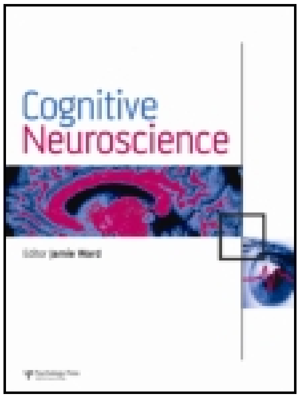

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Francesca Morganti[a], Stefano Stefanini[b] & Giuseppe Riva[cd]

[a] Department of Human and Social Sciences, University of Bergamo, Bergamo, Italy

[b] Fondazione Europea Ricerca Biomedica (FERB), Centro Alzheimer, Ospedale Briolini, Gazzaniga, Italy

[c] Department of Psychology, Catholic University of Milan, Milano, Italy

[d] ATN-P Lab, Istituto Auxologico Italiano IRCCS, Milano, Italy

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From allo- to egocentric spatial ability in early Alzheimer's disease: A study with virtual reality spatial tasks

Francesca Morganti[1], Stefano Stefanini[2], and Giuseppe Riva[3,4]

[1]Department of Human and Social Sciences, University of Bergamo, Bergamo, Italy
[2]Fondazione Europea Ricerca Biomedica (FERB), Centro Alzheimer, Ospedale Briolini, Gazzaniga, Italy
[3]Department of Psychology, Catholic University of Milan, Milano, Italy
[4]ATN-P Lab, Istituto Auxologico Italiano IRCCS, Milano, Italy

The ability to orient in space constitutes a main sign of cognitive impairment in Alzheimer's disease (AD). Presently, a peculiar aspect of topographical disorientation in AD linked with spatial reference frame congruence appears to have been only minimally investigated. We aim to study whether there is a decline in performing the allo- to egocentric translation of spatial knowledge during different types of wayfinding in AD patients. We introduced two virtual reality tasks, the VR-Maze and VR-Road Map tasks, in which we compared 26 AD and 26 healthy, elderly subjects. The results emphasize that there is a specific reduction in performing allo- to egocentric spatial tasks in AD, whereas this reduction is not as evident in equivalent allocentric spatial tasks. The data are consistent with the neurological results regarding the early degeneration of the hippocampus and retrosplenial cortex in AD, which underlies the ability to translate between these two reference frames.

Keywords: Egocentric/Allocentric spatial knowledge; Alzheimer dementia; Virtual reality; Cognitive decline; Neuropsychological assessment.

Topographical orientation is considered a high-level cognitive function that enables agents to navigate familiar and unfamiliar surroundings by integrating different attentional, mnemonic, and perceptual processes (O'Keefe & Nadel, 1978). Within topographical orientation, individuals' abilities for wayfinding are employed because of the capacity to plan and re-plan goal-oriented behaviors and actively acquire knowledge during this interaction. The loss of this capacity appears to be one of the main signs of cognitive impairment in Alzheimer's disease (AD) and the role of reference frames in space, such as egocentric and allocentric points of view is still unclear. According to this perspective the present study aims in evaluating the ability to translate environmental-centered spatial information (allocentric) into body-centered ones (egocentric) in order to perform an efficient wayfinding during the active interaction in a complex environment. Determining a route in a complex setting, in fact, is possible using a set of ego- and allocentric cognitive processes related to the subject's locomotion within an environment that identifies their position in space and the target destination and then outlines the planning of the act (Morganti,

Correspondence should be addressed to: Francesca Morganti, Department of Human and Social Sciences, University of Bergamo, Piazzale S. Agostino, 2, 24129 Bergamo, Italy. E-mail: francesca.morganti@unibg.it

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Carassa, & Geminiani, 2007). Only if an agent is able to create abstract regions with borders and landmarks (route maps) and simultaneously contemplate high-level spatial maps (survey maps) will she/he be able to draw allocentric spatial inferences while engaged in an egocentric exploration. Moreover, as stated by Gunzelmann (2008), establishing correspondence between an egocentric visual scene and an allocentric map is a fundamental process assessed by orientation tasks, and this process requires integrating information across multiple reference frames. Igloi and colleagues (Igloi, Zaoui, Berthoz, & Rondi-Reig, 2009) evidenced the existence of a bidirectional shift between allocentric/egocentric strategies in solving navigation tasks and this evidence suggests a parallel acquisition of the two type of spatial knowledge during interaction. All orientation tasks, such as wayfinding, appear to require the fundamental step of determining how the allo- and egocentric representations correspond.

Recent neuroimaging studies evidenced different contribution of brain areas to egocentric and allocentric spatial knowledge organization. Some fMRI studies on unimpaired subjects have shown how the posterior parahippocampal gyrus is involved in route-based learning (Aguirre, Zarahn, & D'Esposito, 1998) and the hippocampus in the memorization of spatial relationship without landmarks (Maguire, Frackowiak, & Frith, 1997). More recent researches (Epstein, 2005; Wolbers & Buchel, 2005) pointed out that the parahippocampal cortex together with the retrosplenial and posterior parietal cortex is involved in the ability to recognize spatial snapshots and in spatial memory (Hartley, Maguire, Spiers, & Burgess, 2003; Ino et al., 2002). In particular, the parahippocampal area seems to be specifically involved in the recognition of spatial snapshots (Epstein, Parker, & Feiler, 2007) while the retrosplenial cortex is in charge of coding wide scenes that constitute the basis for spatial orientation (Epstein & Higgins, 2007). To the retrosplenial cortex is also assigned the role of locating oneself in space and of combining the head-based information provided by the Papez circuit, with the information about distance, derived from parietal areas (Byrne, Becker, & Burgess, 2007).

Although the acquisition of knowledge is inseparable from its egocentric perspective as described by Wang and Spelke (2002), it cannot be excluded that simultaneously there is also an allocentric reference according to which agents are referring spatial information (Burgess, 2006). Generally, in fact, during a complex environment exploration requiring a prolonged self-motion, it is more efficient to maintain an allocentric map of the environment than to continuously update multiple egocentric representations. The translation between these two systems requires action-oriented egocentric representations derived from allocentric information about self-motion (e.g., the interaction between body referenced right/left turns and environment referenced north/south directions). Thus, in addition to the viewpoint-dependent and action-dependent representation systems, human navigation ability appears to be supported in parallel by a more enduring allocentric representation of the environment (Burgess, 2006, 2008). The neuroscientific evidence of the existence of an allocentric updating process of multiple egocentric representations was supported by the discovery of a reciprocal link between the hippocampus and the entorinal cortex. It suggests that the entorhinal grid cells could combine egocentric motion-related inputs with allocentric environmental-sensory information derived from hippocampus activity (Barry, Hayman, Burgess, & Jeffery, 2007; Hafting, Fyhn, Molden, Moser, & Moser, 2005; McNaughton, Battaglia, Jensen, Moser, & Moser, 2006; O'Keefe & Burgess, 2005).

In the meantime, a large amount of studies have documented the existence of topographic orientation and navigation abilities decline related to advancing age of the subjects without dementia onset (Driscoll, Hamilton, Yeo, Brooks, & Sutherland, 2005; Iaria, Palermo, Committeri, & Barton, 2009; Moffat, 2009; Moffat, Zonderman, & Resnick, 2001). In the literature there are only some indications about the nature of age-related deficits according to egocentric and allocentric types of learning. Wayfinding studies showed how older adults perform egocentric tasks more poorly than their younger counterparts (Head & Isom, 2010) and how younger adults outperform older adults in place-learning tasks, revealing also a substantial age-related alteration in the neural networks supporting allocentric navigation in humans (Moffat, Elkins, & Resnick, 2006).

In recent years, Mitchell and Shiri-Feshki (2009) investigated the impairment of ego- and allocentric memory in patients with Mild Cognitive Impairment (MCI), indicating how the early detection of spatial amnesia could be highly informative regarding the possibility of developing AD. Several other studies have investigated this issue in patients with MCI using either natural or virtual reality-based environments (Burgess, Trinkler, King, Kennedy, & Cipolotti, 2006; Hort et al., 2007; Plancher, Tirard, Gyselinck, Nicolas, & Piolino, 2012; Weniger, Ruhleder, Lange, Wolf, & Irle, 2011). Specifically, when the spatial task required allocentric representation, the performance in both ego- and allocentric spatial tasks appear to be deficitary in MCI populations compared to healthy, aged control groups.

Navigational impairments have also been detected in the early stages of Alzheimer disease (AD) (Nestor, Fryer, Smielewski, & Hodges, 2003; Silverberg et al., 2011), and these deficits may be the discriminating element from other forms of dementia. Several clinically-relevant impairments in navigational skills ("getting lost in familiar places" and "wandering") are often apparent in the early stages of Alzheimer's disease and, in many cases, reports of impaired spatial behavior lead to the recognition of cognitive impairment and diagnosis of dementia (Klein et al., 1999; Serino & Riva, 2013). A study by Jack et al. (1997) indicated that the hippocampus is generally known to atrophy in mild AD; however, this result alone does not sufficiently inform us regarding the correspondence of allo- and egocentric frames of reference. A recent research showed that the entorhinal cortex is one of the first brain regions to be affected in early AD (Suthana et al., 2012). There is also a hypometabolism of the retrosplenial cortex (RSC) and hippocampus in AD patients (Minoshima, Giordani, & Berent, 1997; Pengas et al., 2012; Villain et al., 2008). Notably, these regions and the anatomical connectivity of the RSC to other brain structures—such as the dorsolateral prefrontal cortex, parietal and occipital cortex, anterior thalamic nuclei, and also the hippocampus—could have a key role in determining the correspondence between ego- and allocentric representations (Vann, Aggleton, & Maguire, 2009). Finally, the posterior cingulate region appears to be as vulnerable to neuro-degeneration as the hippocampus (Nestor et al., 2003; Pengas, Hodges, Watson, & Nestor, 2010). In this regard, a recent paper by Bellassen and colleagues (Bellassen, Igloi, Cruz de Souza, Dubois, & Rondi-Reig, 2012) showed how a satisfactory diagnosis of hippocampal-dependent episodic memory impairment in early AD appears as a core challenge and it could be addressed by a specific evaluation of navigation abilities that require hippocampal contribution (e.g., spatio-temporal contextualized wayfinding experimental tasks).

While existing evidence suggests that advancing age is associated with decrements in spatial navigation ability related to different reference frames, the effects of AD on specific aspects of navigational tasks, such as egocentric or allocentric ones, are less well specified. Thus, detecting early cognitive symptoms of topographical disorientation, and the specific contribution of allocentric and egocentric spatial reference on this cognitive decline, is still an essential challenge not only for diagnosis but also for evaluating the progression of the disease.

According to this perspective, we aim to observe whether in AD patients there is a specific impairment in translating the allocentric spatial knowledge acquired from a survey map into the egocentric spatial representations necessary to efficiently perform route-type wayfinding tasks. In our research hypothesis AD patients could be able to perform wayfinding from an allocentric perspective (as assessed by the majority of neuropsychological tests) but it does not directly mean that they will be able to acquire spatial knowledge starting from this perspective and translate it into an egocentric one in order to use it for an efficient wayfinding. Specifically, we consider this allo- to egocentric ability as the key factor to be investigated for an early spatial disorientation assessment in early AD. This research hypothesis appears to be coherent with previously described neurological results in which the early degeneration of the hippocampus and retrosplenial cortex in AD underlies the ability to translate between these two reference frames. By the use of virtual reality we introduce two allo- to egocentric wayfinding tasks that requires an active egocentered wayfinding navigation starting from an allocentric perspective. In the first spatial task, the VR-Maze spatial task, we aim to investigate the ability to actively perform an egocentered wayfinding starting from an equivalent wayfinding performed on a purely allocentric perspective. In the second spatial task, the VR-Road Map task, we would like to understand if there is a difference between imagining the translation between the allocentric and egocentric perspective or to actively perform it during a wayfinding task in a virtual environment.

The main objective of the study is to understand if the allo-to egocentric translation required from both these tasks we proposed is mainly impaired in an early AD population and preserved in the elderly one. If confirmed, this finding could give us an early indicator of the AD onset.

PARTICIPANTS

In this study, we evaluated 26 early-stage Alzheimer's patients (mean age 80.96; *SD* 6.3) recruited at the Briolini Hospital in Bergamo and 26 healthy volunteers as a control group (CG; mean age 77.23; *SD* 5.25) in virtual reality.

MATHERIALS AND METHODS

A neuropsychological examination was performed for both the Alzheimer (AD) and control (CG) groups. The exam included a general cognitive level assessment (by the Mini Mental State Examination), an evaluation of spatial memory functions (by the Corsi's Span and Supraspan Test), an evaluation of executive functions (by the Tower of London), and an attention evaluation (by the Trail Making Test). Specifically, some tests on body representations (Manikin's Test) and visual exploration (Benton Line Orientation Test) were included. To avoid confounding variables, such as sex differences in spatial skills, male and female genders were balanced. Both AD and CG have the same (very low level) expertise in computer use. It was taken into account by a brief yes/no answers auto-evaluation questionnaire (e.g., "Do you habitually use computerized tools in your everyday life?"; "Did you have used computerized tools before?"; "Are you confident with the use of a keyboard to navigate a computerized environment such as a 3D game?"). All subjects participated as volunteers and provided informed consent for their data treatment.

Materials

To test the participants' abilities to explore a complex environment in an egocentric manner using an allocentric map, we used the VR-Maze spatial task (VR-MT) and VR-Road Map task (VR-RMT). They are originally developed as virtual reality tools (Morganti, Marrakchi, Urban, Iannoccari, & Riva, 2009) based on the classic WISC-R Maze sub-tests and Money's Road Map test. See Figure 1 for details. In both virtual environments created for the spatial tasks, no landmark objects were provided as navigation aids, and all buildings appeared with the identical texture. Both the VR-MT and VR-RMT were fully and actively navigable from an egocentric perspective. It means that each participant can choose her/his own path within the environment and actively perform this path exploration by using an input device. By actively interacting with a virtual environment in such a way, an agent can construct in real time a spatial representation by experiencing the cycles of perception and movement that are the basis for the construction of knowledge. This constitutes a core difference in wayfinding within VR, if compared with the possible dissociation between only physical activity (in which participants can actively move into the virtual environment without be allowed to decide the path to explore), or psychological activity (in which participants can decide the path to explore but do not have the possibility to move in the environment); for a more detailed explanation, see Carassa, Geminiani, Morganti, and Varotto (2002). Both the VR-MT and the VR-RMT can be explored in immersive and desktop modalities. Generally, in immersive modality, participants have to wear a head-mounted display in order to see the environment and a motion sensor in order to input decision movement in the same environment; in the desktop modality, participants can see the environment on a computer screen and can input movement by a joypad or a similar device. For this experiment, because of both the absence of statistical

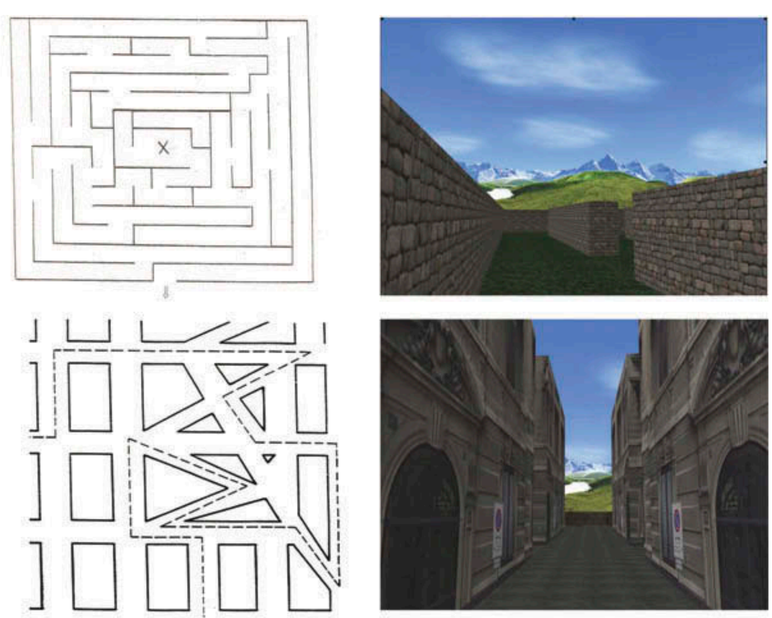

Figure 1. Particulars of the paper and pencil version of the tasks and the snapshots of the VR-MT and VR-RMT 1057 × 793 mm (72 × 72 DPI).

difference between the immersive and non-immersive exploration modalities for wayfinding, evidenced from several authors when the height of the point of view and the visual angle amplitude are equivalent (see Morganti, 2003 for a review), and because of the age-related difficulties in managing immersive devices, we preferred to use the desktop modality. The exploration speed was constant and approximately 5 m and 40° per second. All virtual reality tasks were administered on an Intel Core 2 Duo personal computer and presented on a 15" desktop monitor. The participants were seated in a chair approximately 50 cm from the computer monitor and moved in virtual reality using a narrow keyboard. In order to cope with difficulties elderly participants could have in interacting through a computerized device, we used the QueenKey facilitate keyboard. By using the 2.5 × 2.5 narrow buttons on this keyboard participants can move forward/back and turn left/right. After a brief familiarization period all the participants felt comfortable with the keyboards and were able to move in the virtual environment.

Procedure

The participants were tested individually. Before the beginning of the experimental phase, using a different virtual environment from the experimental one, a 10-minute training session was performed to familiarize the participants with the use of the devices for navigating. During the training phase participants were requested first to move around the environment, avoiding "bumping" into walls and furniture. After, they were requested to reach a target place within the virtual environment in order to find a virtual object. Exclusively for this training phase, if the participant was unable to locate the target object in space, the experimenter guided her/him through vocal cues (e.g., "Let's go straight on and turn left at the second corner"). If the participants had satisfactorily demonstrated their ability to guide themselves within the environment, they were included in the experimental study. Thirty-five AD participants were recruited for the experiment (according to patient's presence in the Briolini Hospital, their voluntary consent to participate the study and their neuropsychological assessment adequateness). Twenty-six showed a good performance after the 10-minute training session, nine of them showed difficulties in the training phase and dropped out (25%). For the control group, 30 participants were recruited and four dropped out after the training phase (20%).

The VR-Maze spatial task

In the VR-Maze spatial task (VR-MT), the participants faced the front of the computer screen and they were provided with one of the paper-and-pencil versions of five different complex mazes (PP-MT). In order to assess allocentric spatial knowledge in the PP-MT, they are requested to draw the path from start to exit trying to find the most efficient way between the two points. After each PP-MT was performed, in order to assess the allo- to egocentric translation of spatial knowledge, we ask participants to use the PP-MT in order to locate the exit point in the corresponding virtual reality version of the mazes (VR-MT). In both maze versions, the start and exit points were obviously indicated. The PP-MT was visible at all times during the VR-MT navigation. For each of the five VR-MT mazes, the north direction in the PP-MT version was depicted at the top of the page, and the corresponding north in the virtual version was indicated by the sun, which was depicted in front of the participant's starting point. To begin the VR-MT exploration, the correspondence between the starting positions on the paper and the virtual version of each maze was obviously indicated to the participants. The participants were not allowed to rotate the paper version of the maze according to the direction navigated in the virtual maze but they were invited to use the north/sun correspondence to re-orient themselves during the virtual navigation. The exit point in the VR-MT was unequivocally recognizable when reached. The wayfinding performance were recorded for each of the five PP-MT and VR-MT. A maze was considered as correctly performed if the participant was able to reach the exit point within the maximum time provided (10 minutes).

The VR-Road Map task

In the VR-Road Map task (VR-RMT), the participants faced the front of the computer screen with the paper version of the Money's Road Map Test (PP-RMT) placed at the base of the screen. The PP-RMT consists of a stylized city map in which participants have to indicate on a 32-step dotted pathway the direction taken at each turn (left or right) in order to follow a designated route. The answers require an egocentric mental rotation, because the dotted pathway follows an erratic trace both away from and towards the subject, who is not allowed to turn the map or to make head and body movements to give the correct answer. Afterward, the participants were asked to use the PP-RMT to specifically navigate the VR-RMT by following the route indicated by the dotted line on the PP-RMT. In this task the participants actively decided which direction to turn at each of the 32 intersections of the VR-RMT and navigate the virtual environment accordingly. The north direction in the PP-RMT was depicted at the top of the page, and the corresponding north direction in the VR-RMT was indicated by the sun, which was depicted in front of the participants' starting point. Before the beginning of the VR-RMT navigation, correspondence to the starting position on the PP-RMT was obviously indicated to the participants. The main objective of this task is to evaluate if the allo- to egocentric translation of spatial knowledge required for the navigation in the simulated virtual reality environment might differ from the one required from a mental imagery simulation of the same environment based on a sketched map. In the first type of simulation (VR-RMT), in fact, the participants have an egocentric perspective on the environment and they are actively able to move within it. In the second type of simulation (PP-RMT), participants have an allocentric perspective on the environment that requires a mental imagery effort to be translated in a possible action. We assume that only being able to perform wayfinding, more than imagining how to perform, requires a peculiar ego- to allocentric translation and it constitutes the element we have to further investigate as the key factor for early AD detection. The participants could see the PP-RMT during the time the virtual exploration occurs but they were not allowed to rotate the paper version according to the direction navigated in the virtual environment. As in the VR-MT, the participants were only allowed to use the north-sun correspondence to re-orient themselves during the virtual navigation. The participants had to state aloud to the experimenter each time they considered one of the 32 turn points as reached. Performance on the VR-RMT was assessed by providing one point for each correct answer; namely, the correct direction (right or left) at each turn for a maximum of 32 points.

RESULTS

An initial comparison between AD and CG groups was performed using neuropsychological tests. Table 1 indicates each test score and significant difference between the groups. The two groups differed not only for the Mini Mental State Examination but also for attention, memory, and visuo-spatial abilities.

For the VR Maze spatial task, the correct execution of each maze was analyzed. A comparison between the AD and CG was performed for the correct execution of the five mazes for both the PP-MT and VR-MT. By using SPSS 20.0 a repeated measure ANOVA (Bonferroni's adjustment) was conducted: 2 Tasks (PP-MT/VR-MT) × 5 Mazes as within factors, and Group (AD/CG) as between variable. Results showed an effect for Task, $F(383, 45)$, $p < .001$, and for the interaction Task × Group, $F(42, 60)$, $p < .001$. There is also an effect for Mazes, $F(7, 64)$, $p < .001$ and for the interaction Mazes × Task $F(4, 52)$, $p < .038$. Between-subjects contrasts revealed a significant effect for Group, $F(89, 22)$, $p < .001$ and for Task $F(383, 45)$, $p < .001$. Comparison for Task × Group confirms that the VR-MT is more difficult to perform than the PP-MT; moreover, the CG showed more correct performances than the AD group in the PP-MT and in the VR-MT. Significant results and means are shown in Tables 2 and 3.

Performance on the VR-RMT was assessed by providing 1 point for each correct answer; namely, the good direction (right or left) at each turn for a maximum of 32 points. We observed significant differences, $F(9, 29)$, $p < .004$, between the AD and CG groups when performing the VR-RMT. The AD group (M = 6.50, SD = 4.21) reached significantly fewer target points than the CG (M = 11.25, SD = 5.55) in the VR-RMT.

TABLE 1
The statistical differences between AD and CG in the neuropsychological assessment

Neuropsychology test	*Between-groups analysis (t-test)*	*Alzheimer*	*Healthy*
Mini Mental State Examination	$F(.872)$ $p < .023$	*M* 21.57 *SD* 2.52	*M* 28.55 *SD* 1.23
Trail Making Test (*A* + B)	$F(.004)$ $p < .001$	*M* 129. 36 *SD* 45.14	*M* 68.15 *SD* 41.58
Tower of London	$F(8.79)$ $p < .020$	*M* 28.00 *SD* 3.94	*M* 32.83 *SD* 1.6
Corsi's span	$F(16.99)$ $p < .001$	*M* 3.6 *SD* .94	*M* 7.61 *SD* 2.87
Corsi's supra span	$F(77.47)$ $p < .001$	*M* 3.55 *SD* 1.27	*M* 20.59 *SD* 9.64
Benton Line Orientation (H)	$F(3.02)$ $p < .001$	*M* 14.33 *SD* 6.43	*M* 28.83 *SD* .98
Manikin's Test	$F(3.86)$ $p < .001$	*M* 17.05 *SD* 3.23	*M* 29.61 *SD* 2.47

TABLE 2
The means and standard deviation values for AD and CG in the VR-MT task

					Int Conf 95%	
Group	*Task*	*Maze*	*Mean*	*SD*	*Inf.*	*Sup.*
AD	PP-MT	1	.923	.053	.816	1.030
		2	.923	.038	.847	.999
		3	.654	.067	.519	.789
		4	.769	.065	.638	.901
		5	.808	.067	.673	.943
	VR_MT	1	.346	.097	.150	.542
		2	.231	.065	.099	.362
		3	.077	.080	−.084	.237
		4	.038	.074	−.110	.187
		5	.000	.071	−.142	.142
CG	PP-MT	1	.923	.053	.816	1.030
		2	1.000	.038	.924	1.076
		3	1.000	.067	.865	1.135
		4	.962	.065	.830	1.093
		5	.923	.067	.788	1.058
	VR_MT	1	.538	.097	.343	.734
		2	.962	.065	.830	1.093
		3	.538	.080	.378	.699
		4	.615	.074	.467	.764
		5	.462	.071	.320	.603

TABLE 3
The ANOVA main results for VR-MT (Bonferroni's adjustment)

Variable	*F value*	*Sig.*	*Effect size*	*Power*
Task	383.45	.000	.885	1.00
Mazes	7.643	.000	.388	.994
Task * Mazes	4.52	.038	.083	.550
Group	89.22	.000	.641	1.00
Task * Group	42.60	.000	.460	1.00
Mazes * Group	2.17	.147	.042	.304
Task * Mazes * Group	.007	.933	.000	.051

A final correlation was conducted between the VR-MT, VR-RMT, and neuropsychological tests proposed to the participants prior to the test phase. The VR-MT results correlated with the Mini Mental State Examination (Pearson's .678, $p < .001$), Corsi's span (Pearson's .505, $p < .001$), Corsi's supra-span (Pearson's .704, $p < .001$), Manikin Test (Pearson's .752, $p < .001$) and Trial Making Test (Pearson's .456, $p < .004$). The VR-RMT results correlated with the Mini Mental State Examination (Pearson's .371, $p < .018$) and Corsi's supra-span (Pearson's .326, $p < .049$).

DISCUSSION AND CONCLUSIONS

The analysis of the performance indicated that a decreasing ability in performing the VR-MT exists in AD, whereas this decrease was not as evident in the PP-MT. Nearly all of the healthy subjects were able to plan a path in the environment when provided with an allo- or egocentric perspective. By contrast, only AD patients appeared to be greatly impaired in the allo- to egocentric translation demanded from the VR-MT. Our results are not only consistent with the result that patients with AD specifically show severe impairment in route learning (Cherrier, Mendez, & Perryman, 2001; Cushman, Stein, & Duffy, 2008; Monacelli, Cushman, Kavcic, & Duffy, 2003) but also with the results from Kalova and colleagues (Kalova, Vlcek, Jarolimova, & Bures, 2005), in which AD patients appear to be specifically impaired in the use of allocentric cues for navigation. We suggest that the results from the VR-MT could be discussed in the interplay between these apparently contrasting results because our spatial task does not investigate pure ego- and allocentric reference frames, but their correspondence. Our data appear to be more consistent with other research results (Laczo et al., 2009; Hort et al., 2007) that emphasize that wayfinding impairment in AD may be dependent on the inability to create and use survey maps of the environment when computing body-centered information for self-orientation, even though there are several main differences between our study and those previously mentioned. One of the main differences is with the procedure they adopted: Both the studies required patients to locate an invisible goal in a circular arena by doing different kinds of pointing. The start-goal relationship and the relative positions in the different subtests they used could be indubitably used to underline deficits in allocentric/egocentric dissociation but are not wayfinding measures. The main focus of our study is to understand how the allo- to egocentric translation can be used in reaching a target place as in everyday wayfinding, and it constitutes in our opinion the main added value of the present study. Moreover, another difference is in the materials we introduce: The VR-MT and VR-RMT are easy-to-use computerized tools that do not require any sophisticated setting up and can be adopted in clinical contexts without specific logistic efforts as they run on a computer desktop. It could constitute a great added value for a neuropsychological evaluation or for a clinical trial that requires the use of technology for the assessment and rehabilitation of spatial knowledge.

Specifically, the results from the VR-MRT emphasize that there is a reduction in Alzheimer's patients in a task that requires them to perform wayfinding from an egocentric perspective while simultaneously using an allocentric map as a spatial knowledge reference. In the VR-RMT, the participants were asked to use the classic Money's Road Map test to guide their turns in the virtual world, and as Schultz (1991) indicated, the paper version of the test is solved primarily by imagining egocentric spatial transformations. Different from the VR-MRT, the subjects reached a decision regarding a turn in front of the screen by acting out the turn they considered appropriate to reach the subsequent turn point. Thus, the participants have to efficiently maintain a stable perspective on the explored world using the allocentric map of the environment in which multiple egocentric representations were continuously updated. The AD patients appeared significantly impaired compared to the CG when continuously translating between allo- and egocentric frames of reference to obtain the required action-oriented egocentric representations derived from allocentric information, as in the VR-RMT. It might be argued that the VR-RMT does not really add any additional knowledge about wayfinding ability if compared to the classical version of the Money's Road Map test, because in the latter participants have to translate between allocentric and egocentric information every time a left/right turn is imagined in a specific target point. In this regard, we believe there is a difference between imagining a right/left turn on a body axis (as in the M-RMT) and performing it in order to obtain a spatial perspective from the simulated world (as in the VR-RMT). Our spatial task, in fact, requires the following steps from participants. First, in the PP-RMT participants look at the map, then imagine how to move on the body axis and finally obtain (and have to keep in mind) the spatial perspective derived from the turn. Then, in the VR-RMT condition, participants first look at the map, then physically turn on the body axis and finally perceive in the simulated world the spatial perspective derived from that turn. We consider that these two different spatial tasks, as they provide different embodied schemas (the first based on imaginative ability, the second on active performance) results in different allocentric-to-egocentric outcomes. Specifically, the VR-MRT, by providing an external representation of the route perspective, may influence perspective taking and provide different performance in spatial orientation than the PP-RMT. From the work of Gray and Fu (2004), we know that when a computer-based interface is well designed, it supports the possibility of placing knowledge in-the-world instead of retrieving it from in-the-head, in order to have it readily available when an agent needs it. According to this embodied vision of human-computer interaction, agents offload cognitive work onto the environment (Wilson, 2002) and it constitutes one of the main advantages of the active interaction supported by the virtual reality interface. The VR-RMT allows guiding orientation by obtaining spatial perspectives from in the world (the different spatial snapshots encountered by the agent after a right/left turn in the virtual environment) rather than retrieving it from in the head (the different inferences on how a perspective would be after a right/left turn in the PP-RMT). Following this interpretation, the main difference between the Money's Road Map Test and the VR-RMT may be related to the difference between simulation and action: Rotating the body on its vertical axis towards the point of reference in virtual reality requires a different allocentric-to-egocentric translation than rotating the body in a mental space. The first is an action that results in a perspective taking while the second is a simulation based on a mental rotation. As pointed out by Hegarty and Waller (2004), there is a dissociation between perspective taking and mental rotation. Perspective taking involves imagining the results of changing one's egocentric frame of reference with respect to the environment. Mental rotation involves imagining the results of changing the positions of objects in the environment, while maintaining one's current orientation in the environment. In the VR-MRT task participants must match the perspective that the virtual scenario is providing them with to their right/left turn intentions in order to match the obtained perspective with the results of each turn, and this matching has to be tightly coupled with internal cognitive processes. The option to offload cognition onto the external visualization provided by VR-RMT (by observing the perspective resulting from a right/left turn) requires an allocentric-to-egocentric translation that appears to be impaired in AD. We must also consider that in the VR-RMT, any turn error causes a discrepancy between the agent's expected and actual position in the environment, which might create a difficulty in subsequent turns. Thus, an error after a wrong turn in the VR-RMT will affect the AD patients more than the CG.

We can partially conclude that an allo- to egocentric translation task is required to emphasize the differences between a non-pathological cognitive decline in the elderly and impairments in this ability connected to Alzheimer's disease. These results appear to confirm recent neuroscientific investigations, which indicate that there are specific impairments in planning spatial tasks in the initial phase of AD, and a compromise in translating allocentric spatial knowledge into the egocentric spatial representations necessary to efficiently perform route-type wayfinding tasks. Moreover, our results appear to be coherent with neurological results in which the early degeneration of the hippocampus and retrosplenial cortex in AD underlies the ability to translate between these two reference frames.

Finally, the VR-MT and VR-RMT correlations with classic neuropsychological tests support our results considering that, not only a general cognitive functionality is assessed from these tasks (as in the Mini Mental State Examination), but specific ego- and allocentric spatial cognitions. Even if we do not assume a total equivalence between the simulated and non-simulated environments, we can nevertheless support the use of virtual reality-based spatial tasks as useful tools for the easiest assessment of allo- to egocentric reference frame correspondence and translation. First, spatial performance in non-simulated settings correlated highly with performance in virtual reality (Cushman et al., 2008), and second, the use of virtual reality-based tasks, such as the VR-MT and VR-RMT, enable us to conduct a more ecological evaluation of the navigational impairment in patients with AD.

In conclusion, our study appears to be congruent with Plancher et al.'s (2012) suggestion according to which, in the early detection of cognitive decline, there is a necessity to introduce a neuropsychological assessment that bears some degree of similarity to the demands of daily life by providing an active and situated cognitive task. Moreover, to focus on the non-verbal behaviors such as the allocentric and egocentric spatial tasks, mainly dependent on the hippocampal activity, appears to be a priority in AD diagnosis. The active wayfinding behavior required from our experimental tasks, and its ability to evaluate the allo- to egocentric translation of spatial encoding appears to be a promising tool for the early detection of Alzheimer's disease.

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