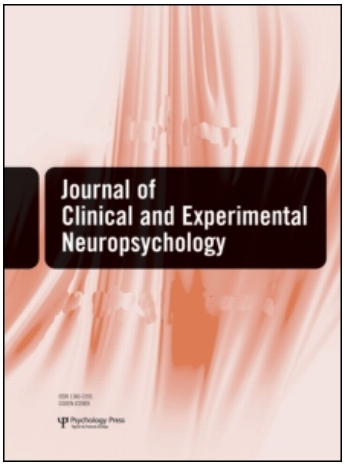

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Visually navigating a virtual world with real-world impairments: A study of visually and spatially guided performance in individuals with mild cognitive impairments

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Visually navigating a virtual world with real-world impairments: A study of visually and spatially guided performance in individuals with mild cognitive impairments

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In recent years, computer technology has evolved such that highly realistic virtual environments (VEs) can be used within a lab setting. Such VEs provide controlled ability to examine behavioral performance across different populations. The primary goal of this investigation was to examine the ability of mild cognitive impaired (MCI) participants to navigate effectively through a realistic, fictional virtual city. A total of 26 healthy control participants (age: 69 ± 7.7 years; Mini-Mental State Examination, MMSE ≥ 29) and 8 MCI patients (age: 72 ± 7 years, MMSE ≥ 26) were recruited. Both groups exhibited similar spatial-navigation ability. However, the MCI groups' ability to use effective visually guided navigation to traverse the VE was significantly compromised compared to healthy controls; a similar performance reduction was also observed when selecting appropriate paths. Though initially groups appear practically indistinguishable in regard to spatially navigating their way through the VE, these data indicate that careful evaluations of behavior in VEs may provide novel ways to differentiate between populations that have historically displayed relatively subtle differences.

Keywords: Mild cognitive impairment; Virtual environment; Visually guided performance; Spatial navigation.

INTRODUCTION

In recent years, use of virtual environments (VE) has increased in neuroscience research, stimulated in part by the explosive growth of computer technology and the video game industry. Virtual environments have been constructed to simulate a number of real-world tasks in variable contexts such as driving (Lundberg et al., 1997; Shechtman et al., 2007; Walshe, Lewis, O'Sullivan, & Kim, 2005), shopping (Whitney et al., 2006), and walking down the street (Nomura, Mulavara, Richards, Brady, & Bloomberg, 2005), to characterize behavioral functioning objectively and with improved ecological validity. They have also been constructed to help facilitate the rehabilitation of individuals with functional impairments, such as acquired brain injuries with consequent cognitive impairments (Broeren, Bjorkdahl, Pascher, & Rydmark, 2002; Buckwalter & Rizzo,

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1997; Christiansen et al., 1998; Glantz, Durlach, Barnett, & Aviles, 1997; Goude, Bjork, & Rydmark, 2007; Rose, Brooks, & Rizzo, 2005; Slobounov, Tutwiler, Sebastianelli, & Slobounov, 2006).

More specifically, VE technology has enabled systematic, laboratory-based investigation of spatial navigation in humans (Maguire, Burgess, & O'Keefe, 1999), including assessment of spatial-knowledge acquisition (Gillner & Mallot, 1998), sex differences (Astur, Ortiz, & Sutherland, 1998), theta oscillations in electroencephalography (Kahana, Sekuler, Caplan, Kirschen, & Madsen, 1999), age changes in route learning (Moffat, Zonderman, & Resnick, 2001), and regional brain activation patterns (Christiansen et al. 1998). These efforts provide a considerable increase in scientific sophistication beyond historical approaches. The key innovation is that navigation within VEs of highly adjustable complexity can be achieved in the egocentric perspective, with much of the relevant information unseen at any specific time (Maguire et al., 1999). Prior to use of VEs, much of the literature involved "table-top" tests of spatial memory, such as mazes or maps (Galea & Kimura, 1993). Although these tools can be well controlled by the experimenter, they assess route learning in allocentric perspective with all spatial information available within a two-dimensional field of view, which is only one component of the range of spatial skills required in ecological navigation (Sandstrom, Kaufman, & Huettel, 1998). This apparent dichotomy between allocentric and egocentric aspects of spatial navigation is also reinforced by clinical literature. Patients with topographical memory impairment, who present with well-intact table-top spatial and geographical knowledge tests, have been described in the literature (McCarthy, Evans, & Hodges, 1996). Conversely, Maguire and Cipolotti (1998) reported a patient with selective preservation of navigation ability in the context of profound verbal and visual memory impairment and poor geographical knowledge, confirming the double dissociation between navigation and table-top spatial tasks. Nadolne (Nadolne & Stringer, 2001) even suggested that paper-and-pencil spatial performance is independent of true way-finding or navigation ability.

Many studies to date have examined spatial navigation in virtual environments using the Morris water maze task (Maguire et al., 1999; Moffat et al., 2001; Sandstrom et al., 1998). Researchers have suggested that landmarks and geometric information are essential elements for navigation (Astur et al., 1998; Maguire et al., 1999; Moffat et al., 2001; Sandstrom et al., 1998). In addition, it has been noted that males often outperform females on spatial-navigation tasks (Astur et al., 1998; Galea & Kimura, 1993; Maguire et al., 1999; Sandstrom et al., 1998), and older participants are reported to travel further and take longer to solve each trial (Kirasic, 1991; Moffat et al., 2001). However, research is limited in examining tasks that would challenge every-day individuals such as navigating the city streets.

Consequently, there is interest in developing VEs as assessment tools to provide an improved probe of deficient spatial-navigation abilities. One obvious application area for such tools is improved detection and classification of individuals with Alzheimer's disease (AD), or those with mild cognitive impairment (MCI) at elevated risk of progressing to AD. Previously, VEs have been employed to examine the ability of individuals with AD and MCI to remember spatially their location or the location of items around them (Burgess, Trinkler, King, Kennedy, & Cipolotti, 2006; Drzezga et al., 2005). Consistent with this work, it has been posited that memory deficits may inhibit navigation within a VE due to damage in cerebral regions such as the hippocampal formation, which is significantly affected by AD pathology (Braak & Braak, 1991). An alternative and supplementary hypothesis, however, is that the inability to navigate throughout a VE or the world in general is linked to deficits in cerebral regions supporting visually guided movements. Successful navigation in a VE suggests intact egocentric spatial ability, implicitly extending to the real world, whereas navigation deficits can occur either due to spatial memory impairment or due to reductions in effective visually guided movements, both challenging the decision-making processes.

Further work is needed to investigate this alternative hypothesis and to investigate the clinical utility and sensitivity of navigational functioning as an early diagnostic marker for MCI and AD populations. The purpose of the present work was to examine carefully the ability of individuals with and without MCI to traverse routes within the Sunnybrook City VE, a realistic but fictional depiction of several city blocks (Figure 1). Both the ability to navigate by memory and visuomotor control in Sunnybrook City were examined and compared to standard neuropsychological measures of spatial navigation.

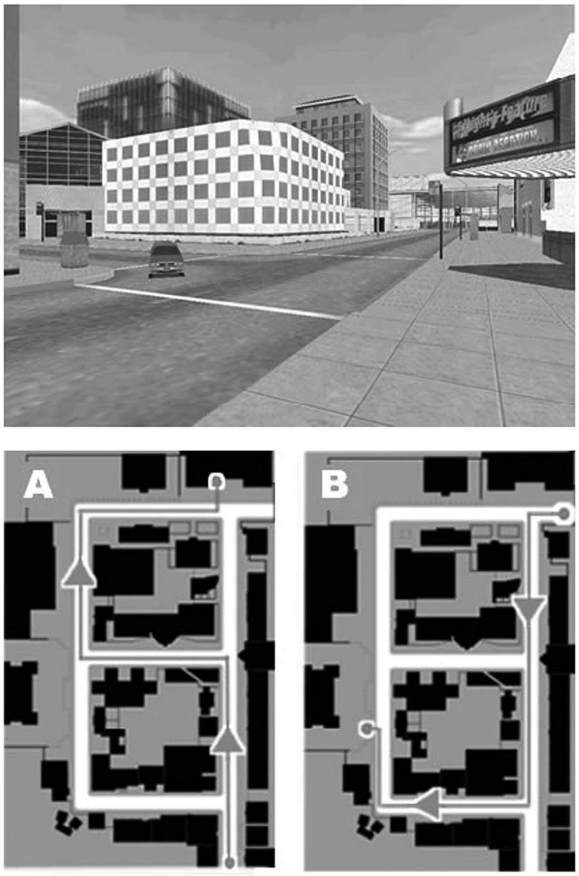

Figure 1. Representative screen capture and map of the virtual city used. Path A (left panel) and Path B (right panel).

METHOD

Participants

Participants were part of the Sunnybrook Dementia Study and were recruited from the Cognitive Neurology Clinic at Sunnybrook Health Sciences Center. All participants had adequate visual and auditory acuity to complete testing. A total of 34 participants were recruited and were divided into two groups matched for age, education, and sex. Initially, the study started with 26 control participants (age 69 ± 7.7 years, range 58–79 years; Mini-Mental State Examination, MMSE ≥ 29; years of education 16.6 ± 0.69; 16 male) and 8 MCI patients (age 72 ± 7 years, range 59–83 years; MMSE ≥ 26; years of education 15.4 ± 1.1; 4 male). However, 8 controls were unable to complete all testing in the VE due to fatigue or illness (N = 2) or computer malfunction (N = 6). In addition, neuropsychological data for 3 controls were unavailable due to computer malfunction. These participants were excluded from the subsequent analysis. All volunteers gave informed consent to participate, and the study was conducted with the approval of the Sunnybrook Health Sciences Center Research Ethics Board.

The MCI patients in this study met Petersen criteria for mild cognitive impairment (Petersen et al., 1999). One patient was defined as amnestic MCI (Dementia Rating Scale, DRS, Memory). All patients received a comprehensive clinical evaluation, including detailed medical history review, neurological examination, routine laboratory investigation, and neuropsychological testing with a standardized test battery.

Neuropsychological tests

The neuropsychological test battery chosen for this study consisted of assessments commonly used within the Sunnybrook Health Sciences Center Clinic. The tests have been well validated historically, assessing spatial ability, executive function, and dementia-related memory deficits with sufficient range of difficulty (floor and ceiling effects) to chart the behavioral course of disease onset and duration. Each participant performed the Rey–Osterrieth Complex Figure Test (RCFT; Copy, Immediate Recall, Delayed Recall); the Trail Making Test (A and B); the Digit Span subtest (Forward and Backward) from the Wechsler Adult Intelligence Scale–Revised; the Dementia Rating Scale (total, attention, initiation, construction, conceptualization, and memory components); and the Mini-Mental State Examination.

VE experimental apparatus

The experiment made use of an existing virtual-reality (VR) platform for the development and display of the VEs (Mraz et al., 2003). The platform consisted of a computer workstation (Dell Inc., 2 GHz Intel Xeon processor, 1 GB RAM, 36 GB HD, 21-inch SVGA monitor, 3Dlabs Wildcat 5110 graphics card) to develop and render complex computer graphics at frame rates close to motion picture quality (approximately 30 frames/second). The VE was developed within a real-time visual environment (WorldUp Release 5.0, Sense8, Inc.) and was presented to the participant using an LCD projector (Boxlight Corp). Interaction was achieved using a modified eight-way gameport joystick (PC Gamepad, Gravis, Inc.). The device allowed recording of both button-press responses as well as navigational control. Joystick calibration was performed using the generic gameport joystick utility provided in the workstation operating system (Windows 2000 SP2, Microsoft Corp.).

The testing platform also included a scan converter (DSC-10224G, Sony Corp.) connected to a video cassette recorder (HS-U650, Mitsubishi Corp.) and a television monitor (KV-13TR10, Sony Corp.). These devices allowed experiences within the VE to be recorded on videotape. Behavioral assessment measures and rating scales based on human observation were therefore easily recorded offline after the experiments were conducted.

VE test

The VE used in this study was a realistic city environment (approximately 2.5 city blocks) called "Sunnybrook City," with capability to "walk" participants through prerecorded paths and for participants to engage in self-directed movement (Ku et al., 2003; Mraz et al., 2003). Two paths (A and B) were chosen with fixed start and end points (Figure 1, top). The paths were not elaborate but were constructed to understand how effectively each group traversed them. The VE task consisted of a set of three learning trials for Path A followed by one learning trial for Path B. For each trial, the participant first viewed the pertinent path through the city passively (Figure 1, top panel). Participants were instructed to pay attention to where various landmarks were located within the city and with respect to one another. After the path was completely viewed, participants were returned to the start position and were required to replicate the path to the best of their abilities. Path B served as an interference condition and was conducted using a separate path design in the same city environment to counteract perceptual priming effects. Following these trials were short-delay (5 min) and long-delay (20 min) recall trials, during which participants navigated Path A by memory alone, with no passive viewing component.

During the long delay, participants completed a questionnaire to quantify the degree of discomfort experienced during VE exposure. This simulator sickness questionnaire (SSQ; Kennedy, Fowlkes, & Lilienthal, 1993) has been used extensively for quantifying symptoms of "cybersickness" that are thought to arise due to effects such as sensory conflict, imperfect representation of sensory stimuli, or imperfect sensorimotor integration within the VE. The SSQ separates simulator sickness into three components: nausea (nausea, stomach awareness, increased salivation, burping); oculomotor discomfort (eyestrain, difficulty focusing, blurred vision and headache); and disorientation (dizziness, vertigo). The components are then combined to give a total SSQ score (min = 0, max = 235.62).

Quantifying task performance in the VE

Spatial memory and visuomotor performance were used to characterize the ability of participants to traverse paths in Sunnybrook City. From videotape, the number of wrong turns was recorded for each trial. From joystick data recorded to computer file (x and y spatial coordinates as a function of time) and the (x, y) coordinates for Paths A and B, three additional measures were recorded: the rate at which participants moved throughout the VE, (i.e., speed in virtual m/s); total completion time for each trial; and a reaction time characterizing the time needed to perform a movement when presented with a turn or directional change.

RESULTS

Neuropsychological tests

Table 1 displays the means and standard deviations for all neuropsychological test variables, for the MCI and control groups. As anticipated, the groups were highly similar when characterized by these measures. Multivariate analysis covaried for age, sex, and education showed only one significant effect between groups occurring on the DRS initiation task, $F(1, 26) = 7.55$, $p < .05$. All remaining variables were not statistically significant.

VE test

A univariate analysis indicated no significant effect between groups based on number of incorrect responses, $F(1, 24) = 0.313$, $p = .76$. Based on these results, both participant groups were similarly successful in navigating Sunnybrook City to learn Paths A and B by memory. This result is also not surprising, given the simplicity of the routes.

However, some differences were revealed through more detailed analysis of how MCI patients and controls traversed paths during the various trials. Considering speed of movement within Sunnybrook City, repeated measures analysis of variance (ANOVA; tests of normality met: Kolmogorov–Smirnov $p < .001$) yielded a significant main effect of group, $F(1, 24) = 4.69$, $p < .05$, and trial for Path A, $F(2, 48) = 10.38$, $p < .001$. However, no interaction effect was observed. Thus, both groups improved at a similar rate across trials, but overall MCI participants moved at reduced speed (Figure 2). Furthermore, effect size calculations for Trials 1–3 (Cohen's $d = 1.50$, 1.35, 1.10), confirmed that MCI and control groups performed quite differently over learning

TABLE 1
Means and standard deviation for control and MCI participants for all neuropsychology measures

Neuropsychological tests	*Mean*	*SD*
DRS		
Total		
Control	140.08	3.16
MCI	136.50	5.80
Attention		
Control	36.52	0.73
MCI	35.87	1.45
Initiation		
Control	36.65	0.64
MCI	34.62	2.97
Construction		
Control	5.73	0.61
MCI	5.62	0.51
Conceptualization		
Control	37.34	1.66
MCI	38.00	1.06
Memory		
Control	23.82	1.11
MCI	22.37	2.50
Rey		
Copy		
Control	34.36	2.15
MCI	34.25	2.12
Imm		
Control	19.04	6.25
MCI	14.75	5.45
Delay		
Control	18.65	5.63
MCI	12.75	5.55
Trail A		
Control	39.52	12.46
MCI	43.75	14.89
Trail A error		
Control	0.04	0.20
MCI	0.12	0.35
Trail B		
Control	100.78	30.14
MCI	125.75	81.15
Trail B error		
Control	1.08	1.27
MCI	0.87	1.72
Digit Span Fwd		
Control	9.00	1.67
MCI	8.00	2.39
Digit Span Bwd		
Control	7.26	2.26
MCI	6.87	1.95

Note. MCI = mild cognitive impairment. DRS = Dementia Rating Scale. Rey = Rey–Osterrieth Complex Figure Test. Imm = Immediate Recall. Delay = Delayed Recall. Trail A, Trail B = Trail Making Test, A and B. Digit Span Fwd = Digit Span Forward. Digit Span Bwd = Digit Span Backward.

trials. No significant differences were observed between the groups on the short-delay and long-delay trials (Table 2).

Lastly, a univariate analysis showed the MCI group exhibited a significant increase in average reaction time compared to controls, $F(1, 24) = 11.24$, $p < .05$ (see Figure 3). Thus, overall the MCI group takes greater amount of time across trials to respond to changes in maze direction.

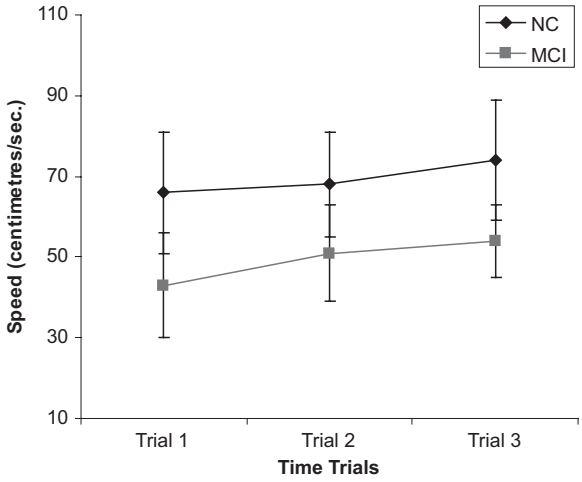

Figure 2. Mean movement and standard deviation values for the normal control (NC) group and the mild cognitive impairment (MCI) group, displayed for the three "Path A" trial conditions.

TABLE 2
Mean and standard deviation of speed of movement for control and MCI participants completing short and long delay trials in Sunnybrook City

	Speed (virtual cm/s)	
Group	*Short delay*	*Long delay*
Control	73.45 ± 18.59	73.84 ± 17.37
MCI	64.00 ± 14.33	64.00 ± 9.45

Note. MCI = mild cognitive impairment. Means and standard deviations are shown.

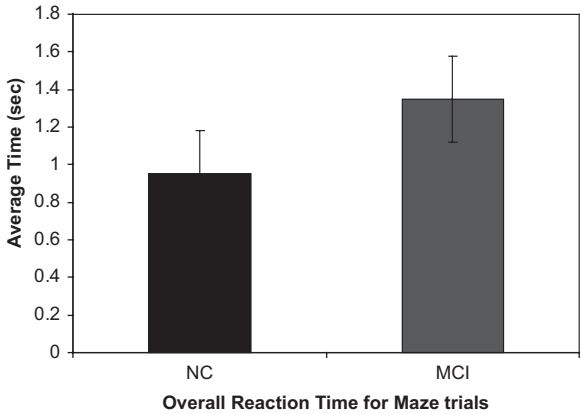

Figure 3. Overall average reaction time and standard deviation values for the normal control (NC) and the mild cognitive impairment (MCI) group.

Relationship between neuropsychological and VE test variables

To examine neuropsychological testing performance, an index of memory was estimated by conducting a factor analysis: memory index = (0.934 × Rey delayed recall) + (0.904 × Rey immediate recall) + (0.611 × forward digit span) + (0.530 × DRS memory). Internal consistency of the memory index was 0.77 as quantified by Cronbach's α. Two measures of the VE task were significantly correlated with the memory index: time to completion on Trial 1 and that on Long Delay Recall. This initial finding was then used to perform an additional factor analysis providing an overall VE navigation index, consisting of a memory component and a movement component. The VE movement index was composed of measures in only Trial 1 (distance traveled and wrong-turn metrics) because the other trials involved repeated exposure:

$$\text{VE memory index} = (\text{long delay completion time}) + Z(\text{Trial 1 completion time})$$

$$\text{VE movement index} = 0.870 \times (\text{no. wrong turns}) + 0.734 \times (\text{distance traveled}) + 0.598 \times (\text{no. double wrong turns})$$

$$\text{VE navigation index} = \text{VR memory index} + \text{VR movement index}$$

The VE indices were subsequently analyzed to explore the relationship with the available neuropsychological test variables. Table 3 illustrates that the VE navigation index was more highly correlated with the VE movement than with the VE memory index and showed significant correlation with the Trail Making Test (A error, and B error). The VE movement and memory indices did not show statistically significant correlations. The VE movement index also was significantly correlated with the Trail Making Test measures (A, A error, B error), whereas the VE memory index was correlated with measures of the Rey immediate recall and delayed recall.

TABLE 3
Pearson correlations between the VE indexes and neuropsychological tests

	VE navigation	*VE movement*	*VE memory*
VE movement	.94**		
VE memory	.58*	.32	
Memory index	−.24	−.13	−.55*
Rey immediate recall	−.25	−.12	−.60**
Rey delayed recall	−.21	−.05	−.54*
Trail Making Test A	.35	.46**	.08
Trail Making Test A error	.49	.41*	.08
Trail Making Test B error	.58*	.47**	.23

Note. VE = virtual environment.
* $p < .05$. ** $p < .01$.

SSQ results showed only a small, statistically insignificant discrepancy in means between the control and MCI groups (43.8 vs. 69.7), $F(1, 18) = 1.77$, $p = .20$. These SSQ scores indicate that on average, participants felt a mild level of discomfort during VE tests, irrespective of group.

DISCUSSION

The results of this study demonstrate that VE technology can be used to assess spatial memory and navigation skills and that the measures of this behavior in a VE are related to those of newer and conventional neuropsychological tests. The VE *memory* index was related to the RCFT (immediate and delayed), but the VE *movement* index was related to the Trail Making Test, which is known to assess visuomotor skills and executive function. These results suggest that navigational learning in a VE is very useful in the assessment of spatial memory. Although not directly assessed in this study, it is likely that the VE navigational-learning task can provide reliable and valid measures of real-world functional abilities.

Research has demonstrated that patients with AD and a MCI can improve their visually guided performance through training activities that may possibly create therapeutic affects (Yan & Dick, 2006). These effects do not only show positive outcomes for improving visually guided performance, but may have broader implications for all types of activities (Loewenstein, Acevedo, Czaja, & Duara, 2004). Thus, engaging patients with MCI and AD in these activities may offer benefits for these individuals that may transfer to real-world activities. To this end, we sought to understand all aspects surrounding the ability of individuals with and without mild cognitive impairments to traverse routes within Sunnybrook City so to help to increase understanding of impaired navigation and visually guided behavior in patients with dementia. One of the primary hypotheses for this research was that MCI participants experience deficits in maze navigation as a result of overt memory impairments, such as learning how best to get from one location to another. The findings from this study, however, demonstrates that patients with

MCI were as successful as normal controls in correct path choices, locating the starting and ending positions and performing with similar rates of error. Thus, their ability to handle these virtual environments, based on initial analysis, indicates that the groups were relatively indistinguishable. These results may have been related to the fact that the VE was a simple design, and thus the MCI participants were not significantly challenged.

The secondary hypothesis for this research suggested that the inability of patients with MCI to navigate a maze might be linked to deficits in visually guided performance and not related to their ability to remember their egocentric position. The evidence presented here demonstrates that performance in navigating the maze was reduced compared to the normal control sample. The performance reduction, however, was manifested as slower movement, rather than impaired route finding. Accordingly, visually guided performance may be initially affected in patients with MCI, and this subtle difference could be a useful marker in the early detection of MCI. Also, we should point out that navigation times were influenced by patients' ability to react to path choices, which could suggest either spatial deficits in way finding or difficulty in producing sensorimotor transformations (e.g., visually guided movements). Thus, further evaluation to separate out these elements could be of great benefit in this research.

One might argue that the maze was not very elaborate, thus explaining why differences in participants were not observed in relation to maze navigation. Subtle differences, however, are often difficult to distinguish between these populations, a result supported by the lack of significant findings in relation to the neuropsychological data in this study. The neuropsychological findings suggest that traditional measures might not be a sensitive enough tool to evaluate MCI's populations, and further examination of spatial memory (with a more complex design) in addition to measuring visually guided performance may provide insight into viable ways to identify deficits observed in these populations. It would be presumptuous to suggest, however, that visually guided performance within this research endeavor explains the results completely, but, to date, examination of this type of performance in these population samples have been rather minimal, and thus we suggest that further examination, especially with the use of these simulated real-world applications such as VEs, could assist in demarking these groups. To this end, interestingly, a four-year follow-up of these MCI patients showed that 4 converted to AD, 1 to progressive aphasia presumably from frontal–temporal degeneration, and 3 continued to have a mild cognitive impairment. Thus, further evaluation of the MCI population using a larger sample may provide additional insight with the use of VEs in a longitudinal study to identify individuals with the greatest propensity for converting to a form of dementia, based on both spatial memory for navigation and visually guided performance assessments.

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