Allocentric spatial judgements by re-mapping egocentric coordinates:
a fMRI study.

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I affirm that I have written the dissertation myself and have not used any sources and aids other than those indicated.

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SUMMARY

Spatial locations of objects can be represented in the brain with respect to different classes of reference frames, either relative to or independent of the subject's position. This fMRI study compared brain activation induced by a condition involving spatial judgements with respect to the body mid-sagittal plane (the egocentric task) with that induced by judgements about the spatial relationship between certain objects (allocentric task). Comparing both conditions to an object discrimination task (control condition) revealed a largely overlapping occipito-parietal network in the right hemisphere. Direct comparisons of the two spatial tasks revealed higher activations for the allocentric spatial task in medial temporal lobe (MTL) structures of the right hemisphere and in frontal areas of the brain, including the anterior cingulate gyrus (ACC) and medial parts of the prefrontal cortex (MPFC). No brain region exhibited a significant higher activation in the egocentric compared to the allocentric task. Results are interpreted according to a transition approach, in that reflexively performed egocentric localisations are re-mapped into an allocentric code of permanent storage. Here we suggest the involvement of the posterior parietal cortex in managing egocentric spatial representations, with some parts being specialised to convey egocentric information to brain areas responsible for the re-mapping. We propose that two densely interconnected structures (MPFC and MTL) could serve this function, initialised by conflict monitoring of the ACC.

1 INTRODUCTION

Spatial orientation, navigation and the systematic exploration of space are essential for survival of most animal species and are also critical for human everyday life. Thus one goal in neuroscience is to understand the mechanisms by which humans orient themselves in space and how their brains create and organise spatial representations.

The spatial location of an object may be, in principle, represented with reference to two fundamental classes of spatial coordinate systems: egocentric and allocentric (Lacquaniti, 1997). In the egocentric spatial frame of reference, spatial locations are coded with respect to relevant body parts, such as the eyes, the head, the trunk or/and the arm. This kind of coding is highly dynamic, needs continuous updating as one moves and is particularly useful for the organization of movements towards objects in space, when for example reaching a target (Snyder, 2000). By contrast, in an allocentric spatial representation the location of an object is represented independent of the observer's position and thus describes the spatial relationship among the component parts of the object or the relative position of multiple objects with respect to each other. Representations encoding these configurational properties of objects may be useful for their identification. Objects, in ecological conditions, are typically seen from a variety of viewer-centred (observer-based) perspectives, suggesting a close interaction between egocentric and allocentric spatial frames of reference (Neggers, Scholvinck, van der Lubbe, & Postma, 2005).

Egocentric frames of reference are typically associated with the posterior parietal cortex. Neurons coding spatial position relative to body parts have been found in the monkey's posterior parietal cortex, (Andersen, Snyder, Bradley, & Xing, 1997; Colby, 1998; Cohen & Andersen, 2002) and in connected regions (Wise, Boussaoud, Johnson, & Caminiti, 1997) of the premotor cortex (Fogassi et al., 1992; Graziano, Hu, & Gross, 1997; Graziano & Gross, 1998). Patients with lesions to the posterior parietal cortex may show inaccurate visuomotor coordination, a disorder termed 'optic ataxia' (Perenin & Vighetto, 1988). Typically such patients are impaired in reaching and grasping for visual objects with both hands in their contralesional peripheral visual field (Karnath & Perenin, 2005). They also show a specific deficit in

perceiving the position of their body midsaggital plane, a fundamental egocentric spatial ability (Perenin, 1997). A series of neuroimaging studies has provided direct evidence of the involvement of parieto-frontal circuits in the egocentric coding of space. A posterior parietal-frontal network, bilateral but more extensive in the right hemisphere is activated when simple stimuli are localized with respect to the body mid-sagittal plane (Vallar et al., 1999). Similar results were reported when employing complex 3-D objects and an egocentric distance estimation task (Committeri et al., 2004). The parieto-frontal activation is larger than when an object-based, i.e. allocentric judgement is performed on the same stimuli (Galati et al., 2000) and is found for body-centred localization tasks with both, visual and tactile stimuli (Galati, Committeri, Sanes, & Pizzamiglio, 2001).

The ability to spatially judge stimuli with respect to the body's mid-saggital plane requires that spatial information is transformed from a retinal to a body-centred coordinate frame. From the conceptual point of view, the prevailing idea has been that this "coordinate transformation" is performed in a serial or hierarchical manner with progressive shifts of target location from retinocentric, to head-centred, to body-centred coordinates by combining information from various modalities (Andersen, Snyder, Li, & Stricanne, 1993). Many parietal areas involved in early processing of visual information do so in an eye-centred frame of reference (Colby, Duhamel, & Goldberg, 1995). A head-centred representation is formed by combining information about eye position and the location of the visual stimulus imaged on the retina. A body-centred coordinate representation is likewise achieved by combining retinal, eye and head position signals. It is generally believed that this combination is achieved by gain modulation (Salinas & Thier, 2000) of eye-centred representations through eye and/or head position signals, i.e. the amplitude of a neuron's visual response is modulated by eye and/or head position information (Andersen et al., 1993). In posterior parietal areas of the monkey, these gain modulated signals form a distributed representation of sensory-target locations that could be principally read out in different egocentric frames of reference, for example in a head-centred or body-centred frame (Andersen et al., 1997; Cohen et al., 2002). Yet, neurons whose activity reflects a convergence of retinal and eye position signals have also been reported in "earlier" areas of the monkey's visual brain, for example in Areas V1 (Trotter & Celebrini, 1999), V3A (Galletti & Battaglini, 1989), MT, and MST (Bremmer, Ilg, Distler, & Hoffmann, 1997) and in the parieto-occipital region (Nakamura, Chung,

Graziano, & Gross, 1999). Thus a head-centred representation of visual space could be computed already at low levels of the visual pathways (Boussaoud & Bremmer, 1999). On the other hand, head position gain fields, which ultimately could be used to achieve an body-centred coordinate frame have been only reported for "later" areas, like the lateral intraparietal area (LIP) of the posterior parietal cortex (Snyder, Grieve, Brotchie, & Andersen, 1998).

Allocentric orientation or frames of reference are probably best understood in terms of an enduring storage of environmental information, in form of relational maps of topographical space that are independent of the observers position. An influential theory was proposed that pointed to the hippocampus as the neural substrate for cognitive maps (O'Keefe & Nadel, 1978), based on the discovery of "place cells" in the rat's hippocampal formation (O'Keefe & Dostrovsky, 1971; Muller, 1996; Best, White, & Minai, 2001), i.e. neurons that exhibit an increased firing rate when the rat arrives at a particular location in space called the "place field". The cognitive map theory proposed that hippocampal place cells are the basic units of the map and that an environment is represented by a collection of place cells, each of which represents a specific region in space. The specific configuration of place cells thus would provide an internal representation of the environment that affords an animal knowledge of its position relative to important locations. Therefore the hippocampus, according to the cognitive-mapping theory, encodes allocentric space, the location of the organism with respect to important places in the environment. Neurons with place fields that encode space in allocentric coordinates have also been identified in the monkeys hippocampal formation (Matsumura et al., 1999; Georges-Francois, Rolls, & Robertson, 1999). More recently, cells that would exhibit a 'place response' were also reported for the human hippocampus, obtained by extracellular recordings from single neurons, while patients with pharmacologically intractable epilepsy performed large scale spatial behaviour in virtual reality (Ekstrom et al., 2003). Lesion to parts of the human medial temporal lobe (MTL), like the parahippocampal gyrus (Aguirre, Zarahn, & D'Esposito, 1998; Bohbot et al., 1998; Bohbot, Allen, & Nadel, 2000), the hippocampus (Spiers, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2001) or lesions to both (Maguire, Burke, Phillips, & Staunton, 1996a), lead to difficulties in storing and/or recalling identity and spatial location of important landmarks, resulting in topographical disorientation (Aguirre & D'Esposito, 1999) in new and/or familiar environments.

Neuroimaging studies using a variety of topographical tasks, such as landmark knowledge, orientation in large scale space and navigation (usually in 'Virtual Reality'), have detected activations in the parahippocampal gyrus (Aguirre, Detre, Alsop, & D'Esposito, 1996; Maguire, Frackowiak, & Frith, 1996b; Maguire, Frith, Burgess, Donnett, & O'Keefe, 1998b; Janzen & van Turennout, 2004), the hippocampal formation (Maguire et al., 1996b; Maguire, Frackowiak, & Frith, 1997; Maguire et al., 1998a; Kumaran & Maguire, 2005), as well as in the posterior parietal cortex (Aguirre et al., 1996; Maguire et al., 1996b; Maguire et al., 1997; Maguire et al., 1998b; Maguire et al., 1998a). Such complex tasks entail spatial operations referred to both, egocentric *and* allocentric orientation, which are difficult to isolate at this particular level of performance. Some attempts to actually disentangle the two reference frames in order to detect neural correlates of allocentric spatial orientation, employing less complex stimuli and tasks, were carried out by only a few authors (Galati et al., 2000; Committeri et al., 2004). In their studies, stimuli were presented, whose spatial location should be evaluated with reference to another visible object and thus represented an object-based (i.e. allocentric) judgement that accessed the spatial relationship between stimuli, independent of the observer's position. Both studies report the activation of posterior parietal-frontal networks responsible for coding allocentric space (when compared to a control condition). Interestingly these areas are implicated in egocentric orientation, although there is also evidence suggesting that some neurons of the posterior parietal cortex (monkey's area 7a) might code targets in a world-centred (i.e. allocentric) spatial frame of reference (Snyder et al., 1998). The mentioned studies addressed the difference between allocentric and egocentric spatial judgements (i.e. spatial judgements with respect to the body). Committeri et al. (2004) identified a bilateral lateral occipital-temporal (LOC) activation for the allocentric compared to an egocentric task. Galati et al. (2000) were not able to show a higher activation for object-centred compared to a viewer-centred spatial tasks, when contrasting the conditions directly. Although their group analysis did not reach statistical significance, they reported that four out of eight measured subjects showed bilateral lingual-hippocampal activations including the parahippocampus.

The present study ties in with the experiments carried out by Galati et al. (2000) and Committeri et al. (2004). Our study was conducted to detect anatomical structures involved in the computation of egocentric (body-centred) and allocentric

(object-centred) spatial representations. We used functional magnetic resonance imaging (fMRI) in normal individuals and compared the pattern of cerebral activations induced by two simple visuo-spatial tasks, requiring the use of different coordinate frames. Subjects were asked to judge the spatial position of dots either with respect to the subjective body midline or with respect to the imagined midline of a rectangle that was present, while maintaining fixation. These two conditions induced subjects to code the spatial position of the same object (the dot), making use of two different coordinate frames (egocentric: with reference to the mid-sagittal plane of the body; allocentric: with reference to the vertical midline of the rectangle). As a control condition we used a non-spatial object discrimination task. Based on reports of Galati et al. (2000) and Committeri et al. (2004) we expected to find a neural network of large overlap that is used by both spatial conditions, but aimed at identifying structures exclusively employed in computing an allocentric or an egocentric spatial frame of reference.

2 METHODS

Subjects

Twelve right-handed participants (5 men and 7 women, mean age: 25.4; SD: 2.8) with no history of neurological or psychiatric illness participated in the study. All subjects gave full written informed consent and the study was approved by the local ethics committee.

Apparatus

A Siemens MAGNETOM SonataVision MR System (Siemens, Erlangen, Germany) operating on 1.5 T and equipped for echo-planar imaging, using a 8-channel head coil system was employed for acquiring anatomical and functional MR images. The nasion was aligned with a laser crosshair projection, so that each participant's head would be approximately centred in the standing magnetic field of the MR system once within the MR bore. Head movements were minimised by mild restraint and cushioning, and participants lay supine in the MR bore.

Visual stimuli were generated using the software "E-Prime" (Psychology Software Tools, Inc., Pittsburgh, USA) on a personal computer located outside the

MR room. Stimuli were projected onto a projection screen mounted on the bench near the feet of the subjects (Fig. 1) using a LCD video projector connected to the personal computer, which was also placed outside of the scanning room. Participants viewed the visual stimuli via a mirror apparatus mounted on the head coil. Subjects had to respond by pressing one of two locally fabricated push buttons connected to the controlling computer.

The projection screen was equipped with an aperture mask having the shape of a rectangle (Fig. 1). By that we made sure that exclusively projection light, which felt through the aperture (i.e. rectangle window) could reach the subjects eyes. The aperture was placed such that the vertical midline of the rectangle was *not* aligned with the body-midline of the subjects, once they were within the scanner. The mask could be adjusted onto the projection screen, so that the vertical midline of the rectangle could be either left or right of the subject's own body-midline. Using this experimental setup we were able to exclude the possibility that subjects could use the edges of the projection as an additional cue in order to spatially judge stimuli according to their mid-saggital plane.

An infrared MR-eye tracker (Cambridge Research Systems Ltd., Rochester, UK) was employed to monitor eye movements. The eyepiece of the tracker was attached to head coil, such that we could measure the position of the subject's right eye during the whole experiment.
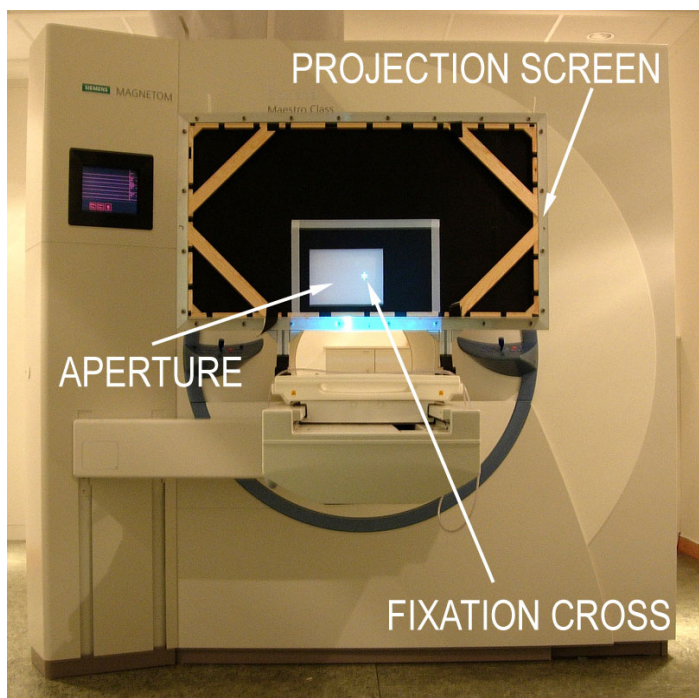

Figure 1: Setup for stimulus presentation in MR environment. Depicted is the MR scanner with inserted bench. Subjects lay supine in the magnet (no subject depicted). At the lower end of the bench a projection screen was mounted, equipped with an aperture mask, which had the shape of a rectangle (note the central fixation cross). The LCD-projection came from the direction, where the photograph was taken and illuminated an area of the mask marked by the larger white rectangle. The whole experiment was performed in complete darkness and subjects exclusively perceived visual stimulation through the small aperture rectangle, whose vertical midline was always shifted with respect to the body-midline of the subjects. The mask could be taken off the projection screen and flipped to the other side, to enable the rectangle being more 'left' or 'right' from the subjects midline.

Stimuli and Tasks

The experiment was carried out in complete darkness, with contrast and brightness values of the LCD-projector minimised in order to reach the lowest possible illumination of the within-environment of the scanner. Because the projection was masked by an aperture, the subjects perceived a rectangle (6.4° (vertical) x 8.6° (horizontal) visual angle), whose vertical midline was displaced by 2° either to the left or to the right of their own body midline. Within the rectangle, a fixation cross was continuously present, which subjects were instructed to fixate during the experiment. The cross could be either placed in a central position, aligned with the subjects mid-saggital plane, or in a peripheral position, i.e. 4.2° either left or right of the location of the central fixation cross depending on the placement of the aperture mask on the projection screen.

We presented an equal number of red and green dots (0.6° visual angel) at 24 different locations within the rectangle. Half of those dots were presented to the left, the other half to the right of the fixation cross, therefore controlling for the amount of visual stimulation in one hemisphere elicited by the dot's presentation. Subjects were instructed to judge the appearing dots according to their spatial location, either (1) with respect to their subjective body midline (egocentric condition) *or* (2) with respect to the vertical midline of the rectangle (allocentric condition) by responding with a left or right button-press. Additionally we employed a feature discrimination task, in which (3) subjects had to indicate the colours of the dots (control condition) by pressing the right button, when perceiving a red dot and the left button, when a green dot was present. Stimulus presentation time for a single dot was 300 msec, followed by 1700 msec time-to-respond period before the next dot appeared (Fig. 2).
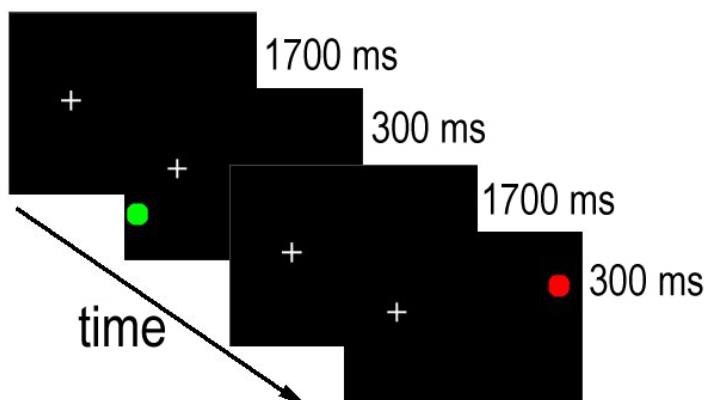

Figure 2: Two typical trails during the experiment. The permanent visual stimulus was a rectangle and a white fixation cross (here: central fixation), which subjects were instructed to look at. For 300 ms a red or green dot was presented and for the next 1700 ms subject responded by judging (1) the spatial location of the dot with respect to their subjective body midline (egocentric condition) or (2) in reference to the vertical midline of the rectangle (allocentric condition) or (3) they evaluated the colour of the presented dots.

Procedure

Prior to the MR imaging participants underwent a 20-minutes training session on a personal computer to familiarise with the tasks. After positioning a participant in the MR system, adjusting the eye tracker and performing an automatic shimming procedure to account for inhomogeneities in the standing magnetic field, we acquired a three-plane T1-weighted scout image to aid slice positioning for subsequent acquisition of functional MR images. Then we acquired functional MR images. Each subject underwent 4 consecutive imaging sessions, each session comprising 347 EPI-volumes. The first six volumes of each session were discarded to discount T1 saturation effects. The experimental task started with the acquisition of the seventh volume.

Each imaging session lasted about 11.5 minutes, two sessions were performed with the aperture mask placed to the right and left of the subjective body-midline, respectively. One session consisted of 12 blocks, comprising 24 pseudo-randomly selected trials each, and blocks were interleaved by condition-specific instructions. Four of the 12 blocks represented one of three task-specific conditions (egocentric, allocentric, control). Out of these four blocks, two were performed with a central fixation, whereas the other two blocks with a peripheral fixation. Thus the experiment had six conditions resulting from the factors "task" (egocentric, allocentric and control) and "fixation" (central and peripheral position). A session was organised in consecutive blocks of different fixations over task-specific condition, i.e. two blocks of one task-specific condition (for example the egocentric one) were successively performed for both types of fixation positions. The sequence of task specific conditions was counterbalanced over sessions as well as the sequence of the fixation conditions. Each experimental block started with a blank screen (for 2 sec) followed by an instruction screen (for 4 sec) and a request to fixate the fixation cross (for 2 sec) before the first of 24 consecutive trials (each 2 sec) of a block could be performed. The instruction screens consisted of a word ('body', 'rectangle' or 'colour') to remind the subject of the kind of task to be performed next, with two smaller words below reminding of the meaning of the two buttons ('left' and 'right' or 'green' and 'red'). Subjects performed four scanning session in total, two sessions with the aperture mask placed to the right and left of the subjective body-midline, respectively. Each participant was randomly assigned to one of twelve possible sequences with which the four imaging sessions could be presented, thus counterbalancing the order

of sessions (i.e. the order with which the aperture mask could be placed) over subjects.

Following the four scanning sessions we performed a calibration task of eye position (*see:* Eye Movement Monitoring) before we acquired high-resolution T1-weighted anatomical volumes.

Eye Movement Monitoring

Participants were instructed to look at a fixation cross during the spatial and non-spatial judgements of the dots, respectively. To control the fixation of the subjects, horizontal eye movements were recorded (sampled at 100 Hz) during the scanning procedure using MRI-compatible infrared oculography (Kimmig, Greenlee, Huethe, & Mergner, 1999). The MR-eye tracker uses the limbus tracking technique. The limbus is the margin between the cornea, which covers the pupil and iris, and the sclera. In this limbus tracker, the eye is illuminated by infrared light, coming from a light emitting diode (LED). The amount of light reflected back from the eye's surface is measured with a photodiode, which gives the position of the eye. A multi-channel display program (DASYLab, National Instruments, Austin, USA) was used to acquire and display the signals derived from the MR-eye tracker. The TTL pulse of the MR scanner at the beginning of each volume acquisition was also recorded and used to trigger the stimulus presentation. A calibration task was performed, which consisted of sequential, multiple fixations (5 times) onto three targets, presented on the midsagittal plane or 4.2° either to the left or right of the central target. The eye movement signals were evaluated manually (i.e. for the occurrence of saccadic eye movements during the trials) using the calibration task of eye position as a reference. We determined the percentage of trails for each task specific condition (egocentric, allocentric, control) that were performed with saccadic eye movements (i.e. saccades within the entire trial interval of 2 sec after onset of the stimulus). Percentages of trials performed without the instructed fixation were analysed across conditions (RM ANOVA) in order to show comparability of the tasks.

Behavioural Response Monitoring

During the scanning sessions the participants had to indicate their judgements by pressing one of two push buttons. We collected their responses and analysed reaction times and response error rates (RM ANOVA's) for the task specific

conditions (egocentric, allocentric, control) in order to compare the difficulty of the tasks.

Since we used the same stimuli in all experimental conditions, it was important to validate that subjects indeed judged according to different spatial frames of reference. For this purpose we separately analysed trials that depending on the spatial task (egocentric or allocentric) must have had different responses, i.e. dots that were presented right of the body-midline but left of the vertical midline of the rectangle or dots left to the body-midline and right to the midline of the rectangle. These *critical trials* were indicative for the accuracy with which the subjects correctly judged according to the two different spatial reference frames. Critical trials constituted approximately 16% of the total trials performed within a certain spatial condition and they were analysed (paired *t*-test) in terms of correct performance rates.

Imaging Parameters

Echo-planar functional MR images (TR = 2 sec, TE = 45 msec, flip angle = 90°, FOV = 192 x 192 mm, image matrix = 64 x 64, voxel size = 3.0 x 3.0 x 4.0 mm + 1 mm gap) were acquired in the axial orientation using blood oxygenation level-dependent (BOLD) imaging (Kwong et al., 1992). Fast imaging sequences such as echo-planar imaging (EPI) can captured stimulus-evoked transient changes in the BOLD-signal (Bandettini, Wong, Hinks, Tikofsky, & Hyde, 1992), which appears to be more closely correlated to local field potentials (LFP) than to spiking activity (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001; Logothetis & Wandell, 2004) and therefore represents local processing within and inputs to brain areas rather than outputs to other regions.

EPI-images consisted of twenty-four axial slices. The planes were individually oriented in parallel to the AC-PC line and covered the whole cerebral volume including the superior half of the cerebellum in all of the subjects. A three-dimensional high-resolution anatomical image was also acquired for each subject (176 sagittal slices, TR = 1300 msec, TE = 3.19 msec, TI = 660 msec, flip angle = 15°, FOV = 256 x 256 mm, image matrix = 256 x 256, voxel size = 1.0 x 1.0 x 1.0 mm).

Imaging Data Analysis

Image preprocessing and statistical analysis were performed using the SPM2 software platform (Wellcome Department of Cognitive Neurology, London, UK), implemented in MATLAB (The MathWorks Inc., Natick, MA, USA).

The functional scans of each participant were corrected for head movements that occurred during the functional MRI data acquisition, with the first scan as a reference. All images were corrected for differences in acquisition time before they were resampled and transformed into a standard space, using transformation parameters determined from the mean-realigned image through an automatic nonlinear stereotaxic normalization procedure (Friston et al., 1995a), resulting in a final voxel size of isotropic 3 mm. The template image that was used is based on average data provided by the Montreal Neurological Institute (Mazziotta, Toga, Evans, Fox, & Lancaster, 1995). To enhance the signal-to-noise ratio and enable intersubject functional anatomical comparison, the images were smoothed by convolution with a 8-mm full width at half maximum (FWHM) gaussian kernel. The time series in each voxel were highpass filtered using a cutoff of 128 sec, and a correction for temporal autocorrelation in the data (AR 1 + white noise) was applied to accommodate serial correlations.

Images were analysed using a two-stage random-effect approach (Holmes & Friston, 1998; Friston, Holmes, & Worsley, 1999). At the first stage, the time series of the functional MR images obtained from each participant was analysed separately. The effects of the experimental paradigm were estimated on a voxel-by-voxel basis according to the general linear model (Friston et al., 1995b). The correctly performed trials of the six experimental tasks were modelled as box-car functions, convolved with a synthetic haemodynamic response function to account for the delay of the BOLD time course. Head movement parameters (translations and rotations around three axes), which were estimated during the preprocessing stage were modelled as additional explanatory variables in order to remove components of the signal correlated to head movements.

For each subject-specific model, linear compounds of the regression parameter estimates (i.e. linear contrasts) were used in order to estimate the size of the effects of interest. Subject-specific contrast images were entered at the second stage into an one-sample *t*-test, testing the null hypothesis that the mean effect size was equal to zero in the population from which our participants were extracted.

For each effect of interest, we obtained a statistical parametric map of the *t* statistic. Clusters of adjacent voxels surviving a threshold of $p < 0.01$ were formed and characterised in terms of spatial extent (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994). The significance of each cluster was estimated using distribution approximations from the theory of gaussian fields resulting in a corrected *p*-value (Worsley et al., 1995; Cao & Worsley, 2001). Cluster-size tests have been widely used in such or similar investigations because of increased sensitivity to spatially extended signals, compared to voxel-intensity tests (Friston, Holmes, Poline, Price, & Frith, 1996; Poline, Worsley, Evans, & Friston, 1997). Activation clusters were retained as significant at $p < 0.05$, corrected.

The statistical parametric maps of the group analysis were superimposed onto a T1-weighted averaged normalized brain of all participants of the study, using the MRIcro software (www.cla.sc.edu/psyc/faculty/rorden/mricro.html). Activations were assigned with the help of automated anatomical labelling based on an anatomical parcellation of the Montreal Neurological Institute (MNI) single-subject brain (Tzourio-Mazoyer et al., 2002), and then manually checked with reference to a standard brain atlas (Nieuwenhuys, Voogd, & van Huijzen, 1991).

3 RESULTS

Behavioural Response Data

Psychophysical data was collected during functional measurements. The difficulty of the three task specific conditions (egocentric, allocentric, control) was comparable as accessed by both, average response times (RT) and error rates (ER), i.e. incorrect judgements about either the location of the dot or the identity of the stimulus. Error rates did not show a statistical difference (egocentric task: 5.4%, SD 4.1%; allocentric task: 4.1%, SD 3.3%; control task: 3.3%, SD 3.2%; $F_{2,22} = 2.94$, $p > 0.05$), so did not the average response times of the subjects over the three conditions (egocentric task: 592 ms, SD 80 ms; allocentric task: 585 ms, SD 93 ms; control task: 596 ms, SD 86 ms; $F_{2,22} = 0.39$, $p > 0.05$).

In order to validate the difference between the two spatial tasks on the behavioural level (i.e. judgements according to different reference frames), 'critical trials' (*see*: methods) were analysed that were indicative for the correct performance

of both tasks. The analysis of the average correct performance rates of critical trials across subjects revealed that they followed the instructions (egocentric task: 77.3%, SD 19.8%; allocentric task: 89.8%, SD 7.8%; t_{11} = -2.10, p > 0.05), which is well above chance level in a 2-alternative forced choice task (2AFC). Thus, subjects judged stimuli according to the egocentric *or* allocentric spatial frame of reference, respectively.

Eye Movement Data

Eye movements were monitored during the experiment in all subjects. Three data sets could not be analysed, because data was corrupted by too much noise due to problems with the eye tracker. Eye-tracking data of the remaining nine subjects revealed that they were able to maintain fixation during the vast majority of trails. On average, participants fixated the cross during the *complete* 2-sec trial period in 94% (SD 6.4%) of the total trials. These results show that the subjects followed the instruction to fixate a central or peripheral target during the spatial and non-spatial judgements. Furthermore, the percentage of trials performed *with* saccadic eye movements (for example towards the presented dots), was comparable across the task specific conditions. In the egocentric task, subjects made saccadic eye movements in 6.4% (SD 6.8%) of the trials, in the allocentric task 5.6% (SD 7.2%), and in the control task 6.2% (SD 5.8%) of the trials were performed without the instructed fixation. No significant difference was found between the three tasks ($F_{2,16}$ = 0.29, p > 0.05).

Brain Activation Patterns

The evaluation of functional imaging data was confined to trials correctly performed by the subjects. We examined the effects of the task specific conditions (egocentric, allocentric, control) across all fixation conditions. We first compared the fMRI responses in each of the two spatial tasks versus the control task in order to reveal the patterns of activation associated with setting a subjective spatial midpoint according to the two different coordinate frames.

The egocentric task activated an occipito-parietal cluster mainly of the right hemisphere comprising the precuneus, the superior parietal lobule, the intraparietal sulcus, and extended to the superior and middle occipital gyri. Additionally the cluster covered the precuneus of the left hemisphere, but the task activated brain regions

predominantly in the right hemisphere (Fig. 3: egocentric activations are indicated by red colour). The allocentric task activated a occipito-parieto-frontal network exclusively of the right hemisphere (Fig. 3: allocentric activations are indicated by green colour). The occipito-parietal cluster showed activation of the precuneus, superior parietal lobule, intraparietal sulcus and the posterior part of the angular gyrus, extending to the superior and middle occipital gyri. Activated frontal areas were located near the intersection of the precentral and the superior frontal sulcus and comprised the middle and superior frontal gyri, an area known as the frontal eye field (FEF). The spatial extent of the occipito-parietal activation was comparable to that in the egocentric condition, but activated an additional structure (i.e. posterior part of the angular gyrus). Remarkably, the occipito-parietal cluster detected in the egocentric condition activated only slightly more voxels (*see*: Table 1), which might be attributed to an additional activation of the left hemispheric precuneus that was absent in the allocentric condition. Both spatial tasks show a large amount of overlap in occipito-parietal regions, indicated by yellow colour in Figure 3. Main peaks of activation of the allocentric and egocentric task compared to the control condition, respectively are listed in the upper part of Table 1.

In order to identify brain regions that are critically involved in either of the two spatial tasks, we contrasted them directly. We first examined the activation associated with the egocentric compared to the allocentric spatial task (i.e. egocentric > allocentric) and found *no* significant cluster that would exhibit a stronger involvement during body-centred compared to object-centred spatial judgements. When comparing the allocentric to the egocentric task directly (allocentric > egocentric), we detected two clusters of activation, which showed significantly higher fMRI responses during the object-based compared to the body-centred spatial judgements (Fig. 4). One of these clusters was localised in the medial temporal lobe (MTL); the other one in frontal brain regions. The MTL activation comprised the middle temporal gyrus, the parahippocampal gyrus and the anterior edge of the hippocampus of the right hemisphere. The cluster extended medially into the tegmental area of the midbrain. The frontal cluster indicated activation including the bilateral gyri recti (ventromedial part of the orbito-prefrontal cortex) and superior frontal gyri. Additionally we detected activation of the anterior cingulate gyrus of the left hemisphere. Main peaks of activation of the allocentric compared to the egocentric condition are listed in the middle part of Table 1.
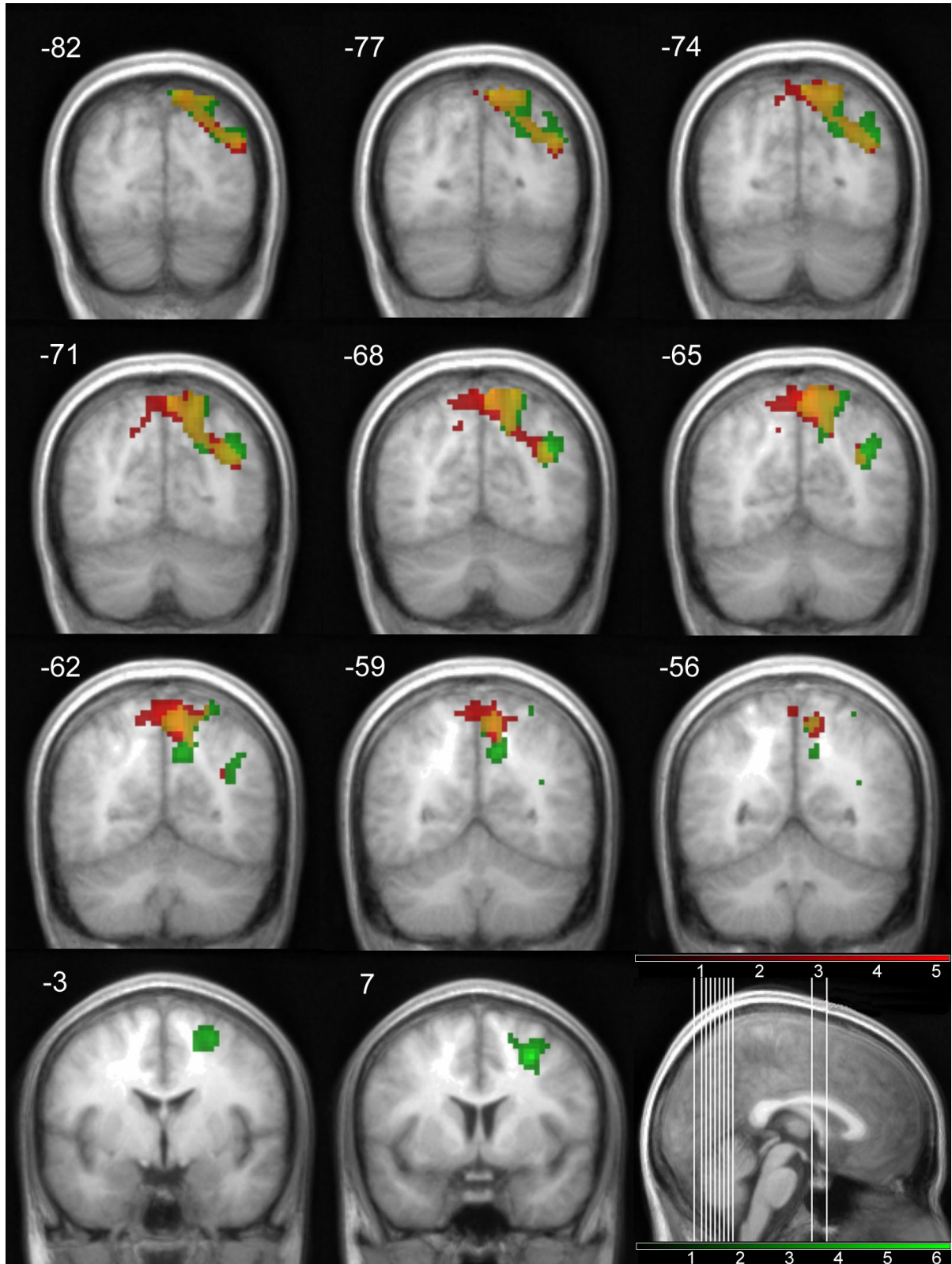
Figure 3. Statistical parametric maps showing areas activated ($p < 0.05$, corrected) by the egocentric task (red) and by the allocentric task (green), when compared to the control condition, respectively. The overlap of both contrasts is depicted by yellow colour. White numbers in the upper left corners of the brain slices indicate stereotaxic coordinates (mm) in the coronal plane. Group comparisons of twelve subjects are superimposed on a T1-weighted normalized averaged brain. The structural image in the lower right corner of the figure indicates the origin of the displayed coronal slices, including colour-bars illustrating *t*-values for the performed comparisons. *See*: upper part of Table 1 for main peaks of activations.
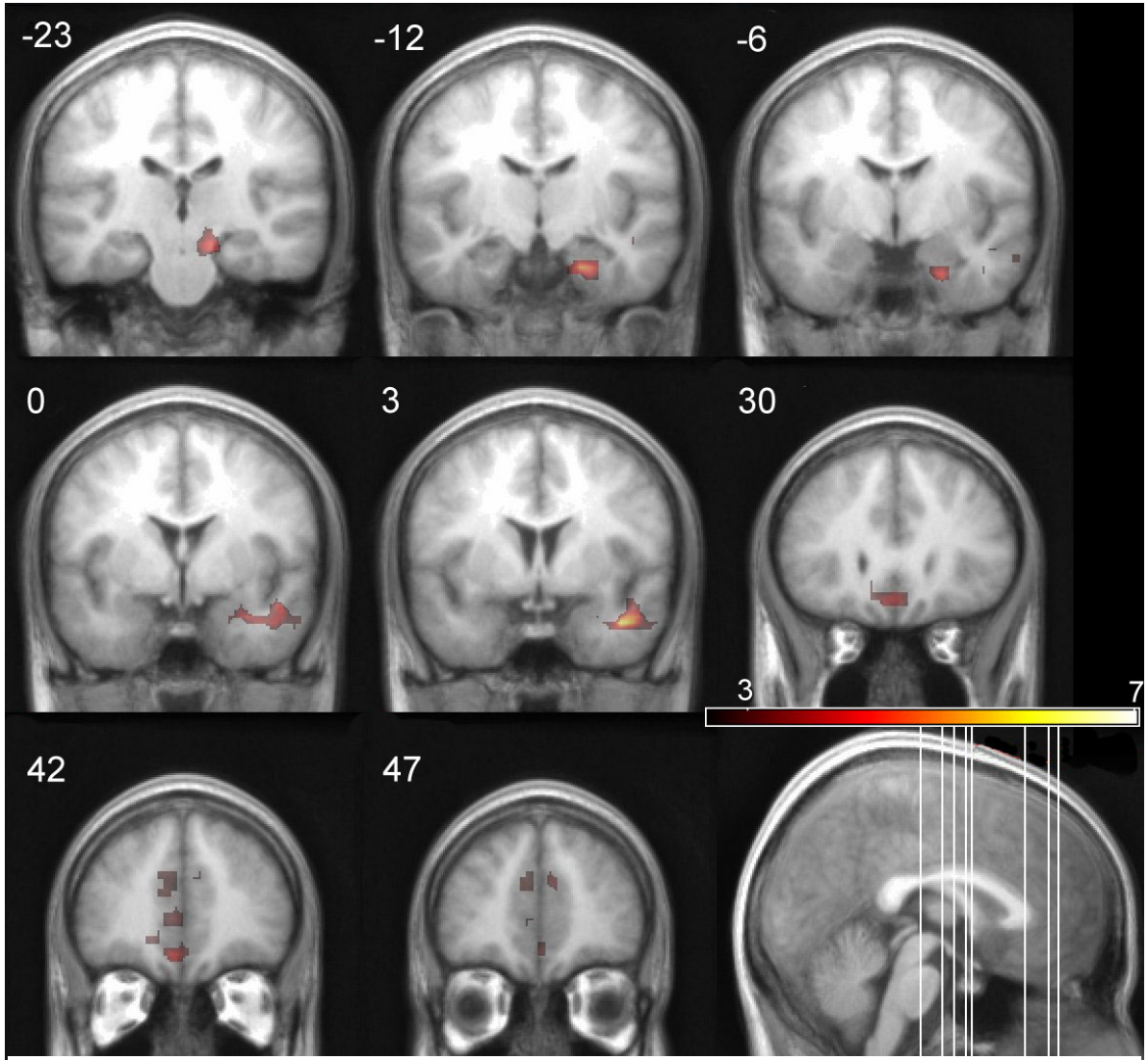
Figure 4. Statistical parametric map showing areas activated ($p < 0.05$, corrected) by the allocentric, when compared to the egocentric task. White numbers in the upper left corners of the brain slices indicate stereotaxic coordinates (mm) in the coronal plane. Group comparisons of twelve subjects are superimposed on a T1-weighted normalized averaged brain. The structural image in the lower right corner of the figure indicates the origin of the displayed coronal slices, including the colour-bar illustrating *t*-values for the performed comparison. *See*: middle part of Table 1 for main peaks of activation.

Finally we looked at activations in the control task. When compared to the egocentric spatial task, the feature discrimination task activated a cluster in occipital areas. It comprised the calcarine sulci, bilaterally and the middle and inferior occipital gyri of the right hemisphere (Fig. 5). A slightly different pattern emerged, when comparing the control to the allocentric spatial task. Again an occipital cluster was detected, but the spatial extent was much smaller, confined to the right hemisphere and covered the middle occipital gyrus (Fig. 6). Main peaks of activation of the control compared to the egocentric and the allocentric condition, respectively are listed in the lower part of Table 1.
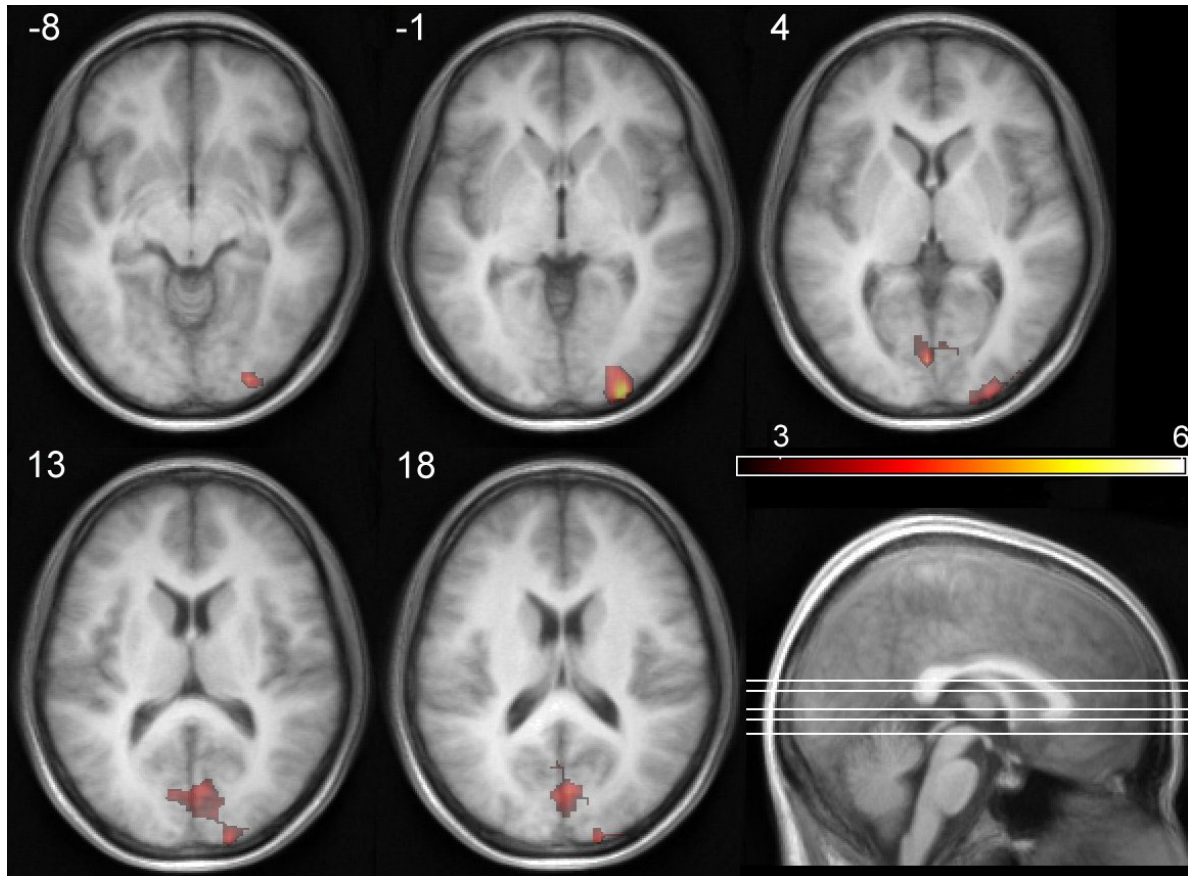
16

Figure 5. Statistical parametric map showing areas activated ($p < 0.05$, corrected) by the control task, when compared to the egocentric condition. White numbers in the upper left corners of the brain slices indicate stereotaxic coordinates (mm) in the transversal plane. Group comparisons of twelve subjects are superimposed on a T1-weighted normalized averaged brain. The structural image in the lower right corner of the figure indicates the origin of the displayed transversal slices, including the colour-bar illustrating *t*-values for the performed comparison. *See*: Table 1 (lower part) for main peaks of activation.
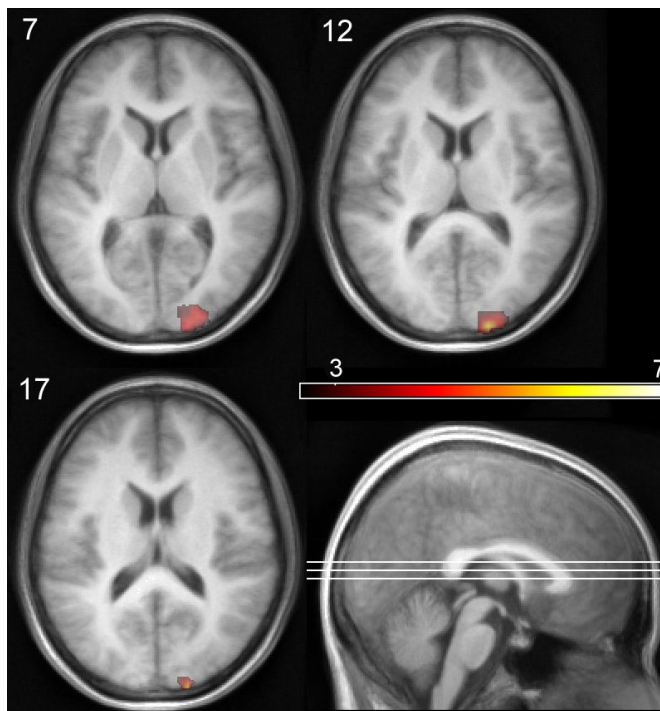

Figure 6. Statistical parametric map showing areas activated ($p < 0.05$, corrected) by the control task, when compared to the allocentric condition. White numbers in the upper left corners of the brain slices indicate stereotaxic coordinates (mm) in the transversal plane. Group comparisons of twelve subjects are superimposed on a T1-weighted normalized averaged brain. The structural image in the lower right corner of the figure indicates the origin of the displayed transversal slices, including the colour-bar illustrating *t*-values for the performed comparison. *See*: Table 1 (lowest part) for main peaks of activation.

Table 1. Regions and main peaks of activation of performed comparisons in this study. Extent of the regions and its location are given by the first and second column, respectively. For each peak inside each region, we then report its location in terms of gyral anatomy and MNI coordinates as well as its *t*-value (with 11 degrees of freedom) from the appropriate statistical parametric map.

Cluster (Voxel)	Region	Peaks	MNI-Coordinates X	Y	Z	*t*-value
	Egocentric Task > Control Task					
647	Right Posterior Parietal Cortex	Precuneus	6	-69	66	5.13
		Superior Parietal Lobule	18	-69	66	4.29
		Intraparietal Sulcus	30	-72	36	3.56
	Right Occipital Cortex	Middle Occipital Gyrus	42	-81	27	4.17
		Superior Occipital Gyrus	23	-84	47	2.98
	Left Posterior Parietal Cortex	Precuneus	-3	-66	63	4.40
	Allocentric Task > Control Task					
633	Right Posterior Parietal Cortex	Precuneus	12	-60	42	4.47
		Superior Parietal Lobule	18	-69	66	4.27
		Intraparietal Sulcus	24	-75	36	3.31
		Angular Gyrus	45	-69	36	3.19
	Right Occipital Cortex	Middle Occipital Gyrus	39	-69	33	4.69
		Superior Occipital Gyrus	24	-84	49	3.68
159	Right Frontal Eye Field (FEF)	Middle Frontal Gyrus	30	6	48	6.56
		Superior Frontal Gyrus	24	-6	57	4.44
	Allocentric Task > Egocentric Task					
291	Right Temporal Areas	Middle Temporal Gyrus	42	3	-27	6.77
		Parahippocampal Gyrus	21	-12	-27	5.32
		Hippocampus	30	-2	-23	3.30
	Brainstem	Tegmentum mesencephalis	15	-23	-15	4.43
317	Left Frontal Areas	Gyrus Rectus	-3	36	-18	5.28
		Anterior Cingulate Gyrus	-9	33	0	4.84
		Superior Medial Frontal Gyrus	-6	51	18	3.24
	Right Frontal Areas	Gyrus Rectus	3	30	-15	3.80
		Superior Medial Frontal Gyrus	9	48	21	3.40
	Control Task > Egocentric Task					
514	Right Occipital Cortex	Middle Occipital Gyrus	30	-102	0	5.88
		Inferior Occipital Gyrus	27	-93	-6	4.88
		Calcarine Sulcus	3	-78	18	4.27
	Left Occipital Cortex	Calcarine Sulcus	-3	-84	3	4.80
	Control Task > Allocentric Task					
165	Right Occipital Cortex	Middle Occipital Gyrus	18	-102	15	6.71

4 DISCUSSION

The present study was conducted to detect anatomical structures involved in the computation of egocentric and allocentric spatial representations. We compared brain activation induced by a condition involving spatial judgements with respect to the body mid-sagittal plane (the egocentric task) with that induced by the judgements about the spatial relationship between certain objects (allocentric task), while keeping a central or peripheral fixation. Comparing both spatial conditions to a feature discrimination task (control condition) revealed a largely overlapping occipito-parietal network in the right hemisphere, but also exclusive brain areas associated with either of the two spatial tasks. The object-centred spatial judgements additionally activated the frontal eye field (FEF) and the posterior part of the angular gyrus of the right hemisphere, whereas the body-centred spatial judgements in addition activated the precuneus of the left hemisphere. Direct comparisons of the two spatial tasks revealed higher activations for the allocentric spatial task in the medial temporal lobe of the right hemisphere (i.e. medial temporal gyrus, parahippocampus and hippocampus) and in frontal areas of the brain, including the anterior cingulate gyrus and ventro-medial and superior medial prefrontal cortex, respectively. There was no brain region that exhibited a significant higher activation in the egocentric compared to the allocentric condition.

In the present study we report functional imaging data that neither can be due to differences in task difficulty, nor can be interpreted in terms of differential eye movements during task performance. Both, task difficulty (as accessed by error rates and reaction times) and eye movements (failure rate to maintain fixation) were comparable in all of the employed conditions. Finally, the presented results cannot be attributed to differences in stimuli and responses, since we applied the same visual stimulation similarly in all of the tasks, while requiring identical responses. The tasks differed only in the behaviourally relevant criteria (i.e. instructions). Subjects responded according to the criteria, reflected by an objective measure of following the given instruction (i.e. accuracy rates for 'critical' spatial trials).

The egocentric compared to the control condition activated occipito-parietal areas with a definite right-sided asymmetry (Fig. 3). These results are similar to other human neuroimaging studies investigating body-centred spatial judgements (Vallar et

al., 1999; Galati et al., 2000; Galati et al., 2001; Committeri et al., 2004). Interestingly, the present study failed to replicate the involvement of premotor areas in performing the egocentric task. This might be attributed to the possibility that the task employed to test egocentric orientation was inherently different from those used by former studies carried out in the field. While those experiments were exclusively performed under free-viewing conditions, we introduced a target cross that subjects should fixate during their body-centred spatial judgements. It might be possible that a stable fixation onto a spatial location (fixation cross) that does not coincide with the target (dot) to be judged, actually diminishes the effect size in premotor areas. In order to clarify this question and to gain higher comparability, it would be interesting to re-evaluate the present data in terms of a volume of interest analysis (VOI), which was applied by some authors (Vallar et al., 1999; Galati et al., 2000).

Although the present study differed from the mentioned experiments in premotor activations, it also revealed many common brain regions in the posterior parietal cortex modulated by the egocentric task. These areas include the precuneus, the superior parietal lobule and the intraparietal sulcus. Thus, our results are also consistent with findings from electrophysiology. Neurons coding spatial target position relative to body parts have been identified in many areas of the monkey's posterior parietal cortex, especially around the intraparietal sulcus (Andersen et al., 1997). Many of these neurons share an eye-centred representation of visual space (Colby et al., 1995), and are modulated by multimodal extra-retinal signals, such as eye-position and head-on-trunk signals (Andersen et al., 1993). As a result, areas in the posterior parietal cortex can from a distributed representation of space that in principle, could be read out in different egocentric frames of reference, for example in head-centred or body-centred frames (Cohen et al., 2002). The subjects in the present study were instructed to judge spatial locations according to their subjective body-midline. But since the subject's head- and body-midline were aligned while performing half of the trials with fixation on their mid-saggital plane, the presented imaging data does not allow for conclusions about the specific egocentric reference frame (i.e. eye-, head- or body-centred) that was actually used in order to perform correctly. In fact, the extent to which these coordinate systems are truly independent of each other is not yet clear (Halligan, Fink, Marshall, & Vallar, 2003), but obviously subjects utilized certain *egocentric* spatial reference frames while executing the task, indicated by their high behavioural performance.

The activation of posterior parietal areas by the egocentric task, is also in line with neuropsychological findings on optic ataxia. This deficit in visuomotor coordination can be observed after dorsal lesions, and both the precuneus and the superior parietal lobule were thought to play a fundamental role in the genesis of this clearly egocentric disorder (Perenin et al., 1988). Using new techniques (Rorden & Karnath, 2004), a recent re-evaluation of critical lesions resulting in optic ataxia, identified the central 'core' of lesion overlap in more ventrolateral areas of the posterior parietal cortex (Karnath et al., 2005). The critical lesion site was localised at the junctions between superior occipital cortex and inferior and superior parietal lobules, respectively, and extended to the precuneus near the occipito-parietal junction. The areas of activation by the egocentric task show partial overlap with the lesion localisation in right brain-damaged optic ataxia patients reported by Karnath & Perenin (2005), although large parts of the lesion concerned more ventrolateral areas compared to our functional imaging data. One area of overlap comprises the precuneus and is illustrated in Figure 7.
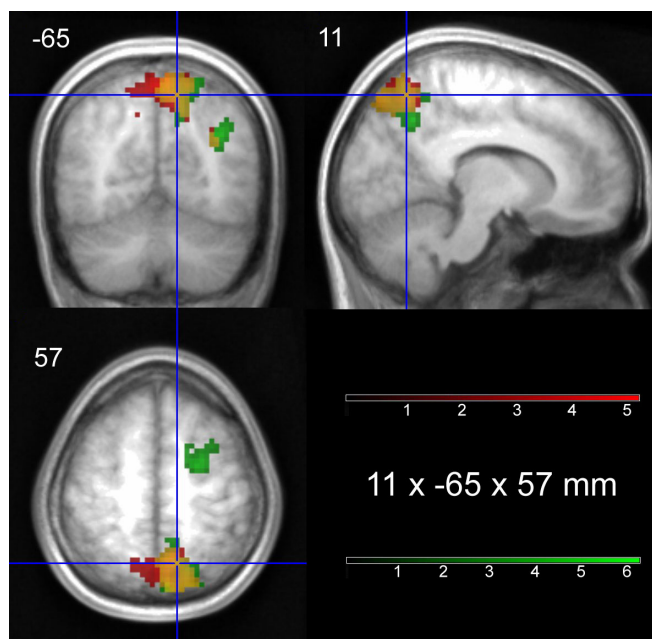

Figure 7. Statistical parametric maps showing areas activated ($p < 0.05$, corrected) by the egocentric task (red) and by the allocentric task (green), when compared to the control condition, respectively. The overlap of both contrasts is depicted by yellow colour. Blue crosses and white numbers indicate MNI-coordinates (mm) after converting Talairach coordinates (Talairach & Tournoux, 1988) given by Karnath & Perenin (2005; pp. 1566), for one region of the lesion location of a right brain-damaged optic ataxia group. The crosses centre the precuneus in the coronal, saggital and transversal plane and are superimposed on a T1-weighted normalized averaged brain of the 12 tested subjects. Colour-bars illustrate *t*-values for the performed comparisons.

In conclusion, evidence from single cell recordings in monkeys, functional neuroimaging in humans as well as results from human lesion studies suggest that the posterior parietal cortex is a crucial component for egocentric spatial orientation, responsible for the creation and maintenance of spatial representations in egocentric coordinates. The biological significance of the posterior parietal cortex, whose

projections strongly innervate premotor areas (Wise et al., 1997), is probably related to the preparation of goal directed movements (such as orienting the head and eyes towards objects, reaching, or grasping it), which require coding the spatial position of targets with respect to the motor effectors.

The allocentric spatial task (compared to the control condition) activated a occipito-parieto-frontal network exclusively in the right hemisphere (Fig.3). These results replicate findings of Galati and colleagues (2000), who identified right-lateralised activations in the superior parietal lobule (SPL), the intraparietal sulcus (IPS) and the frontal eye field (FEF) during object-centred spatial judgements. Interestingly, nearly all areas activated by *their* allocentric task, were also activated during the egocentric spatial judgements (Galati et al., 2000), and thus support our finding of a large overlap between both spatial tasks in occipito-parietal regions of the right hemisphere (Fig.3: overlap indicated in yellow). A very similar degree of overlap between the two conditions was also reported by Committeri and colleagues (2004), who described large overlapping occipito-parietal activations in both hemispheres. Their study showed essentially no difference between body- and object-centred spatial judgements in posterior parietal brain regions. This finding is in line with our result, when examining the activation associated with the egocentric compared to the allocentric spatial task (i.e. egocentric > allocentric). We also found no significant cluster that would exhibit a stronger involvement during body-centred compared to object-centred spatial judgements. Nevertheless, our findings together with reported results of Committeri and colleagues (2004) do not agree with evidence provided by Galati and colleagues (2000). These authors detected a clear preference of the posterior parietal cortex for body- versus object-centred tasks. In order to clarify this discrepancy, our data would have to be re-evaluated by means of volume of interest (VOI) analysis, which was employed by Galati and colleagues (2000). This analysis is much more sensitive to small differences between conditions, whereas the methods applied by the present study and Committeri and colleagues (2004) was much more conservative, lacking specific hypothesis about the assumed anatomical localisation of areas involved in the spatial tasks.

Besides this inconsistency there is a high level of similarity between the three studies. All of them report a strong overlap of parietal regions activated by both, the allocentric and egocentric spatial task. One possible interpretation would be that the posterior parietal cortex with its strong projection to premotor areas is mainly involved

in managing egocentric spatial representations, with some portions being also able to make use of object-centred frames of reference (Galati et al., 2000). In this subset of areas, allocentric frames are created by further combining the egocentric representations with additional extra-retinal inputs, which may help to build up world-centred representations (Snyder et al., 1998), i.e. the object-based code is created as a further processing step, in a subset of the same areas that build up egocentric codes. However this interpretation, although appealing, seems unlikely when examining the actual amount of overlap between both spatial tasks. The study of Galati and colleagues (2000) showed nearly exclusively activations by the allocentric task *within* areas that were also active during the egocentric condition. A striking overlap between both spatial tasks in occipito-parietal areas was also reported by Committeri and colleagues (2004). Our study revealed that 65% of the area activated by the egocentric condition was also activated during allocentric spatial judgements. The high percentage of overlap raises the question, if the brain can actually "afford" a state of being equipped with an oversized "hybrid-system" that is able to compute multiple object-centred frames on top of egocentric coordinates, when only little benefit can be expected by using object-centred frames in the preparation of goal directed movements. Orienting the head or eyes towards an object and reaching out in order to point at it, within a fraction of a second and reasonable precision, are high level egocentric abilities and therefore should be only accomplishable by a highly specialised system. Furthermore the degree of specialisation within that system should allow the organism to even react reflexively and automatic to sensory information that is immediate and salient. Lesions to this highly specialised system lead to deficits in visuomotor coordination (i.e. optic ataxia) and in perceiving the position of the body midsaggital plane (Perenin, 1997), a fundamental egocentric spatial ability. Interestingly, the areas of activation by the allocentric task (as in the egocentric condition) show partial overlap with the lesion location in right brain-damaged optic ataxia patients reported by Karnath & Perenin (2005) (Fig. 7). Thus, another interpretation about the meaning of activation elicited by the allocentric task in posterior parietal regions seems to be likely. It might be possible that the posterior parietal cortex with its strong projections to premotor areas is *exclusively* involved in managing egocentric spatial representations, and that only some portions (especially of the right hemisphere) are actually specialised to convey their egocentric

information to other brain areas responsible to re-map the egocentric content into an allocentric code.

This hypothesis is supported when examining the pattern of activation after comparing the allocentric with the egocentric spatial task (allocentric > egocentric; *see* Fig.4). Here, we detected prominent frontal cortical activations comprising the anterior cingulate gyrus in the left hemisphere, the bilateral superior medial frontal gyri as well as parts of the orbito-prefrontal cortex, together with activations in the medial temporal lobe (i.e. hippocampal, parahippocampal and middle temporal gyrus of the right hemisphere). The prefrontal cortex (PFC) is a brain region that has been associated with processes of cognitive control (Miller & Cohen, 2001). The term 'cognitive control' refers to mechanisms that can override or augment reflexive and habitual reactions in order to direct action or thought in accord with behaviourally relevant criteria (Miller, 2000; Rainer, Asaad, & Miller, 1998). The PFC is thought to do so by providing 'bias signals' throughout much of the rest of the brain, affecting not only sensory processes but also systems responsible for response execution or memory retrieval. The aggregate effect of these bias signals is to guide the flow of information along pathways that establish the proper mappings between the visual input, the behaviourally relevant criteria and the motor output needed to correctly perform a task (Miller et al., 2001). This is especially important when two different responses are possible and the task-appropriate response must compete with a stronger alternative, for example with a prepotent response alternative. Prepotent responses refer to reflexive or automatic actions that are either innate or established through a considerable amount of experience (Miller, 2000). Egocentric spatial judgements (or orientation) might actually meet these characteristics, and thus might exert automatic egocentric response tendencies in the face of an allocentric task instruction. The PFC has been implicated in inhibition of those automatic response tendencies (Mesulam, 1998; Nobre, Coull, Frith, & Mesulam, 1999), and in the implementation of performance adjustments, due to proper re-mapping of inputs, instructions and outputs (MacDonald, Cohen, Stenger, & Carter, 2000; Kerns et al., 2004; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuiss, 2004).

Nevertheless, theories of cognitive regulation, which would enable the re-mapping of specific relations, suggest a system with *two* necessary components: one to implement control and another to monitor performance and to signal when adjustments in control is actually needed. An influential theory suggests that the latter

is performed by the anterior cingulate cortex (ACC) in terms of 'conflict monitoring' (Carter et al., 1998; Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; Botvinick, Cohen, & Carter, 2004). These authors hypothesised that the ACC responds to the occurrence of conflicts in information processing and that this conflict signal triggers strategic adjustments in cognitive control, which serve to prevent conflict in subsequent performance. The theory is based on the observation that ACC engagement is typically associated with tasks that (1) require the overriding of prepotent responses, tasks that (2) require the selection among a set of equally permissible responses, or tasks that (3) involve the commission of errors (Barch et al., 2001; Ridderinkhof et al., 2004). Computational models demonstrated that ACC activation in each of these contexts could be explained based on a single function – the detection of conflict (Botvinick, Braver, Barch, Carter, & Cohen, 2001). In the present study, the allocentric task showed an increased activation in the ACC of the left hemisphere, when compared to the egocentric condition, and consequently showed no difference in the reversed contrast. Additionally, both spatial tasks did not differ in terms of committed errors and task difficulty. On the basis of these observations we have to conclude that the ACC engagement in the allocentric spatial task represents a conflict, in the form of a competition between the correct response and the one that has to be overridden, i.e. the allocentric task required the overriding of a prepotent response tendency.

These prepotent response tendencies might be attributed to the high degree of specialisation found within the egocentric localisation system. It enables the organisms to reflexively access the location of objects in egocentric space. These automatic spatial judgements might result in tendencies to respond according to an egocentric coordinate system. In order to follow the instruction to judge spatial locations with respect to an object-centred reference frame, it would be necessary to re-map the reflexively performed egocentric localisation. This re-mapping, in parts, is probably carried out by employing resources of the PFC after a conflict (i.e. between task-appropriate response tendency and the stronger egocentric alternative) has been detected by the ACC. This dissociation between the roles of PFC and ACC has been shown in different versions of the Stroop-task (MacDonald et al., 2000; Kerns et al., 2004). For example Kern and colleagues (2004) demonstrated that conflict-related activity in the ACC predicted both, a greater prefrontal cortex activation *and* performance adjustments, supporting the view that the ACC has a role in conflict

monitoring and triggering the implementation of control processes performed by the PFC.

Although the proposed egocentric-to-allocentric re-mapping hypothesis seems to be probable, other interpretations for the involvement of the PFC during allocentric spatial judgements might be possible. Prefrontal activation has also been associated with either a working memory function or with rule representation (Miller, 2000; Miller et al., 2001). These two functions are not mutually exclusive and, in fact, are likely to be complementary (Schoenbaum & Setlow, 2001). Working memory enables the organism to hold in 'mind's eye' the contents of conscious awareness, even in the absence of sensory input, by maintaining an active representation of information for a brief period of time (Baddeley, 2003). One might reason that during the allocentric spatial task, subjects had to actually actively represent the imaginary rectangle midline that they were required to spatially judge. Here, we cannot rule out this probability, although the argument would be questionable, since the subjects should consequently also be able to maintain an active representation of their body-centred midline in the same areas. Similar arguments apply for acquiring or representing the 'abstract rule' behind the two spatial tasks (i.e. the instruction). Another indication that these interpretations are less likely, comes from the precise anatomical location of the frontal activations. The present study detected activity in superior-medial and orbito-prefrontal areas, whereas spatial working memory and rule representations are predominately mediated by the dorsolateral PFC (Courtney, Petit, Haxby, & Ungerleider, 1998; Miller, 1999). Additionally these interpretations would lack an explanation for the involvement of the ACC in the allocentric but not in the egocentric spatial task. Taking these facts into account, it seems more likely that the activations of frontal brain regions during the allocentric spatial task, are in favor for a re-mapping hypothesis. Instead of "just" representing the imaginary rectangle midline in working memory, frontal activation may rather be actively involved in re-mapping an egocentric into an allocentric midline representation.

The frontal lobes seem to be especially suited for this type of re-mapping activity. The PFC as an interconnected set of neocortical areas, has a unique, but overlapping pattern of connectivity with virtually all sensory cortical and motor systems and with a wide range of subcortical structures. It also has widespread projections back to these systems that may allow to exert a 'top down' influence on a wide range of brain processes (Miller, 2000). Interestingly orbital and medial PFC

show a dense connectivity with medial temporal lobe (MTL) structures – those areas found in the present study to be involved in allocentric spatial judgements (Fig.4). This includes direct and indirect (via the medial dorsal thalamus) connections with the hippocampus and associated neocortex and the amygdala (Miller et al., 2001), structures critical for long-term memory and the processing of internal states. Therefore, these two interconnected structures (PFC and MTL) are very likely to be responsible for re-mapping a given, reflexively perceived egocentric content into an allocentric code.

The allocentric code is probably best understood in terms of an enduring storage of environmental information, in form of relational maps of topographical space that are independent of the observers position. The 'cognitive map' theory proposed the hippocampus as the neural substrate for allocentric orientation (O'Keefe et al., 1978). Neurons with place field responses that encode space in allocentric coordinates have been identified in the monkey's hippocampal formation (Matsumura et al., 1999; Georges-Francois et al., 1999), and were also reported for the human hippocampus (Ekstrom et al., 2003; Burgess & O'Keefe, 2003). Neuropsychological data in humans demonstrated a crucial role of the MTL, including the hippocampal formation and the parahippocampal gyrus, in allocentric spatial learning and memory (Aguirre et al., 1998; Bohbot et al., 1998; Spiers et al., 2001). For example, patients with temporal lobe damages could neither remember the locations of the landmarks in space nor specific spatial relationships among the landmarks and had deficits in a radial arm maze task (Maguire et al., 1996a; Abrahams, Pickering, Polkey, & Morris, 1997). Similar conclusions about the involvement of the MTL for environmental-centred spatial representations come from neuroimaging studies using a variety of topographical tasks, such as landmark knowledge or orientation and navigation in large scale space. These experiments revealed activations of the parahippocamus (Aguirre et al., 1996; Maguire et al., 1998b) and the hippocampus (Maguire et al., 1996b; Maguire et al., 1998a), which were associated with allocentric object location memory and/or wayfinding through complex environments, a task that probably also requires allocentric processing of spatial locations. Thus, evidence from single cell recordings, functional neuroimaging in humans as well as results from human lesion studies suggest the importance of the hippocampal formation and the parahippocampal gyrus for allocentric information processing.

The present study showed higher activation of the middle temporal gyrus, the parahippocampus and the anterior edge of the hippocampus in the right hemisphere, when comparing the object-centred to the body-centred spatial task (Fig.4). These results underline the importance of MTL structures for allocentric orientation and are in line with evidence that suggest the parahippocampal gyrus as a neural substrate for object-in-place representations within a larger system for topographical learning in humans (Maguire, 1997). Furthermore, our results are also consistent with claims that the right but not the left hippocampal formation appears to have a bias toward the processing of spatial relationships and thus are in accordance with the cognitive map theory (Burgess, Maguire, & O'Keefe, 2002; Kumaran et al., 2005).

However, the interesting finding of the present study is in fact that our subjects were not explicitly instructed to encode or retrieve the spatial location of the dots with respect to the object. Indeed they were performing a perceptual task followed by a fast indication of their judgements. This is remarkable, since most of the studies finding similar activations in the MTL relied on complex tasks that would involve memory processes or even active navigation (Aguirre et al., 1996; Maguire et al., 1996b; Maguire et al., 1998b; Maguire et al., 1998a). Another interesting comparison concerns the level of complexity of employed stimuli. Whereas the above mentioned studies investigated the formation of spatial representations in large-scale environments by using computerized or real-world landscapes (i.e. 3-dimensional), the present study simply presented coloured dots on a 2-dimensional rectangle. In that, the present experiment revealed impressive effects, namely that our study might generalise those findings obtained with much more complex tasks and stimuli, to the degree of similarity between those studies and the present experiment. Our study revealed activations in MTL structures associated with spatial judgements according to an object-centred frame of reference. Consequently, the similarity between all the studies could be characterised by the requirement to process spatial relationships that are independent of the observer' position (i.e. by using an allocentric coordinate system). Nevertheless, here we cannot rule out the possibility that our subjects also utilized major memory components (encoding or retrieval) in order to perform correctly, despite the perceptual nature of the employed task.

The results of the present study have important implications, when interpreted in the light of the more general concept of human topographical orientation. One way to assess this concept is by considering the manner of acquisition of environmental

information. In the environmental psychology domain, it is commonly argued that there are three predictable stages in acquiring knowledge about the surroundings (Maguire et al., 1996a). It is posited that the first stage consists of structuring a representation of several stable landmarks from experience. This is ultimately accomplished within an egocentric system, where the locations of landmarks are encoded in relation to the self. This most basic level of representation therefore involves being able to recognise important objects and their topological relationships (such as proximity) within the egocentric perceptual field. The second major stage is the development of route knowledge that connects the landmarks into sequential chains or routes, i.e. representations that include information about navigation from one location to another. The final stage of cognitive map development is when an allocentric representation develops, where routes and landmarks form a configuration that includes information of routes that have never been traversed. The exact nature of the transition from one stage into another is still largely unknown (Maguire et al., 1996a). Since the present experiment was able to more directly access possible components of human spatial orientation, our results may actually contribute to a better understanding of the transition steps from egocentric into allocentric spatial representations.

Finally, the plausibility of the presented functional imaging data is additionally supported by the observed, specifically involved areas of activation associated with the control condition. Subjects performed a feature discrimination task in that they judged the colour of the presented stimuli. When compared to both spatial tasks, higher activations were revealed in early visual areas of the occipital cortex (Fig.5 and Fig.6). This is in line with results obtained by studies using similar tasks and demands (Fink, Dolan, Halligan, Marshall, & Frith, 1997; Galati et al., 2000). It is largely accepted that selective visual attention can strongly influence perceptual processing, even for apparently low-level visual stimuli (Reynolds & Chelazzi, 2004). The modulation of visual processing by attention has been reported for both, striate and extrastriate cortical areas of the occipital cortex (Somers, Dale, Seiffert, & Tootell, 1999; Kastner, De Weerd, Desimone, & Ungerleider, 1998) and was shown to be organised in retinotopic fashion (Tootell et al., 1998). Furthermore, an increased activity related to attention has been detected even in the absence of visual stimulation in the extrastriate cortex (Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999). Our results are in line with the notion that selective attention

might operate in the visual cortex by facilitating processing of selected stimuli and presumably filtering out unwanted information over circumscribed regions of visual space (Pinsk, Doniger, & Kastner, 2004). The increased activity in occipital areas may reflect a 'top-down' bias of neural signals in favour for an attended location of the stimulus, which might derive from the connectivity with a fronto-parietal network (Tong, 2003).

The present study was conducted to detect anatomical structures involved in the computation of egocentric and allocentric spatial representations. We interpreted the obtained functional imaging data according to a transition approach, in that a given, reflexively performed egocentric localisation is re-mapped into an allocentric code of permanent storage. We suggested that the posterior parietal cortex with its dense projections to premotor areas is exclusively involved in managing egocentric spatial representations, and that only some portions of these structures (especially of the right hemisphere) are actually specialised to convey their egocentric information to other brain areas responsible for the re-mapping. We pointed out that it would be possible that two densely interconnected structures (PFC and MTL) could serve this function after a conflict between response tendencies (due to the propotent characteristics of egocentric spatial judgements) had been detected by the ACC. It is probable that the roles of PFC and MTL in serving the re-mapping function are actually dissociable. It might be for example possible that the PFC is predominantly involved in primarily re-mapping egocentric into allocentric coordinates, whereas the MTL is more likely to serve the representation of the emerging allocentric coordinate frame. Unfortunately, the present data does not allow for conclusions about the distinct contributions of the PFC and the MTL for the re-mapping process. Certainly, due to their connectivity and intense cross-communication, they are likely to achieve the re-arrangement of egocentric contents into an allocentric code together.

It might be interesting for further research to be able to describe in more detail the distinct contributions of the fronto-parietal network, the prefrontal cortex and the medial temporal lobe for the re-mapping process. One approach for example, could be based on the suggestion that there are temporal differences of information processing between the ventral and dorsal visual pathways (Milner & Goodale, 1995). Information processing in the dorsal stream, dedicated to control of action, was proposed to be accomplishable within much shorter time compared to the perceptual processing in the ventral stream. This suggestion is in line with reports

about visually evoked onset response latencies of single neurons across the monkey's visual brain (Schmolesky et al., 1998). These authors found that onset latencies were, on average, 25 ms shorter in the frontal eye field (FEF), which can be interpreted as a quite "late" structure in the dorsal stream, than actually in area V4, a quite "early" region of the ventral processing pathway. Therefore one hypothesis could be that information processing in prefrontal areas precedes processing in the MTL, which would point to a primarily re-mapping function of the PFC in contrast to a more representational function of the MTL. In order to be able to more precisely describe relationships of the involved structures, one might employ effective connectivity analyses (i.e. Dynamic Causal Modeling, DCM). The aim of DCM is to estimate and make inferences about the influence that one neural system exerts over another and how this is affected by the experimental context (Friston, Harrison, & Penny, 2003; Penny, Stephan, Mechelli, & Friston, 2004). It would be interesting to see if this approach would be able to shed more light onto the discussed topic and to clarify remaining questions.

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