Neuropsychologia 47 (2009) 59–69

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Egocentric memory impaired and allocentric memory intact as assessed by virtual reality in subjects with unilateral parietal cortex lesions

Godehard Weniger[a,b], Mirjana Ruhleder[a,c], Stefanie Wolf[a,c], Claudia Lange[a,c], Eva Irle[a,c,*]

[a] Department of Psychiatry and Psychotherapy, University of Göttingen, Von-Siebold-Str. 5, D-37075 Göttingen, Germany
[b] Department of Social and General Psychiatry, University of Zürich, Switzerland
[c] Department of Psychiatry and Psychotherapy, University of Göttingen, Germany

ARTICLE INFO

Article history:
Received 18 May 2008
Received in revised form 29 July 2008
Accepted 15 August 2008
Available online 22 August 2008

Keywords:
Navigation
Virtual park
Virtual maze
3D MRI
Inferior parietal cortex
Precuneus

ABSTRACT

Present evidence suggests that medial temporal cortices subserve allocentric representation and memory, whereas egocentric representation and memory mainly depends on inferior and superior parietal cortices. Virtual reality environments have a major advantage for the assessment of spatial navigation and memory formation, as computer-simulated first-person environments can simulate navigation in a large-scale space. However, virtual reality studies on allocentric memory in subjects with cortical lesions are rare, and studies on egocentric memory are lacking. Twenty-four subjects with unilateral parietal cortex lesions due to infarction or intracerebral haemorrhage (14 left-sided, 10 right-sided) were compared with 36 healthy matched control subjects on two virtual reality tasks affording to learn a virtual park (allocentric memory) and a virtual maze (egocentric memory). Subjects further received a comprehensive clinical and neuropsychological investigation, and MRI lesion assessment using T_1, T_2 and FLAIR sequences as well as 3D MRI volumetry at the time of the assessment. Results indicate that left- and right-sided lesioned subjects did not differ on task performance. Compared with control subjects, subjects with parietal cortex lesions were strongly impaired learning the virtual maze. On the other hand, performance of subjects with parietal cortex lesions on the virtual park was entirely normal. Volumes of the right-sided precuneus of lesioned subjects were significantly related to performance on the virtual maze, indicating better performance of subjects with larger volumes. It is concluded that parietal cortices support egocentric navigation and imagination during spatial learning in large-scale environments.

1. Introduction

Currently, spatial navigation and memory is modelled as a process supported by allocentric (i.e., world-centred) spatial representations, being independent to the observer, and egocentric (i.e., body-centred) spatial representations, which relate to the body axes (O'Keefe & Nadel, 1978). Allocentric spatial representations include prominent and salient environmental features ('places') that may serve as navigationally relevant locations for the purpose of spatial orientation and memory storage. On the other hand, egocentric spatial representations include the sensorimotor representation of whole-body, head and gaze motion, the mental representation of distance, time and number of routes that have been travelled, and the temporo-spatial relationship of all information.

A number of studies have reported that individuals with medial temporal lobe damage are impaired in finding their way within their locomotor environment ('topographical disorientation and amnesia') (Abrahams, Pickering, Polkey, & Morris, 1997; Astur, Taylor, Mamelak, Philpott, & Sutherland, 2002; De Renzi, Faglioni, & Villa, 1977; Landis, Cummings, Benson, & Palmer, 1986; Maguire, Burke, Phillips, & Staunton, 1996; Spiers, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2001b). Single case studies provided evidence that bilateral hippocampal lesions are associated with allocentric memory impairment (Holdstock, Mayes, Cezayirli, Aggleton, & Roberts, 1999; Holdstock et al., 2000; King, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2002; Maguire, Nannery, & Spiers, 2006; Spiers, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2001a), whereas other studies reported the right parahippocampal gyrus as the common area of damage across cases (Bohbot et al., 1998; Epstein, DeYoe, Press, Rosen, & Kanwisher, 2001; Habib & Sirigu, 1987; Nyffeler et al., 2005).

Topographical disorientation and amnesia were also reported in the presence of parietal (Barrash, Damasio, Adolphs, & Tranel, 2000; Cogan, 1979; De Renzi et al., 1977; Suzuki, Yamadori, Hayakawa, & Fujii, 1998) and retrosplenial (Maguire, 2001) lesions. However, individuals with topographical disorientation or amnesia vary with respect to specific spatial deficits (Aguirre & D'Esposito, 1999).

* Corresponding author. Tel.: +49 551 398950; fax: +49 551 3912712.
E-mail address: eirle@gwdg.de (E. Irle).

0028-3932/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2008.08.018

Bilateral parietal lesions seem to be frequently related to a form of egocentric disorientation or amnesia, implying deficits to localize visual space, to orientate properly towards objects in space, to track and reach objects in space, or to form new topographical memories (Cogan, 1979; Kase, Troncoso, Court, Tapia, & Mohr, 1977; Levine, Warach, & Farah, 1985; Stark, Coslett, & Saffran, 1996; Wilson et al., 2005). Functional imaging studies frequently reported parietal cortex activations in topographic navigation tasks, although to a larger degree in tasks demanding position judgments when compared with tasks demanding landmark recognition (Aguirre & D'Esposito, 1997; Aguirre, Detre, Alsop, & D'Esposito, 1996; Burgess, Maguire, Spiers, & O'Keefe, 2001; Epstein, Graham, & Downing, 2003; Maguire, Frackowiak, & Frith, 1997).

So far, the majority of studies investigating topographical orientation and memory in individuals with brain damage relied on clinical descriptions, or used traditional neuropsychological paper and pencil tests. More recently, studies tried to assess topographical learning using complex real life surroundings (Barrash et al., 2000; Bohbot et al., 1998; Epstein et al., 2001; Maguire et al., 1996). The development of virtual reality technology has brought a major progress to the study of spatial navigation and memory. Virtual realities have a major advantage for the assessment of spatial navigation and memory formation, as computer-simulated first-person environments can simulate navigation in a large-scale space. There are now a large number of studies investigating allocentric memory in healthy individuals using virtual reality environments and functional imaging (e.g., Aguirre & D'Esposito, 1997; Aguirre et al., 1996; Burgess et al., 2001; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003). However, studies on egocentric representation and memory of visual space using virtual reality environments are lacking.

In the present study, we studied neuropsychological and virtual reality task performance of 24 subjects with unilateral parietal cortex lesions due to infarction or haemorrhage and 36 healthy comparison subjects. Two virtual reality tasks affording the navigation in a virtual park (allocentric memory) and a virtual maze (egocentric memory) were applied. The goals of our study were (a) to test the suitability of virtual reality environments for the assessment of spatial memory in subjects with cortical lesions, (b) to assess whether subjects with parietal cortex lesions are impaired in learning the virtual maze, (c) to assess whether subjects with parietal cortex lesions are impaired in learning the virtual park, and (d) to analyse whether lesion characteristics such as size, laterality, and the exact location of lesions are related to virtual reality task performance of subjects with parietal cortex lesions.

2. Methods

2.1. Participants

2.1.1. Subjects with parietal cortex lesions

The study group comprised 24 subjects with focal parietal cortex lesions (14 left-sided, 10 right-sided), due to infarction or intracerebral haemorrhage within the territory of the medial cerebral artery (Tables 1 and 2). Screening the MRT records of the neurological department of the University of Göttingen identified subjects. Subjects older than 70 years, with a native tongue other than German, or with a history of psychiatric or other neurological disease were excluded. Only subjects with lesions covering substantial parts of the parietal cortex were included. Subjects were assessed at least 12 months after onset of clinical symptoms.

2.1.2. Healthy controls

Subjects with parietal cortex lesions were compared with 36 healthy control subjects recruited for the study by an advertisement in a local newspaper (Table 1). Only subjects without a history of neurological or psychiatric disorder were studied. Subjects were paid for their participation and matched subjects with parietal cortex lesions in terms of age, sex, and years of education.

After complete description of the study to the subjects informed written consent was obtained. The Ethical Committee of the Medical Faculty of the University of Göttingen had approved of the study design.

2.2. Lesion analysis

2.2.1. MRI acquisition and analysis

Subjects received MRI scanning using a 1.5-T Philips Gyroscan machine at the day of the assessment, including T_1, T_2 and FLAIR sequences. Scanning parameters of the T_1-weighted three-dimensional sequence were as follows: TE = 6.0 ms; TR = 24.0 ms; flip angle = 30°; FOV = 256; slice plane = sagittal; matrix = 256 × 256; slice thickness = 1.3 mm; slice number = 130; acquisition mode = three-dimensional. Volumetric analysis was done on the basis of 3D-MRIs. The images were transferred to a computer workstation and processed using the CURRY® software (version 4.5; Neurosoft Inc., El Paso, Tex.). Images were reformatted into continuous 1-mm thick slices. Intracranial volume and regional brain volumes were calculated with automated multistep algorithms and 3D region-growing methods that are limited by grey value thresholds. Simultaneous 3D visualization of brain structures and manual tracings allowed a precise identification and delineation of regions of interest. All regions of interest included grey and white matter volumes.

2.2.2. Parietal cortex lesion size

2.2.2.1. Precuneus. The anterior border of the precuneus was defined by the postcentral sulcus, the posterior border by the parietooccipital sulcus, the ventrolateral boundary by the intraparietal sulcus and the inferior medial border by a line passing through the cingulate/subparietal sulcus that extended into the parietooccipital sulcus. Manual markings were made on coronal slices by drawing a straight line between the intraparietal sulcus and the cingulate/subparietal sulcus and its posterior extension. The resulting volume (Fig. 1) includes precuneus and related superior parietal cortices (Brodmann areas 5, 7 and 31).

2.2.2.2. Postcentral gyrus. The anterior border of the postcentral gyrus was defined by the central sulcus. On the medial surface, a line vertical to the AC–PC line was drawn between the central and cingulate sulcus. The posterior border was defined by the postcentral sulcus, the ventrolateral border by the Sylvian fissure and the inferiomedial border by the posterior cingulate sulcus. Manual markings were made on coronal slices by drawing a straight line between the central and postcentral sulcus. The resulting volume (Fig. 1) includes the primary somatosensory cortex (Brodmann areas 1–3).

2.2.2.3. Inferior parietal cortex. The anterior border of the inferior parietal cortex was defined by the postcentral sulcus, the dorsal border by the intraparietal sulcus and the ventrolateral border by the Sylvian fissure. A line passing through the Sylvian fissure was extended in the same orientation posteriorly and served as post-Sylvian ventrolateral boundary. An oblique plane orientated along the length of the parieto-occipital sulcus defined the posterior border. Manual markings were made on coronal slices by drawing a straight line between the Sylvian fissure/post-Sylvian boundary and the intraparietal sulcus. The resulting volume (Fig. 1) includes the supramarginal and angular gyri (Brodmann areas 39 and 40).

In a previous study (Irle, Lange, Weniger, & Sachsse, 2007), sufficient intrarater and interrater reliabilities have been obtained. The intraclass correlation coefficients for this procedure were $r = 0.99$ (intrarater) and $r = 0.95$ (interrater) for the precuneus, $r = 0.99$ (intrarater) and $r = 0.98$ (interrater) for the postcentral gyrus and $r = 0.96$ (intrarater) and $r = 0.93$ (interrater) for the inferior parietal cortex.

2.2.3. Parietal cortex lesion localization

Lesion territories were localized by one of us (E.I.) who was unaware of the results of the behavioural assessments. MR scans of the present assessment as well as MR and CT scans obtained at the time of the insult were used for lesion localization. Lesion areas were mapped onto appropriate atlas templates (Talairach & Tournoux, 1988), and involvement of cortical (Brodmann areas) as well as subcortical regions was assessed. Table 2 summarizes lesioned cortical areas for individual subjects, and gives the Talairach coordinates of the lesion centre. In three subjects with parietal cortex lesions, the T_1-weighted three-dimensional sequence could not be obtained. Parietal cortex size reduction in these subjects (Table 2) was estimated by calculating areas covered by the lesion in each slice using a standard grid, and by summing up these areas across slices.

2.3. Neuropsychological assessment

Subjects received a comprehensive neuropsychological assessment of intellectual, attentional and mnemonic performance with special emphasis on spatial functioning. A short form of the *Wechsler Adult Intelligence Scale-Revised* (*WAIS-R*) (Tewes, 1991) was given to derive an estimate of general intellectual capacity. Memory was assessed with the *Wechsler Memory Scale-Revised* (*WMS-R*) (Wechsler, 1987). Spatial performance was assessed with four subtests (dot counting, position discrimination, number location, and cube analysis) of the German version of the *Visual Object and Space Perception Battery* (*VOSP*; Beckers & Canavan, 1992; Warrington & James, 1991), one subtest (remembering a short route, immediate) of the *Rivermead Behavioural Memory Test* (*RBMT*; Wilson, Cockburn, & Baddeley, 1992), and one subtest (city map) of the *Lern-und Gedächtnistest-3* (*LGT-3*; Bäumler, 1974), which affords to memorize a complex route marked on a city map. Subjects had

Table 1
Demographic and clinical characteristics of all subjects

Characteristic	Subjects with left-sided parietal cortex lesions ($n = 14$)	Subjects with right-sided parietal cortex lesions ($n = 10$)	Control subjects (n = 36)	Statistic	P
Age (years)	59 ± 9	59 ± 11	58 ± 9	$\chi^2 = 0.20$	0.931[a]
Education (years)	9.3 ± 1.3	9.3 ± 2.3	9.6 ± 1.7	$\chi^2 = 0.52$	0.771[a]
Handedness, right:left	10:4	8:2	32:2		0.077[b]
Sex, female:male	5:9	5:5	17:19		0.761[b]
Lesion aetiology, ischemia:haemorrhage	13:1	8:2			0.550[b]
Duration since symptom onset (mo)	21 ± 8	19 ± 10		$U = 45.5$	0.393[c]
Intracranial volume (ml)	1482 ± 99	1464 ± 103	1499 ± 141	$\chi^2 = 0.54$	0.764[a]
Left precuneus volume (ml)	24 ± 7[d]	24 ± 5[d]	30 ± 7	$T(2) = 10.16$	**0.006**[e]
Left postcentral gyrus volume (ml)	13 ± 3[d]	15 ± 3[f]	16 ± 3	$T(2) = 7.17$	**0.028**[e]
Left inferior parietal cortex volume (ml)	22 ± 3	23 ± 5	24 ± 6	$T(2) = 2.85$	0.240[e]
Right precuneus volume (ml)	26 ± 9	25 ± 5	31 ± 8	$T(2) = 4.32$	0.115[e]
Right postcentral gyrus volume (ml)	14 ± 2	13 ± 2[d]	16 ± 2	$T(2) = 14.28$	**0.001**[e]
Right inferior parietal cortex volume (ml)	25 ± 5	19 ± 4[d,f]	25 ± 6	$T(2) = 11.85$	**0.003**[e]
WAIS-R, verbal IQ	107 ± 13[g]	107 ± 22	119 ± 13	$\chi^2 = 9.09$	**0.011**[a]
WAIS-R, performance IQ	115 ± 18[g]	112 ± 11[g]	126 ± 18	$\chi^2 = 6.85$	**0.032**[a]
WMS-R, verbal memory	99 ± 21[g]	110 ± 21	118 ± 14	$\chi^2 = 8.76$	**0.013**[a]
WMS-R, visual memory	113 ± 11[g]	113 ± 14[g]	123 ± 12	$\chi^2 = 10.03$	**0.007**[a]
WMS-R, delayed recall	107 ± 15[g]	115 ± 12[g]	124 ± 16	$\chi^2 = 13.11$	**0.001**[a]
WMS-R, attention/concentration	84 ± 16[g]	92 ± 18	98 ± 12	$\chi^2 = 9.82$	**0.007**[a]
VOSP, dot counting	9.8 ± 0.4	9.9 ± 0.3	9.9 ± 0.2	$\chi^2 = 2.66$	0.265[a]
VOSP, position discrimination	19.1 ± 1.4	19.9 ± 0.3	19.7 ± 0.8	$\chi^2 = 4.21$	0.122[a]
VOSP, number location	9.5 ± 0.7	9.4 ± 1.1	9.4 ± 1.5	$\chi^2 = 1.55$	0.460[a]
VOSP, cube analysis	9.1 ± 1.2	9.8 ± 0.4	9.6 ± 0.9	$\chi^2 = 4.25$	0.119[a]
Block Design (*WAIS-R*)	10 ± 2[g]	10 ± 2	12 ± 3	$\chi^2 = 8.15$	**0.017**[a]
Rivermead behavioural memory test					
Remembering a short route, immediate	4.8 ± 0.4	4.9 ± 0.3	4.9 ± 0.3	$\chi^2 = 0.19$	0.911[a]
Lern-und Gedächtnistest, City map	14.8 ± 4.2	15.3 ± 4.0	15.4 ± 5.6	$\chi^2 = 0.57$	0.753[a]
Virtual reality tasks					
Virtual park, errors	12.4 ± 6.9	11.7 ± 6.2	11.9 ± 7.3	$\chi^2 = 0.12$	0.940[a]
Virtual maze, errors	24.7 ± 7.7[g]	25.6 ± 6.2[g]	17.3 ± 9.7	$\chi^2 = 10.82$	**0.004**[a]

Table values are mean ± S.D. unless indicated otherwise. Significant differences are given in boldface type. *WAIS-R*: Wechsler Adult Intelligence Scale-Revised, Verbal IQ estimates were derived from Information and Similarities, Performance IQ estimates from Picture Completion and Block Design Scores; *WMS-R*: Wechsler Memory Scale-Revised; *VOSP*: visual object and space perception battery.

[a] Kruskal–Wallis one-way ANOVA.
[b] Fisher's exact test (two-tailed).
[c] Mann–Whitney *U*-test.
[d] Significantly different when compared with control subjects (one-way ANCOVA-type statistic adjusting for intracranial volume; $P < 0.05$).
[e] One-way ANCOVA-type statistic adjusting for intracranial volume.
[f] Significantly different when compared with subjects with left-sided lesions (one-way ANCOVA-type statistic adjusting for intracranial volume; $P < 0.05$).
[g] Significantly different when compared with control subjects (Mann–Whitney *U*-test; $P < 0.05$).

to reproduce this route about 20 min later on a similar plan. As a screening instrument for the assessment of spatial inattention or neglect the subtest 'neglect' of the computer-driven *Testbatterie zur Aufmerksamkeitsprüfung* (*TAP*; Zimmermann & Fimm, 1993) was used. This test affords subjects to detect stimuli in various locations on the screen while fixating a central target.

2.4. Virtual reality tasks

The virtual reality environments were realized using previously described techniques (Weniger & Irle, 2006). The environments were three-dimensional, fully coloured and textured and presented a first-person view. The tasks were presented on a 21-in. screen. Subjects controlled their movements with a joystick. Prior to the tasks, subjects underwent a training session in a similar virtual reality environment. There were two virtual reality tasks (virtual park, virtual maze) each replicated five times. The order of the tasks was alternated between subjects.

2.4.1. Virtual park and virtual maze

The virtual park environment (Fig. 2c and d) comprised nine points of two-way intersection and 11 cul-de-sacs. Each cul-de-sac contained a pot, but only one pot contained money. Subjects were instructed to find the shortest way to the pot with money in it. Landmarks (house, garden, car, tree, lake, river, bridge, playground, mountain, etc.) were spread throughout the environment, allowing subjects to learn routes based solely on these landmarks. The virtual maze environment (Fig. 2a and b) comprised six points of two-way intersection and seven cul-de-sacs containing pots, from which one contained money. The maze consisted of brick walls, a similarly coloured floor and a blue sky. All intersections appeared identical when approached from different directions. As the maze did not include any landmarks, egocentric navigation strategies were necessary to solve the task.

In each trial of the virtual park and the virtual maze, subjects started at the same location and then had to find the target that remained in the same location across trials. Subjects were not able to see the target or the survey perspective (cf. Fig. 2a and c) from the starting position or from other vantage points in the environments.

2.4.2. Data analysis

Subjects learning performance was characterized by the number of errors (visiting a pot not containing money) committed across trials of the virtual park and the virtual maze, respectively. After finishing the task, subjects completed a questionnaire indicating what kind of navigation strategies they used in the virtual park (storage of landmarks, or egocentric cues, or survey perspective) and the virtual maze (storage of egocentric cues or survey perspective), respectively. The questions described the specific navigation strategies and required a yes/no answer. For example, subjects were asked whether they used landmarks like mountain, house, bridge etc. to find their way to the goal (storage of landmarks), whether they tried to construct a kind of map of the virtual environment in their mind (survey perspective), or whether they tried to memorize their imagined head, body and gaze motion at different decisions or time points of the virtual environments (egocentric cues). Subjects were also given the opportunity to describe their navigation strategies in a free field response and were given oral support, since egocentric strategies are likely to be stored in an implicit manner (Weniger & Irle, 2008), requiring a free field format to translate them into verbal frames of memory. Possible side

Table 2
Lesion characteristics and virtual reality performance of subjects with parietal cortex lesions

Subject number	Lesion side	Lesion characteristics							Virtual reality performance	
		Cortical areas with lesions (Brodmann areas, BA)[a]	Lesion centre (Talairach coordinates)			Precuneus size reduction (BA 5, 7, 31)[b]	Postcentral gyrus size reduction (BA 1–3)[b]	Inferior parietal size reduction (BA 39, 40)[b]	Virtual park: total errors	Virtual maze: total errors
			X	*Y*	*Z*					
297	Left	**1–3, 5, 7, 31**, 40	−22	−36	43	43	5	0	22	33
090[c]	Left	1–3, 4, 7, 13, **40**, 41	−46	−23	26	37	2	26	3	12
270	Left	**1–3**, 4, 5, 7, **40**	−35	−30	35	32	13	13	11	16
103	Left	**1–3**, 4, 5, 7, **40**	−26	−31	39	16	14	10	25	26
258	Left	**1–3**, 4, 6, 13, **40**	−32	−16	33	0	12	26	7	31
239[c]	Left	7, **39**, **40**	−39	−27	34	14	0	38	17	22
298	Left	**13**, **22**, **39**, **40**	−50	−40	30	12	4	11	14	17
236	Left	13, 18, 19, **22**, **39**, **40**	−49	−44	30	0	17	40	4	16
099	Left	**1–3**, **4**, **6**, 7, **40**, **44**	−41	−8	35	14	46	42	3	21
205	Left	**1–3**, **7**	−34	−29	54	18	0	0	18	30
094	Left	**1–3**, **4**, 6, **7**, 40	−36	−10	38	6	31	0	14	23
299	Left	**1–3**, 7, 40	−28	−37	32	6	16	4	8	35
311[c]	Left	**1–3**, 4, 6, **13**, **22**	−45	−22	25	0	6	0	13	35
108[c]	Left	**1–3**, **40**	−37	−25	50	0	6	12	15	29
288	Right	**1–3**, 4, 6, 7, **40**	40	−26	30	0	33	34	11	21
096[c]	Right	1–3, 5, **7**	22	−34	51	16	0	0	19	27
104	Right	**1–3**, **4**, 5, 6, 7	30	−13	49	25	23	0	0	31
254	Right	**1–3**, **4**, 6	36	−15	43	0	42	0	19	24
294	Right	1–3, **13**, 22, **40**	47	−22	25	0	0	21	13	28
133	Right	**1–3**, 7, **40**	25	−32	40	0	35	17	7	15
324	Right	**1–3**, 13, 22, **39**, **40**	45	−39	24	0	18	23	16	34
112[c]	Right	**1–3**, 4	32	−25	37	0	17	0	5	30
114[c]	Right	5, 7, **39**, **40**	34	−27	35	0	0	26	11	17
241	Right	**7**, 13, **22**, **39**, **40**	38	−48	33	19	8	47	16	29

[a] Areas with substantial lesions are given in boldface type.
[b] Percentage of volume reduction in the lesioned compared with the non-lesioned hemisphere.
[c] Subcortical lacunar lesions.

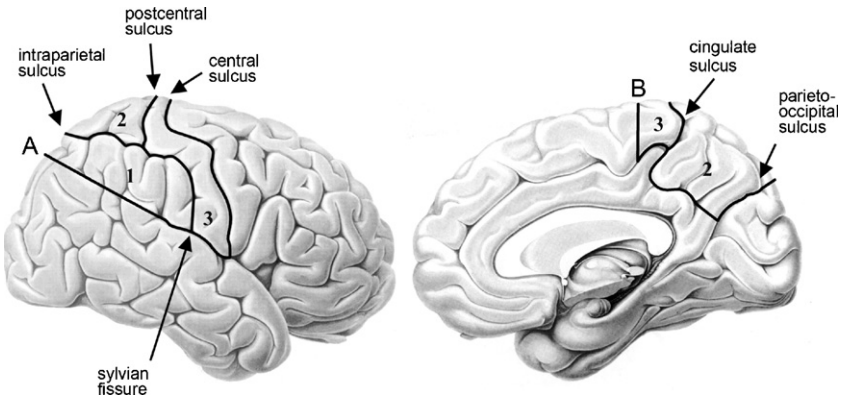

Fig. 1. Boundaries defining the inferior parietal cortex (1), precuneus (2) and postcentral gyrus (3) on the lateral (left) and medial (right) brain surface. Sulcal boundaries are labelled with black lines. A = posterior extension of the line passing through the Sylvian fissure serving as post-Sylvian ventrolateral boundary. B = vertical line connecting the central and cingulate sulcus serving as anteriomedial boundary.

effects like nausea, disorientation or oculomotor symptoms were assessed with the *Simulator Sickness Questionnaire* (*SSQ*; Kennedy, Lane, Berbaum, & Lilienthal, 1993). Subjects were further asked to rate their spatial abilities in every day life (on a five-point scale), and to describe their present experience with computers.

2.5. Statistical analysis

Kruskal–Wallis one-way analyses of variance (ANOVA) and Mann–Whitney *U*-tests were applied to compare differences between groups on demographic, clinical and neuropsychological variables, and on intracranial volume. Regional brain volumes of lesioned subgroups and control subjects were compared by non-parametric analyses of covariance (ANCOVA) (Brunner, Domhof, & Langer, 2002) adjusting for intracranial volume. Frequencies were compared using the exact test of Fisher. Performance on the virtual reality tasks was analysed by ANOVAs comparing errors of subjects with parietal cortex lesions and controls across tasks and trials. Multivariate comparisons with small sample sizes were performed using a non-parametric version of the classical mixed model (Brunner et al., 2002). Regression analyses were used to examine the relationship between regional brain volumes and virtual reality task performance.

All analyses were two-tailed, and the alpha was defined at 0.05. Statistical computations were performed using the *Statistical Analysis System* (*SAS* for Windows, Version 8.02; non-parametric ANOVAs and ANCOVAs: http//www.ams.med.uni-goettingen.de/de/sof/ld/makros.html) and the *Statistical Package for the Social Sciences* (*SPSS* for Windows, Version 14.0).

3. Results

3.1. General

Parietal cortex lesioned subjects and control subjects did not differ on age, education, handedness, and sex (Table 1). Left-sided and right-sided lesioned subjects did not differ regarding lesion aetiology and regarding the time that had elapsed since the onset of clinical symptoms.

At the time of the present assessment, residual neurological symptoms included weakness or uncoordination (subject nos. 99,

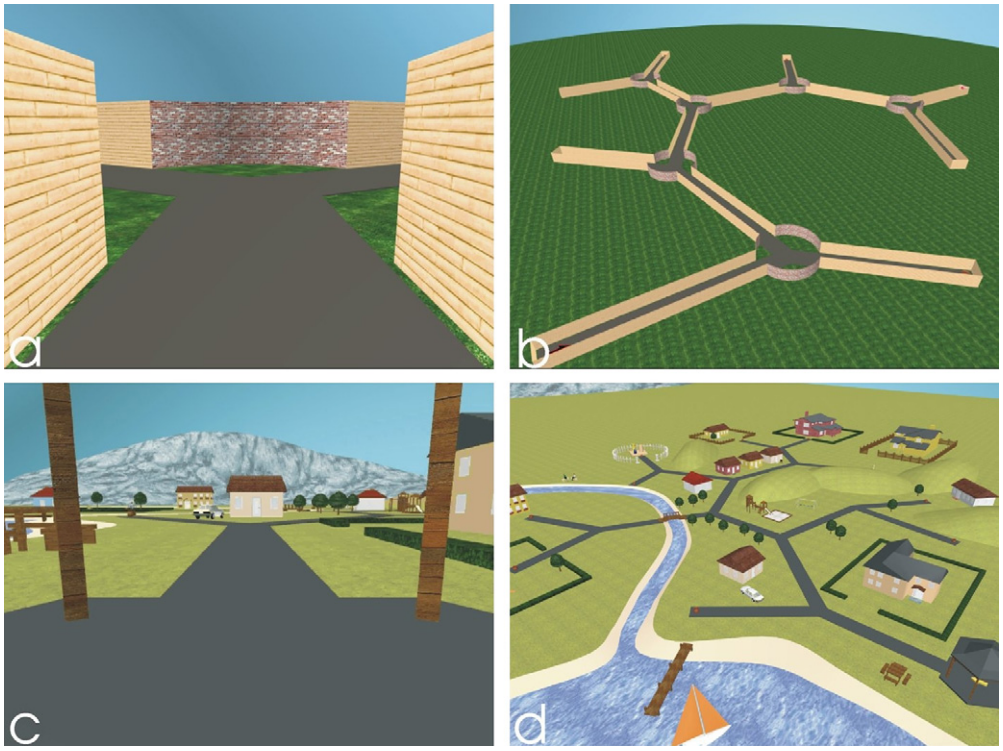

Fig. 2. Grey scale rendering of subject view (a and c) and aerial view (b and d) of the virtual maze (a and b) and the virtual park (c and d). Actual stimuli were in full colour. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

108, 239, 258, 288 and 324) and hypaesthesia (nos. 103, 112 and 133). Two subjects developed symptomatic epilepsy (no. 114: focal sensory seizures; no. 298: secondary generalized seizures). One subject (no. 96) presented with mild ataxia and vertigo. Three subjects (nos. 94, 288 and 324) showed symptoms of depression at the time of the assessment.

Two subjects (nos. 94 and 298) with left-sided lesions performed on the subtest 'neglect' (*TAP*) with >2 < 10 omissions in the left and right hemifield, respectively. However, neglect could not be clinically confirmed in these subjects. None of the other subjects showed signs of neglect on the 'neglect' subtest of the *TAP*. None of the subjects suffered from apraxia, aphasia, agnosia, or optic ataxia at the time of the assessment.

3.2. Anatomical results

Lesion localization (see Section 2.2.3) confirmed substantial parietal cortex lesions in all subjects. Eight subjects presented with side damage to the temporal cortex (insula, superior temporal gyrus) (subject nos. 90, 258, 298, 236, 311, 294, 324, 241), and 11 subjects with side damage to the frontal cortex (premotor, motor cortex) (nos. 90, 270, 103, 258, 99, 94, 311, 288, 104, 254 and 112). Seven subjects showed subcortical lacunar lesions in the striatum, thalamus or brain stem (nos. 90, 239, 311, 108, 96, 112 and 114). Details of lesioned areas for each subject can be seen from Table 2.

Lesioned subjects did not display white matter hyperintensities (WMHs) according to a three-point scale (normal, focal, confluent) adapted from Fazekas, Chawluk, Alavi, Hurtig, and Zimmerman (1987), except for three subjects (nos. 96, 108 and 239) presenting with some focal changes. Mild global cerebral atrophy was observed in two subjects (nos. 94 and 297).

Volumes of left- and right-sided precuneus, postcentral gyrus and inferior parietal cortex (see Section 2.2.2), and intracranial volumes are summarized in Table 1. Intracranial volumes of lesioned and control subjects did not differ significantly. Left-sided lesioned subjects had smaller volumes of the left precuneus and postcentral gyrus than controls, and right-sided lesioned subjects had smaller volumes of the right postcentral gyrus and inferior parietal cortex, and left precuneus than controls. Comparisons regarding right precuneus and left inferior parietal cortex were not significant.

3.3. Neuropsychological results

Subjects with left-sided parietal cortex lesions did not differ from subjects with right-sided parietal cortex lesions on any neuropsychological measure (Table 1). However, both left-sided and right-sided lesioned subjects showed impaired performance on the *WAIS-R* when compared with control subjects. Memory performance as assessed with the *WMS-R* was also impaired in both groups of subjects, however, subjects with left-sided lesions showed somewhat stronger impairments than subjects with right-sided lesions on *Verbal Memory, Delayed Recall and Attention/Concentration* (Table 1).

Left- and right-sided lesioned subjects did not differ from controls on the four spatial perceptional subtest of the *VOSP* (cp. Table 1). Three lesioned and two control subjects performed below the 5% cut off score on one of the four subtests, respectively. Lesioned subjects were also unimpaired on the immediate recall of the subtest 'remembering a short route' of the *RBMT* (Table 1). The majority of subjects performed with five points (maximum performance). Two left-sided, one right-sided lesioned, and three control subjects performed with four points (borderline performance). Results on the *LGT-3* (remembering a complex route on a city map) were also normal. Only three subjects with left- (no. 297) or right-sided (nos. 241 and 254) lesions performed more than 1 SD below the mean of the control sample.

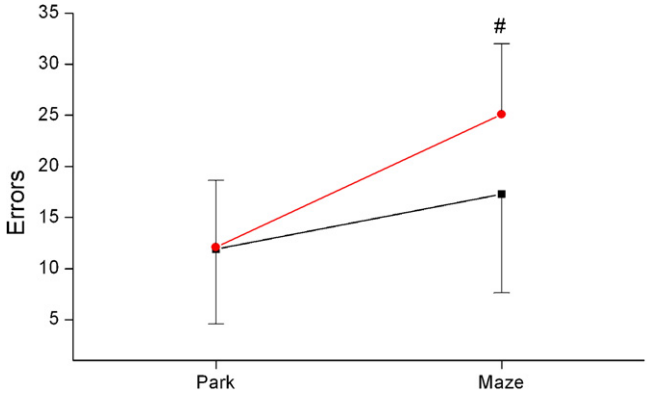

Fig. 3. Errors performed in the virtual park and virtual maze. Horizontal lines indicate group means and standard deviations. (●) Subjects with parietal cortex lesions; (■) control subjects; (#) significant difference ($P < 0.001$) between groups.

3.4. Virtual reality task performance

All lesioned and control subjects succeeded in navigating within the virtual environments, and none of them experienced side effects (i.e., simulator sickness). Lesioned and control subjects did not differ on ratings of their every day spatial navigational competence ($P = >0.70$) and on their experience with computers ($P = >0.60$). Lesioned as well as control subjects did not display sex differences on virtual maze or virtual park performance (*U*-tests; *P*-values > 0.60).

3.4.1. Effects of lesion laterality

A non-parametric 2 (*hemisphere*) × 2 (*task*) × 5 (*trial*) ANOVA comparing the errors committed by subjects with left-sided ($n = 14$) and right-sided ($n = 10$) parietal cortex lesions across the five trials in the virtual park and the virtual maze revealed significant effects of *task* ($QF(1) = 58.62$; $P < 0.001$), *trial* ($QF(3.35) = 12.46$; $P < 0.001$), and *task* × *trial* ($QF(3.19) = 13.70$; $P < 0.001$). The effect of *hemisphere* was not significant, as was true for the *hemisphere* × *task*, *hemisphere* × *trial* and *hemisphere* × *task* × *trial* interaction. Therefore, subjects with left- and right-sided lesions were combined for further analyses into one group.

3.4.2. Comparison of subjects with parietal cortex lesions and controls across both tasks

The overall 2 (*group*) × 2 (*task*) × 5 (*trial*) ANOVA comparing the errors committed by subjects with parietal cortex lesions ($n = 24$) and controls ($n = 36$) across the five trials in the virtual park and the virtual maze revealed significant effects of *group* ($F(1) = 6.96$; $P = 0.011$), *task* ($F(1) = 40.81$; $P < 0.001$) and *trial* ($F(4) = 43.62$; $P < 0.001$), and a significant *group* × *task* ($F(1) = 6.95$; $P = 0.011$) (cp. Fig. 3), *group* × *trial* ($F(4) = 5.49$; $P < 0.001$) and *task* × *trial* ($F(4) = 20.46$; $P < 0.001$) interaction. Post hoc analyses revealed that subjects with parietal cortex lesions were impaired on the virtual maze ($T = 3.37$; $P < 0.001$) but not on the virtual park ($T = 0.113$; $P > 0.90$). Both lesioned ($F(1) = 33.02$; $P < 0.001$) and control subjects ($F(1) = 32.00$; $P < 0.001$) significantly improved across trials in the virtual park. On the virtual maze, however, only control subjects ($F(1) = 8.74$; $P < 0.001$) but not lesioned subjects ($F(1) = 2.36$; $P = 0.058$) significantly improved across trials.

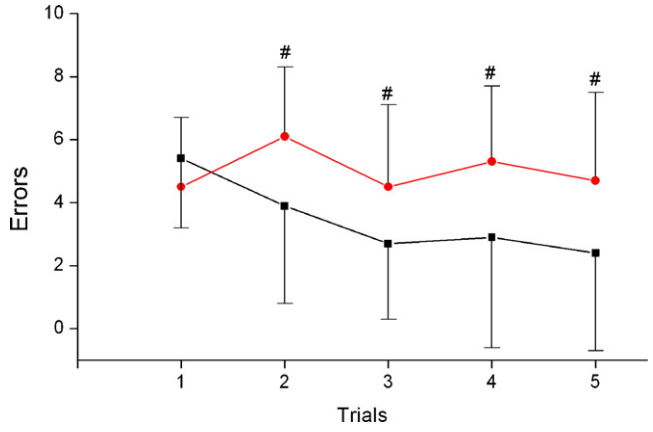

Fig. 4. Errors performed across the five trials administered in the virtual maze. Group means and standard errors are given. (●) Subjects with parietal cortex lesions; (■) control subjects; (#) significant difference ($P < 0.010$) between groups.

3.4.3. Virtual maze

A 2 (*group*) × 5 (*trial*) ANOVA comparing the errors committed by lesioned subjects and controls across the five trials of the virtual maze revealed a significant effect of *group* ($F(1) = 11.38$; $P = 0.001$) and *trial* ($F(4) = 4.88$; $P = 0.001$), indicating worse performance of lesioned subjects compared with controls. The *group* × *trial* interaction ($F(4) = 5.10$; $P = 0.001$) was also significant, indicating less learning progress across trials of lesioned subjects compared with controls (Fig. 4).

3.4.4. Virtual park

A 2 (*group*) × 5 (*trial*) ANOVA comparing the errors committed by lesioned subjects and controls across the five trials of the virtual park revealed a significant effect of *trial* ($F(4) = 90.40$; $P < 0.001$), indicating a significant learning progress of both groups across trials. The effect of *group* and the *group* × *trial* interaction was not significant, demonstrating similar performance of lesioned subjects and controls (Fig. 5).

3.4.5. Navigation strategies

In the virtual park, the majority of subjects reported to have memorized landmarks (controls: 79%; subjects with lesions: 67%), followed by memorizing a survey perspective (26%; 13%) or egocentric cues (18%; 17%). None of the controls, and 8% of lesioned subjects reported no specific strategy. In the virtual maze, the majority of subjects reported to have memorized egocentric cues (controls: 71%; lesioned subjects: 46%), and only some reported to have memorized the survey perspective (9%; 13%). However, 24% of the control subjects and 42% of the lesioned subjects reported that they did not use a specific navigation strategy. None of our study subjects reported to have verbalized a sequence of left and right turns.

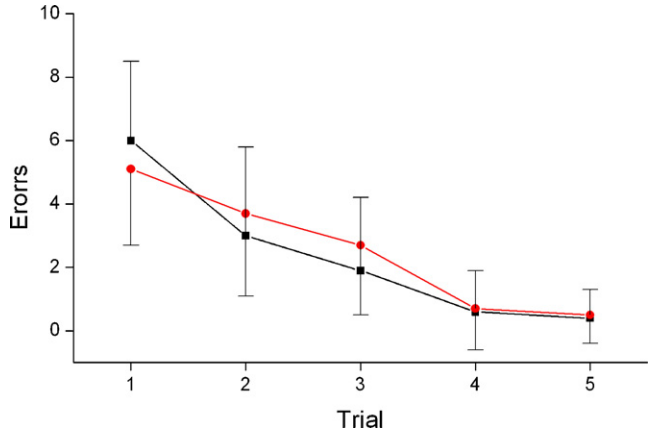

Fig. 5. Errors performed across the five trials administered in the virtual park. Group means and standard errors are given. (●) Subjects with parietal cortex lesions; (■) control subjects.

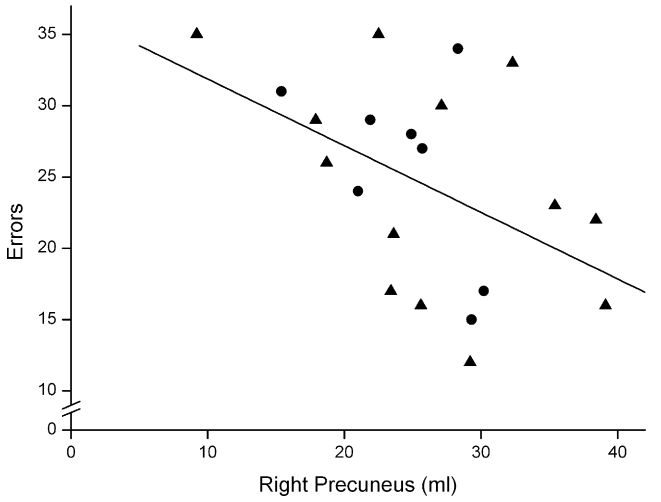

Fig. 6. Relationship between right precuneus volume and errors performed in the virtual maze of subjects with parietal cortex lesions. (●) Subjects with right-sided parietal cortex lesions; (▲) subjects with left-sided parietal cortex lesions.

Subjects with lesions did not differ significantly from control subjects on the navigation strategies used for each task (Fisher's exact test; $Ps > 0.20$). The same is true when the use of any strategy vs. the use of no strategy was compared (Fisher's exact test; $Ps > 0.16$). The amount of errors committed by control subjects in the virtual park and the virtual maze did not differ depending on the navigational strategies used (Kruskal–Wallis one-way ANOVAs; $Ps > 0.60$). The same is true for subjects with parietal cortex lesions ($Ps > 0.40$).

3.5. Influence of specific parietal cortex volumes on spatial performance

The volumes of left- and right-sided precuneus, postcentral gyrus and inferior parietal cortex of subjects with parietal cortex lesions were entered into multiple regression analyses (method: stepwise; significance level for selecting variables: $\alpha = 0.05$). Intracranial volume was entered as a further predictor to control for premorbid global brain size. Considering virtual maze performance, the volumes of the right-sided precuneus ($R^2 = 0.22$, $P = 0.010$) significantly predicted task performance (cf. Fig. 6), and the addition of the other variables did not significantly improve the prediction. All other regression models with the same predictors and virtual park performance, or performance on the *VOSP*, *LGT-3*, *RBMT*, *WMS-R* or *WAIS-R* as dependent variables were not significant.

3.6. Influence of specific lesion locations on virtual task performance

Subjects with lesions covering the intraparietal sulcus ($n = 8$; nos. 297, 270, 103, 239, 94, 288, 114 and 241) did not differ on virtual maze performance from subjects without such lesions ($n = 16$) (23 ± 6 errors vs. 27 ± 7 errors; $U = 40.0$; $P = 0.213$).

Subjects with side damage to the temporal cortex (insula, superior temporal gyrus) ($n = 8$; see Section 3.2 and Table 2) did not differ

on virtual maze performance from subjects without such lesions ($n = 16$) (25 ± 9 vs. 25 ± 6; $U = 59.5$, $P = 0.787$). The same is true for subjects with side damage to the frontal cortex (premotor, motor cortex) ($n = 11$), which did not differ from subjects without such lesions ($n = 13$) (25 ± 7 vs. 26 ± 7; $U = 66.5$, $P = 0.776$).

White matter hyperintensities (WMHs; $n = 3$; see Section 3.2) or subcortical lacunar lesions ($n = 7$) were also not related to specific impairments on the virtual maze (WMHs: 26 ± 4 vs. 25 ± 7; $U = 28.5$, $P = 0.898$; lacunar lesions: 25 ± 8 vs. 25 ± 7; $U = 57.0$, $P = 0.901$).

3.7. Influence of neurological and neuropsychological deficits on virtual task performance

Eleven lesioned subjects presented with residual neurological symptoms at the time of the assessment (see Section 3.1). However, performance on the virtual maze did not differ between these subjects and lesioned subjects without residual neurological symptoms ($n = 13$) (24 ± 6 vs. 26 ± 8; $U = 57.5$, $P = 0.424$).

Two subjects with left-sided lesions (nos. 94 and 298) presented with omissions on the 'neglect' subtest of the *TAP* (see Section 3.1). However, these subjects performed with fewer errors on the virtual maze when compared to the average performance of subjects with parietal cortex lesions (cp. Tables 1 and 2).

In order to assess a possible influence of subclinical hemiinattention or neglect on virtual task performance, we compared the frequency of subjects' left and right turns on the first trial of both tasks, respectively. Each three control subjects turned either only left or only right on the first trial of the virtual maze, and two further control subjects turned only left on the first trial of the virtual park. One subject with a right-sided lesion (no. 294) made only right turns on the first trial of the virtual maze. The average number of left and right turns of control subjects (virtual park, left turns: 6 ± 3, right turns: 5 ± 3; virtual maze, left turns: 4 ± 3, right turns: 5 ± 2), subjects with left-sided lesions (virtual park, left turns: 6 ± 2, right turns: 5 ± 2; virtual maze, left turns: 4 ± 1, right turns: 5 ± 2) and subjects with right-sided lesions (virtual park, left turns: 4 ± 2, right turns: 5 ± 2; virtual maze, left turns: 4 ± 3, right turns: 5 ± 2) did not differ significantly (Kruskal–Wallis one-way ANOVAs; χ^2 between 0.10 and 2.31, P-values between 0.315 and 0.952).

Seven 2 (*group*) $\times$ 5 (*trial*) ANCOVAs were performed, comparing the errors committed by lesioned subjects and controls in the virtual maze and *Verbal IQ, Performance IQ, Block design* (*WAIS-R*), *Verbal Memory*, *Visual Memory*, *Delayed Recall* and *Attention/Concentration* (*WMS-R*) as covariates, respectively. After partialing out the respective covariate, the factor *group* remained always significant (F-values between 4.739 and 8.403; Ps < 0.05).

4. Discussion

4.1. Suitability of virtual reality environments for investigating spatial memory in subjects with cortical lesions

Our results demonstrate the suitability of virtual reality environments for the study of spatial navigation and memory in subjects with cortical lesions. Virtual realities have a major advantage for the assessment of spatial memory formation, as computer-simulated first-person environments can simulate navigation in a large-scale space. The results of our study further demonstrate that assessment of spatial functions in virtual realities yields sensitive and specific results. Our subjects presented with focal and unilateral lesions, leading to an unimpaired behaviour on several traditional neuropsychological spatial tests (*VOSP*, *LGT-3*, *RBMT*). However, subjects were strongly impaired in the virtual maze and unimpaired in the virtual park, lending support to the idea that spatial memory is subserved by separable ventral and dorsal cortical areas (Aguirre & D'Esposito, 1997; Burgess et al., 2001).

All of our subjects succeeded in navigating within the virtual environments. The majority of subjects reported to have used allocentric navigation strategies in the virtual park, and egocentric navigation strategies in the virtual maze. None of our subjects experienced side effects ('simulator sickness'). We have already demonstrated that normal volunteers (Kesztyues et al., 2000; Weniger et al., submitted for publication), individuals with temporal lobe epilepsy (Weniger & Irle, 2006) and individuals with schizophrenia (Weniger & Irle, 2008) succeed to navigate in the same virtual reality environments as used in the present study, and that none of them experienced simulator sickness.

So far, only few studies used virtual reality environments to assess spatial mnemonic functions of individuals with medial temporal lobe damage (Astur et al., 2002; King et al., 2002; Maguire et al., 2006; Spiers et al., 2001a, 2001b), or to improve spatial functions in subjects with unilateral neglect (Ansuini, Pierno, Lusher, & Castiello, 2006; Castiello, Lusher, Burton, Glover, & Disler, 2004; Glover & Castiello, 2006). The vast progress of computer technologies now offers practical and economical opportunities to assess spatial memory and cognition of clinical samples by using virtual reality paradigms.

4.2. Impaired egocentric memory after parietal cortex lesions

Our results demonstrate a strong impairment of subjects with parietal cortex lesions to learn their way in a virtual maze lacking any topographical landmarks (Figs. 3 and 4). To our knowledge, the present study is the first to investigate egocentric learning and memory storage in a virtual maze and to test the effects of parietal cortex lesions on task performance. Egocentric memory deficits of subjects with parietal cortex lesions could not be explained by pure navigational deficits, as they were similarly efficient as control subjects to navigate within the virtual park.

Our subjects with parietal cortex lesions presented also with some general memory problems (as assessed with the *WMS-R*; cp. Table 1). Our finding of a role of the parietal cortex for egocentric spatial memory thus adds to the many other parietal lobe contributions to human memory, as more recently highlighted in lesion and functional imaging studies (for review see Cabeza, 2008; Cavanna & Trimble, 2006; Ciaramelli, Grady, & Moscovitch, 2008; Vilberg & Rugg, 2008).

The present results are supported by a recent fMRI study (Weniger et al., submitted for publication) that applied the same virtual maze as used in the present study in healthy volunteers. During learning the maze, we found activity increases within the most posterior temporal lobe, along the parieto-occipital sulcus (including the precuneus), in the postcentral gyrus and the retrosplenial cortex. Activity changes were bilateral, but more pronounced on the right side.

Currently, spatial representation is modelled as a process supported by a network of cerebral cortical regions. Whereas allocentric representation of spatial context is considered to principally depend on medial temporal cortices, posterior and medial parietal cortices are thought to provide the representation and encoding of egocentric coordinates. Lesion studies using rats and monkeys have suggested that posterior parietal cortices are involved in the encoding and long-term retention of kinaesthetic information playing an important role in spatial learning tasks (McDaniel et al., 1995; Quintana & Fuster, 1993; Rogers & Kesner, 2006; Save & Moghaddam, 1996; Save, Guazzelli, & Poucet, 2001). A recent study on patients with right middle cerebral artery stroke (Grimsen, Hildebrandt, & Fahle, 2008) suggests that egocentric visual search deficits are associated with fronto-parietal lesions,

whereas allocentric search deficits are rather related to ventral temporal lesion sites.

However, it must be kept in mind that the virtual reality tasks used in the present study are not pure egocentric or allocentric tasks. In every day practice, conjoint usage of allocentric and egocentric information in spatial navigation and learning is likely (Burgess, 2006). This applies also to large-scale virtual environments being used for the investigation of spatial navigation and learning. Even if a virtual environment is specifically designed to assess allocentric processing, a person may learn to navigate within this environment by using egocentric information instead of the provided objects and landmarks. *Vice versa*, a virtual maze might be solved by constructing a survey perspective, which is an allocentric frame of memory. However, most of our subjects reported to have memorized egocentric cues. Furthermore, subjects were forced to learn the maze by egocentric cues, because the maze did not contain any landmarks and all intersections appeared identical when approached from different directions. Translation of egocentric memories into a survey perspective of the maze should be possible only in later trials of the task, when most or the entire maze has already been stored in an egocentric frame of memory. Thus, we think it justified assuming that the virtual maze impairments or our parietal cortex lesioned subjects were predominantly caused by egocentric memory deficits.

4.3. Preserved allocentric memory after parietal cortex lesions

In contrast to the results of the virtual maze, subjects with parietal cortex lesions were unimpaired on the virtual park (Figs. 3 and 5). We are not aware of previous studies investigating allocentric navigation and memory storage of subjects with parietal cortex lesions in a virtual park. So far, only few studies investigated allocentric memory of individuals with medial temporal lobe damage by use of virtual realities, and consistently reported impairments in these subjects (Astur et al., 2002; King et al., 2002; Maguire et al., 2006; Spiers et al., 2001a, 2001b). Functional imaging studies in healthy volunteers also suggest that medial temporal cortices, i.e. the hippocampus and parahippocampal cortex subserve allocentric navigation and memory storage (Aguirre & D'Esposito, 1997; Aguirre et al., 1996; Burgess et al., 2001; Epstein et al., 2003; Iaria et al., 2003; Maguire et al., 1997). Thus, we assume that the virtual park used in our study can be principally solved with intact medial temporal cortices. In none of our subjects lesions encroached upon cortices of the medial temporal lobe (see Section 3.2 and Table 2).

We included two spatial memory tests ('remembering a short route' of the *RBMT* and 'city plan' of the *LGT-3*) in our neuropsychological test battery. 'Remembering a short route' (*RBMT*) affords the subject to repeat the way the experimenter has gone through a real environment (a room). The test may be classified as testing allocentric memory. The rather difficult test 'city plan' (*LGT-3*) affords one to memorize a complex route on a city plan, and to reproduce it later on a similar plan. Memorizing allocentric survey knowledge may best solve this test. In none of the tests we could observe consistent impairments of subjects with parietal cortex lesions (Section 3.3). As assumed for the virtual park, subjects with parietal cortex lesions were possibly able to solve these tests because their intact medial temporal lobes were sufficient for normal allocentric task performance.

4.4. Intraparietal cortex and egocentric memory

Single unit recordings in monkeys and lesion studies in monkeys and humans have suggested that the posterior parietal cortex around the intraparietal sulcus (bordering superior parietal BA 7 and inferior parietal BA 40) is involved in an eye- and head-centred representation of visual space (Andersen, Essick, & Siegel, 1985; Andersen, Bracewell, Barash, Gnadt, & Fogassi, 1990; Heide & Kömpf, 1998; Heide, Blankenburg, Zimmermann, & Kömpf, 1995; Li & Andersen, 2001; Medendorp, Goltz, Vilis, & Crawford, 2003; Mullette-Gillman, Cohen, & Groh, 2005; Ventre-Dominey & Vallee, 2007), suggesting a gaze-centred updating of visual space during spatial navigation. We have analysed the lesions of our subjects with regard to intraparietal sulcus involvement and identified eight subjects. However, these subjects did not perform differentially to subjects without lesions of the intraparietal sulcus (see Section 3.6). We assume that differential effects of localization subgroups possibly may have been obscured by the fact that subjects with parietal cortex lesions displayed extraordinarily strong impairments on the virtual maze ('floor effect'; cp. Fig. 4).

4.5. Precuneus and egocentric memory

Using regression analyses, we found a significant relationship between right-sided precuneus volume and performance on the virtual maze (Fig. 6), indicating larger precuneus volumes in parietal cortex-lesioned subjects with better performance on the virtual maze. Other regression models using virtual park performance or performance on the other spatial tests as dependent variables, were not significant (cp. Section 3.5).

Functional imaging studies have highlighted the role of medial and posterior parietal cortices in computing egocentric spatial representations (Burgess et al., 2001; Neggers, van der Lubbe, Ramsey, & Postma, 2006; Rosenbaum, Ziegler, Winocur, Grady, & Moscovitch, 2004; Spiers & Maguire, 2007), and route encoding (Janzen & Weststeijn, 2007; Shelton & Gabrieli, 2002; Wolbers, Weiller, & Büchel, 2004). The role of the precuneus may be seen in gathering an imaginable representation of the world around and within us, thus enabling a continuous perspective of the organism relative to its environment (Gusnard & Raichle, 2001). Accordingly, the precuneus was shown to be activated during tasks requiring visuo-spatial and motor imagery, episodic memory retrieval, and self-processing operations, namely first-person perspective taking (for review see Cavanna & Trimble, 2006). Vogeley and Fink (2003) suggested from a review of the literature that the general pattern of activation evoked by first-person perspective taking includes medial parietal, inferior parietal, and medial frontal cortices.

However, it must be kept in mind that functional imaging studies investigating first-person perspective taking regularly demonstrate recruitment of the very medial aspects of the precuneus (medial parts of BA 7, and BA 31) (for review see Cavanna & Trimble, 2006). On the other hand, human lesion studies involving medial parietal cortices are rare (we are aware of one case study; see Suzuki et al., 1998), as is true for the present study, in which only one subject (no. 297) presented with lesions encroaching the medial surface of the parietal cortex (Table 2).

4.6. Methodological considerations

We have carefully controlled for possible effects of general cognitive and mnemonic disturbance, residual neurological symptoms and unspecific neural lesions on virtual reality task performance of subjects with parietal cortex lesions, and did not find evidence for an influence of all these factors. However, we cannot completely exclude that these factors exerted some influence on virtual reality task performance. As well, lesion size and coverage (see Table 2) pretended a rigorous test of localization subgroups. Future studies using more homogeneous and focal lesion groups should elucidate

the role of specific parietal cortices in egocentric representation and memory formation.

Specifically, it could be speculated that hemi-inattention or neglect may have contributed to virtual task impairment of subjects with parietal cortex lesions. However, we consider this possibility rather unlikely for the following reasons: First, neglect could not be clinically confirmed in any subject, and two subjects performing with omissions in the 'neglect' subtest of the *TAP* showed virtual task performance comparable to that of other lesioned subjects. Second, it seems unlikely that virtual maze performance, but not virtual park performance, should have been influenced by subclinical hemi-inattention or neglect. Third, by analysing the routes travelled through the virtual park and maze, we could not find evidence for a left or right preference of lesioned subjects, meaning that subjects most probably explored the left and right hemifield of the virtual environments equally. Nevertheless, future studies should record gaze direction and saccades of subjects with parietal cortex lesions in order to elucidate perceptional and attentional contributions to large-scale virtual task performance.

For control subjects, the egocentric task might have been more difficult than the allocentric task (cf. Fig. 3). This raises the concern that the egocentric task simply detected unspecific deficits in parietal cortex lesioned subjects due to high sensitivity. However, Weniger and Irle (2008) using the same virtual environments as the present study found intact egocentric and impaired allocentric memory in schizophrenia subjects, indicating a double dissociation of spatial memory in parietal and schizophrenia subjects. Therefore, we consider our main results truly due to specific egocentric deficits and specific parietal cortex lesions, and not due to simple task differences.

We found a significant relationship between right-sided precuneus size of lesioned subjects and performance on the virtual maze. However, the strength of this relationship is modest, and volumes of the affected and unaffected hemispheres were combined, respectively (see Section 3.5). Thus, the resulting correlation contains normal interindividual, as well as pathological, variance. Furthermore, precuneus size showed a greater variability than postcentral or inferior parietal cortex size (cf. Table 1), thus questioning the specificity of this brain–behaviour relationship. In line with this, our current fMRI study with healthy volunteers (Weniger et al., submitted for publication) revealed not only precuneus, but also postcentral gyrus activation during virtual maze performance. On the other hand, an exploratory analysis of the control group revealed no correlation between precuneus size and virtual maze performance (but similar variance of precuneus size; Levene test; $P = 0.372$), indicating that precuneus lesions were a powerful predictor of virtual maze performance in lesioned subjects. Taken together, we consider the present result preliminary and hope that fMRI studies presently done in our department elucidate in more detail the roles of specific parietal cortices in egocentric navigation and memory formation.

Our study assessed spatial memory in a large-scale environment. As a consequence, the tasks differed with respect to visual cues and complexity. Current evidence indicates complementary roles of allocentric and egocentric representations depending on the number of landmarks remembered and the size and familiarity of the environment (Burgess, 2006). Future studies using more specific virtual reality paradigms are needed to elucidate the influence of intrinsic task structure on allocentric and egocentric memory performance.

Acknowledgements

We express our appreciation to the subjects who participated in this study. The authors wish to thank K. Märtens for assistance in subjects' assessment, and J. Siemerkus, M. Mehlitz and A. Raguse who assisted with programming and analysing of the virtual reality tasks. Research was supported by grant IR 15/8-2 and RI 1000/1-1 from the Deutsche Forschungsgemeinschaft.

References

Abrahams, S., Pickering, A., Polkey, C. E., & Morris, R. G. (1997). Spatial memory deficits in patients with unilateral damage to the right hippocampal formation. *Neuropsychologia*, *35*, 11–24.

Aguirre, G. K., & D'Esposito, M. (1997). Environmental knowledge is subserved by separable dorsal/ventral neural areas. *Journal of Neuroscience*, *17*, 2512–2518.

Aguirre, G. K., & D'Esposito, M. (1999). Topographical disorientation: A synthesis and taxonomy. *Brain*, *122*, 1613–1628.

Aguirre, G. K., Detre, J. A., Alsop, D. C., & D'Esposito, M. (1996). The parahippocampus subserves topographical learning in man. *Cerebral Cortex*, *6*, 823–829.

Andersen, R. A., Essick, G. K., & Siegel, R. M. (1985). Encoding of spatial location by posterior parietal neurons. *Science*, *230*, 456–458.

Andersen, R. A., Bracewell, R. M., Barash, S., Gnadt, J. W., & Fogassi, L. (1990). Eye position effects on visual, memory, and saccade-related activity in areas LIP and 7a in the macaque. *Journal of Neuroscience*, *10*, 1176–1196.

Ansuini, C., Pierno, A. C., Lusher, D., & Castiello, U. (2006). Virtual reality applications for the remapping of space in neglect patients. *Restorative Neurology and Neuroscience*, *24*, 431–441.

Astur, R. S., Taylor, L. B., Mamelak, A. N., Philpott, L., & Sutherland, R. J. (2002). Humans with hippocampus damage display severe spatial memory impairments in a virtual Morris water task. *Behavioural Brain Research*, *132*, 77–84.

Barrash, J., Damasio, H., Adolphs, R., & Tranel, D. (2000). The neuroanatomical correlates of route learning impairment. *Neuropsychologia*, *38*, 820–836.

Bäumler, G. (1974). *Lern- und Gedächtnistest-3 (LGT-3)*. Göttingen: Hogrefe.

Beckers, K., & Canavan, A. G. M. (1992). *VOSP Testbatterie für visuelle Objekt-und Raumwahrnehmung*. Bury St Edmunds and Göttingen: TVTC Thames ValleyTest Company and Testzentrale: TVTC Thames Valley Test Company and Göttingen.

Bohbot, V. D., Kalina, M., Stepankova, K., Spackova, N., Petrides, M., & Nadel, L. (1998). Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex. *Neuropsychologia*, *36*, 1217–1238.

Brunner, E., Domhof, S., & Langer, F. (2002). *Nonparametric analysis of longitudinal data in factorial experiments*. New York: Wiley.

Burgess, N. (2006). Spatial memory: How egocentric and allocentric combine. *Trends in Cognitive Sciences*, *10*, 551–557.

Burgess, N., Maguire, E. A., Spiers, H. J., & O'Keefe, J. (2001). A temporoparietal and prefrontal network for retrieving the spatial context of lifelike events. *NeuroImage*, *14*, 439–453.

Cabeza, R. (2008). Role of parietal regions in episodic memory retrieval: The dual attentional processes hypothesis. *Neuropsychologia*, *46*, 1813–1827.

Castiello, U., Lusher, D., Burton, C., Glover, S., & Disler, P. (2004). Improving left hemispatial neglect using virtual reality. *Neurology*, *62*, 1958–1962.

Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: A review of its functional anatomy and behavioural correlates. *Brain*, *129*, 564–583.

Ciaramelli, E., Grady, C. L., & Moscovitch, M. (2008). Top-down and bottom-up attention to memory: A hypothesis (AtoM) on the role of the posterior parietal cortex in memory retrieval. *Neuropsychologia*, *46*, 1828–1851.

Cogan, D. G. (1979). Visuospatial dysgnosia. *American Journal of Ophthalmology*, *88*, 361–368.

De Renzi, E., Faglioni, P., & Villa, P. (1977). Topographical amnesia. *Journal of Neurology Neurosurgery and Psychiatry*, *40*, 498–505.

Epstein, R., DeYoe, E. A., Press, D. Z., Rosen, A. C., & Kanwisher, N. (2001). Neuropsychological evidence for a topographical learning mechanism in parahippocampal cortex. *Cognitive Neuropsychology*, *18*, 481–508.

Epstein, R., Graham, K. S., & Downing, P. E. (2003). Viewpoint-specific scene representations in human parahippocampal cortex. *Neuron*, *37*, 865–876.

Fazekas, F., Chawluk, J. B., Alavi, A., Hurtig, H. I., & Zimmerman, R. A. (1987). MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *American Journal of Radiology*, *149*, 351–356.

Glover, S., & Castiello, U. (2006). Recovering space in unilateral neglect: A neurological dissociation revealed by virtual reality. *Journal of Cognitive Neuroscience*, *18*, 833–843.

Grimsen, C., Hildebrandt, H., & Fahle, M. (2008). Dissociation of egocentric and allocentric coding of space in visual search after right middle cerebral artery stroke. *Neuropsychologia*, *46*, 902–914.

Gusnard, D. A., & Raichle, M. E. (2001). Searching for a baseline: Functional imaging and the resting human brain. *Nature Reviews Neuroscience*, *2*, 685–694.

Habib, M., & Sirigu, A. (1987). Pure topographical disorientation: A definition and anatomical basis. *Cortex*, *23*, 73–85.

Heide, W., & Kömpf, D. (1998). Combined deficits of saccades and visuo-spatial orientation after cortical lesions. *Experimental Brain Research*, *123*, 164–171.

Heide, W., Blankenburg, M., Zimmermann, E., & Kömpf, D. (1995). Cortical control of double-step saccades: Implications for spatial orientation. *Annals of Neurology*, *38*, 739–748.

Holdstock, J. S., Mayes, A. R., Cezayirli, E., Aggleton, J. P., & Roberts, N. (1999). A comparison of egocentric and allocentric spatial memory in medial temporal lobe and Korsakoff amnesics. *Cortex*, *35*, 479–501.

Holdstock, J. S., Mayes, A. R., Cezayirli, E., Isaac, C. L., Aggleton, J. P., & Roberts, N. (2000). A comparison of egocentric and allocentric spatial memory in a patient with selective hippocampal damage. *Neuropsychologia*, *38*, 410–425.

Iaria, G., Petrides, M., Dagher, A., Pike, B., & Bohbot, V. D. (2003). Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: Variability and change with practice. *Journal of Neuroscience*, *23*, 5945–5952.

Irle, E., Lange, C., Weniger, G., & Sachsse, U. (2007). Size abnormalities of the superior parietal cortices are related to dissociation in borderline personality disorder. *Psychiatry Research: Neuroimaging*, *156*, 139–149.

Janzen, G., & Weststeijn, C. G. (2007). Neural representation of object location and route direction: An event-related fMRI study. *Brain Research*, *1165*, 116–125.

Kase, C. S., Troncoso, J. F., Court, J. E., Tapia, J. F., & Mohr, J. P. (1977). Global spatial disorientation: Clinico-pathological correlations. *Journal of the Neurological Sciences*, *34*, 267–278.

Kennedy, R. S., Lane, N. E., Berbaum, K. S., & Lilienthal, M. G. (1993). Simulator sickness questionnaire: An enhanced method for quantifying simulator sickness. *International Journal of Aviation Psychology*, *3*, 203–220.

Kesztyues, T. I., Mehlitz, M., Schilken, E., Weniger, G., Wolf, S., Piccolo, U., et al. (2000). Preclinical evaluation of a virtual reality neuropsychological test system: Occurrence of side effects. *Cyberpsychology & Behavior*, *3*, 343–349.

King, J. A., Burgess, N., Hartley, T., Vargha-Khadem, F., & O'Keefe, J. (2002). Human hippocampus and viewpoint dependence in spatial memory. *Hippocampus*, *12*, 811–820.

Landis, T., Cummings, J. L., Benson, D. F., & Palmer, E. P. (1986). Loss of topographic familiarity: An environmental agnosia. *Archives of Neurology*, *43*, 132–136.

Levine, D. N., Warach, J., & Farah, M. (1985). Two visual systems in mental imagery: Dissociation of "what" and "where" in imagery disorders due to bilateral posterior cerebral lesions. *Neurology*, *35*, 1010–1018.

Li, C. S., & Andersen, R. A. (2001). Inactivation of macaque lateral intraparietal area delays initiation of the second saccade predominantly from contralesional eye positions in a double-saccade task. *Experimental Brain Research*, *137*, 45–57.

Maguire, E. A. (2001). The retrosplenial contribution to human navigation: A review of lesion and neuroimaging findings. *Scandinavian Journal of Psychology*, *42*, 225–238.

Maguire, E. A., Burke, T., Phillips, J., & Staunton, H. (1996). Topographical disorientation following unilateral temporal lobe lesions in humans. *Neuropsychologia*, *34*, 993–1001.

Maguire, E. A., Frackowiak, R. S. J., & Frith, C. D. (1997). Recalling routes around London: Activation of the right hippocampus in taxi drivers. *Journal of Neuroscience*, *17*, 7103–7110.

Maguire, E. A., Nannery, R., & Spiers, H. J. (2006). Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain*, *129*, 2894–2907.

McDaniel, W. F., Via, J. D., Smith, J. S., Wells, D. L., Fu, J. J., Bishop, J. F., et al. (1995). Unilateral injury of posterior parietal cortex and spatial learning in hooded rats. *Behavioural Brain Research*, *70*, 165–179.

Medendorp, W. P., Goltz, H. C., Vilis, T., & Crawford, J. D. (2003). Gaze-centered updating of visual space in human parietal cortex. *Journal of Neuroscience*, *23*, 6209–6214.

Mullette-Gillman, O. A., Cohen, Y. E., & Groh, J. M. (2005). Eye-centered, head-centered, and complex coding of visual and auditory targets in the intraparietal sulcus. *Journal of Neurophysiology*, *94*, 2331–2352.

Neggers, S. F., van der Lubbe, R. H., Ramsey, N. F., & Postma, A. (2006). Interactions between ego- and allocentric neuronal representations of space. *NeuroImage*, *31*, 320–331.

Nyffeler, T., Gutbrod, K., Pflugshaupt, T., von Wartburg, R., Hess, C. W., & Müri, R. M. (2005). Allocentric and egocentric spatial impairments in a case of topographical disorientation. *Cortex*, *41*, 133–143.

O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford: Clarendon Press.

Quintana, J., & Fuster, J. M. (1993). Spatial and temporal factors in the role of prefrontal and parietal cortex in visuomotor integration. *Cerebral Cortex*, *3*, 122–132.

Rogers, J. L., & Kesner, R. P. (2006). Lesions of the dorsal hippocampus or parietal cortex differentially affect spatial information processing. *Behavioral Neuroscience*, *120*, 852–860.

Rosenbaum, R. S., Ziegler, M., Winocur, G., Grady, C. L., & Moscovitch, M. (2004). I have often walked down this street before": fMRI studies on the hippocampus and other structures during mental navigation of an old environment. *Hippocampus*, *14*, 826–835.

Save, E., & Moghaddam, M. (1996). Effects of lesions of the associative parietal cortex on the acquisition and use of spatial memory in egocentric and allocentric navigation tasks in the rat. *Behavioral Neuroscience*, *110*, 74–85.

Save, E., Guazzelli, A., & Poucet, B. (2001). Dissociation of the effects of bilateral lesions of the dorsal hippocampus and parietal cortex on path integration in the rat. *Behavioral Neuroscience*, *115*, 1212–1223.

Shelton, A. L., & Gabrieli, J. D. (2002). Neural correlates of encoding space from route and survey perspectives. *Journal of Neuroscience*, *22*, 2711–2717.

Spiers, H. J., & Maguire, E. (2007). A navigational guidance system in the human brain. *Hippocampus*, *17*, 618–626.

Spiers, H. J., Burgess, N., Hartley, T., Vargha-Khadem, F., & O'Keefe, J. (2001). Bilateral hippocampal pathology impairs topographical and episodic memory but not visual pattern matching. *Hippocampus*, *11*, 715–725.

Spiers, H. J., Burgess, N., Maguire, E. A., Baxendale, S. A., Hartley, T., Thompson, et al. (2001). Unilateral temporal lobectomy patients show lateralized topographical and episodic memory deficits in a virtual town. *Brain*, *124*, 2476–2489.

Stark, M., Coslett, H. B., & Saffran, E. M. (1996). Impairment of an egocentric map of locations: Implications for perception and action. *Cognitive Neuropsychology*, *13*, 481–523.

Suzuki, K., Yamadori, A., Hayakawa, Y., & Fujii, T. (1998). Pure topographical disorientation related to dysfunction of the viewpoint dependent visual system. *Cortex*, *34*, 589–599.

Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.

Tewes, U. (1991). *HAWIE-R, Hamburg-Wechsler-Intelligenztest für Erwachsene. Revision 1991*. Huber: Bern.

Ventre-Dominey, J., & Vallee, B. (2007). Vestibular integration in human cerebral cortex contributes to spatial remapping. *Neuropsychologia*, *45*, 435–439.

Vilberg, K. L., & Rugg, M. D. (2008). Memory retrieval and the parietal cortex: A review of evidence from a dual-process perspective. *Neuropsychologia*, *46*, 1787–1799.

Vogeley, K., & Fink, G. R. (2003). Neural correlates of the first-person-perspective. *Trends in Cognitive Sciences*, *7*, 38–42.

Warrington, E. K., & James, M. (1991). *VOSP visual object and space perception testbattery*. Bury St Edmunds: TVTC Thames Valley Test Company.

Wechsler, D. (1987). *WMS-R, Wechsler memory scale-revised*. San Antiono: Psychological Corporation.

Weniger, G., & Irle, E. (2006). Posterior parahippocampal gyrus lesions in the human impair egocentric learning in a virtual environment. *European Journal of Neuroscience*, *24*, 2406–2414.

Weniger, G., & Irle, E. (2008). Allocentric memory impaired and egocentric memory intact as assessed by virtual reality in recent-onset schizophrenia. *Schizophrenia Research*, *101*, 201–209.

Weniger, G., Siemerkus, J., Schmidt-Samoa, C., Mehlitz, M., Baudewig, J., Dechent, P., et al. (submitted for publication). The human parahippocampal cortex subserves egocentric spatial learning during navigation in a virtual maze.

Wilson, B., Cockburn, J., & Baddeley, A. (1992). *The rivermead behavioural memory test*. Bury St Edmunds: TVTC Thames Valley Test Company.

Wilson, B., Berry, E., Gracey, F., Harrison, C., Stow, I., Macniven, J., et al. (2005). Egocentric disorientation following bilateral parietal lobe damage. *Cortex*, *41*, 547–554.

Wolbers, T., Weiller, C., & Büchel, C. (2004). Neural foundations of emerging route knowledge in complex spatial environments. *Brain Research Cognitive Brain Research*, *21*, 401–411.

Zimmermann, P., & Fimm, B. (1993). *Testbatterie zur Aufmerksamkeitsprüfung (TAP), Version 1.02*. Freiburg, FRG: Psytest.