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Egocentric and allocentric memory as assessed by virtual reality in individuals with amnestic mild cognitive impairment

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ABSTRACT

Present evidence suggests that medial temporal cortices subserve allocentric representation and memory, whereas egocentric representation and memory also depends on parietal association cortices and the striatum. 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. Twenty-nine patients with amnestic MCI (aMCI) were compared with 29 healthy matched controls on two virtual reality tasks affording to learn a virtual park (allocentric memory) and a virtual maze (egocentric memory). Participants further received a neuropsychological investigation and MRI volumetry at the time of the assessment. Results indicate that aMCI patients had significantly reduced size of the hippocampus bilaterally and the right-sided precuneus and inferior parietal cortex. aMCI patients were severely impaired learning the virtual park and the virtual maze. Smaller volumes of the right-sided precuneus were related to worse performance on the virtual maze. Participants with striatal lacunar lesions committed more errors than participants without such lesions on the virtual maze but not on the virtual park. aMCI patients later converting to dementia ($n = 15$) had significantly smaller hippocampal size when compared with non-converters ($n = 14$). However, both groups did not differ on virtual reality task performance. Our study clearly demonstrates the feasibility of virtual reality technology to study spatial memory deficits of persons with aMCI. Future studies should try to design spatial virtual reality tasks being specific enough to predict conversion from MCI to dementia and conversion from normal to MCI.

1. Introduction

Mild cognitive impairment (MCI) is considered as a stage of cognitive, especially mnemonic impairment beyond what is considered normal for age, but not of sufficient magnitude as to warrant the diagnosis of dementia or Alzheimer's disease (AD) (Petersen & Negash, 2008; Petersen et al., 1999). Several studies have demonstrated reduced hippocampal size in individuals with amnestic MCI (aMCI) when compared with healthy controls (for review see Wolf et al., 2003). Hippocampal size reduction in aMCI (approximately 10–15%) is, however, less strong than that observed in individuals with clinically probable AD (up to 40%; for review see Barnes et al., 2009).

Individuals with aMCI were repeatedly shown to progress to clinically probable AD at higher rates (about 10% per year) compared with healthy age-matched controls (Bowen et al., 1997; Petersen et al., 1999; Tierney et al., 1996; for review see Mitchell & Shiri-Feshki, 2009). Reduced medial temporal cortex volumes and mnemonic and executive dysfunction have been repeatedly shown to predict conversion to dementia (Chen et al., 2001; den Heijer et al., 2006; Jack et al., 1999; Marquis et al., 2002; Tabert et al., 2006). However, these markers rarely surpass 70% sensitivity and specificity, thus demanding the development of an accurate marker (Modrego, 2006).

Persons with aMCI often complain spatial deficits, i.e. being impaired in finding their way within their locomotor environment ('topographical disorientation'; Cogan, 1979; De Renzi, Faglioni, & Villa, 1977). Accordingly, recent studies have found that patients with aMCI have reduced metabolism and grey matter volumes within the parietal lobe, being most pronounced in dementia converters (Bozzali et al., 2006; Chetelat et al., 2005; Fouquet et al., 2009; Hämäläinen et al., 2007; Pagani et al., 2010; Pennanen et al., 2005). Parietal cortex grey matter losses are significantly stronger in patients with mild AD when compared with patients with aMCI (Apostolova et al., 2007). Earlier neuropathological studies have already suggested that AD-related degenerative changes start in allocortical areas, i.e. hippocampus and entorhinal cortex, and later spread in a predictable manner across the

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Table 1
Demographic, clinical and neuropsychological characteristics of all subjects.

Variable	Participants with aMCI ($n=29$)	Healthy controls ($n=29$)	Statistic	P
Age (year)	59 ± 9	59 ± 8	$t(56)=0.11$	0.910
Education (year)	9.9 ± 2.0	9.6 ± 1.7	$t(56)=-0.72$	0.474
Sex (female:male)	7:22	10:19		0.565[a]
MCI subtype (n)				
Amnestic single domain	22			
Amnestic multiple domain	7			
Mini mental state examination	28 ± 2			
Beck depression inventory	8.1 ± 4.6	5.4 ± 4.2	$t(49)=-2.21$	**0.032**
WAIS-R (Similarities)	11.8 ± 3.6	13.2 ± 2.7	$t(56)=1.71$	0.093
WCST (perseverative errors)	19.0 ± 13.7	18.3 ± 15.5	$t(54)=-0.17$	0.868
WMS-R (Verbal Memory)	95 ± 16	117 ± 14	$t(54)=5.73$	**<0.001**
WMS-R (Visual Memory)	101 ± 19	124 ± 12	$t(54)=5.49$	**<0.001**
WMS-R (Delayed Recall)	91 ± 17	124 ± 16	$t(54)=7.76$	**<0.001**
WMS-R (Attention/Concentration)	89 ± 14	97 ± 9	$t(54)=2.79$	**0.007**
Spatial performance				
WAIS-R (Block Design)	7.5 ± 2.8	9.9 ± 2.9	$t(56)=3.25$	**0.002**
VOSP (dot counting)	9.9 ± 0.3	9.9 ± 0.2	$t(52)=0.59$	0.586
VOSP (position discrimination)	19.7 ± 0.8	19.7 ± 0.8	$t(52)=0.11$	0.914
VOSP (number location)	9.3 ± 1.0	9.7 ± 0.7	$t(52)=1.81$	0.076
VOSP (cube analysis)	9.5 ± 1.1	9.7 ± 0.7	$t(52)=0.90$	0.375
RBMT				
Remembering a short route, immediate	4.6 ± 0.8	4.9 ± 0.3	$t(46)=2.01$	**0.050**
Lern- und Gedächtnistest-3 (city map)	10.8 ± 5.9	15.5 ± 5.3	$t(52)=3.07$	**0.003**
Virtual reality tasks				
Virtual park, errors	15.6 ± 6.7	10.6 ± 7.3	$t(56)=-2.72$	**0.009**
Virtual maze, errors	27.4 ± 8.7	17.4 ± 9.8	$t(55)=-4.10$	**<0.001**

Table values are mean ± SD unless indicated otherwise. Significant differences are given in boldface type.
aMCI, amnestic mild cognitive impairment; SD, standard deviation; *WAIS-R*, *Wechsler Adult Intelligence Scale-Revised*; *WCST*, *Wisconsin Card Sorting Test*; *WMS-R*, *Wechsler Memory Scale-Revised*; *VOSP*, *Visual Object and Space Perception Battery*, *RBMT*, *Rivermead Behavioural Memory Test*.
[a] Fisher's exact test.

isocortex, including parietal association cortices (Braak & Braak, 1991).

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. Allocentric representation of spatial context is considered to depend mainly on medial temporal cortices, especially in the right hemisphere (e.g., Burgess, Maguire, Spiers, & O'Keefe, 2001). On the other hand, egocentric representation of space is mainly modulated by right-sided parietal association cortices and subcortical regions, especially the striatum (Burgess et al., 2001; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003; Maguire et al., 1998).

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. We have already demonstrated that normal volunteers (Kesztyues et al., 2000; Weniger et al., 2010) and individuals with temporal lobe epilepsy (Weniger & Irle, 2006), parietal cortex infarction (Weniger, Ruhleder, Wolf, Lange, & Irle, 2009) or schizophrenia (Weniger & Irle, 2008) succeed to navigate in virtual reality environments and that none of them experienced simulator sickness. The vast progress of computer technologies now offers practical and economical opportunities to assess spatial memory and cognition in clinical samples using virtual reality paradigms.

In the present investigation, we studied virtual reality task performance of 29 patients with aMCI and 29 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 tasks were identical to those applied in previous investigations of our group (Weniger & Irle, 2006; Weniger & Irle, 2008; Weniger et al., 2009; Weniger et al., 2010). Special emphasis was laid on the assessment of combined grey and white matter parietal cortex volumes, which were shown to predict virtual task performance in patients with middle cerebral artery infarction (Weniger et al., 2009). The goals of our study were (a) to assess whether participants with aMCI are impaired in learning the virtual park and the virtual maze, (b) to assess whether participants with aMCI have reduced hippocampal and parietal cortex size, (c) to analyse whether hippocampal and parietal cortex size is related to virtual task performance, (d) to explore the influence of striatal lacunar lesions on virtual task performance, and (e) to assess whether brain measures and behavioural measures of dementia converters differ from those of non-converters.

2. Methods

2.1. Participants

2.1.1. Participants with amnestic mild cognitive impairment (aMCI)

The study group comprised a consecutive sample of 29 patients with aMCI (Table 1), having been referred to the outpatient memory clinic of the Department of Psychiatry and Psychotherapy, University of Göttingen. The diagnosis of aMCI was made according to Petersen and Negash (2008), i.e. if the patient met the following criteria: (1) memory complaint, (2) memory status not normal for age, (3) not demented, and (4) normal activities of daily living. Dementia was diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*; American Psychiatric Association, 1994). Patients being younger than 40 years or presenting with a history of neurological or severe medical illness, or a history of psychotic disorder or major depression were excluded. Patients were clinically re-assessed 6 years later in order to define those patients having progressed to dementia.

Subtypes of MCI were diagnosed by aid of the *Wechsler Memory Scale-Revised* (*WMS-R*; Wechsler, 1987) (amnestic subtype), and the *Wechsler Adult Intelligence Scale-Revised* (*WAIS-R*; Tewes, 1991) and the *Wisconsin Card Sorting Test* (*WCST*;