Spatial analysis in the human cerebral cortex: Behavioural and functional magnetic resonance studies of spatial transformations in visual perception and imagery

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Table of contents

Introduction

The questions

In the year 1896 George Malcolm Stratton (1865-1957), psychologist at Stanford University, made an astonishing discovery. For eight days his only visual input came through a system of lenses that produced a 180° inversion. In the course of the experiment, he experienced striking conflicts between the directional cues from gravity and tactile exploration on the one hand and those from visual information on the other. But after a week the world started to appear normal to him, although he was still wearing the inverting goggles (Stratton 1896; 1897). 50 years later, the Innsbruck group around Theodor Erismann and Ivo Kohler had subjects wear an upside-down reverting mirror and perform as many activities of daily life as possible and reported rapid adaptation of motor functions and a replication of Stratton's perceptual results. The neuronal mechanisms underlying this rapid adaptation of perceptual coordinates to the new visual input, however, were not investigated, partly because the methods available at the time did not easily lend themselves to such an undertaking. However, 50 years after Erismann and Kohler and 100 after Stratton, the progress of non-invasive neuroimaging techniques, which can be applied to human subjects, allows such an investigation of neuronal plasticity during the adaptation to inverting spectacles. We therefore sought to replicate "the most famous experiment in the whole of experimental psychology" (Gregory 1997, p. 92) and monitor changes in cortical function during the adaptation to inverting spectacles with daily functional magnetic resonance imaging (fMRI) sessions. While the earlier studies had relied on introspective reports of the subjects and the experimenters' observation of their performance in everyday tasks, we aimed for a quantifiable measure of the neuronal plasticity supposed to underlie the behavioural changes. Furthermore, we added formalized laboratory tests in order to verify that the subjects really experienced a full-blown inversion of the perceptual image.

We hypothesized that if these introspective reports could be replicated and verified the underlying neuronal mechanism should take place at the level of retinotopic visual areas, or higher visual areas, or both. Our first

neuroimaging approach therefore consisted in the retinotopic mapping of the early visual areas before, during, and after the experiment. This method allows to decide whether

a) the "perceptual rewriting of reality" (Gregory, *ibid*.) that is supposed to take place during adaptation to inverting spectacles is accompanied by a *rewiring* of retino-cortical pathways or

b) the retinotopy of early visual areas remains stable and the adaptation to mirror vision has to be attributed to cortical mechanisms at a higher level.

The introspective, psychophysical and fMRI data of four subjects who wore inverting spectacles or mirrors are presented and discussed in chapter 1.

While this study investigated the complex interplay of perceptual and motor adaptation and visuo-spatial coordinate transformation, the following chapter is primarily concerned with the higher-level cortical processes that underlie the successful performance of visuo-spatial transformation tasks, using a reading paradigm. Subjects were asked to read words and phrases whose orientation was transformed in a number of ways (rotation, lateral mirror image, vertical mirror image). It is evident from everyday experience that the cognitive demands of this task are quite different from those of simple reading. This is also reflected in the longer reaction times that are required for the performance of a semantic or syntactic judgement on the transformed items compared to items that are presented in conventional orientation. We again acquired functional magnetic resonance images during the performance of these different tasks in order to elucidate the cortical mechanisms that are activated during reading of transformed, but not normal text. On the basis of the cognitive subtraction theory it is supposed that these mechanisms represent the spatial transformation component of the mirror reading task.

Because of the problematic nature of this theory (see chapter 4) and in order to obtain converging evidence for spatial transformation areas in the human cerebral cortex, we performed a further experiment (chapter 3) of spatial analysis, using the mental clock paradigm that was introduced into experimental psychology by Paivio (1978) and into neuropsychology by

Grossi et al. (1989). Here subjects were presented with pairs of clock times and were required to choose the one in which the hour and minute hand formed the smaller angle. The times were presented acoustically, necessitating a transformation into symbolic representations from which the angular size difference could be inferred. This paradigm relies on visual mental imagery and not on visually presented material, and therefore excludes confounding effects of cortical processing of visual information. Furthermore, the mental comparison of analogue clocks might share some of the cortical mechanisms involved in the spatial analysis of objects that are presented in a non-canonical orientation, such as transformed text. We therefore sought to determine the extent of the overlap between the foci of cortical activation, as detected by fMRI, during the two tasks (chapters 2 and 3). A considerable overlap, particularly in the region of the parietal cortex that is commonly implicated in coordinate transformations, could indicate a common mechanism for spatial analysis that is required for the successful execution of both tasks, the recognition of visually presented transformed text and the comparison of mentally generated analogue clocks. Such a result would be of interest for the debate on the nature of visual imagery and the extent to which it shares the cortical pathways for visual perception. Moreover, it would contribute to our understanding of the manifold functions of the parietal lobe and its functional topography, which is of particular importance in the light of the frequent occurrence of clinical lesions to this region of the brain.

The methods

The functional neuroanatomy of cognitive processes in the human brain can be approached noninvasively at high spatial resolution with imaging techniques that record changes in regional cerebral blood flow (rCBF) and blood oxygenation. Of the two main available methods, positron emission tomography (PET) and fMRI, we used the latter because of its higher spatial and temporal resolution, the possibility to analyse single subject data and to

measure the same subject repeatedly, even, as in the experiments with inverting goggles, every day. FMRI relies on the blood oxygenation level-dependent (BOLD) contrast mechanism, first reported by Ogawa et al. in 1990 (Ogawa et al. 1990a, 1990b; Ogawa and Lee 1990) and widely applied to generate functional maps of the human brain since the pioneering studies of 1992 (Ogawa et al. 1992; Kwong et al. 1992; Bandettini et al. 1992).

The BOLD contrast mechanim for MRI is based on the use of deoxyhemoglobin as an endogenous intravascular paramagnetic contrast agent (Turner and Jezzard 1994; Aine 1995). Whilst hemoglobin is diamagnetic in the oxygenated state (HbO_2), it becomes paramagnetic when it is dissociated from oxygen (deoxyhemoglobin: Hb) (Pauling 1936; Sanders and Orrison 1995). This means that when it is placed in a magnetic field it will produce local distortions of this field and thus affect the MR behaviour of water proton nuclei and attenuate the signal intensity in MR images that are weighted for transverse relaxation time (T_2) or apparent transverse relaxation time (T_2^*) (Ogawa et al. 1990a, 1990b; Ogawa and Lee 1990; Kim and Ugurbil 1997; Turner et al. 1997). It is supposed that neuronal activity is accompanied by an increase in rCBF and oxygen delivery that exceeds the extraction by the elevated oxygen consumption and leads to a reduction of the blood level of deoxyhemoglobin (Grinvald et al. 1991; Kim and Ugurbil 1997; Raichle 1998; see Fig. 0.1).

Relationship of Blood Flow & Metabolism
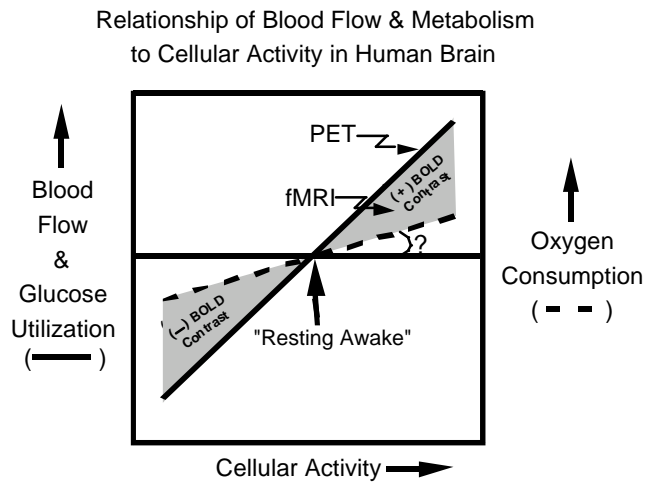to Cellular Activity in Human Brain

Figure 0.1: Diagram of the relationship of blood flow, glucose utilization, and tissue oxygen consumption to neuronal activity in the brain (from Raichle 1998). Blood flow and glucose utilization changes exceed changes in oxygen consumption. It is yet to be determined to what extent oxygen consumption changes at all. Blood flow changes and changes in glucose utilization are measured by PET, using radioactively labelled oxygen or fluoro-deoxyglucose, respectively (Aine 1995). The contrast that arises when changes in blood flow exceed changes in oxygen consumption (BOLD signal) is measured by fMRI.

This reduction of the concentration of the paramagnetic agent, which follows the presumed onset of the neuronal activity with a lag of approximately 4 seconds (hemodynamic delay), results in an increase in the signal intensity of T_2 and T_2^* -weighted MR images (increased BOLD signal).

MRI and FMRI data acquisition

All fMRI images shown in this thesis were obtained with a 1.5 Tesla Magnetom Vision clinical scanner (Siemens Medical Systems, Erlangen, Germany) equipped with a head coil designed for rapid gradient field switching that permits echo-planar imaging (EPI). This technique allows the acquisition of a single image in less than 100ms (Stehling et al. 1991; Blamire et al. 1992; DeYoe et al. 1994; Kim and Ugurbil 1997; Schmitt et al. 1998) and is therefore the method of choice for multi-slice fMRI. The acquisition parameters (number and distance of slices, distance factor, repetition time, field of view [FOV]) were varied according to the requirements of the experiments and are described in the methods sections of the

respective chapters. In all fMRI scanning sessions we also acquired co-registered 3D anatomical data sets that could be used for subsequent 3D visualization of the activation data. We routinely acquired a 3D magnetization prepared rapid gradient echo sequences (MP-RAGE) of 180 slices (voxel size: 1 mm^3) and a duration of 8 min 32 s. This sequence allows the acquisition of high-contrast (T1), full-head data sets with millimeter resolution in a comparatively short time (Mugler and Brookeman 1990). In order to obtain an even better contrast between grey and white matter of the brain each subject underwent a 3D T1-FLASH scan (TR=30 ms; TE=5 ms; Flip angle [FA] 40°) of 180 slices (voxel size: 1 mm^3) and a duration of 25 min. These 3D data sets were used for white/grey matter segmentation and surface reconstruction.

Data analysis and visualization

Data analysis, registration and visualisation were performed with the fMRI software package BrainVoyager (Goebel et al. 1998a,b). Prior to statistical analysis, the time series of functional images was aligned for each slice in order to minimize the signal changes related to small motions of the subject during the acquisition. The realigned time series were at first spatially filtered by convolving each EPI - image with a bidimensional gaussian smoothing kernel with Full Width at Half Maximum (FWHM) = 2 pixels, and then temporally filtered by convolving each pixel's time-course with a smoothing gaussian kernel with FWHM = 3 samples. Furthermore, the linear drifts of the signal with respect to time were removed from each pixel's time-course.

After these pre-processing steps, the cerebral regions responding to the stimulus were identified by means of a correlation analysis (Bandettini et al. 1993). The reference vector used in our analysis was a "box-car" ideal vector which assumed a value of "0" during the control period and "1" during the imagery period.

In order to take into account the hemodynamic delay of the activation signal, the correlation coefficient was evaluated for each pixel by shifting the original reference vector by one sample. Activated brain areas were selected in the

correlation maps by imposing a conservative intensity threshold for the correlation coefficients (r > 0.4, corresponding to $p < 10^{-4}$; uncorrected).

2D statistical maps were converted into polychromatic images and incorporated into the 3D MP-RAGE or T1-FLASH data sets through interpolation to the same resolution (voxel size: 1 mm^3). This allowed to superimpose 3D statistical maps onto the 3D anatomical data sets. Since the 2D functional and 3D structural measurements were performed within the same recording session, co-registration of the respective data sets could be computed directly based on the Siemens slice position parameters of the T2*-weighted functional measurement (number of slices, slice thickness, distance factor, Tra-Cor angle, FOV, shift mean, off-center read, off-center phase, in plane resolution) and on parameters of the T1-weighted 3D MP-RAGE or T1-FLASH measurements (number of sagittal partitions, shift mean, off-center read, off-center phase, resolution) with respect to the initial overview measurement (scout).

For each subject the structural 3D data sets were transformed into Talairach space. Talairach transformation was performed in two steps. The first step consisted in rotating the 3D data set of each subject to be aligned with the stereotaxic axes. For this step the location of the anterior commissure (AC) and the posterior commissure (PC) and two rotation parameters for midsagittal alignment had to be specified manually in the 3D MPR data set. In the second step the extreme points of the cerebrum were specified. These points together with the AC and PC coordinates were then used to scale the 3D data sets into the dimensions of the standard brain of the Talairach and Tournaux atlas (Talairach and Tournoux 1988) using a piecewise affine and continuous transformation for each of the 12 defined subvolumes. The individual Talairach 3D maps were averaged across subjects and superimposed on a normalized anatomical 3D data set. Prior to averaging, the functional 3D maps were smoothed with a gaussian kernel of 5mm FWHM.

The 3D T1-FLASH recordings were used for a surface reconstruction of both hemispheres. The white/grey matter border was segmented with a region-growing method. The discrimination between white and grey matter was improved by several manual interactions (e.g., labeling subcortical structures

as "white matter"). The white/grey matter border was finally tesselated in a single step using two triangles for each side of a voxel located at the margin of white matter. The tesselation of a single hemisphere typically consists of roughly 240,000 triangles. The reconstructed surface is subjected to iterative corrective smoothing (100-200 iterations). An iterative morphing algorithm (Goebel et al. 1998 a) was used to let the surface grow smoothly into the grey matter. Through visual inspection, this process was halted when the surface reached the middle of grey matter (approximately layer 4 of the cortex). The resulting surface was used as the reference mesh for the visualization of functional data. The iterative morphing algorithm was further used to inflate each hemisphere (chapter 3) or the posterior part thereof (chapter 1). An inflated hemisphere possesses a link to the folded reference mesh so that functional data may be shown at the correct position of the inflated representation. This link was also used to keep geometric distortions during inflation to a minimum with a morphing force that keeps the area of each triangle of the inflated hemisphere as close as possible to the value of the folded reference mesh. This display of functional maps on an inflated hemisphere allows the topographic representation of the three-dimensional pattern of cortical activation without loss of the lobular structure of the telencephalon (Figure 3.2).

Chapter 1

A psychophysical and functional imaging study of adaptation to inverting spectacles

1.1 Abstract

The adaptation to inverting prisms and mirror spectacles was studied in four subjects over periods of six to ten days. Subjects showed rapid adaptation of visuomotor functions, but did not report return of upright vision. The persistence of the transformed visual image was confirmed by the subjects' perception of shape from shading. No alteration of the retinotopy of early visual cortical areas was seen in the functional magnetic resonance images. These results are discussed in the context of previous claims of upright vision with inverting prisms and mirror spectacles.

1.2 Introduction

The psychology of perception produced few dogmas more deeply entrenched in the general mind than the return of upright vision during adaptation to inverting spectacles. Stratton's (1897) claim that he saw the world in its canonical orientation on the sixth day with inverting prisms was followed by attempts to reproduce his findings in 1928 and 1952 (see Kottenhoff 1961, Gregory 1998b). A number of studies at Innsbruck University with upside-down reverting mirrors (Kohler 1964) also resulted in reports of upright vision after one week. These alleged perceptual changes occurred concomitantly with the improvement of motor functions. On the other hand, the introspective data from a series of Japanese inversion and up-down reversal experiments, conducted on a similar time scale, suggested that throughout the experiment the awareness of visual transposition remained stronger than the sense of reality of the new vision (Yoshimura 1996). Thus, more than 100 years after

Stratton's report, the controversy that arose from his claims is "still unresolved" (Gregory 1998b).

The interest in visual inversion and distortion experiments was recently fuelled by the opportunity to investigate mechanisms of oculomotor and visuomotor adaptation at the single cell level. Left-right inverting prisms lead to a rapid change in the gain of the vestibulo-ocular reflex (Melvill Jones 1982, 1988), which has been associated with altered response properties of neurons in the flocculus (Lisberger & Fuchs 1978; Lisberger 1994). Sugita (1996) studied the adaptation to right-left reverting prisms in monkeys and reported that, after six weeks, 43 out of 119 cells recorded from in V1 were found to respond to ipsilateral as well as contralateral stimulation. These cells, however, had no preference for orientation or direction of motion, which suggests deterioration of function rather than compensation. The limited adaptability of early visual areas is also documented by experiments in kittens and adult cats that experienced a rotated visual field following cyclotorsion of the eyes. Neither the developing nor the adult cats were able to adjust behaviourally to the distorted visual input and within a few days developed a near complete neglect of the visual modality. This neglect was associated with a remarkable loss of responsiveness and response selectivity in neurons of the primary visual cortex (Singer 1979a, 1979b, 1982a). In adult cats, these neuronal modifications were reversible when normal vision was restored (Singer 1982b), but no similar effect was observed in kittens. Thus in early visual areas distortions of retinal coordinates do not appear to lead to compensatory readjustments but rather to dedifferentiation, as postulated by Fiorentini (1972). Truly compensatory processes seem to be confined to higher visual and visuomotor areas, particularly in the parietal cortex. Clower (1996) studied the gradual improvement of visually guided movements of human subjects whose visual input was distorted by prism spectacles and found increased regional cerebral blood flow in the contralateral posterior parietal lobe during the adaptation.

Little, if any attention was paid to the question whether the motor adaptation that occurs during the wearing of inverting spectacles is indeed matched by a concomitant perceptual adaptation. We thus performed a series of

experiments with inverting prisms and mirror spectacles in human subjects in order to try and reproduce the earlier reports of return of upright vision and identify the underlying neuronal mechanisms using functional magnetic resonance imaging.

1.3 Methods

Four healthy, right-handed volunteers took part in the experiment (age range 20-28 years, mean 25 years, all male). Written informed consent was obtained from all subjects and appropriate measures for their safety taken. Subjects were monitored around the clock during the experiment. One subject (author DL) wore a pair of inverting prisms (rotation through 180°; prism system custom made by Carl Zeiss Augenoptik, Aalen) for ten days, exactly replicating the duration and the optical inversion mechanism of Stratton's (1897) experiment, with the exception that a binocular mechanism was used (the system was adjusted for far targets, but the left prism could be covered during the exploration of the near environment). The three others wore a custom made upside-down reverting mirror of the type used in the Innsbruck experiments (see Figure 1.1) for seven, eight, and ten days, replicating the optical mechanism and duration of the pioneering mirror experiments of Kundratitz and Marte (1947; see Kottenhoff 1961). During the experiment subjects had no visual input other than through these optical devices (or similar devices mounted on the MRI head coil). Eyes were blindfolded at night. Subjects had to perform their everyday tasks with as little help as possible. The days were filled with tests in the institute, walks, visits to the zoo or the museum, and other recreational activities.

Figure 1.1: Subject DK wearing the upside down reverting optical system. The visual field of the subject does not extend beyond what is seen through the mirror. The maximum visual field is 85° wide and 22° high.

Behavioural tasks

The daily programme in the institute included the following psychophysical tests:

a) *Inverted and normal reading of phrases.* Subjects were shown 198 phrases in blocks of 24 each, half of which were presented in conventional orientation. The other half was presented in the respective transformation, i.e. inverted or upside-down. Subjects were requested to make a syntactic decision (phrase or pseudophrase), and reaction times were measured.

b) *Perception of shape from shading.* We used a stimulus described by Ramachandran (1988), presenting a central target circle, which was surrounded by six circles with the opposite contrast distribution. Subjects

had to decide whether the perceived hemisphere pointed inward or outward ("eggs": Figure 1.2 A). As a second shape from shading stimulus we used squares that were composed of two neighbouring bright edges and two dark edges ("squares": Figure 1.2 B). These squares evoke the illusion of buttons. Subjects had to decide whether the buttons pointed inward or outward. These stimuli rely on the reversal of depth perception that is brought about by shifting the light-source of cast shadows from above to below (Gregory, 1998b). This extraction of 3D shape from shading depends on retinal rather than gravitational cues and is assumed to be carried out early in visual processing (Kleffner and Ramachandran, 1992).

c) *Building three-dimensional objects.* Subjects had to copy three-dimensional objects of four, six, and ten components with a set of building bricks.
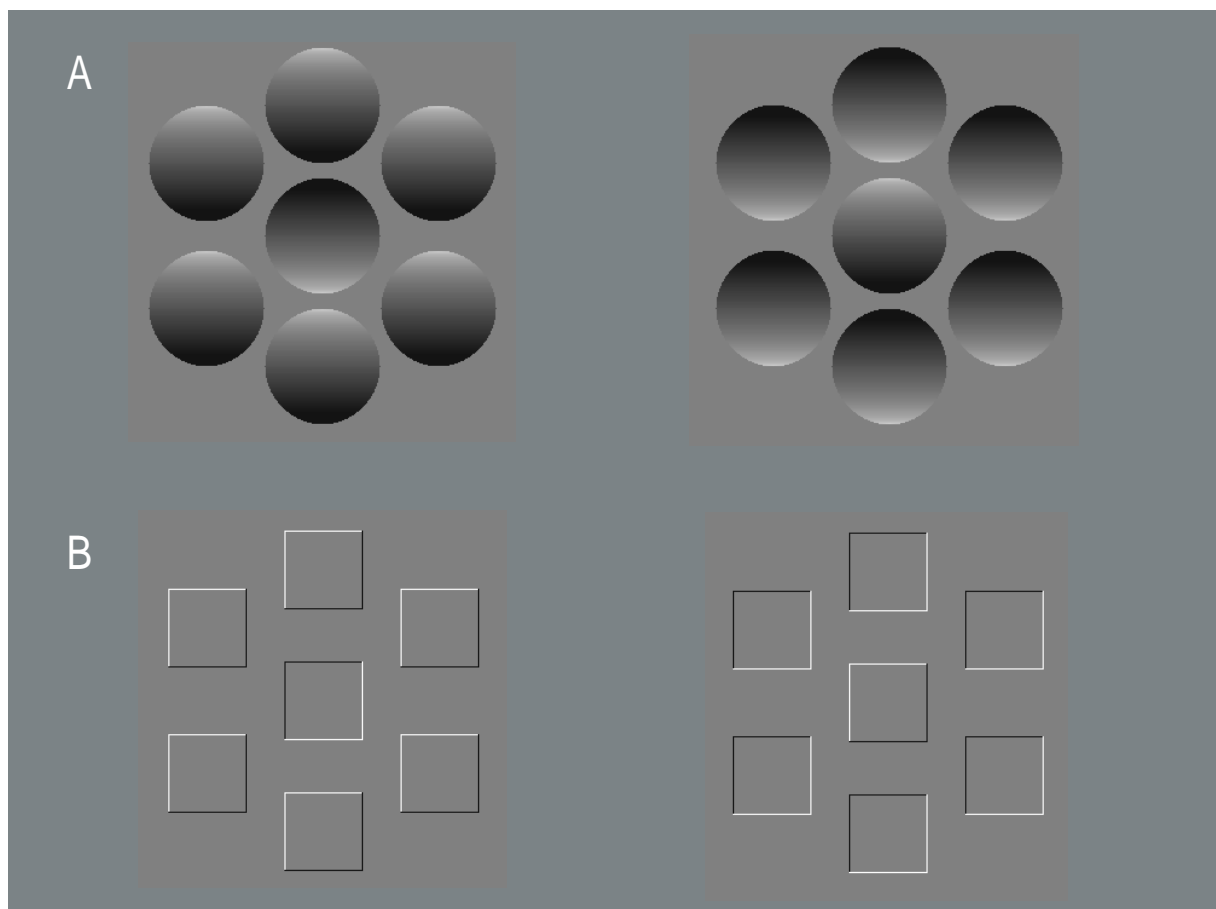
Figure 1.2: The stimuli for the extraction of three-dimensional shape from shading. A: A central target circle is surrounded by six circles with the opposite contrast distribution. Subjects report whether they perceive the central stimuli as eggs or cavities. B: Squares are composed of two neighbouring bright edges and two dark edges. Subjects decide whether the buttons point inward or outward

Functional magnetic resonance imaging

The stimulus for fMRI retinotopic mapping was a checkerboard disk segment subtending 45° of visual angle, which rotated clockwise starting at the left horizontal meridian (360° in 96 s; see Figure 1.3). Each mapping experiment consisted of four repetitions of a full rotation and was performed every (DL) or every other day (UK, AH, DK) at 1.5 T (Siemens Magnetom Vision) using the standard head coil and a gradient echo EPI sequence. The Siemens Magnetom gradient overdrive allowed functional scans with high spatial and temporal resolution (1 volume = 12 axial slices; TE = 69 ms, FA = 90°, FOV = 210 x 210 mm^2, voxel size 1.6 x 1.6 x 3.0 mm^3). Retinotopy of polar angle was revealed with cross-correlation analysis. The high-resolution 3D data sets of subject AH were aligned to each other, transformed into Talairach space (Talairach and Tournoux 1988), and used for surface reconstruction and inflation of the posterior part of the brain as described in the general methods section.
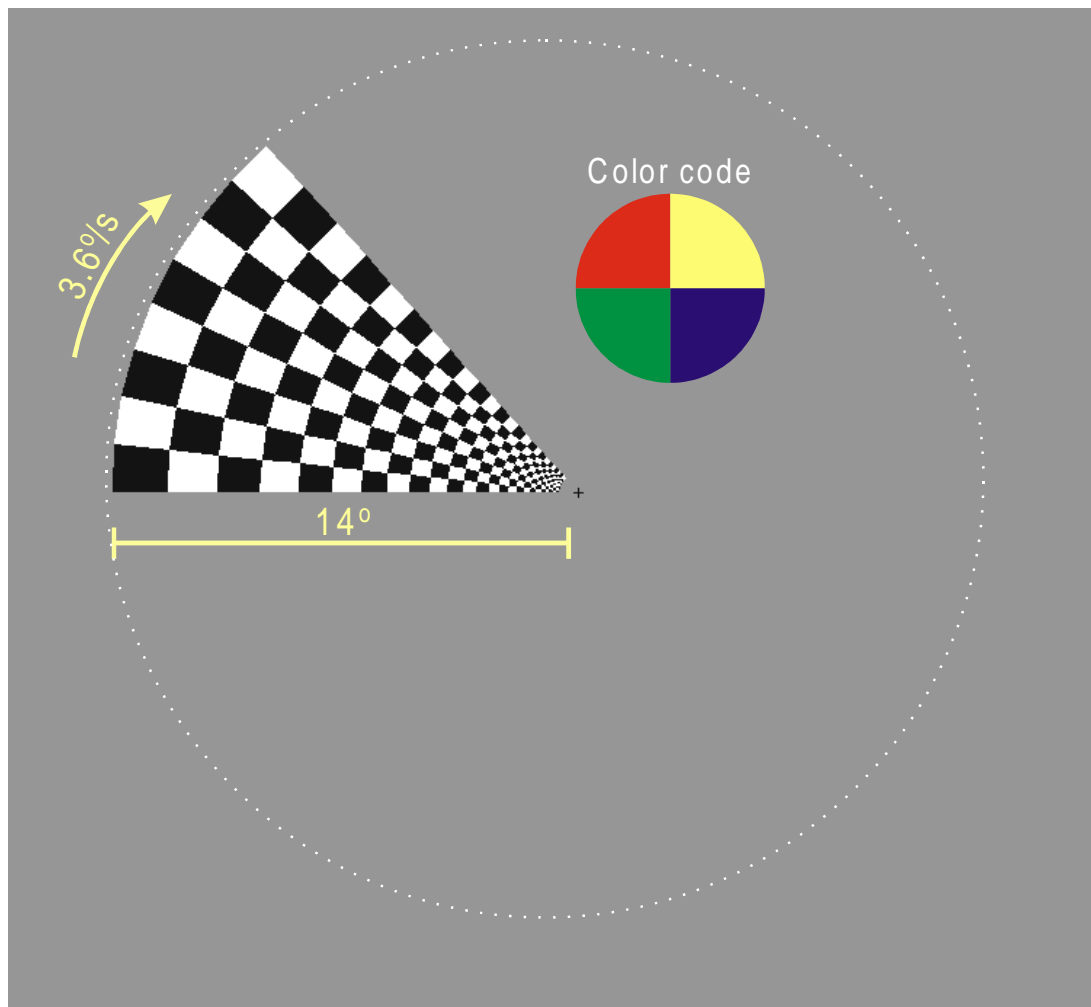
Figure 1.3: The stimulus for fMRI retinotopic mapping. A checkerboard disk segment subtending 45° of visual angle rotated clockwise starting at the left horizontal meridian (360° in 96 s).

A

B

V1d V1v V2v VP

C

Day 0   Day 1   Day 3

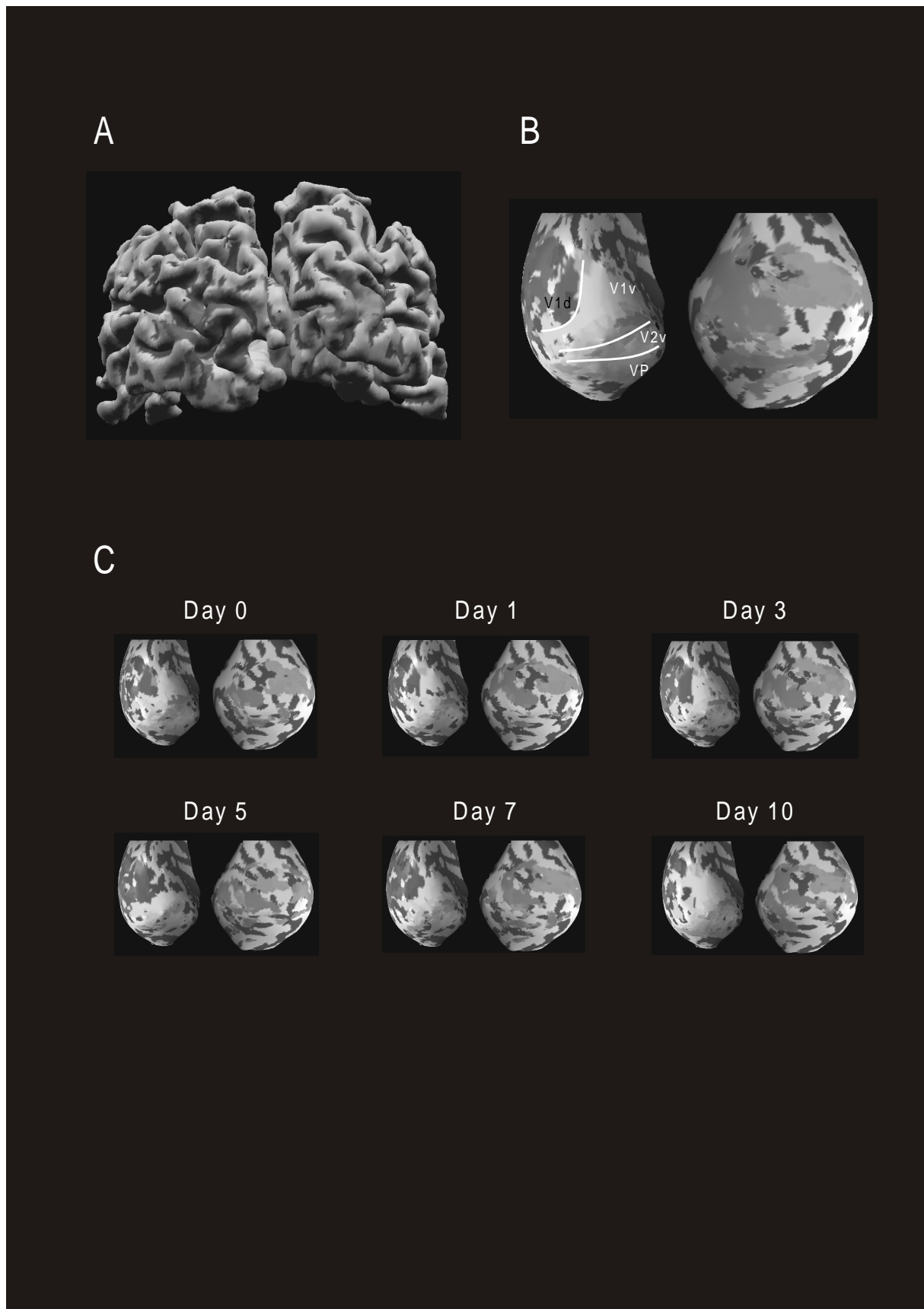Day 5   Day 7   Day 10

Figure 1.4: Results of boundary determination of retinotopic cortical areas V1 and V2 of subject AH and of retinotopic polar angle mapping during the mirror experiment. A: Posterior view of the reconstructed surface of the posterior portions of both hemispheres of

the subject's brain. The average of the polar angle maps of days 0 (baseline), 1, 3, 5, 7 and 10 (post-experimental) of the mirror experiment is projected onto the reconstructed surface (r > 0.33). Responses to stimulation in the right upper visual field are coded yellow (horizontal meridian, h. m.) to orange (vertical meridian, v. m.), in the right lower visual field blue (h. m.) to turquoise (v. m.), in the left upper visual field red (h. m.) to orange (v. m.), and in the left lower visual field green (h. m.) to turquoise (v. m.). B: Posterior-medial view of the same surface with the same map after cortex inflation (only retinotopic cortex shown). Area boundaries (white lines) are drawn for the left hemisphere at vertical and horizontal meridian representations. C: The same view as in B. Polar angle maps are shown for days 0, 1, 3, 5, 7, and 10 (r > 0.33 for all maps). The topography retinotopic visual cortex, as indicated by the colour code, remained stable throughout the experiment.

1.4 Results

All subjects showed a rapid adaptation of motor skills. On the third day of the experiment, they were capable of walking freely without a stick. Subjects performed all tasks of everyday life with none or minimal aid. During the second half of the experiment, they were able to find their way in a crowded department store and to ride a bicycle. The execution of very fine movements, however, was slowed down and remained so until the end of the experiment. For instance, the building of three dimensional objects still took twice the baseline time on the last day of the experiment. In the mirror experiments it took four days until subjects were able to read the clock correctly. Subjects were barely able to write in a conventional orientation on the first day, but improved quickly. One subject even wrote daily letters. Reading of phrases in conventional orientation improved markedly during the experiment, but reaction times remained above those for mirror reading until the spectacles were taken off (see Figure 1.5).
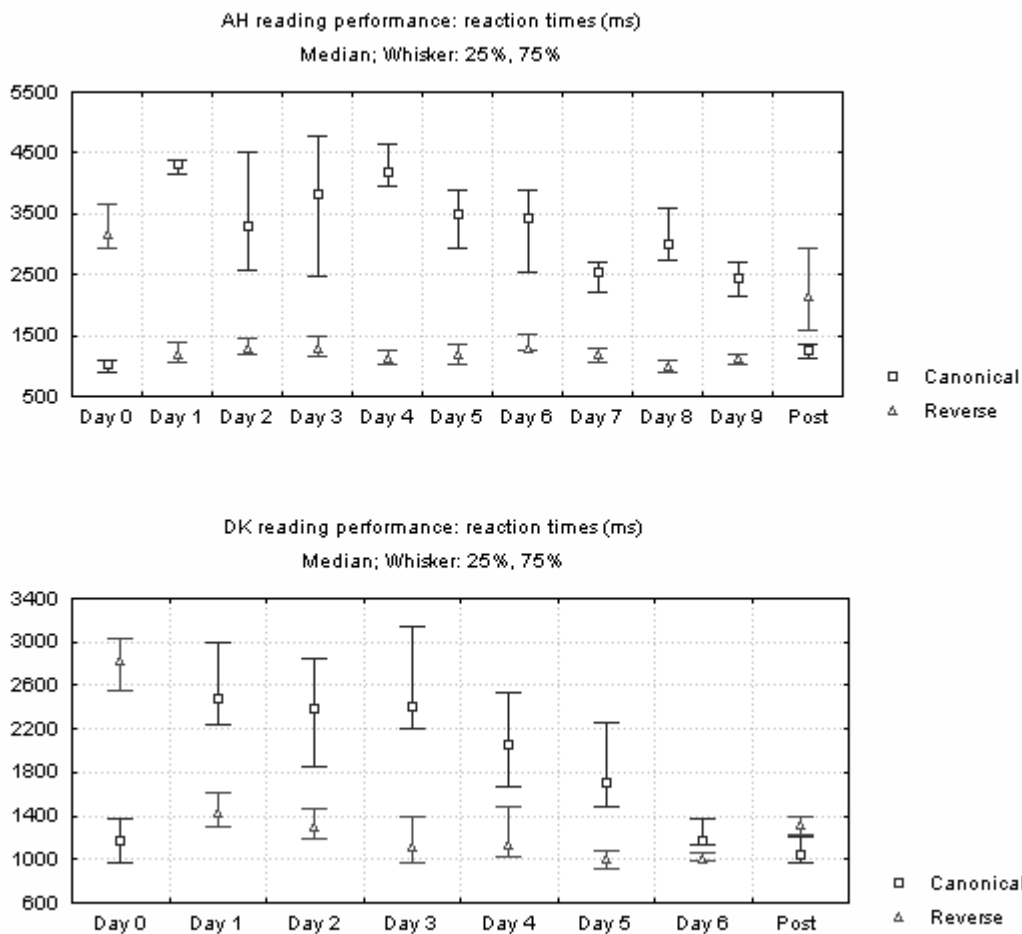
Figure 1.5: Reaction times (syntactic decision) for canonical presentation of phrases (non-canonical retinal input through mirror reversal) improved gradually during the experiment but remained higher than for reverse presentation (canonical retinal input through mirror reversal). This indicates that the canonically presented phrases were still perceived to be oriented non-canonically on the last day of the experiment. The postexperimental data for the canonical presentation show a return to the pre-experimental baseline (Day 0), while the learning effect for the non-canonical retinal input is preserved. (A) Reaction times of subject AH on days 0 (baseline), 1-9 (wearing the mirror) and 10 (post-experimental). (B) Reaction times of subject DK on days 1 (baseline), 2-7 (wearing the mirror) and 8 (post-experimental).

In the shape from shading task, one subject showed increasing ambiguity from day 5 onwards (i.e. 75% of the responses were compatible with the conventional orientation), but the responses of the others remained in accordance with the transformed orientation throughout the experiment (Figure 1.6).
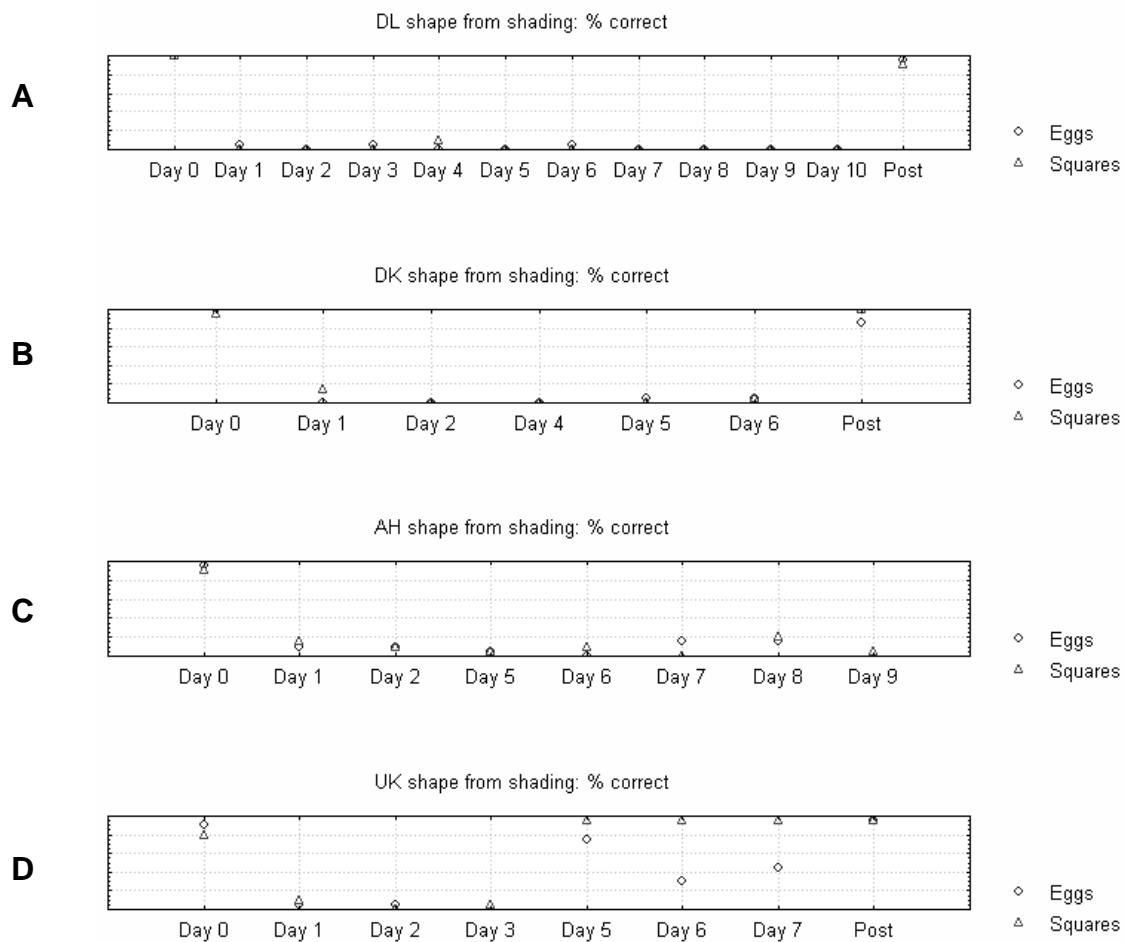
19

Figure 1.6: The extraction of three-dimensional shape from shading was determined by the orientation of the light source relative to retinal coordinates during the entire experiment in three out of four subjects. This indicates that, contrary to Stratton's (1896; 1897) assumption, adaptation to inversion or reversal of the visual field is not accompanied by a post-retinal mechanism that reverts non-canonical input to its canonical orientation. (A-D) Performance (percent correct) in the two shape from shading tasks ("eggs" and "squares"). The correctness of the response was judged by the direction of the light source as presented, i.e. "false" responses during the experiment indicate mirror reversal of the perceived image. Only subject UK (panel D) showed a partial switch of the perceived orientation during the experiment (from day 5), but responses remained ambiguous. The postexperimental performance showed a return to baseline levels (panels A,B,D).

The subjects reported that at times they had the impression that they themselves, rather than the world around them, had been turned upside-down, but that they *knew* that this was not the case. But no subject claimed that he had regained upright vision or that his visual image matched his body sense at any point during the experiment (Linden 1997), not even when they

were exploring the visual scene by touch (on the rôle of tactile exploration in the previous accounts of adaptation to mirror vision see Gregory 1997). Subjects felt dizzy for the first few hours with the inverting/mirror spectacles, and dizziness returned for about half an hour when they had taken off the spectacles at the end of the experiment. This was the only abnormal aftereffect that the return to normal vision had on the subjects. They did not show any difficulty in readjusting to the conventional view of the world. The functional magnetic resonance images showed no change of the retinotopy of the primary visual cortex from baseline levels during the experiment (Figure 1.4). In sum, the subjects' introspective reports and their performance in the psychophysical tests during the adaptation period showed a persistence of the previous visual coordinates. The retinotopy of early visual areas remained stable throughout the experiment.

1.5 Discussion

Our four subjects showed a visuomotor adaptation to inverted and mirror vision that was similar to that reported in previous studies (Kottenhoff 1961). Yet the results of the perceptual tasks and the subjects' reports about their experience suggest that this visuomotor adaptation did not rely on a return of upright vision. These psychophysical and introspective data as well as the results of the fMRI retinotopical mapping and the rapid re-adaptation after the removal of the goggles provide converging evidence against the hypothesis of early remapping. The subjects' rapid behavioural adaptation to the new spatial structure of the visual image might then be explained by the learning of new motor patterns and increased skill at spatial transformations (Held and Freedman 1963) rather than an adjustment of the perception of the world, seen through the mirror or prism, to the conventional orientation.

The fact that none of our subjects reported upright vision during the experiment is in keeping with parts of the previous literature. Of the five classical experiments with inverting spectacles, only two (Stratton 1897, Snyder & Pronko 1952) resulted in reports of upright vision of some sort. In

the three other cases, visuomotor adaptation occurred without major changes of perception (Ewert 1928, see Kottenhoff 1961). The five subjects who wore upside-down reverting mirrors at Innsbruck University for periods of five days to two weeks during the years 1947-1954 all showed rapid and partly spectacular motor adaptation, including the ability to ride a bicycle or to go skiing. Around day 3 of the experiment they reported an increasing ambiguity of the visual image. Sometimes they would see an object upside-down, sometimes in its conventional orientation, depending on the context and the extent to which the violation of gravity was felt to interfere with the visual image. These effects can be described as an interpretation of the visual image guided by previous knowledge about the external world and information about one`s own position in it rather than as fully-fledged upright vision (Kottenhoff 1961). Even Stratton himself, who otherwise gave the least ambiguous account of perceptual changes, conceded the importance of the appropriate "mental attitude of the observer toward the present scene" (Stratton 1896). It is also worth considering that none of the previous investigators tested their subjects' claim to upright vision with context-independent tasks, such as the *Reading* and *Shape from shading* task used in our study.

Knowledge about the neural mechanisms and the brain regions, particularly in the parietal lobe, involved in visuomotor adaptation and visuospatial transformations comes from lesion studies, recordings in behaving animals (Colby 1998), and functional imaging experiments on humans (Goebel et al. 1998b; Poldrack et al. 1998). The adaptation of visually guided reaching to the distortion of visual input by prism spectacles leads to an activation of the contralateral posterior parietal cortex (Clower 1996). A region in the intraparietal sulcus that is involved in the spatial transformations required for mirror reading will be identified in chapter 2. The parietal cortex thus has a prominent rôle in the visuospatial processing that is needed for the correct execution of reading and motor tasks during mirror vision.

In agreement with the results of previous electrophysiological studies on the effects of inverted vision (Singer 1979a&b, 1982a&b, Yinon 1982) there was no evidence for a remapping of retinal coordinates in early visual areas. Whether other, more subtle changes, such as reduced excitability or tuning of

neurons, took place cannot be decided because these parameters could not be measured with fMRI. However, the rapid recovery of normal function after restitution of normal vision seems to exclude any major modifications of basic functions in lower visual areas.

Chapter 2

Spatial transformations of visual information: The cortical systems for mirror reading and oculomotor control separated by fMRI

2.1 Abstract

Echoplanar functional magnetic resonance imaging (fMRI) was used to localize the cortical areas involved in the analysis of spatially transformed letterstrings. Significant increases of the blood oxygen level-dependent (BOLD) signal for transformed versus normal reading were observed in the superior parietal lobule (SPL), along the intraparietal sulcus (IPS), in the frontal eye fields (FEF), and in the latero-occipital area LO. The respective contributions of oculomotor and spatial transformation areas to this activation pattern were separated by means of a control condition involving the execution and suppression of eye movements. Areas activated in association with the control of eye movements included the superior parietal lobule and the frontal eye fields. The cooperation of different brain areas was analysed by correlating the time course of task-dependent BOLD signal changes in these areas. This correlation analysis revealed coactivation of occipito-temporal object recognition areas and a spatial transformation area in the intraparietal sulcus during the reading of transformed letterstrings. We suggest that cortical systems that are coactivated during complex cognitive tasks can be differentiated by the correlation analysis of BOLD signal time courses in spatially separate brain areas.

2.2 Introduction

The ability to transform mentally the orientation of objects in space is an important mechanism for perceptual constancy and the recognition of previously seen objects (Jolicoeur 1996). The astonishing capacity of both

humans and animals to adapt behaviourally to long-term inversions and distortions of visual input reflects the importance of such transformations in many situations of everyday life (Walsh 1996). Knowledge about the neural mechanisms and the brain regions involved has come from lesion studies, recordings in behaving animals, and more recently, functional imaging experiments on humans. Lesions to the parietal lobe of man have been reported to result in impairment of a number of higher visual and visuomotor functions, including visually guided eye (Pierrot-Deseilligny et al. 1986) and hand movements (Jeannerod et al. 1996) and the correct motor response to objects reflected in mirrors (Ramachandran 1997). Functional imaging studies with human subjects showed the involvement of posterior parietal cortex in location matching (Haxby et al. 1994) and in the mental rotation of two- (Alivisatos and Petrides 1997) and three-dimensional objects (Cohen et al. 1996) as well as that of the body (Bonda et al. 1996; for review see Petit 1997).

Neurophysiological studies in alert behaving monkeys have shown the involvement of parietal neurons in processes that require spatial analysis of visual signals and preparation of visually guided movements (Sakata et al. 1997; Andersen et al. 1990). Neurons in the lateral intraparietal area LIP and in area 7a are thought to play a rôle in the location of targets and in the prevention of perceptual disruptions that are owed to eye movements (Colby and Duhamel 1996; Battaglini 1997). Sakata et al. (1997) also reported neurons in the caudal intraparietal sulcus that were selective for the axis-orientation or surface-orientation of objects in three-dimensional space. Results from monkey studies suggest that classical object recognition areas are also involved in the spatial transformation of objects and that the cooperation of parietal and occipitotemporal areas is required for the accurate discrimination of rotated shapes (Walsh and Butler 1996).

The goal of the present series of experiments was to contribute to the identification of structures involved in spatial visual transformations and to establish correlations between psychophysical performance and neuronal activation. In particular, we were interested in relations between occipito-

temporal areas involved in object recognition and areas of the parietal cortex devoted to the processing of spatially transformed objects.

Because visual recognition and transformation tasks often involve eye movements, the identification of visual centres responsible for spatial processing and spatial transformations requires the ability to distinguish between networks involved in oculomotor processes and spatial transformations, respectively (Milner and Goodale 1995). Recent reports of mirror agnosia in patients with normal oculomotion (Ramachandran 1997) and of an isolated perceptual deficit in analysing mirror objects (Turnbull and McCarthy 1996) suggest that the systems for spatial transformation and eye movements are indeed anatomically separate. In order to differentiate between these two systems, we compared the activation patterns associated with tasks that required the spatial transformation of letterstrings (*Transformed Words* and *Inverted Lines*) with a control condition that involved the execution and suppression of eye movements (*Oculomotor Control* task).

2.3 Methods

Functional magnetic resonance imaging and stimulus presentation

Five healthy, right-handed human subjects were scanned in the *Transformed Words* experiment (age range 27 to 28 years, two female), five in the *Inverted Lines* experiment (age range 19 to 33 years, mean 26 years, one female) and five, including three of the previous, in the session with *Inverted Lines* and *Oculomotor Control* (age range 19 to 35 years, mean 26.5 years, all male). The experiments were undertaken with the understanding and written consent of each subject. Functional magnetic resonance imaging was performed at 1.5 T (Siemens Magnetom Vision) using the standard head coil and a gradient echo EPI sequence. The Siemens Magnetom gradient overdrive allowed functional scans with high spatial and temporal resolution

(1 volume = 15 axial slices; TE = 69 ms, FA = 90°, FOV = 210 x 210 mm^2, voxel size 1.6 x 1.6 x 5.0 mm^3). Visual stimuli were delivered under computer control (Digital DECpc Celebris XL 590) to a high-luminance LCD projector (EIKI LC-6000). The image was back-projected onto a frosted screen positioned at the foot end of the scanner. Visual stimuli were generated using the Microsoft Direct X graphics library and a Matrox Mystique graphics board.

Interindividual statistical analysis

The data for statistical comparisons between conditions across subjects consisted of the mean time course of all voxels of an analysed area. Based on this data the mean of the raw fMRI signal for each subject and condition in a given experiment was computed. These mean values were analysed by means of ANOVA and post-hoc pairwise comparisons using stimulus condition as a within-group factor. The obtained p-values were corrected for multiple comparisons. Values of percent signal change averaged across subjects were computed on the basis of the difference between the mean values of the fMRI signal in each experimental condition and the mean fMRI signal in the fixation periods for each individual subject.

The *Inverted Reading* experiments

Each experiment consisted of the acquisition of 128 volumes (TR = 4000 ms), starting and ending with fixation periods of 4 volumes each, and alternating stimulus and fixation periods of 8 volumes (= 32 s) in between. We performed two series of experiments with inverse reading. In the first (*Transformed Words*), subjects were shown normal and spatially transformed German words and pseudo-words of five letters each (covering 3° of visual angle) in the order presented in Figure 2.1. In the second (*Inverted Lines*), subjects were shown German phrases and pseudo-phrases of four words each (covering 14° of visual angle), alternating normal and rotated presentation. The transformations were indicated by a cue (the string "R_ _ _ _" displayed in the respective transformation), which was visible during the

last two volumes of the preceding fixation period. Subjects had to discriminate between words and pseudowords (semantic decision) in the *Transformed Words* experiment and between phrases and pseudophrases (syntactic decision) in the *Inverted Lines* experiment (Rösler et al. 1993). The rate of presentation of the phrases/pseudophrases in the *Inverted Lines* experiment was triggered by the subject's response in order to reach a constant level of overall attention. The presentation of words and pseudowords was at random and involved on average the same number from each category. During the experiments, reaction times and correctness of answers were recorded by means of a fibre-optic answer-box.

Block	Presentation	Description of stimulus
1	geben	Normal
2	geben	Lateral mirror image
3	uǝqǝƃ	Rotated word
4	ƃǝqǝu	Rotated letters
5	geben	Normal
6	geben	Vertical mirror image
7	uǝqǝƃ	Rotated word
8	ƃǝqǝu	Rotated letters

Figure 2.1: Stimulus paradigm of the *Transformed Words* experiment. The eight periods of stimulus presentation alternated with fixation periods (of eight volumes each). A cue that indicated the type of transformation was shown during the last two volume measurements of the preceding fixation period.

The *Oculomotor Control* experiment

In the third experiment, each subject performed the *Inverted Lines* task and an *Oculomotor Control* task in the same recording session, which allowed for

a precise comparison of activated regions in the two tasks. The *Oculomotor Control* task consisted of the acquisition of 128 volumes (TR = 4000 ms) starting and ending with fixation periods of 8 volumes each. After the first fixation period, five stimulus blocks of 16 volumes (= 64 s) were alternated with fixation periods of 8 volumes (= 32 s) in between. In the stimulus periods, a small square (0.3°) appeared randomly on either the left or the right side of the fixation cross for 300 ms at a distance of 7.5°. Subjects were instructed to make a saccade to the target square and to return immediately to the fixation cross in the first, third and fifth stimulus period (eye movement blocks). In the second and fourth stimulus period, subjects were instructed to fixate the cross while the target square appeared and disappeared (eye movement suppression blocks). In the first and third stimulus period, the interval between successive appearences of the square was reduced gradually from 3 to 0.9 s while in the second and fourth stimulus period, the interval increased gradually from 0.9 to 3 s. In the fifth stimulus block the square appeared repeatedly with a constant interval of 2 s.

2.4 Results

Behavioural results

The reaction times of the lexical decision task in the *Transformed Words* experiment were significantly higher for transformed than for normal words (p < 0.01; see Figure 2.2). The vertical mirror image required the longest average reaction time for correct responses (1988 ms), followed by the rotation of the single letters of a word in the picture plane (preserving the reading direction) (1795 ms), the lateral mirror images (1717 ms), the rotation of entire words (1543 ms) and words in normal presentation (1033 ms). The average reaction times for correct syntactic decisions in the *Inverted Lines* experiment ranged from 1255 ms to 1640 ms (mean 1436 ms) for normal presentation and from 1912 ms to 3109 ms (mean 2411 ms) for rotation in the picture plane.
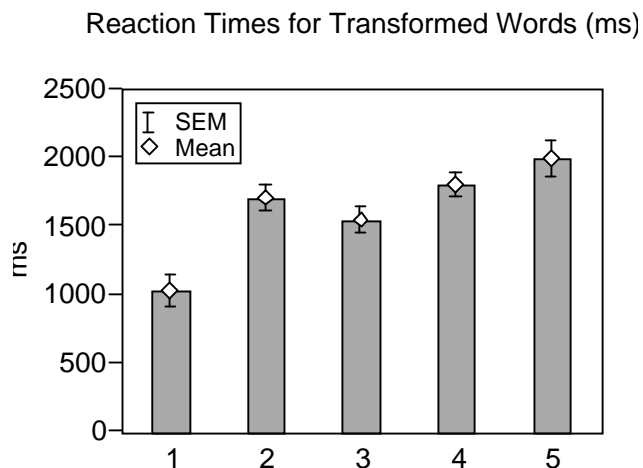
Reaction Times for Transformed Words (ms)

Figure 2.2: Reaction times in the *Transformed Words* experiment. Mean and standard error of reaction times for correct responses in the lexical decision task over five subjects. Stimulus conditions: 1 = normal orientation; 2 = lateral mirror image; 3 = rotated words; 4 = rotated letters; 5 = vertical mirror image.

BOLD signal increases during inverted reading

A significant increase of the BOLD signal for normal vs. inverted reading (task-dependent activation) was observed in four cortical areas in both the *Transformed Words* and *Inverted Lines* experiments ($p < 0.05$). These areas were located in the left SPL, along the IPS bilaterally, in the left occipito-temporal cortex (comprising the posterior fusiform gyrus and occipitotemporal sulcus), and in the posterior bank of the left precentral sulcus. The Talairach coordinates of the areas that showed task-dependent activation in all subjects are summarized in Table 2.1. In addition, some subjects showed significant task-dependent activation in the right SPL (3/10), the right precentral sulcus (4/10), and the right occipitotemporal cortex (3/10). In the *Transformed Words* task, activation showed a trend to be higher for the rotation of single letters and the mirror images than for the rotation of entire words (see Figure 2.3). This corresponded to the level of difficulty as reflected in the recorded response latencies (see Figure 2.2). Further areas that were activated during the reading task, but did not show a significantly different modulation for the transformed conditions, included early visual areas and inferior frontal cortex.

For the subjects of the *Inverted Lines* experiment, further correlation maps were computed based on the BOLD signal time course of the left occipito-temporal area (presumed area LO, see Malach et al. 1995). These maps showed a high correlation (r > 0.75) of task-dependent activity in the *Inverted Lines* task between area LO and an area at the posterior T-junction of the left intraparietal sulcus (Figure 2.4, see Ono et al. 1990). This was the only parietal area that exhibited high correlation values in all analysed subjects. The individual Talairach coordinates of both areas are provided in Table 2.2 for the four subjects who performed the *Inverted Lines* and the *Oculomotor Control* tasks in the same session.

Area	Talairach coordinates (mean of 10 subjects)	SD
Left upper IPS	-23, -68, 47	2.14, 2.90, 4.17
Right lower IPS	29, -68, 28	1.77, 4.12, 5.34
Left lower IPS	-25, -71, 25	3.00, 4.87, 4.69
Left SPL	-33, -48, 51	3.23, 5.66, 3.63
Left LO	-49, -73, - 7	4.04, 3.24, 4.43
Left FEF	-43, - 1, 37	3.20, 3.59, 3.77

Table 2.1: Locations of areas differentially activated by inverse reading (*Transformed Words* and *Inverted Lines* experiments).

Subject	LO	Spatial transformations (IPS)	Oculomotor control (SPL)
1	-46, -76, -13	-23, -68, 47	-36, -41, 62 (L)
2	-48, -63, - 6	-25, -67, 54	-31, -45, 40 (L)
3	-44, -77, -11	-20, -72, 46	16, -52, 56 (R)
4	-44, -75, - 6	-21, -71, 41	-27, -52, 40 (L)
Mean	-46, 73, - 9	-22, -70, 47	-31, -46, 47 (L)
SD	1.91, 6.55, 3.56	2.22, 2.38, 5.35	4.50, 5.57, 12.77 (L)

Table 2.2: Locations (Talairach coordinates) of left LO, of the spatial transformation area at the posterior T-junction of the left IPS and of the oculomotor area in the SPL (L = left hemisphere; R = right hemisphere).
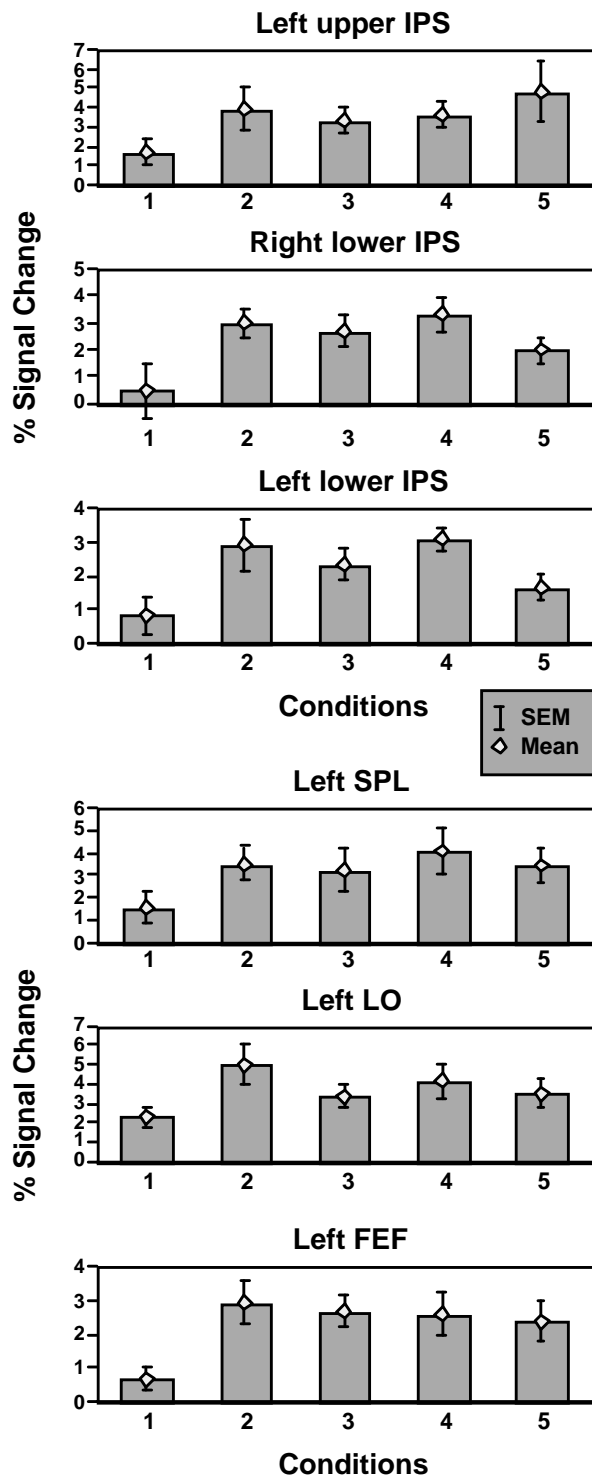
Figure 2.3: Activation levels of selected regions during the *Transformed Words* experiment. Mean and standard error of task-dependent BOLD signal change in the stimulus conditions as compared to the fixation periods over five subjects. Stimulus conditions: 1 = normal orientation; 2 = lateral mirror image; 3 = rotated words; 4 = rotated letters; 5 = vertical mirror image. For the averaged Talairach coordinates of activated areas see Table 2.1.

BOLD signal increases during overt and covert eye movements

A significant increase of the BOLD-signal for overt and covert eye movements was found in the frontal eye field (FEF), the supplementory eyefield (SEF) and in the anterior portion of the SPL. The time course of the hemodynamic response in these regions roughly followed the supplied reference function (see Figure 2.4). The slopes of the reference function correspond to changes in presentation rate of the saccade target. A comparison between the parietal area activated most strongly in the *Inverted Lines* task (see above) and the parietal region activated in the *Oculomotor Control* experiment revealed that they are located at clearly separated positions and that the intersubject variability is markedly higher for the oculomotor area than for the spatial transformation area. For the respective Talairach coordinates see Table 2.2. The averaged functional map across the four subjects who perfomed both experiments in the same session revealed that during the *Oculomotor Control* experiment, the activity in the FEF was stronger and more extended than activity in the SEF, whereas the opposite was the case in the *Inverted Lines* experiment (see Figure 2.4 C).
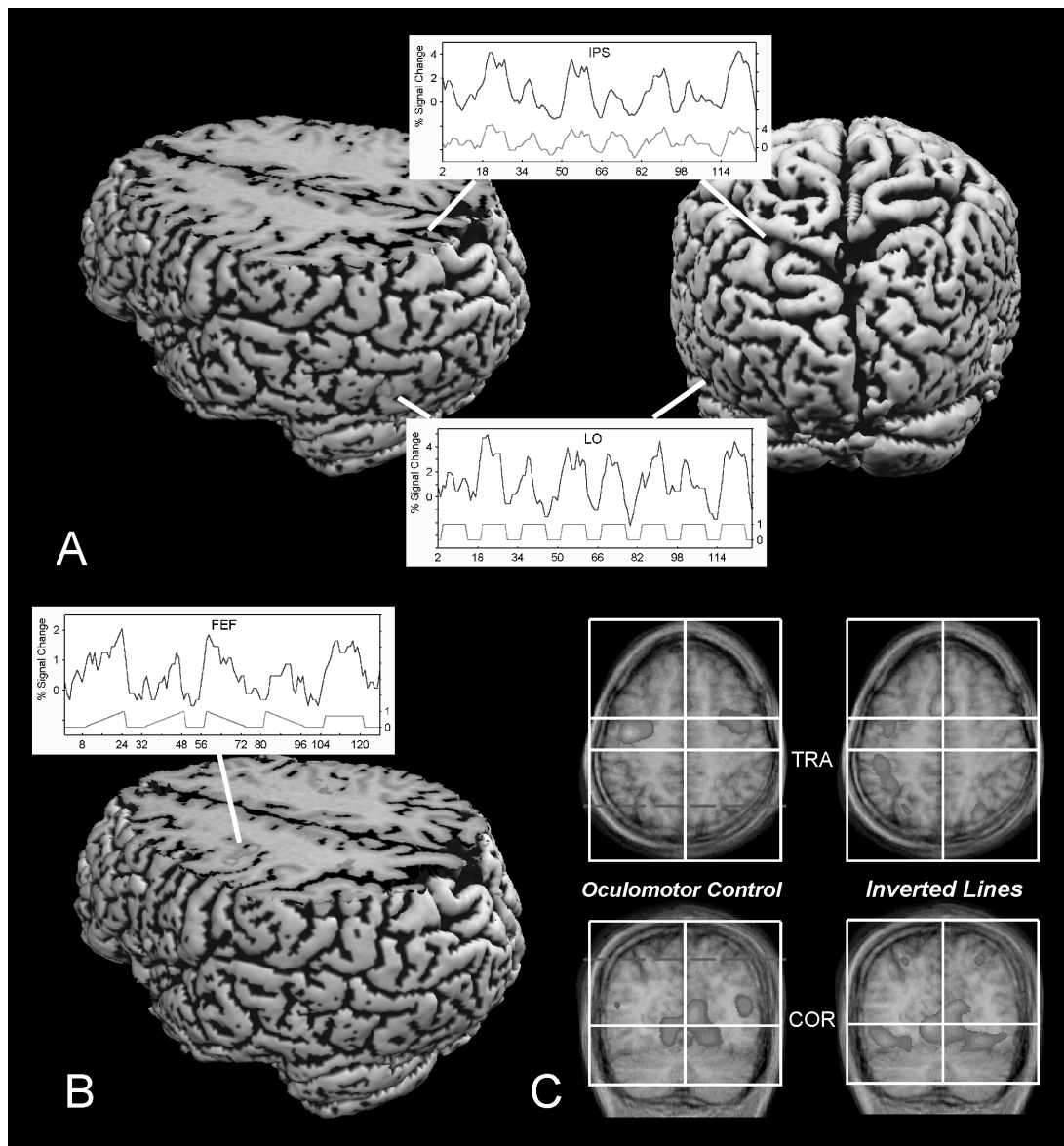
Figure 2.4: Main cortical areas activated in the *Inverted Lines* and *Oculomotor Control* experiments. Left hemispheres are shown on the left side of each picture. (A) The reconstructed 3D views show activated regions of a single subject performing the *Inverted Lines* task that were identified by correlation analysis of the BOLD signal changes in left LO (r>0.7). The regions include right LO, the posterior T-junction of the left IPS and a more anterior left parietal area. Lower panel shows time course of signal changes in left LO (red) as identified with the simple reference function (green = normal reading, blue = inverted reading). Upper panel shows time course of signal changes in the posterior T-junction of the left IPS (red), the area with the highest correlation with the LO time course (blue). (B) Reconstructed 3D view shows activated regions that were identified in the *Oculomotor Control* experiment. They include left and right FEF and a region in the anterior left IPS. Panel shows time course of signal changes in left FEF (red) as identified with the specified reference function (green = eye movement blocks, blue = eye movement suppression

blocks; slopes reflect the changes in presentation rate of the target). (C) Two slices of functional data averaged across four subjects and superimposed on averaged anatomical data. Axial slice shows left and right FEF in the *Oculomotor Control* experiment (left side). Because of the effects of intersubject averaging, small areas with high spatial variability are often not visible on averaged maps. This explains the absence of anterior parietal areas that are visible in the data of individual subjects. The two slices of the *Inverted Lines* experiment (right side) show the parietal region at the posterior T-junction of the IPS, SEF, left FEF, and a region containing LO and the posterior fusiform gyrus. White lines indicate Talairach space, blue lines indicate posiiton of coronal (y = -63) and transversal (z = 47) cuts.

2.5 Discussion

Brain activity associated with the execution and suppression of eye movements was located in the posterior bank of the precentral sulcus and in the superior parietal lobule bilaterally. These areas also showed a task-dependent BOLD signal increase during the spatial transformation of letterstrings. In addition, this task was associated with BOLD signal increases along the intraparietal sulcus and in occipitotemporal object recognition areas.

The activation of the posterior bank of the precentral sulcus, presumed to be the human homologue of monkey frontal eye fields (Paus 1996), can be attributed to both covert and overt shifts of visual attention (Nobre et al. 1997) because a BOLD signal increase of the same scale was observed in the Oculomotor Control task (see Figures 2.3 and 2.4). However, the posterior T-junction of the IPS, the area that showed the highest activation associated with inverted reading in the parietal lobe, was not active during tasks that only involved the execution or suppression of eye movements. It should therefore be an area that is specifically related to spatial transformations. This claim is supported by Kosslyn's (1994) finding of increased cerebral blood flow in a left parietal area with very similar coordinates (-33, -73, 44) in a PET study of 12 subjects who had to identify objects seen from a non-canonical point of view. Various areas in the parietal lobe were suggested by Cohen et al. (1996) as being responsible for the mental rotation of three-dimensional objects. Mental rotation of the object is one main strategy for the

solution of problems that require an adjustment of viewpoint and object orientation. The inverted reading task could be solved by performing mental rotations of the words or letters, or reversal of the object along one axis, in the case of the mirror images. Thus the BOLD signal increase in the T-junction of the intraparietal sulcus is likely to reflect the additional spatial transformations required for the accurate recognition of the word. The correlation between BOLD signal intensity and task difficulty as reflected by reaction times further supports this interpretation.

Visual object recognition is a perceptual function in which the occipitotemporal cortex is implicated. We observed task-dependent activity particularly in the areas in the fusiform gyrus and around the left occipitotemporal sulcus that have been implicated in the processing of letterstrings (Price et al. 1996; Puce et al. 1996) and in the postero-lateral part of the fusiform gyrus, an area termed the lateral occipital cortex (LO) and regarded to be the human homologue of monkey areas TEO and TE by Malach et al. (1995). Both the gyral localization and the Talairach coordinates of our area met the criteria for LO given by Malach. This complex, which is not activated by eye movements (Malach et al. 1995), showed a high correlation with the parietal spatial transformation area in its task-dependent activity during inverted reading. Such a correlation between occipitotemporal object recognition areas and parietal spatial transformation areas might be brought about by cortico-cortical projections like those described in the monkey from the IPS and 7a to TE and TEO (Andersen et al. 1990) and implicated in the attentional modulation of inferotemporal cortical activity (Desimone and Duncan 1995).

Recent lesion studies (Turnbull and McCarthy 1996; Turnbull et al. 1997) have shown a dissociation between the abilities to recognize objects and to assess their orientation or to make enantiomorphic discriminations. Such a dissociation could be due to the lesion of a specific visuospatial area in the parietal cortex. In one of the patients, enantiomorphic discrimination was impaired only for objects, not for letters. This could either indicate that there are parietal areas specialized for the spatial transformation of objects and that of letters, respectively, or that the lesion affected the connections

between a parietal area that subserves enantiomorphic transformations in general and areas in the occipito-temporal cortex that are specialized for the recognition of objects or letters. We prefer the latter interpretation because it does not require the hypothesis of distinct parietal areas specialized for the transformation of different classes of objects, but relies on co-operation between occipitotemporal modular areas for object recognition (Kanwisher et al. 1996) and visuospatial areas in the intraparietal sulcus for spatial transformations.

In their PET study of the mental rotation of alphanumeric stimuli, Alivisatos and Petrides (1997) found specific activity in the head of the right caudate nucleus. The absence of such an activation in our data might be due to technical constraints. For the fMRI mapping of deep nuclei, fast low angle shot (FLASH) sequences seem to be more appropriate than the EPI technique, which was used in our study because of its suitability for full scale brain mapping (Kim and Ugurbil 1997).

The evidence from previous studies as to the laterality of brain processes involved in visuospatial transformations is equivocal. Kosslyn et al. (1994) found task-dependent inferior parietal lobe activity only in the right hemisphere, Alivisatos and Petrides (1997) only in the left. Our results do not support any strong theory of laterality. Although activation tended to be stronger and more consistent in left hemisphere regions, a number of subjects showed significant bilateral activation of temporal, parietal, and frontal areas.

Using the high spatial resolution of fMRI, we demonstrate that the cortical network for spatial transformations of letterstrings and for overt and covert attention shifts, which are coactivated in tasks of inverted and mirror reading, are anatomically separate. The correlation of BOLD signal between parietal and occipitotemporal areas during a task requiring the spatial transformation of letterstrings suggests cooperative interactions between these areas. These results extend recent data from lesion studies, which suggest that parieto-temporal cooperation is required for visual spatial analysis. A different cortical network, including parietal regions and the frontal eye fields, is activated during the execution and suppression of eye movements. This

study also demonstrates that correlation analysis of the task-dependent modulation of the hemodynamic signal in anatomically separate brain areas is a fruitful strategy for differentiating the specific function that a particular area fulfills in coactivated networks.

Chapter 3

Matching two imagined clocks: The functional anatomy of spatial analysis in the absence of visual stimulation

3.1 Abstract

Do spatial operations on mental images and those on visually presented material share the same neural substrate?

We used the high spatial resolution of functional magnetic resonance imaging to determine whether areas in the parietal lobe that have been implicated in the spatial transformation of visual percepts are also activated during the generation and spatial analysis of imagined objects.

Using a behaviourally controlled mental imagery paradigm, which did not involve any visual stimulation, we found robust activation along the intraparietal sulcus (IPS) in both hemispheres. We could thus identify the subset of spatial analysis-related activity that is involved in spatial operations on mental images in the absence of external visual input.

This result clarifies the nature of top down processes in the dorsal stream of human cerebral cortex and provides evidence for a specific convergence of the pathways of imagery and visual perception within the parietal lobes.

3.2 Introduction

Focal lesions of cerebral cortex may determine selective defects of visual mental imagery (Farah 1984; Trojano and Grossi 1994). This suggests that the ability to revisualize objects or events in the mind relies on the integrity of specific neural structures. Most patients with selective imagery defects show lesions of left infero-medial occipital areas (Farah 1988, 1989), or of left temporo-parietal or temporo-parieto-occipital regions (Trojano and Grossi 1994). This variability of the functional and morphological neuroimaging

findings in these patients has so far prevented a general agreement about the neural basis of mental imagery.

Recent investigations identified closely overlapping field-specific defects in visual perception and imagery in hemianopic patients (Farah et al. 1992; Butter et al. 1997), supporting the hypothesis that visual perception and visual imagery share a common neural substrate in occipital lobe structures. However, other authors demonstrated that patients with cortical blindness (Goldenberg et al. 1995; Chatterjee and Southwood 1995) or with visual object recognition impairments (Behrmann et al. 1992; Jankowiak 1992) may show preserved visual imagery, a finding that seems to be at odds with the above hypothesis.

The parallel between vision and imagery might not be restricted to the involvement of occipital structures. On the basis of studies suggesting that there are two visual systems, one for identifying objects and one for locating them (Ungerleider and Mishkin 1982), it has been proposed that visual object and spatial imagery are functionally independent processes which must rely on different underlying neural systems (Levine et al. 1985; Farah et al. 1988). This theoretical framework requires that patients with topographic disorientation show selective deficits in imagery for spatial location (Levine et al. 1985). This distinction was supported by a recent case report of a patient who showed a dissociation between preserved visual and impaired spatial processing in imagery tasks. While her ability to represent objects visually was intact, she failed in tasks that require mental rotation, recall of spatial position or execution of spatially based imagery operations (Luzzatti et al. 1998).

The extent to which visual imagery and visual perception share common neural networks has also been addressed by means of modern neuroimaging techniques, with conflicting results about the involvement of primary visual cortex (PVC) in mental imagery (Kosslyn et al. 1993, Kosslyn et al. 1997, Roland and Gulyas 1994, Moscovitch et al. 1994). Another focus of functional imaging studies was the identification of cortical structures that subserve the generation of mental images of objects, such as the left inferior temporal lobe (D'Esposito et al. 1997).

In the present study we used fMRI to explore the neural correlates of a behaviourally controlled spatial imagery task, aiming to verify the localization of spatial mental imagery.

The experimental condition was derived from the mental clock test (Paivio 1978), which has been used to study defects of spatial mental imagery (Grossi et al. 1989); this paradigm is particularly suitable for the fMRI investigation of mental imagery because it involves a behavioural control that can be performed on-line during scanning. Subjects are asked to imagine pairs of times that are presented acoustically and to judge at which of the two times the clock hands form the greater angle. Clinical data show that both cerebral hemispheres are involved in accomplishing this task: one patient with left temporo-parieto-occipital damage failed only in the imagery condition, while another patient with an extensive right parieto-temporal lesion failed in both the perceptual and the imagery condition but only when the hands had to be imagined on the left half of the clock face (Grossi et al. 1989). This effect of right-hemisphere damage on performance of the "o'clock test" has been replicated in a second study (Grossi et al. 1993).

From this lesion-based evidence on the cortical substrate of spatial mental imagery we expected to see an increase of neuronal activity, as reflected by the BOLD signal, in the parietal lobes bilaterally during the mental clock test. More specifically, we expected activity in the upper portions of the intraparietal sulci, including the T-junction described in chapter 2, because this task, like the inverted reading paradigms, requires a spatial transformation of the material. In addition, our analysis of cortical metabolism, included the entire cortex in order to assess the coactivation of other brain areas during the performance of the task.

3.3 Methods

Subjects

We recruited seven right-handed post-graduate students (4 male, 3 female; mean age 27 years; range 23-32), who gave informed consent to participate in the study. None of the subjects was taking any medication or was affected by neurologic or psychiatric conditions. All of them were unaware of the purposes and predictions of the experiment at the time of testing.

Experimental procedure

Subjects were asked to imagine two analogue clock faces based on the times that were presented verbally by the examiner (e.g. 9.30 and 10.00). We selected 50 pairs of times, involving only half-hours (i.e. 7.30) or hours (i.e. 9.00); in half of the conditions, the correct answers corresponded to numerically greater times (i.e. 3.00 vs. 1.00), and in the other half to numerically smaller times (i.e. 8.30 vs. 11.00) in order to avoid subjects considering only the numerically greater pairs. The clock faces were balanced for the side on which the hands had to be imagined and presented in pseudo-random order. Subjects had to push a button with their right index finger if the hands of the first clock formed the greater angle, or their left index finger for the second. Subjects' responses were registered by a optic fibre answer box and analysed for accuracy.

As a control task, we asked subjects to judge which of the two times was numerically greater. Material, presentation modality and response modality were the same as in the imagery task, but the control condition required only a verbal-semantic judgement, which did not rely on the activation of imagery processes.

The two tasks were alternated in blocks of ten trials (total number of trials= 100); every trial block was preceded by the appropriate instruction. Trials were presented every five seconds. In a pre-experimental session all subjects completed an angle comparison task on visually presented pairs of

analogue clocks and several practice trials of both the imagery and the control task to become familiar with material, tasks and response modality. Following the common procedure for imagery paradigms, subjects were asked to keep their eyes closed during the scanning session. To exclude the possible confound of eye movements, subjects were also requested to keep their eye position steady. Control scans with open eyes and infrared eye-tracking were performed on two subjects (see results section).

FMRI data acquisition

A time-series of 105 functional volumes was acquired using a BOLD sensitive single shot Echo Planar (EPI) sequence (TE =66 msec; FA = 90° ; matrix size =128 X 128) with an interscan temporal spacing of 5 s. Each functional volume consisted of 15 slices, with a thickness of 4 mm and a FOV of 180 mm x 180 mm, located along oblique planes parallel to the plane crossing the anterior and posterior commissure.

Each functional time-series consisted of 5 "resting" volumes (25 sec, discarded from further analysis) followed by 100 acquisitions during which the imagery condition was periodically alternated with the corresponding control condition every 10 acquisitions (every 50 s).

3.4 Results

Behavioural results

Subjects performed the imagery task without difficulties, and none of them made more than three errors (mean correct responses: 47.5±2.3). The "semantic" task proved to be slightly easier than the imagery task (mean correct responses: 48.3±1.4). However, the difference between the two tasks was not significant (t= 2; p= NS).

FMRI results

The contrast between imagery and control conditions yielded an increase of the BOLD signal in several parietal and frontal regions. The individual correlation maps (r>0.5) showed a bilateral activation in the IPS (BA 7), in the fronto-basal region centered on the ascending ramus of the lateral sulcus and on parts of the inferior frontal gyrus (BA 45), and in the anterior insula in all subjects. The middle frontal gyrus including the dorsolateral prefrontal cortex (DLPFC, BA 6, 8) was bilaterally activated in 5/7 subjects, the superior frontal gyrus including the supplementary motor area (SMA) in 4 volounteers, and the frontal eye fields in 3. The inferior occipito-temporal region (BA 37) was also activated (4/7 left, 3/7 right).

The analysis of the averaged correlation map (n=7, r>0.25) confirmed the main results of the individual analysis. The largest clusters of activation were located bilaterally along the IPS. Foci of activation were found in the superior, inferior and anterior portions of the IPS (Figures 3.1 and 3.2A, Table 3.1). Smaller foci of activity were also visible in the inferior frontal and perisylvian region of both sides (Table 3.1). These areas of group activation correspond to those that were found consistently in the individual correlation maps. The DLPFC, SMA, FEF and the occipito-temporal cortex, which were activated only in some volunteers (see Figure 3.2B), did not appear in the averaged map with the selected rigorous threshold.
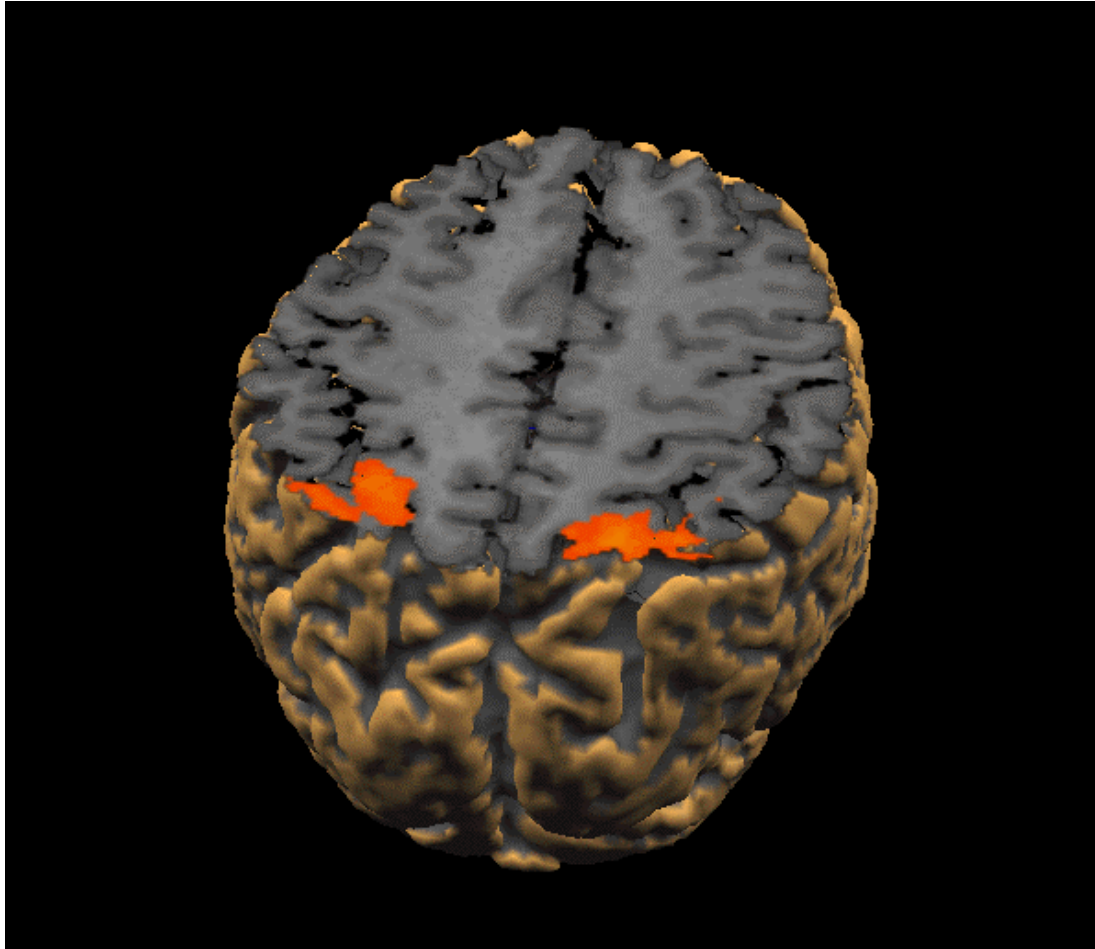
Figure 1: 3D correlation map in Talairach space (axial cut at z=44) of BOLD contrast during experimental versus control conditions averaged over seven subjects and superimposed on an individual normalized surface-rendered brain (left hemisphere on left side). The prominent bilateral clusters of activation in the upper intraparietal sulcus area are clearly visible. Activation thresholded at r>0.5 ($p<10^{-5}$; uncorrected).
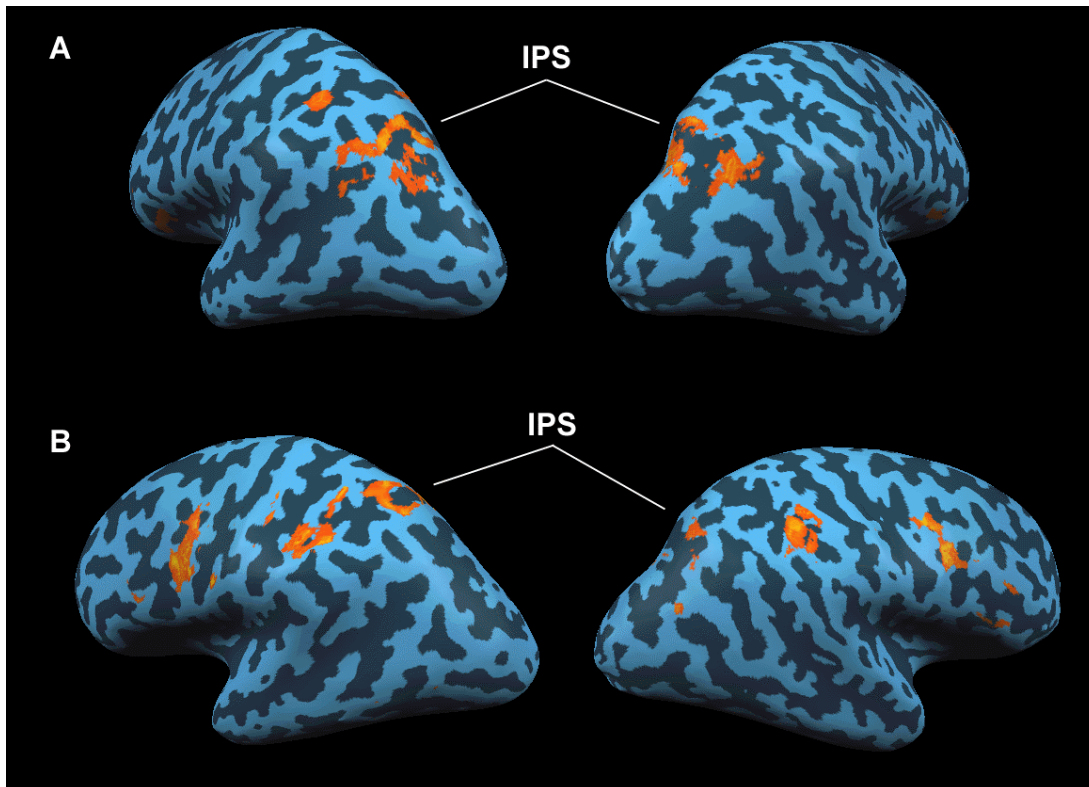
Figure 2: Correlation maps of average and individual BOLD signal during experimental versus control conditions superimposed on inflations of the two hemispheres of a surface-rendered individual 3D anatomy (left hemisphere on left side). (A) The same map as in Figure 1, postero-lateral view (r>0.25). The lines indicate the clusters of activation in the upper intraparietal sulcus. (B) Individual 3D correlation map, lateral view (r>0.5; $p<10^{-5}$; uncorrected). In addition to the spatial transformation area in the intraparietal sulcus, prominent activation is also present in the anterior superior parietal lobe and the dorsolateral prefrontal cortex. Note that the IPS activation in the right individual map matches that obtained by group analysis. However, in the left hemisphere the individual results (more rostral) differ from those of the group analysis (within the range of variability described in Table 3.1). This underlines the importance of a combination of individual and group statistics.

Anatomical area	Brodmann areas	X	Y	Z	No. of voxels	r
Left upper IPS	7	-24 (-20±4,35)	-70 (-74±3,37)	44 (42±4,24)	243	0.73
Right upper IPS	7	22 (21±2,50)	-76 (-75±2,71)	43 (42±0,82)	261	0.72
Left lower IPS	7	-22 (-23±2,08)	-72 (-76±4,79)	31 (33±2,58)	53	0.63
Right lower IPS	7	24 (25±1,83)	-80 (-78±2,75)	31 (33±1,73)	52	0.63
Left anterior IPS	7	-31 (-33±3,16)	-48 (-46±4,43)	38 (34±2,75)	77	0.64
Left perisylvian	45/ insula	-31 (-33±5,51)	23 (22±3,06)	12 (8±4,00)	39	0.58
Right perisylvian	45/ insula	44 (43±4,51)	16 (17±2,52)	4 (5±1,73)	96	0.57

Table 3.1: Locations, extension and significance of the activated brain areas during the "imagery vs. semantic comparison" task.

The position of each area is given as the Tailarach coordinates of the centre of mass of the supra-threshold (r>0.25) clusters in the 3D-average map. Additionally, the mean values (± s.d. of 7 subjects) of the Tailarach coordinates of the centre of mass of each cluster as selected in the individual correlation maps (r>0.5; p<10^{-5}; uncorrected) are reported in brackets. The comparison of these values shows that each centre of mass of a cluster in the average map lies within two standard deviations of the distribution of the centres of mass of the respective clusters in the individual maps. The number of voxels was used to quantify the extension of the areas. R indicates the cross-correlation coefficient between the reference vector and averaged time-courses of the area averaged across subjects.

Eye movements

The experiment was repeated with two subjects, who were requested to keep their eyes open, while their eye movements were monitored by the fMRI compatible Ober2 (Permobil Meditech, Timra, Sweden) infrared eye tracking system (Aisenberg 1996), sampling the horizontal and vertical positions of both eyes at 120 Hz. This system has already been used for fixation control in a recent study of attentional effects on fMRI activity in human MT/MST

(O'Craven 1997). We could thus confirm that subjects maintained fixation during the entire experiment.

The magnetic artefacts produced by the eye monitoring device affected the quality of the EPI signal, but only in areas anterior to the clusters of activation described above. The BOLD activation pattern during eye monitoring did not differ significantly from that reported above.

3.5 Discussion

The mental clock test requires the generation of multipart mental images (Trojano and Grossi 1994). These mental images served as the substrate of a spatial comparison task, which all of our subjects performed at a high level of accuracy. The related metabolic activation of the cerebral cortex (as measured by an increase of the fMRI BOLD signal) was most prominent in the posterior parietal lobes of both hemispheres. Additional activation was observed in occipitotemporal and anterior perisylvian areas. However, no activity was observed in the primary visual cortex at the selected rigorous threshold.

The absence of imagery-related PVC activation has some impact on the debate on the cortical representations of mental imagery because the present study employed a behavioural on-line control to ensure the actual generation of mental images. Our results therefore confirm the recent findings that certain imagery conditions, particularly those which rely on abstract patterns and schematic figures require the activity of primary visual areas only to a small extent (Goebel et al. 1998a) or not at all (Mellet et al. 1996). Furthermore, it is worth noting that some but not all of our subjects showed an activity in BA 37, which has been identified as the possible specific neural correlate of the generation of object mental images (D'Esposito et al. 1997). This finding confirms that BA 37 may play a rôle in different kinds of imagery tasks but would suggest that this area is not specifically involved in spatial analysis.

Activation of the inferior frontal cortex was observed in PET studies of grasp observation (Rizzolatti 1996), imagined grasping (Grafton et al. 1996), and imagined construction of 3D-objects (Mellet et al. 1996). Our finding of activation of the inferior frontal gyri during the imagery condition of the mental clock test suggests that this area is involved in spatial mental imagery even when the task does not explicitly require motor imagery. The activation of the DLPFC, which was observed in a number of our subjects, has been associated with the attentional demand involved in different kinds of mental imagery (Mellet et al. 1996; Goebel et al. 1998a) and with tasks of working memory (Ungerleider et al. 1998).

Activation of posterior parietal areas has been related to the spatial transformation of visually presented stimuli (Cohen 1996; Alivisatos and Petrides 1997). In a recent PET study of mental rotation (Alivisatos and Petrides 1997) the left inferior parietal cortex and the right postero-superior parietal cortex were seen to participate in the processing of mirror images of letters or digits. Activation of the superior parietal lobule and of the intraparietal sulcus in both hemispheres (but more consistently in the left) has been described in a recent fMRI study of the analysis of spatially transformed words and phrases, which also separated this spatial transformation-related activation from general attentional effects (Goebel et al. 1998b; see chapter 2). The main foci of spatial transformation-related activation were located in the superior parts of the intraparietal sulci in very close proximity to the largest clusters in the average analysis of the present study (within one standard deviation, see Tables 3.1 and 1.1). The construction of three-dimensional mental images from auditory instructions, as studied by PET (Mellet et al. 1996), involved a distributed system of frontal, occipital, and parietal areas. The parietal activation, however, was most prominent in the right precuneus and supramarginal gyrus and did not involve the IPS region. This absence of IPS activation might reflect the specific nature of the task of Mellet et al. (1996), which did not require the spatial comparison between objects and was not performed through mental rotation.

The majority of earlier studies of mental rotation and related tasks suffered from the possible confound of saccade-related activation in the parietal lobe (Milner and Goodale 1995). The spatial transformation-related activation of

the IPS region that was observed by Goebel et al. (1998b) could be separated from the activity related to overt (saccades) and covert attention shift by additional control tasks and correlation analysis of the BOLD signal time course. In the present study, we excluded the contribution of saccadic activity to the task-related BOLD signal changes by controlling eye movements during the scanning session.

Goebel et al. (1998b) identified a "spatial transformation area" in the parietal lobe. Their spatial transformation task, as well as those of Alivisatos and Petrides (1997) and Cohen et al. (1996), was performed on visually presented material. The present study shows that the same area in the superior IPS is active when the spatial task is performed on mental images. This similarity of activation patterns can be explained in two ways: The superior IPS might be instrumental in the computation of spatial transformations, regardless of whether the material is present in the visual field or merely as a mental image. Alternatively, any spatial transformation task, whether it involves visually perceived or imagined material, might require the implicit generation of mental visual representations (Kosslyn and Sussmann 1995).

In sum, whilst this study did not address the separation of the single subcomponents of spatial mental imagery (Trojano and Grossi 1994), the comparison of our results with those of recent studies of spatial transformations of visually presented material indicates that the analysis of visual space in perception and imagery has a common neural basis in the parietal lobes. It can be suggested that the neural networks involved in the processes of spatial transformation might be shared by several cognitive functions, including visual spatial imagery.

Chapter 4: General discussion

Subjects who wore inverting and mirror spectacles over periods of six to ten days, showed a rapid visuomotor adaptation and were able to interact correctly with the surrounding world after a few days. This adaptation was not accompanied by a return of upright vision, as assessed by their own introspective reports, reading performance and the extraction of three-dimensional shape from shading, nor was any change in the retinotopy of early visual areas observed in the functional magnetic resonance images. In addition, it took subjects only minutes to re-adapt to the canonical visuomotor patterns when the goggles had been removed. This dissociation of visuomotor and perceptual adaptation contradicts established views about the changes brought about by inversions of visual input. It does, however, confirm an analysis of the inversion studies that regards the reports of upright vision to refer to reinterpretations of the inverted visual image rather than genuine inversions of the orientation of the perceived image. Since Stratton's first reports, psychologists and physiologists alike have been searching to explain the ability of the adult brain to reverse the visual world within one week in order to restore upright vision. Like Leonardo da Vinci in his quest for the second crossing (see Gregory 1998a), they might have been pursuing yet another mythical mechanism.

Chapter 1 shows that the short-term adaptation to a rotated or reverted visual world does not rely on perceptual inversion and does not produce changes in the retinotopic maps of the occipital cortex. Yet adaptation, for example of motor and reading function, does take place. The design of conditions that emulate the cognitive tasks faced by subjects with mirror vision for functional brain imaging experiments allowed the investigation of the cortical mechanisms that subserve such adaptive processes. The results of our (chapter 2) and other recent functional imaging studies show that areas in the parietal lobes are instrumental in the execution of the coordinate transformations that are required for complex visual and visuomotor tasks on material that is presented in a distorted or non-canonical manner. It was crucial for the interpretation of these cognitive experiments to separate the

parietal areas for visuospatial transformation from the attentional and oculomotor networks. Using functional neuroimaging, we could thus contribute to the debate in cognitive psychology on the possibility of the separation of mental rotation and oculomotor control (Milner and Goodale, 1995). The work of Koriat et al. on reaction times in reading and recognition of rotated words and letters (Koriat and Norman 1985; Koriat et al. 1991) indicated the possibility that tasks of image matching and image transformation require the implicit contribution of visual mental imagery (Kosslyn and Sussman 1995). Our results on the overlap between the cortical systems that subserve the reading of transformed letterstrings and the matching of *imagined* clocks (chapter 3) converge with these behavioural data. Kosslyn and Sussman (1995) suggested that "there is no such thing as immaculate perception". Although the dissociations between perceptual and imagery deficits observed in patients with brain lesions urge caution against the view that all of visual perception relies on the ability to generate mental images, it can certainly be agreed that imagery "may play an integral role in perception".

The convergent evidence from functional imaging studies of different paradigms of visuo-spatial analysis, including both visually presented and imagined material, is also important on methodological grounds. The studies that formed the basis for chapters 2 and 3 employed cognitive subtraction paradigms. An experimental task that involved spatial analysis was compared to a control task on the same material that did not. The interpretation of the functional imaging results relies on the assumption that the subtraction of the control condition from the experimental condition (formalized in the 1-0 box-car reference function) yields the component of cerebral activation that is specific for or can be attributed to the function of interest, in this case spatial analysis. This approach is potentially very useful for avoiding the contamination of activation data by unspecific effects, but suffers from two inherent drawbacks. The control task, in order to be behaviourally controllable, must involve a cognitive component of its own and therefore cannot simply be defined as the experimental task minus the specific cognitive component of interest. Secondly, the cognitive subtraction

approach assumes that the cognitive components of a task add up linearly (pure insertion). But it cannot be excluded that these components interact. In this case it would be difficult to separate a specific cognitive function and its neuronal substrate from the other components of a task (Friston et al. 1996). This difficulty can be overcome by factorial (Friston et al. 1996) or parametric (Cohen 1997; Büchel et al. 1998) designs of functional imaging studies. Alternatively, like in the present series of studies, one can combine evidence from the comparison between different experimental and control conditions that all aim at the isolation of the cognitive function of interest. In the present case, both the contrast between mirror and conventional reading and that between the spatial comparison of mental clocks and the assessment of numerical order resulted in an activation of specific parietal lobe areas. This convergence of activation results from different studies increases the probability of specific effects related to the investigated function over that of unspecific subtraction effects. Yet it will be desirable to pursue the investigation of the mental clock paradigm using

a) a control condition that is matched not only for difficulty (as in the present study) but also for reaction time and attentional demand

b) a parametric design that overcomes the disadvantages of cognitive subtraction paradigms using pairs of times at different degrees of difficulty (Paivio, 1978). In functional imaging studies, this approach will involve a departure from the classical block design and the use of an event-related single-trial design (Munk et al., 1998; Linden et al., 1998).

The results reported in chapters 2 and 3 thus confirm that imagery and perception share partly overlapping cortical structures (Frith and Dolan, 1997; Mellet et al., 1998). On the basis of the lesion and functional imaging studies of the involvement of striate and extrastriate cortical areas, Farah (1995) suggested that "mental imagery is the efferent activation of some subset of the brain's visual areas, subserving the same types of functions (what, where, color, spatial attention, and so on) in imagery and in perception." Our finding of closely overlapping activation of parietal spatial transformation areas during perceptual (chapter 2) and imagery (chapter 3) tasks indicates

that this theory might also hold true for the higher areas of visual processing in the parietal lobe.

The relationship of the functional imaging results reported here to the neuropsychological lesion literature deserves particular attention. We confirmed the lesion-based evidence for a specific spatial transformation system in the parietal lobe that is anatomically separate from the parietal eye fields (Ramachandran 1997; Turnbull and McCarthy 1996; see chapter 2). Lesion data also suggested that the recognition of objects that are presented in a non-canonical orientation requires co-operation of this parietal spatial transformation system with occipito-temporal object recognition areas (Turnbull and McCarthy 1996; Turnbull et al. 1997; see chapter 2). This was confirmed by our finding of co-activation of areas LO and IPS during reading of transformed text (Figure 2.4). With the application of fMRI to the mental clock task (chapter 3) we were able to confirm the lesion-based hypotheses that the spatial analysis of imagined visual material involves structures in the parietal lobes bilaterally (Grossi et al., 1989; Grossi et al., 1993) and that these structures are distinct from those that subserve the mere generation of visual images (Luzzatti et al, 1998). Such a confirmation of neuropsycho-logical data by functional neuroimaging is essential for the evaluation of the rôle of that lesion-based hypotheses can play in the investigation of the normal human brain.

The comparison of the cortical systems for the spatial transformation of visually presented material and overt and covert attention shifts shows a considerable overlap in frontal and parietal areas, but also clear specializa-tions in the IPS spatial transformation areas (chapter 2). The performance of spatial matching operations on imagined material, on the other hand, seems to rely on a subset of the respective perceptual system (chapter 3). Further work is needed to elucidate the mutual interactions of visual perception and visuospatial imagery and the extent to which the two can be separated. Ultimately, this work will benefit from a combination of the most advanced functional neuroimaging techniques with the study of the perceptual and imagery performance of patients with parietal lobe damage.

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Zusammenfassung

Die vorliegende Dissertation berichtet über eine Serie von Verhaltens- und funktionellen Bildgebungsstudien zu experimentalpsychologischen Paradigmata, die eine räumliche Analyse und Koordinatentransformation von Material der visuellen Wahrnehmung oder Vorstellung beinhalten. Nach einer Einführung in die Prinzipien und Techniken der funktionellen Kernspintomographie, der hier benutzten Methode für die Messung von Gehirnaktivität, werden die Versuche einer Replikation des berühmten Stratton'schen Umkehrbrillen-Experiments dargestellt (Kapitel 1). Unsere vier Probanden zeigten zwar eine zügige Anpassung der visuomotorischen Funktionen an die neue visuelle Umwelt, berichteten aber, anders als Stratton, nicht, daß sie die Welt nach einigen Tagen mit der Umkehrbrille wieder normal sähen. Diese Persistenz des umgekehrten Bildes wurde durch eine psychphysische Testbatterie bestätigt. Des weiteren ergaben die funktionellen Kernspinmessungen, daß sich die kortikale retinotope Organisation im Verlaufe des Experiments nicht geändert hat. Da sich also Strattons Haupteffekt, das Aufrechtsehen durch die Umkehrbrille nach einwöchiger Adaptation, nicht replizieren ließ, werden andere Möglichkeiten der Interpretation der verschiedenen Umkehrexperimente der letzten hundert Jahre vorgeschlagen.

Dieses Ergebnis einer funktionellen Anpassung ohne größere Änderungen der visuellen Wahrnehmung (und ohne Veränderungen der Repräsentation der Netzhautareale in der Sehrinde) führte zu der Hypothese, daß die erforderlichen Transformationen auf einer höheren Stufe der kortikalen Hierarchie der visuellen Verarbeitung erfolgen. Zur Testung dieser Hypothese wurde eine funktionelle Kernspinstudie des Umkehrlesens durchgeführt (Kapitel 2). Hierbei lasen die Probanden Wörter und Sätze in Spiegelschrift oder auf dem Kopf. Der neuronale Mechanismus der räumlichen Transformationen, die zur Bewältigung dieser Aufgabe nötig sind, konnte in bestimmten Regionen des Parietallappens, die zwischen den Probanden sehr konstant waren, lokalisiert werden. Weiterhin fand sich eine Koaktivierung okzipitootemporaler Objekterkennungs-Areale. Die Spezifizität der parietalen Aktivierungsfoci wurde durch ein Kontrollexperiment bestätigt,

in welchem das kortikale System für räumliche Transformationen von den Netzwerken der allgemeinen visuellen Aufmerksamkeit und der Augen-bewegungskontrolle unterschieden werden konnte.

In einem weiteren Experiment wurden die räumlichen Funktionen des Parietallappens unter dem Vorzeichen der visuellen Vorstellung untersucht. Als Paradigma wurde der "mental clock" – Test verwendet, bei welchem die Probanden die Winkel der Zeiger zweier Uhren vergleichen müssen, deren Zeiten nur akustisch vorgegeben werden (Kapitel 3). Diese Aufgabe erfordert die Generierung eines entsprechenden Vorstellungsbildes und dessen räumliche Analyse, stellt also sowohl ein kontrolliertes Vorstellungs-Paradigma als auch einen Test räumlicher Funktionen dar, der nicht auf visuell präsentiertem Material beruht. Das parietale Aktivierungsmuster, das der Analyse der Winkel dieser vorgestellten Uhren zugeschrieben werden konnte, entsprach weitgehend demjenigen, das mit der räumlichen Transformation von Buchstaben verbunden war. Es handelt sich also wahrscheinlich um ein kortikales System für räumliche Analyse und Koordinatentransformationen, das nicht auf eine visuelle Stimulation angewiesen ist, sondern auch bei bloßer visueller Vorstellung aktiv werden kann.

Die vorgelegten Resultate werden im Kontext neuerer neuropsychologischer Befunde zu Defiziten räumlicher Analyse und Vorstellung bei Läsionen des Parietallappens diskutiert (Kapitel 4). Auch die methodologischen Probleme der kognitiven Subtraktion, die in unseren Studien teilweise benutzt wurde, werden behandelt. Dabei wird erläutert, inwiefern diese für die Beurteilung der vorgelegten Studien nur von untergeordneter Bedeutung sind. Nichts-destoweniger schlagen wir Modifikationen der experimentellen Paradigmata im Sinne des parametrischen Designs und des "event-related functional magnetic resonance imaging" vor, die bei zukünftigen Studien einen vollständigen Verzicht auf die kognitive Subtraktion ermöglichen dürften. Schließlich wird die Bedeutung der vorgelegten Ergebnisse für die Erforschung der Anpassungsfähigkeit des menschlichen Gehirns und des Verhältnissses von Vorstellung und visueller Wahrnehmung dargelegt.

Summary

This thesis reports a series of behavioural and functional neuroimaging studies of cognitive tasks that require the spatial analysis and transformation of visually presented and imagined material. After an introduction to the principles and techniques of functional magnetic resonance imaging, the tool for the assessment of brain activation used in these studies, we describe the attempt to replicate Stratton's famous experiment with inverting spectacles (chapter 1). Our four subjects showed rapid adaptation of visuomotor functions, but, unlike Stratton, did not report return of upright vision. The persistence of the transformed visual image was confirmed by the subjects' perception of shape from shading and other psychophysical tests in the laboratory. No alteration of the retinotopy of early visual cortical areas was seen in the functional magnetic resonance images. These results are discussed in the context of previous claims of upright vision with inverting prisms and mirror spectacles.

This result of functional adaptation without major perceptual changes (and without changes of the retinal representation in the early visual cortical areas) led to the hypothesis that the required transformations might be subserved by cortical areas that occupy a higher place in the visual processing hierarchy. We therefore performed an fMRI study of reading of words and phrases in non-canonical orientations (chapter 2). The execution of this task of visuospatial transformation was accompanied by an activation of areas in the intraparietal sulcus whose location was highly consistent between subjects. It also involved areas in the lateral occipital lobe that are known to contribute to the processing of visual objects, confirming lesion data that suggest that the co-operation of these parietal and occipito-temporal areas is required for the spatial transformation of visually presented material. The task-specificity of the foci in the intraparietal sulcus was demonstrated by a control experiment that involved covert and overt attention shifts and allowed us to separate the cortical system for visuospatial transformations from that for visual attention.

In order to obtain converging evidence for the localization of the cortical system for spatial analysis and to decide whether this system requires visual

input for its activation we applied functional magnetic resonance imaging to the mental clock task (chapter 3). This behaviourally controlled mental imagery paradigm consists in the acoustic presentation of pairs of clock times and requires the subjects to choose the one in which the hour and minute hand form the larger angle. The performance of this task was accompanied by an activation of the very same areas along the intraparietal sulcus that were active during the mirror reading task. This result suggests that at least some of the spatial transformation areas of the human cerebral cortex do not require visual stimulation for their activation, but are also recruited when tasks of coordinate transformations or angle comparison are performed on imagined material.

The results of these three studies are then discussed in the context of recent neuropsychological findings of deficits in spatial transformations and imagery in patients with parietal lobe lesions (chapter 4). Furthermore, the methodological problems of cognitive subtraction paradigms are evaluated for their impact on the present studies. We suggest possible modifications of the experimental design for future studies that are made possible by recent advances in event-related functional magnetic resonance imaging. Finally, we discuss the contribution of the presented results to a number of current topics in cognitive and neuropsychology, such as the functional plasticity of the human brain and the relationship between visual perception and imagery.

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