietal cortex; PS, preceding stimulus; STS, superior temporal sulcus; VIS, early visual processing areas; VPS, putative visual posterior sylvian area.

decided to label the activation in the superior temporal gyrus in our study “VPS” because of its better fit with the localization of VPS (or VTS) described in the human and animal literature [Dieterich et al., 2003; Guldin and Grüsser, 1998; Karnath, 2001; Thier et al., 2001].

The apparently higher activation associated with the presentation of the ‘Filehne’-type stimulus as compared with the pure SPEM stimulus is due to the presence of the dot pattern background during the PS and CS stimuli but is not relevant to the aims of the present study.

SPEM involves a network of cortical and subcortical areas largely overlapping with those involved in planning and

executing saccades [Krauzlis, 2004; Petit and Haxby, 1999; Petit et al., 1997; Rosano et al., 2002]. The SPEM stimulus in experiment I and the CS in experiment II involve both, SPEM and two saccades. Thus, resulting from the abovementioned overlap between areas involved in SPEM and in saccades activations resulting from these two kinds of eye movements cannot be clearly distinguished in our experiments.

The stimulus and experimental parameters in our study have been chosen according to those used by Haarmeier and Thier who were the first to show a modification of the ‘Filehne’ illusion by preceding stimuli (conditioning stimuli) [Haarmeier and Thier, 1996]. In that study the ‘Filehne’

illusion was not significantly over-ridden by a motion aftereffect. Prolonged stimulation of the retina by a pattern moving continuously into one direction induces an illusory perception of motion of a subsequently presented stationary pattern into the opposite direction - a phenomenon, which is known as the motion aftereffect (MAE) [Barlow and Hill, 1963; Huk et al., 2001; Wohlgenuth, 1911]. In contrast to the temporal behavior of the MAE, which decays exponentially in time [Keck and Pentz, 1977], the 'Filehne' illusion showed a tendency to increase in time when it was studied at various interstimulus-intervals (0.5, 3.0, 6.0 s) [Haarmeier and Thier, 1996]. Retina stimulation by a moving pattern in our study was very brief (0.3 s). Taken together with these previous findings on the different temporal behaviors of the 'Filehne' illusion and the MAE it can thus be ruled out that the observed effect is due to a MAE.

Furthermore, the parametric effects on the BOLD response to the CS in VPS and PPC are unlikely to be due to deviations from the required SPEM velocity of $11^\circ/\text{s}$. A recent study found that BOLD activity in MT+ correlates positively with the velocity of SPEM [Nagel et al., 2006]. In our data, we did not find parametric effects on the BOLD response to the CS in MT+ or in the FEF. Thus, such effects in VPS and PPC are unlikely to be induced by systematic deviations of the SPEM velocity during the CS.

Another potential concern could be an influence of the BOLD response to the PS on that to the subsequent CS, because the two stimuli had been narrowly spaced (6.6 s). To address this issue, we modeled the responses to the PS and the CS using different overlaps of the hemodynamic response. At a smaller overlap effects at the downward slope of the BOLD-response to the PS are less strongly modeled and would have more influence on the CS. Our results show that the effects to the CS were abolished or decreased at a less strongly modeled overlap, thus the effects observed in the present study cannot be explained by possible carry-over effects of the BOLD response to the PS. Giving further proof, an ANOVA with repeated measures did reveal an effect of the factor 'CS' but not of the factor 'PS'. In other words, significant effects in right PPC and left VPS arose at the level of the CS but failed significance at the earlier level of the factor 'PS' itself.

Thinking of areas potentially underlying the percept of a stable world even during eye movements in humans one might speculate that it is an achievement of the visual motion complex MT+. In humans, MT+ is located at the dorsal end of the inferior temporal sulcus [Dukelow et al., 2001; Watson et al., 1993]. It is also involved in perceived motion without retinal image motion caused by a motion after effect [Goltz et al., 2003]. However, in accordance with an event-related potential (ERP) study of Haarmeier and Thier [1998] our data do not support this hypothesis. The peak amplitudes of both the parieto-occipital N300 and the frontal P300 but not of earlier components differed between two 'Filehne' conditions and hence corresponded to the subjective percept of visual motion. According to

the authors, the late components imply the dependency of subjective motion perception on a parieto-fronto-occipital network rather than on earlier stages in the stream of visual motion processing up to area V5.

Left VPS responded to the parametric variation in our study. Previous single-cell recordings in rhesus monkeys [Thier et al., 2001] suggest that an area near the dorsal end of the lateral sulcus, labeled as VPS, might be relevant for perceptual stability. Therefore, we speculate that the temporo-parietal activation focus appearing in our data represents a human analogue of VPS.

Furthermore, the BOLD response in the right PPC covaried with the parametric variation in our study. Visual neurons in the lateral intraparietal region (LIP) are strongly connected to the frontal eye fields (FEF). These areas may construct an eye-centered representation of oculomotor space in order to guide current or intended eye movements based on a corollary discharge of the eye movement command [Colby and Goldberg, 1999]. Area LIP indeed exhibits a robust topographic organization in a delayed saccade task [Serenio et al., 2001]. In analogy to the remapping of visual space in the lateral intraparietal area of monkeys [Duhamel et al., 1992], Medendorp et al. [2003] reported the evidence that an area at the same location updates its topographic representation for goal directed movements in a gaze-centered reference frame in humans.

Because the sample size in our study is rather small there may be more cortical areas in which a modulation of the BOLD-response by the background motion velocity of the preceding stimulus is present but in which the level of significance was not reached due to a lack of power. This could be true for example for the visual motion complex MT+ and the frontal eye fields. Nonetheless the effect in VPS and PPC (see Fig. 3) is remarkably robust showing in all of the six subjects.

According to the inferential theory of perception perceptual stability during eye movements is achieved through the comparison of the retinal signal with an internal reference signal encoding for eye movements. Taken together, our data suggest that temporal and parietal brain regions such as VPS and PPC strongly contribute to referential calculation and thus, the achievement of perceptual stability during eye movements.

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