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Review

The contribution of virtual reality to the diagnosis of spatial navigation disorders and to the study of the role of navigational aids: A systematic literature review

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ABSTRACT

Introduction: Spatial navigation, which involves higher cognitive functions, is frequently implemented in daily activities, and is critical to the participation of human beings in mainstream environments. Virtual reality is an expanding tool, which enables on one hand the assessment of the cognitive functions involved in spatial navigation, and on the other the rehabilitation of patients with spatial navigation difficulties. Topographical disorientation is a frequent deficit among patients suffering from neurological diseases. The use of virtual environments enables the information incorporated into the virtual environment to be manipulated empirically. But the impact of manipulations seems differ according to their nature (quantity, occurrence, and characteristics of the stimuli) and the target population.
Methods: We performed a systematic review of research on virtual spatial navigation covering the period from 2005 to 2015. We focused first on the contribution of virtual spatial navigation for patients with brain injury or schizophrenia, or in the context of ageing and dementia, and then on the impact of visual or auditory stimuli on virtual spatial navigation.
Results: On the basis of 6521 abstracts identified in 2 databases (Pubmed and Scopus) with the keywords « navigation » and « virtual », 1103 abstracts were selected by adding the keywords "ageing", "dementia", "brain injury", "stroke", "schizophrenia", "aid", "help", "stimulus" and "cue"; Among these, 63 articles were included in the present qualitative analysis.
Conclusion: Unlike pencil-and-paper tests, virtual reality is useful to assess large-scale navigation strategies in patients with brain injury or schizophrenia, or in the context of ageing and dementia. Better knowledge about both the impact of the different aids and the cognitive processes involved is essential for the use of aids in neurorehabilitation.

1. Introduction

Finding one's way around an environment, whether or not it is familiar, is a common situation for humans. People frequently need to move from one point to another, according to a trajectory that may or may not be known in advance, using different elements – external aids, landmarks or other sources of relevant information. This ability is essential, because it underpins the person's autonomy and his or her participation in society. Spatial navigation has raised interest, and has been the subject of much research in mammals (including humans) on account of its particular integrative role in linking functions in the areas of neurophysiology, learning, memory and cognition [1].

For a number of years, numerous clinical descriptions of brain-injured patients presenting selective losses of the ability to find their way have been undertaken. This disorder has been termed "topographical disorientation" [2]. But there is wide diversity in the types of topographical disorientation observed in these

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patients, and also in the type of brain injury incurred [3]. In addition, the evaluations used to characterise the disorders have been diverse and non-standardised [4].

To start with, tests of spatial cognition on a small scale were elaborated, in the form of "pencil-and-paper" tests, such as the Rotation Mental Test [5] or the Guilford and Zimmermann spatial orientation test. Hegarty et al. [6] showed only partial correlation between paper-and-pencil visuo-spatial tests on a small scale and tests in large-scale virtual or real environments. Spatial navigation in large spaces thus seems to require skills other than those assessed in paper-and-pencil tests. This study concluded to poor ecological validity of pencil-and-paper tests, and confirmed the usefulness of assessing spatial navigation in a large-scale environment, whether real of virtual. Indeed, several authors, among whom Cushman et al. [7], have shown a correlation in navigation performances between real and virtual environments.

The progress in computing and its widespread use from the 1990s have enabled the modelling of simulated environments that are close to reality, known as virtual reality environments. Virtual reality rapidly demonstrated its potential usefulness in clinical practice, in particular in the areas of cognitive evaluation and rehabilitation, and well as for the study of cognitive processes in humans [4]. The evaluation of navigation in a virtual environment has various advantages over evaluation in real situations [8]: it enables better scientific monitoring, it can allow for deficits and disabilities that sometimes make evaluation problematic in real situations, it is less costly, and also safer. From a functional and behavioural viewpoint, it enables immediate feedback on performances in various sensory forms and modes, controlled administration of cues so as to improve performances in a learning approach, and it also enables "time-out" to make room for discussion and the inclusion of different methods.

Following the publication of numerous studies that have shown the advantages of the virtual setting in the area of spatial cognition, it seemed important to us to perform an up-to-date review on the contributions of the use of virtual reality in the exploration of spatial navigation, especially in populations with cognitive impairments. These patients are particularly likely to present spatial cognition disorders, which are highly damaging for social participation in their ordinary environments [2,3]. In addition, the clinical use of virtual environments, because it enables more strict experimental control than working in a real environment, makes it possible to measure the influence of different components brought into play on spatial navigation performances. Thus environmental cues are used as sensory cues of the bottom-up type, and provide scope for investigation, where the use of virtual reality has much to contribute. The review presented here has two objectives: the first is to detail the clinical use of virtual reality in spatial navigation in populations with cognitive disorders; the second is to provide an update on the literature on the impact on virtual spatial navigation of using visual and auditory environmental cues.

2. Methods

This review was conducted on two medical databases, PubMed and Scopus (for the Scopus database, only articles in the area of the health sciences were searched). The following Mesh keywords were used: "navigation", "virtual", "ageing", "dementia", "brain injury", "schizophrenia", "stroke", "cue", "help", "aid", and "stimulus". The basic search algorithm was "navigation AND virtual" to which all the other keywords were associated in turn. The processing of results was performed according to Prisma guidelines. Articles published in English in the area of the life sciences from 2005 to June 2015 were retained. The articles were selected on the basis of title and abstract. The final selection was discussed by the three authors of the present article (MC, PAJ, ES) with respect to the two objectives defined above. A flow diagram (Fig. 1) illustrates the article selection procedure.

In all, 44 articles complying with the first objective and 19 with the second objective were retained. The main characteristics of these articles are summed up in Tables 1 and 2 using the following characteristics: first author, virtual environment used, population (numbers and type) study objective and main result.

3. Results

3.1. Contributions of spatial navigation in virtual reality in different populations presenting cognitive disturbances

3.1.1. Spatial navigation and normal ageing

The effect of ageing on navigation skills in large spaces has been widely described [9]. Generally speaking, the remembrance of spatial configurations and landmarks during navigation loses precision with age [10], while paradoxically, learning a route from an aerial view appears, according to certain authors, to be preserved [11]. More specifically, different studies in virtual reality setting have shown alterations in the allocentric processing of information (i.e. spatial configurations) among elderly subjects using a virtual water maze [12], other maze models (wall maze, radial maze) [13–16], or virtual city districts [17,18]. Similarly, other studies using mazes or other virtual environments evidence difficulties in acquiring spatial representations thought to result from an age-linked decline in hippocampus function, which appears to spontaneously direct elderly subjects towards the use of egocentric strategies [19–23]. A recent study comparing a virtual and a real city district however showed that elderly subjects encounter greater difficulties than young subjects in finding their way, this being related to decline in executive functions, while the spatial knowledge acquired in the virtual environment did not significantly differ between the two groups. This age-linked executive decline, affecting planning and the choice of appropriate navigation strategies, is confirmed by different studies [9,12]. However certain elderly subjects retain better abilities to adapt their strategies [14]. This observation is not however confirmed in the study by Carelli et al. [13]. Finally, for certain authors, failure to efficiently integrate sensory-motor information could also be implicated in the deterioration of spatial navigation skills [25–28]. Overall, virtual reality studies indicate that navigation disturbances in the course of normal ageing is multi-determined, and has origins that can be mnesic (allocentric processing associated with hippocampus function), executive (strategic processing associated with front-lobe function) or related to sensory-motor integration (integration of the itinerary associated with the retrosplenial cortex).

3.1.2. Spatial navigation and Alzheimer-type dementia

Altered large-scale spatial cognition in Alzheimer-type dementia (ATD) has been described in different studies using virtual reality [7,17,29,30]. The study by Ballassen et al. [31] suggests that memory of the temporal type in the course of a navigation task, which tends to be related to allocentric strategies, is a selective behavioural marker for ATD. Topographical disorientation is often considered to be a prodromal sign of this pathology, and has led authors to use virtual environments in order to objectify the early signs and evidence the underlying neurological correlates [32–34]. Weniger et al. [30] retrospectively compared the spatial navigation performances of a group of patients with mild cognitive impairment (MCI) that evolved towards ATD and a group of MCI patients who did not evolve towards ATD. The authors did not

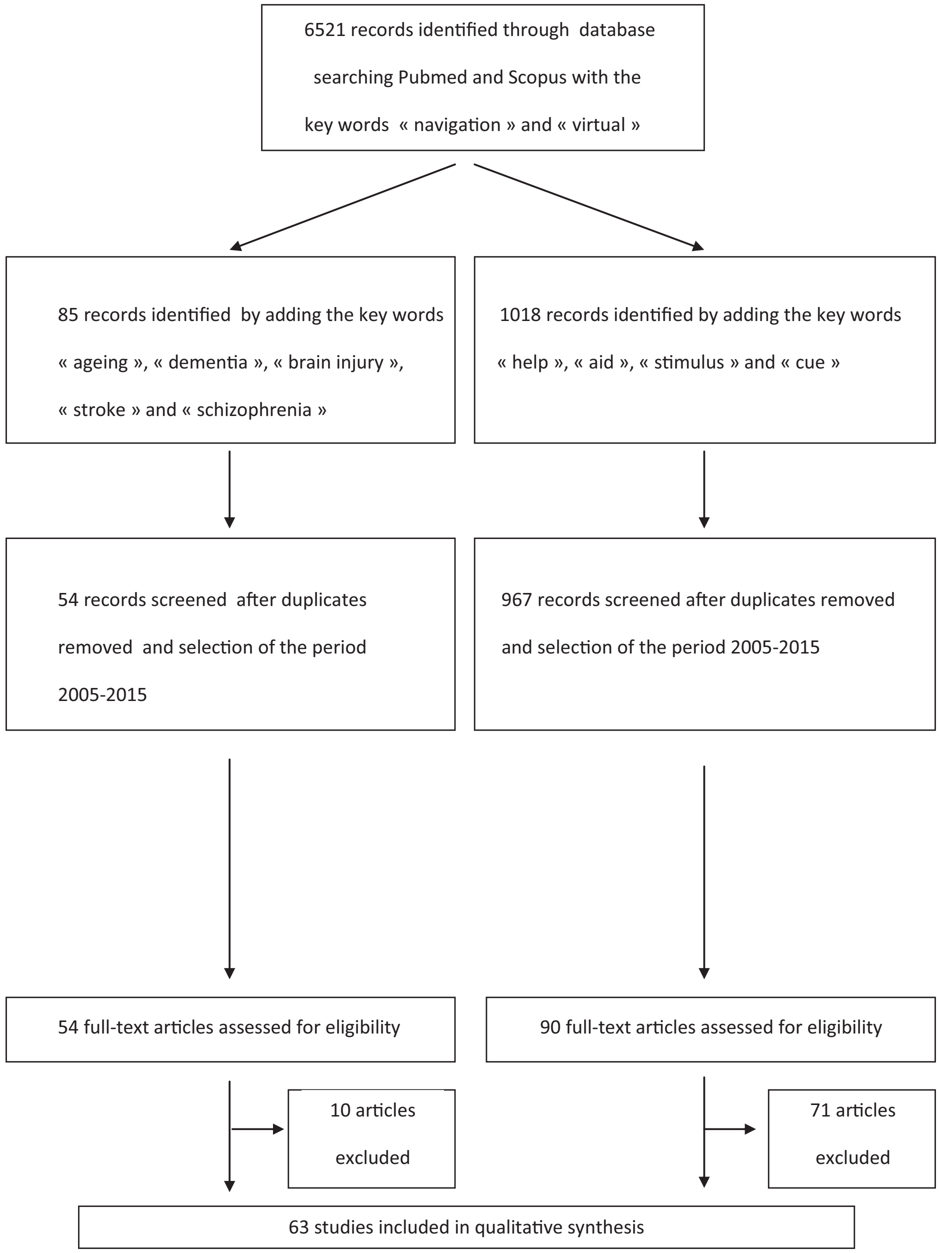

Fig. 1. Flow diagram.

evidence any differences between these two populations in virtual reality navigation performances, whatever the conditions (allocentric or egocentric). They did however observe that the size of the hippocampus was significantly smaller in the MCI-ATD group than in the MCI group that did not progress to dementia. In this study, the lack of specificity of the different navigation tasks assigned with respect to the different navigation strategies (allocentric or egocentric) possibly prevented the differentiation of the two groups.

Cushman et al. [7] compared navigation in real and virtual environment in populations of young, healthy elderly, MCI and ATD subjects, and they found strong correlations between the results obtained in the two environments for the four groups, thus demonstrating the robust ecological validity of virtual environments. This study, and also that by Zakzani et al. [17], showed that ATD patients, and to a lesser degree MCI patients, exhibited deficits in recalling landmarks, itineraries and the configuration of the environment explored. However, in complementary manner, in a more recent study, Kessels et al. [35] observed that implicit memory of objects placed at decisional locations in the path-finding task was not impaired in ATD patients presenting atrophy of the middle temporal lobe in comparison with healthy subjects. In addition, Burgess et al. [36] earlier noted selective impairment of the allocentric component of spatial memory in ATD, and Drzezga et al. [37], among ATD or MCI patients, observed greater difficulty in inhibiting the intervention of cerebral processes non-relevant to the navigation task compared to healthy subjects. The authors thus concluded that spatial navigation disturbances are robust clinical signs for ATD and MCI. Better understanding of their manifestations, and the elaboration of tasks specific to allocentric navigation in virtual environments, could improve prognosis for progress from early cognitive impairment to dementia. The use of virtual environments is in this respect a particularly valuable approach for the understanding and evaluation of these phenomena that generally show themselves on a large scale and in ordinary living settings.

Table 1
Articles selected with the keywords "ageing" and "dementia".

Authors/year	Main aim	*n*	HC	VE setting*	Other investigation	Main result
Normal aging	Normal aging effects on large scale spatial cognition					
Konishi (2013) [16]	To examine the effects of aging on the hippocampus and caudate nucleus during navigation			Virtual maze	fRMI	Aging process involves a shift from using the hippocampus toward the caudate nucleus during navigation
Taillade (2013) [24]	To assess wayfinding and spatial learning in relation to executive et memory decline			Virtual district		Memory and executive declines hamper spatial navigation in older people
Adamo (2012) [26]	To examine the impact of aging on path integration from avalaible sensorimotor informations			Virtual path		Aging impacts path integration. Result in VE* is poorer than in real setting
Harris (2012) [25]	To explore age differences in path integration both with and without landmark information			Virtual landscape		In a VE* that provided only optic flow information, older participants exhibited deficits in path integration
Wiener (2012) [22]	To investigate age-related differences in repeating and retracing a learned route			Virtual maze		The older participants had greater problems during route retracing than during route repetition
Yamamoto et al. (2012) [11]	To investigate whether increasing age has equal consequences for all types of spatial learning			Virtual town		spatial learning through exploratory navigation is particularly vulnerable to adverse effects of aging, whereas elderly adults may be able to maintain their map reading
Head (2010) [10]	To explore age effects on spatial navigation abilities considering the multiple cognitive and neural factors that contribute to successful navigation			Virtual maze	TDM	Age differences are observed in both wayfinding and route learning
Mahmood (2009) [27]	To investigate age-related differences in participants' ability to determine linear distances, angular rotations, and angular displacement exclusively from visual input			Virtual path		There are age-related deficits in the ability to perform visual return-to-origin tasks
Moffat (2007) [12]	To examine age differences in virtual environment navigation and to assess possible relationships between navigation and structural integrity of hippocampal and extrahippocampal brain regions			Virtual maze	fMRI	Individual differences in regional brain volumes as well as performance on the tests of memory and executive functions contributed to age differences
Moffat (2006) [23]	to examine age differences in functional brain activation during virtual environment navigation			Virtual maze	fMRI	There is an age specific neural networks supporting spatial navigation
Lövdén (2005) [28]	To examine the impact of improved sensorimotor demands on spatial navigation among elderly subjects			Virtual maze		Walking support attenuated age-related decrements in navigational learning
Normal aging	Navigational strategies adaptation					
Harris (2014) [18]	To test the ability of young and old participants to switch from learned routes to finding novel shortcuts			Virtual town		Older participants are impaired in both strategy switching and allocentric processing informations
Morganti (2014) [14]	To test the ability to switch from allocentric to egocentric processing			Virtual maze		Virtual performance is significatively related to the overall cognitive level and age
Bohbot (2012) [21]	To investigate navigational strategies across the life span			Virtual maze		The proportion of subjects using spatial strategy decreases across the life span, in favor of response strategies
Harris (2012) [15]	To explore the effects of age on strategy switching during spatial navigation			Virtual maze		Elderly subjects show a specific "switch-to-place" deficit that could account for apparent impairments in both navigational strategy switching and allocentric processing
Rodgers (2012) [19]	To assess age differences in strategy preference in humans			Virtual maze		Elderly patients preferentially use egocentric strategy
Liu (2011) [20]	To determine the effect of age and gender upon different orientation strategies in virtual environments			Virtual town		Age-related declines in navigation are common across all orientation strategies and confirm gender-specific effects in different spatial domains
Pathological aging	Pathological aging on spatial cognition		HC			
Tarnanas (2015) [34]	To investigate deficits in spatial navigation, prospective memory, and executive function in MCI	25	Yes	Virtual museum	EEG	The VE discriminate the presence of MCI
Bellassen (2012) [31]	To compare temporal memory among various groups following a navigation task	27	Yes	Virtual maze		Temporal order memory tested in a spatial navigation task may provide a selective behavioral marker of AD*
Caffò (2012) [33]	To investigate categorical spatial memory deficits using a virtual navigation-based reorientation task	51	Yes	VE*		VE may represent an evaluation supplement for spatial memory deficits in prodromal stages of Alzheimer's dementia
Nedelska (2012) [29]	To determine whether allocentric spatial navigation impairment would be proportional to right hippocampal volume loss irrespective of general brain atrophy	42	Yes	Virtual maze		The right hippocampus plays a critical role in allocentric navigation, particularly when cognitive impairment is present

Table 1 (*Continued*)

Pathological aging	Pathological aging on spatial cognition		HC			
Kessel (2011) [35]	To examine memory for objects relevant for navigation in patients with Alzheimer's dementia	21	Yes	Virtual maze		Subjects with AD* show implicit memory for directional landmarks
Weniger (2011) [30]	To compare spatial performance according to cortical areas involved in navigation among MCI* subjects	29	Yes	Park and maze	fMRI	Various cortical areas are reduced among patients in relation to spatial performance
Carelli (2011) [13]	To investigate how the transfer from survey (map-like) to route representations is affected after a brain lesion	8	Yes	Virtual maze		Executive functions and visuo-spatial abilities deficits appeared to be more relevant for predicting patients' results in performing the VR Maze task
Pengas (2010) [32]	To compare topographical memory between various population of patients with AD* or MCI*	69	Yes	Virtual town		Virtual test discriminates between patients with AD*, MCI and healthy subjects
Zakzanis (2009) [17]	To examine age- and Alzheimer's disease-related differences in route learning and memory using VR	2	Yes	Virtual town		No difference exists in the landmak recognizing task between older subjects and subjects with dementia
Cushman (2008) [7]	To compare a real-world navigation test with a VE version simulating the same navigational environment	26	Yes	Virtual corridor		Close correlations exist between real-world and virtual navigational deficits that increased across groups
Burgess (2006) [36]	To explore the case of a patient thought to be in the very early stages of AD	1	Yes	Virtual town		This case indicates a new category of topographical disorientation with impaired allocentric spatial memory
Drzezga (2005) [37]	To evaluate both cerebral activation and deactivation in various population including HC, MCI, and AD	21	Yes	Virtual maze	PETsca	Development of AD appears to be characterized by a progressive impairment of cross-modal cerebral deactivation functions

VE: virtual environment; AD: Alzheimer dementia; MCI: mild cognitive impairment; f MRI: functional magnetic resonance imaging.

3.1.3. *Spatial navigation and acquired brain injury in adults*

Evaluation and rehabilitation using virtual reality are two major clinical orientations that have been explored in research on spatial navigation disturbances among subjects in the aftermath of acquired brain injury. Better comprehension of the navigation strategies affected in their relationship with the brain lesions is likewise an important line of research in this population. Different authors have thus shown that among adult patients having sustained head trauma, there are difficulties in acquiring allocentric spatial representations or representations of the configuration of an environment [38,39]. The virtual environments used by these authors to dissociate allocentric and egocentric spatial representations are based on the Morris water task paradigm [40,41]. More recently, among amnesic patients presenting hippocampus lesions, the same team confirmed that the subjects were assisted in their navigation towards a target by proximal landmarks (egocentric strategy) but not if these markers were distant from the target (allocentric strategy) [42]. On the other hand, in a recent study, Weniger et al. [43] demonstrated that patients with left or right focal parietal lesions failed to learn an itinerary in a virtual maze (egocentric strategies coming into play in a learning task of the route type), while their performance in a virtual park (allocentric strategies deployed to learn an itinerary of the configuration of the environment type) was normal. These authors also showed that subjects' right precuneus volume was significantly predictive of performance in the virtual maze, and suggested that the parietal cortex could underpin egocentric strategies in spatial learning skills in large-scale environments. Carelli et al. [13] for their part showed that a group of 8 brain-injured patients (3 with a left hemisphere lesion, 2 with a right hemisphere lesion, 2 with bilateral lesions) had difficulty implementing efficient spatial navigation strategies in a virtual maze from a map of the maze on which they had previously plotted the way to the exit, suggesting difficulties in the transfer of knowledge of the configuration of the environment type to follow an itinerary of the route type. Van der Hamm et al. [44], in a case-based approach, demonstrated a dual dissociation by comparing the spatial navigation performances between two patients presenting right parietal-occipital lesions. In these two patients, the spatial strategies were not affected in the same manner, since one had difficulty in the temporal organisation of the itinerary but not in the recognition of the scenes, and the reverse was true for the other. These authors also confirmed that the main complaints from the patients concerning their topographical disorientation were not detected by the traditional neuropsychological tests as efficiently as with the virtual navigation tests. In an original study, Slobounov et al. [45] compared a group of athletes who had sustained mild brain injury with a matched control group in a virtual navigation task calling on spatial memory. These authors observed that while performances did not show significant differences between the two groups, the brain activation recorded under magnetic resonance imagery (MRI) in the brain injury group showed an increase in brain activity (significantly greater than in the control group) in the parietal cortex, the right dorsal-lateral prefrontal cortex and the right hippocampus. According to these authors, different types of lesion associated with neurone losses and local changes in cellular metabolism could explain certain focal hyperactivations and the recruitment of additional cerebral resources.

The evaluation of patients following a stroke and presenting unilateral spatial neglect affecting navigation was recently the subject of work by Buxbaum et al. [46,47]. In their first study [46], these authors evidenced the sensitivity of the virtual test to detect unilateral spatial neglect problems that that were not detected using the traditional neglect battery, and they showed strong correlations with a navigation task in real environment. The second study [47] confirmed the metric qualities of the virtual reality navigation test on 70 patients presenting right cerebral vascular lesions.

Few studies to date have explored the use of virtual reality in rehabilitation programmes for patients exhibiting topographical disorientation. In a very recent study, the feasibility of a rehabilitation programme using virtual reality among patients following a stroke was tested [48]. The rehabilitation approach was of the top-down type, and showed that the use of virtual environments enabled patients to learn alternative navigation strategies suited to their particular cognitive deficits.

Caglio et al. [49] used simulated navigation tasks in virtual environment to improve mnesic functions in a young head-trauma patient, thus using the multimodal cognitive nature of spatial

Table 2
Articles selected with the keywords "brain injury", "stroke" and "schizophrenia".

Authors/year	Main aim	*n*	HC	VE setting*	Other investigation	Main result
Brain injury & stroke	Description of process and behavioral assessment					
Buxbaum (2012) [48]	To assess a large sample of patients with the aim of developing a clinically useful version of the Virtual Reality Lateralized Attention Test (VRLAT)	70	Yes	Virtual path		The VRLAT is a sensitive, valid, and reliable measure of hemispatial neglect
Carelli (2011) [13]	To investigate how the transfer from survey (map-like) to route representations is affected after a brain lesion	8	Yes	Virtual maze		Effect of brain lesions on the transfer map/navigation
Van der Ham (2010) [45]	Presentation of two cases with navigation problems resulting from parieto-occipital right hemisphere damage	2	X	VE*		A double dissociation between spatial and temporal deficits was found
Slobounov (2010) [46]	To investigate the possibility of residual functional deficits in recently concussed but asymptomatic individuals	15	Yes	Virtual corridor	fMRI	Concussed athletes showed larger cortical networks during encoding than HC
Goodrich-Hunsaker (2010) [43]	To evaluate the importance of the hippocampus in spatial learning and memory	5	Yes	Virtual maze	fMRI	Results confirm the role of hippocampus in human navigation and provide a new link between its mnemonic and navigational roles
Weniger (2009) [44]	To compare subjects with brain injury and healthy control on two virtual reality tasks affording to learn a virtual park (allocentric memory) and a virtual maze (egocentric memory)	24	Yes	Virtual maze and park	fMRI	Left- and right-sided lesioned subjects did not differ on task performance but compared with HC, subjects with parietal cortex lesions were impaired learning the virtual maze
Buxbaum (2008) [47]	To report data from participants with right hemisphere stroke on a new VR navigation test	9	X	Virtual path		The VR test detected lateralized attention deficits in participants whose performance was within the normal range on other neglect tests
Livingstone (2007) [40]	To assess among subjects with TBI what are the spatial strategies impaired	11	Yes	Virtual maze		Navigation of TBI survivors was not impaired when the proximal cues were present but was impaired when proximal cues were absent
Skelton (2006) [41]	To test subjects with TBI in a virtual Morris water maze	17	Yes	Virtual maze		TBI survivors navigated to a visible platform but could not learn the location of the invisible platform
Brain Injury & Stroke	Intervention programs					
Claessen (2015) [49]	To investigate the feasibility of a virtual navigation training to instruct chronic stroke patients to adopt an alternative navigation strategy	6	X	VE*		The navigation strategy that patient use can be influenced after a short training procedure
Caglio (2012) [50]	To describe and evaluate the efficacy of a navigational training program in a ma with TBI	1	X	VE*	fMRI	Intensive training in virtual navigational tasks may result in an enhancement of memory function in brain-damaged adults
Schizophrenia	Description of process and behavioral assessment					
Ledoux (2013) [53]	To scan people with schizophrenia and healthy patients while being tested on navigating in a virtual town	28	Yes	Virtual town	fMRI	Between-group comparisons revealed significantly less activation among patients relative to controls in the left middle frontal gyrus, and right and left hippocampi
Wilkins (2013) [52]	To investigate the strategies used by patients with schizophrenia to solve navigation tasks	21	Yes	Virtual maze		Importance of considering individual strategies when investigating memory and navigation performance among various groups of patients with schizophrenia
Siemerkus (2012) [54]	To observe in fMRI patients with positive symptoms while finding their way in a virtual maze	16	Yes	Virtual maze and park	fMRI	*Les activations des régions pertinentes sont plus marquées dans le groupe contrôle*
Weniger (2008) [51]	To compare subjects with recent-onset schizophrenia with healthy subjects on two virtual reality tasks affording the navigation and learning of a virtual park (allocentric memory) and a virtual maze (egocentric memory)	25	Yes	Virtual maze and park		The more global neural network supporting egocentric spatial learning seems to be less affected than the declarative hippocampal memory system in early stages of schizophrenia

VE: virtual environment; TBI: traumatic brain injury.

navigation to improve impaired functions. In this single-case study, on the basis of functional MRI imagery, the authors suggest that this type of intensive training using virtual tasks might increase the activation of the hippocampus and para-hippocampus regions.

3.1.4. Spatial navigation in schizophrenia

Spatial navigation disorders among schizophrenic patients have been the focus of specific interest in the literature. These patients present altered spatial cognition, in particular regarding spatial strategies of the allocentric type, while egocentric strategies based

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on landmark-direction associations appear to be preserved, with normal to subnormal performances in comparison with healthy subjects [50–52]. The authors of these studies used virtual mazes with landmarks outside the laze derived from the real world (buildings, trees, mountains etc.) to objectify the dissociations on navigation strategies. Ledoux et al. [53], under functional MRI, observed a decrease on hippocampus and middle frontal gyrus activity in these patients in a way-finding task. They suggested that these patients had difficulty associating spatial information with contexts in which it appeared, affecting the formation of cognitive maps. A study by Simierkus et al. [54] under functional MRI however showed than in some of these patients specifically presenting positive symptoms, there was difficulty in recruiting the brain areas required for egocentric learning of spatial information. The authors indicate that this could be related to altered consciousness that these patients with positive schizophrenia symptoms have of themselves and of their relationship with the environment.

3.1.5. Overview

Recent studies on large-scale spatial cognition among subjects presenting cognitive disturbances show first of all the interest of using virtual reality to assess navigation strategies, hitherto inadequately explored using the classic pencil-and-paper tests on small scale. This research confirms that large-scale navigation requires the concurrent processing by the brain of different types of information in the course of navigation, enabling a subject to find his or her way towards a given destination [55]. It shows complementarily between spatial representations of the allocentric type [55,56] and those of the egocentric type [57,58], and the way in which navigation strategies can be selectively affected depending on the brain networks that have been damaged (for a review of the neuroanatomical determinants of large-scale spatial navigation see Chrastil [59]). One perspective afforded by the use of virtual environments simulating reality and appearing in the most recent research concerns the scope for improving the specificity of the virtual tasks assigned to patients for diagnostic and predictive purposes. Large-scale spatial cognition is in itself an excellent integrative model of global brain functioning that is directly linked to complex navigation behaviours in everyday life [60].

3.2. The impact of visual or auditory environmental cues on virtual spatial navigation

One of the central questions when using virtual environments to assess spatial navigation functions is that of the differences in the sensory-motor cues between real and virtual settings. Indeed, the motor control involved in the management of navigation using a keyboard or a joystick is not the same as that implemented in actually walking. The proprioceptive and vestibular information involved in these two types of navigation is also different. Grant and Magee [61] thus showed that participants guided along a real route found the places more easily in the real-environment test than those that had learnt the route in virtual setting (i.e. actually walking in situ, or navigating with a joystick). This was not however evidenced in another study [62]. Williams et al. [63] observed that judgement errors in perspective were greater and latencies longer in repositioning and rotation tasks for subjects in virtual environment compared to those in real environment. Wallet et al. [64] showed that poorer-quality visual information (textured versus non-textured environment) in a virtual city district led to a deficit in the transfer of information in the same, real city setting, independently from whether the initial learning situation for the itinerary was active or passive, which is in favour of the preponderance of visual processing of information over motor information.

One of the lines of research concerns the delivery of complementary sensory-motor information that is poorer when virtual environments are used. Ruddle et al. [65] thus showed that the use of a treadmill exerciser associated with a task consisting in localising items in a supermarket decreased the distances covered and improved the precision of the estimates of distances between products. Larrue et al. [66] demonstrated that the reconstruction of a trajectory in a real environment was performed better when the trajectory had been learnt in either real or virtual situation using a treadmill and rotations of the upper body, in comparison with learning in virtual environment with a joystick or with a treadmill but without upper body rotation. However, a recent study on a task involving a search for goods in a shopping mall also showed that among elderly people difficulties generated by the combination of the virtual environment and the treadmill had a negative impact on performance, where the task required frequent shifts in field of vision in order to move towards the objects [67]. Indeed, adding sensory-motor information or walking during navigation puts elderly or brain-injured subjects in a double-task situation (motor task in moving around and balancing and cognitive task for the navigation parameters) [28], which may have reduced performances. It does however seem that active navigation (motor and cognitive) is beneficial for navigation among young subjects [68].

Despite these differences in terms of sensory-motor cues, a certain number of studies are in favour of the similarity of the processes involved in learning and finding a trajectory in real and virtual environments [7,69,70]. There does indeed appear to be a compensation for the loss of idiothetic information in navigation in virtual environments [71].

Nevertheless, while virtual reality enables the simulation of certain aspects of the real world, it also makes it possible to go beyond reality [72]. This is the case in particular when stimuli are added to a virtual environment in the software. These stimuli can be defined as additional information provided by the virtual system that increases the amount of information present in the environment. However their absence from the environment does not prevent completion of the task. These stimuli can be contextual, that is to say linked to the performance of the task, or non-contextual, that is to say they bear no relationship to the task to be performed.

These sensory stimuli can be of different types–auditory, visual, tactile or olfactory. They can be administered separately or in combination in the course of the performance of the task.

Different studies have assessed the impact of visual or auditory environmental cues delivered by the virtual system on navigation or spatial learning tasks.

3.2.1. Visual cues and virtual spatial navigation (Table 3)

The visual cues used were first of all created in a manner that was analogous with aids available for navigation in an unfamiliar real environment. For instance, Darken and Sibert [73] proposed a virtual map, and they reported a significant impact of this element on navigation performance in a virtual environment among healthy subjects. Sjölinder et al. [74] showed that the use of a map in a virtual environment was useful to improve comprehension of the spatial layout of information, but it slowed participants in their progression on account of the mobilisation of greater cognitive capacities, and also because of the repeated switches between the egocentric perspective of the participant and the allocentric perspective of the map. Parush and Berman [75] showed that at the outset of their test navigation with a map proved more difficult than navigation with a list of instructions for movement, but that this difference became non-significant as the duration of navigation was prolonged. Likewise, the existence of landmarks made the navigation more difficult at the outset, but the difficulty lessened as the navigation went on. The deterioration in

Table 3
Visual stimuli and virtual spatial navigation: articles selected with the keywords “cue”, “help”, “aid” and “stimulus”.

Authors (year)	Population	*n*	VE setting	Main aim	Main result
Smyth (2007)	Healthy subjects	16	Vehicle simulator	Study summarized in the section “auditory stimuli”	Study summarized in the section “auditory stimuli”
Yi (2015)	Mild Alzeihmer	28	Vehicle simulator	Study summarized in the section “auditory stimuli”	Study summarized in the section “auditory stimuli”
Broadbent (2015)	48 children aged 5, 7 and 9 years and 18 participants with William syndrome.	66	Two virtual environment mazes (with and without landmarks)	To examine whether individuals with William syndrome are able to employ a sequential egocentric strategy to guide learning and the retracing of a route	Participants with William syndrome showed significantly greater detriment for route learning and retracing a recently learned route when the landmarks were removed. Typically developing children were able to keep an egocentric navigation strategy when landmarks were removed, contrary to participants with William syndrome
de Condappa (2014)	Healthy subjects	52	A virtual route with 4-way intersections and 2 landmarks at each intersection	To examine the cognitive processes and ocular behavior associated with on-going navigation strategy choice	Participants chose the correct movement direction in 62% of all trials
Slölinger (2005)	24 younger subjects et 24 older subjects	48	Online grocery	To examine the influence of a map on navigation and acquisition of spatial knowledge in a virtual ecological environment	The use of a map improved the understanding of the spatial configural knowledge, but slowed down the navigating subjects. The older participants needed more time to solve the tasks, et showed more difficulties to create configural knowledge
Parush and Berman (2004)	Healthy subjects	109	A T-shaped environment divided into 4 rooms	To evaluate the influence of a route list and a map on acquisition of route and survey spatial knowledge	The initial navigation with a map was harder than with a route list, but this difference became insignificant at the end of the learning phase. A similar pattern was found for the impact of landmarks. Performance degradation upon removal of the navigation aids was less for those that navigated with a map as compared to a route list. Performance degradation upon removal of the navigation aid was less for those that navigated with landmarks as compared to no landmarks
Burigat and Chittaro (2007)	Healthy subjects	48	An air base surrounded by urban areas and an empty sphere	To compare 3 navigation aids (2D and 3D directional arrows pointing towards objects that users had to reach and a 2D radar metaphor) on pointing out the location of objects or places	The 3 navigation aids were helpful for navigation. The 3D directional arrows outperformed the others, except for experienced users. There was a difference between experienced and unexperienced users when using the 2D aids
Livingstone (2007)	11 subjects with traumatic brain injury and 12 control subjects	23	A Morris virtual water maze	To investigate the pattern of preserved or impaired cognitive mechanisms of wayfinding among survivors of traumatic brain injury	The navigation of traumatic brain injury participants was not impaired when the proximal cues were present (egocentric mode) but was impaired when proximal cues were absent (allocentric mode). The addition of distal landmarks did not allow the elaboration of a cognitive map
Van der Brink (2013)	23 30-month-old children and 22 35-month-old children	45	4 ED environments: a beach, an open square, a snow and a park landscape	To investigate orientation abilities on the basis of visual spatial cues in 2-3-year-old children	Neither age group benefited from landmarks present in the environment, suggesting that successful task performance relied on the use of optic flow cues, rather than object-to-object relations
Andersen (2012)	Healthy subjects	7	An eight-arm radial maze	To determine by analysing the oculomotor movements if there is a sex difference in wayfinding with variation of the landmarks' number	Women rely more to landmarks (2 or 6) to navigate than men. The landmarks fixations were associated with an increase in task completion time. The more increased the number of landmarks, the more increased the landmarks fixation time
Boggus (2010)	Healthy subjects	17	A virtual maze	To compare the use of distance field illumination and 4 other navigation aids: directional arrows, a line extending in the direction of a goal, a path from the user to the goal and a map showing the locations of the user and goals	The distance field illumination is an effective cue for aiding in visual search and spatial navigation
Harris (2012)	27 younger subjects and 29 older subjects	56	A dark grey floor with white dots and mountain scenery with landmarks	To explore age differences in path integration (distance and direction estimation and triangle completion) both with and without landmark information	Without landmark information, older participants exhibited deficits in path integration in terms of distance reproduction, rotation reproduction, and triangle completion. With landmark information, an age difference in triangle completion was also found

performance was less marked when navigation aids were removed among participants who had navigated with a map and those who had navigated in an environment with landmarks.

Other authors chose to add visual cues that were unlike cues found in a real environment. For instance, Burigat and Chittaro [76] compared the effect of two navigation aids for location pointing among healthy subjects: 2D and 3D arrows indicating the name, the direction, and the distance of the target, and a 2D radar effect using colored points. They showed that in a large virtual geographical environment the 3 aids were useful for navigation by participants whether or not they had experience of navigation in virtual environments. The 3D aid was more effective that the other two types for non-experienced participants, and there were significant differences in performance between experienced and non-experienced performers with the 2D aids. Boggus and Crawfils [77] demonstrated that progressively lighting up the path to follow to the target was a possible cue technique for navigation in virtual environment.

Finally, different authors have studied the impact of adding or altering landmarks in the virtual environment to be explored. Livingstone et al. [38] for instance had traumatic brain injury subjects perform a wayfinding task in a virtual environment rather like the Morris water maze. They showed that adding landmarks close to the target favoured spatial navigation among these patients (egocentric mode), making their performance comparable to that of the control subjects. In contrast, adding distant visual landmarks did not enable this population of brain-injured patients to elaborate a cognitive map. In addition to this, Andersen et al. [78] evidenced a longer duration of navigation in correlation with the number of instances of eye fixation on landmarks, and found that fixating increased with the number of landmarks in the virtual environment.

Like the Livingstone et al. study [38], other studies have assessed the impact of visual cues on spatial navigation among subjects with difficulties in topographical orientation:

Harris et al. [25] showed an effect of age on performance in the integration of a trajectory, based on optic flow. In the condition with no landmarks elderly subjects had more difficulty in tasks involving estimations of direction or distance, and in the triangle completion task. It can be noted here that the pattern of responses differed between older and younger subjects depending on the distance, the range of the rotation required and the type of task assigned (lesser variability in individual responses, poorer performances for large triangles, over-estimation of rotations for small triangles, under-estimation of large triangles). The only difference linked to landmarks was the greater inter-individual differences among elderly subjects for rotations, only in the condition with landmarks.

Broadbent et al. [79] studied the ability of young adults with a Williams syndrome to learn and reproduce an itinerary performed in a virtual maze, with and without landmarks. These subjects relied more on the landmarks to learn and reproduce a trajectory and had greater difficulty in returning to an egocentric strategy in the absence of landmarks than normally-developing children aged 5, 7 and 9.

Van der Brink et al. [80] for their part used 4 environments representing a beach, an open yard, a snowy landscape and a park, and showed that children of two and a half and three drew no benefit from the presence of landmarks in the environment in a task consisting in maintaining the orientation of the scene.

These different studies reflect the diversity of the impact of visual stimuli on virtual spatial navigation, with notable differences according to the populations studied, the cues used and the way in which they were administered.

3.2.2. Auditory cues in spatial navigation (Table 4)

The impact of auditory cues on spatial navigation was first of all studied in real environments or in augmented reality, and in different populations, for instance maritime navigation among partially blind subjects, or explorations among patients with topographical orientation disorders, resulting for example from brain injury. In this respect, Fickas et al. [81] assessed performances in a route-following task in 4 conditions: aerial map, map orientated according to the viewpoint of the user, auditory instructions and text instructions. The brain-injured patients presenting severe cognitive disorders derived the most assistance from auditory instructions, which is in line with the results of the study by Sohlberg et al. [82] performed in a real urban environment on patients with severe brain trauma.

The studies performed in virtual situations have had different objectives, such as testing the validity of a virtual environmental setup [83,84], reproducing a cognitive task in virtual environment [85], or assessing the impact of auditory stimuli on virtual spatial navigation among healthy subjects compared to patients presenting topographical disorientation.

Concerning the impact of auditory stimuli on virtual spatial navigation in healthy participants, several studies are available.

First, Ardito et al. [86] assessed the impact of auditory stimuli on navigation in a virtual environment reproducing a painting exhibition. Three auditory environments were tested:

- a piece of music semantically associated with each item in the exhibition (functional role);
- a musical background delivered throughout the navigation (aesthetic role);
- no auditory stimulus.

The participants were instructed to remember certain elements in the exhibition on which they were to click in the course of navigation. There was no effect of the music on the number of errors in the task, nor on the speed of execution. One hypothesis made by these authors was that the semantic link between the music and the items in the exhibition was too weak. They therefore reiterated the study forming two groups of participants: one was informed explicitly of the semantic link between the music and the environment, and the other was not. The performances this time were better among participants informed of the link between the auditory stimuli and the environment.

Smyth et al. [87], using a driving simulator, assessed the impact of visual directional cues (yellow arrows), auditory cues (verbal instructions) or the two combined on a navigation task. Among 16 military participants they evidenced an increase in navigation speed with the directional cues. When they added to the workload in this navigation (dual task) fewer elements in the virtual environment (here the number of vehicles passed) were remembered. Likewise, Viaud-Delmon et al. [88] studied the manner in which auditory stimuli could affect memorisation of a virtual spatial environment, here the Morris water maze. The main result of this study was that the participants managed to memorise the spatial localisation of a target without visual information (using only auditory clues). By altering the topographic characteristics of the auditory cues used, these authors showed that removal of a proximal auditory cue or a change in the perimeter of the explored zone did not significantly prolong the duration of the task, in contrast with the rotation of auditory cues or the switching of two cues.

There are also a few studies on the impact of auditory stimuli on virtual spatial navigation among patients presenting topographical orientation disorders.

Sanchez et al. [89] showed that an auditory virtual environment enabled 7 visually impaired children aged 10–12 to find their orientations, move around and acquire mental spatial representations and information for the majority (74%). Alfonso et al. [90] showed that the distance to the auditory cues had an effect on the

Table 4
Auditory stimuli and virtual spatial navigation: articles selected with the keywords "cue", "help", "aid" and "stimulus".

Authors (year)	Population	N	VE setting	Main aim	Main result
Yi (2015)	Mild Alzeihmer	28	Vehicle simulator	To investigate the effectiveness of the GPS (visual or audio informations) in assisting drivers with mild Alzheimer in finding their destination safely	The driving performance score was highest in the audio-only setting, moderate in the normal setting and lowest in the visual-only setting. Drivers using the audio-only setting and normal setting were more likely to successfully find their destination than participants using the visual-only setting
Smyth (2007)	Healthy subjects	16	Vehicle simulator	To evaluate the impact of visual (yellow arrows), audio (instructions) or both directional cues on a navigation task combined to a cognitive task	The participants drove significantly faster with the road-turn cues than with just the map. They recalled fewer vehicle sightings with the cognitive tests than without them. They reported higher perceived workload with the cognitive tests than without them
Sorkin (2005 and 2006)	Subjects with schizophrenia	39 patients /21 control subjects	A virtual maze, inspired by the Wisconsin Card Sorting Test	To diagnose the schizophrenia patients with the rules deduction virtual task	A classification procedure based on the subjects' performance profile (with 4 performance measures: the distractor effect, the errors made while the subject was learning the rule, the number of consecutive errors and the response time) correctly predicted 85% of the schizophrenic patients (and all of the comparison subjects)
Ardito (2007)	Healthy subjects	40 (First part) then 10	the Einstein Tower	To evaluate if a musical background provides a support to user navigation and achievement of the search task in the Einstein Tower	First part: no fonctional role of the musical background on navigation performance was showed (but the semantic link between music and the search task was not explicitly told). If the participants were explicitly told about the relationship between music and virtual scene, the music had a fonctional role on the navigation speed
Viaud-Delmon (2014)	Healthy subjects	11	An auditory equivalent of the Morris water maze	To study how a spatial scene can be memorized on the basis of auditory and idiothetic cues only	Participants succeeded in memorizing the spatial localization of a target without visual informations (using auditory cues only). The absence of the closest landmark did not seem to impact the performance. The rotation of the 3 landmarks and the switch (inversion of two landmarks) lengthened the search time. The modification of the perimeter of the exploration area did not impair the search strategy of the participants.
Sanchez (2012)	Blind children 10-12-year-old	7	Audio-based Environment Simulator (AbES)	To evaluate the impact of the use of an audio and haptic-based videogame on the development of orientation, mobility, orientation and spatial knowledge skills in school-age blind learners	Participants mainly succeeded the proposed activities (minimum: 74%)
Degara (2014)	Healthy subjects	8	A virtual environment where subjects must guide an avatar to a target point using only auditory cues in a computer	To compare two spatial virtual sonification navigation system: the Neate-Yang method (with distance-to-target mapping, obstacle detection and directional mapping) and the Villa's method (with target object sonification, obstacle collisions, angular distance and panning)	Participants were able to find the target 62% of the times using Neate-Yang's sonification method. When using Villa's method, subjects were not able to get to the target
Maidenbaum (2013)	Blind adults	23	A virtual corridor with an angle and with a virtual Eye-Cane	To investigate whether blind and blindfolded users can navigate down a virtual twisting corridor using only the Virtual-EyeCane's single point distance parameter	All participants both sighted and blind, were able to navigate all routes with a virtual Eye-Cane successfully following minimal training
Afonso (2010)	18 blindfolded sighted, 18 late blind and 18 healthy participants	54	A physical and virtual space with 6 virtual sounds	To investigate the role of auditory information on spatial knowledge acquisition by blind participants	The time necessary to create a spatial mental knowledge increases with the distance of the auditory cues. The blindfolded sighted participants were selectively impaired in their ability to generate precise spatial representations from locomotor experience

construction of mental representations of the space in which the cues were located, and that blind people more easily formed spatial representations in the setting of movement through a virtual auditory environment than people normally sighted. Maidenbaum et al. [91] for their part showed that virtual auditory setups, such as a virtual white cane, favoured navigation among visually impaired subjects.

Yi et al. [92], among patients with early Alzheimer's disease, showed that compared to visual GPS, auditory instructions improved spatial navigation performances and generally enabled subjects to reach their destination.

3.2.3. Impact of the characteristics of the virtual environmental cues used

In the literature there are arguments in favour of an influence of presentation and content of the cues used on the navigation performances of participants.

For instance, Riley et al. [93] showed that automatic instructions were more helpful to patients with a consolidation deficit (linked to severe mnesic or dysexecutive disturbances). Thus administration of the implicit type and procedural processing of the sensory cues could be very useful in this population.

The moment at which the stimulus occurs, and whether it is transient or lasting also seem to be important. The fleeting administration of a stimulus could no doubt increase the degree of attention in the subject at a key moment in the navigation, although no study was found assessing this aspect.

The existence of a sematic correspondence between the stimulus administered and the task appears to increase the impact of the stimulus used, in particular when the task performed calls on high-level perceptual abilities [86,94].

The nature of the cue or aid (visual, olfactory, auditory, tactile, etc.) could also be of importance [92].

The gradual lighting-up or the illumination of the pathway according to the distance remaining to the target could also be useful [77].

Concerning landmarks used as cues, Stankiewicz and Kalia [95] showed that structural landmarks were better encoded than objects, and that the informativeness of a landmark determined its memorisation. Caduff and Timpf [96] defined different types of landmark salience: perceptual salience refers to the ability of an object to generate exogenous attention by its particular characteristics (shape, colour, size etc.); cognitive salience involves the endogenous orientation of attention as a result of knowledge possessed or informative cues; contextual salience refers to the influence of the environment and the task to be performed on the ability to focus attention on a particular landmark. Janzen and van Turennout [97] showed that objects placed at decisional points, as well as those that the subject would expect to encounter in a passive spatial navigation task, were recalled better than those placed randomly. Han et al. [98] for their part, using 3 virtual navigation experiments, demonstrated that when the localisation of objects was useful to the navigation, because of attentional focalisation, the remembrance of these objects that had become landmarks and the acquisition of allocentric spatial representations were improved.

Different stimuli appear either as facilitators or as hindrances in navigation tasks. But their real impact can vary with a number of parameters, including the amount of information provided, the moment when it is given, and the population concerned.

4. Conclusion

Virtual reality is a valuable, fast-expanding tool. In the area of spatial navigation it enables assessment of patients in dynamic situations that are close to reality, which is an advantage over traditional assessment approaches of the pencil-and-paper type. It also provides better understanding of the mechanisms at play in navigation. Finally, in addition to the evaluation of deficits, it also affords scope for assessing solutions aiming to improve performances in navigation activities, and thus foster greater participation in daily life for affected subjects.

The use of environmental cues as navigation aids could have several applications in the future with the foreseeable progress in technology:

- assistance in rehabilitation and retraining of patients with spatial navigation difficulties;
- improvement of autonomy in the home for these patients.

Better knowledge of the impact of the characteristics of the aids or cues used and the cognitive processes involved seems essential for their appropriate use. As shown by this systematic review, although some research has got underway along these lines, there is still much to be done to understand how to render interventions with neurological patients efficacious.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Hartley T, Maguire E, Spiers H, et Burgess N. The well-worn route and the path less travelled: distinct neural bases of route following and wayfinding in humans. Neuron 2003;37:877–88.
[2] Aguirre G, et D'Esposito M. Topographical disorientation: a synthesis and taxonomy. Brain 1999;122:1613–28.
[3] Barrash J. A historical review of topographical disorientation and its neuroanatomical correlates. J Clin Exp Neuropsychol 1998;20:807–27.
[4] Rizzo AA, Buckwalter JG. Virtual reality and cognitive assessment and rehabilitation: the state of the art. Stud Health Technol Inform 1997;44:123–46.
[5] Vandenberg SG, Kuse AR. Mental rotations, a group test; 1978.
[6] Hegarty M, Montello DR, Richardson AE, Ishikawa T, Lovelace K. Spatial abilities at different scales: individual differences in aptitude-test performance and spatial-layout learning. Intelligence 2006;34:151–76.
[7] Cushman LA, Stein K, Duffy CJ. Detecting navigational deficits in cognitive aging and Alzheimer disease using virtual reality. Neurology 2008;71:888–95.
[8] Rizzo A, Schultheis M, Kerns K, Mateer C. Analysis of assets for virtual reality applications in neuropsychology. Neuropsychol Rehabil 2004;14:207–39.
[9] Lithfous S, Dufour A, Despres O. Spatial navigation in 798 normal aging and the prodromal stage of Alzheimer's disease: 799 insights from imaging and behavioral studies. Ageing Res Rev 2012;800:201–13.
[10] Head D, Isom M. Age effects on wayfinding and route learning skills. Behav Brain Res 2010;209:49–58.
[11] Yamamoto N, DeGirolamo GJ. Differential effects of aging on spatial learning through exploratory navigation and map reading. Front Aging Neurosci 2012;14:14.
[12] Moffat SD, Kennedy KM, Rodrigue KM, Raz N. Extrahippocampal contributions to age differences in human spatial navigation. Cereb Cortex 2007;17:1274–82.
[13] Carelli L, Rusconi ML, Scarabelli C, Stampatori C, Mattioli F, Riva G. The transfer from survey (map-like) to route representations into virtual reality mazes: effect of age and cerebral lesion. J Neuroeng Rehabil 2011;8:6.
[14] Morganti F, Riva G. Virtual reality as allocentric/egocentric technology for the assessment of cognitive decline in the elderly. Stud Health Technol Inform 2014;196:278–84.
[15] Harris MA, Wiener JM, Wolbers T. Aging specifically impairs switching to an allocentric navigational strategy. Front Aging Neurosci 2012;4:29.
[16] Konishi K, Etchamendy N, Roy S, Marighetto A, Rajah N, Bohbot VD. Decreased functional magnetic resonance imaging activity in the hippocampus in favor of the caudate nucleus in older adults tested in a virtual navigation task: navigational strategies in healthy aging. Hippocampus 2013;23:1005–14.
[17] Zakzanis KK, Quintin G, Graham SJ, et al. Age and dementia related differences in spatial navigation within an immersive virtual environment. Med Sci Monit 2009;15:CR140–5.
[18] Harris MA, Wolbers T. How age-related strategy switching deficits affect wayfinding in complex environments. Neurobiol Aging 2014;35:1095–102.
[19] Rodgers MK, Sindone JA, Moffat SD. Effects of age on navigation strategy. Neurobiol Aging 2012;33. 202.e15-202.e22.
[20] Liu I, Levy RM, Barton JJS, et al. Age and gender differences in various topographical orientation strategies. Brain Res 2011;1410:112–9.

[21] Bohbot VD, McKenzie S, Konishi K, Fouquet C, Kurdi V, Schachar R, et al. Virtual navigation strategies from childhood to senescence: evidence for changes across the life span. Front Aging Neurosci 2012;4:28.
[22] Wiener JM, Kmecova H, de Condappa O. Route repetition and route retracing: effects of cognitive aging. Front Aging Neurosci 2012;4:7.
[23] Moffat SD, Elkins W, Resnick SM. Age differences in the neural systems supporting human allocentric spatial navigation. Neurobiol Aging 2006;27:965–72.
[24] Taillade M, Sauzéon H, Dejos M, Arvind Pala P, Larrue F, Wallet G, et al. Executive and memory correlates of age-related differences in wayfinding performances using a virtual reality application. Aging Neuropsychol Cogn 2013;20:298–319.
[25] Harris MA, Wolbers T. Ageing effects on path integration and landmark navigation. Hippocampus 2012;22:1770–80.
[26] Adamo DE, Briceño EM, Sindone JA, Alexander NB, Moffat SD. Age differences in virtual environment and real world path integration. Front Aging Neurosci 2012;4:28.
[27] Mahmood O, Adamo D, Briceno E, Moffat SD. Age differences in visual path integration. Behav Brain Res 2009;205:88–95.
[28] Lövdén M, Schellenbach M, Grossman-Hutter B, Krüger A, Lindenberger U. Environmental topography and postural control demands shape aging-associated decrements in spatial navigation performance. Psychol Aging 2005;20: 683–94.
[29] Nedelska Z, Andel R, Laczó J, Vlcek K, Horinek D, Lisy J, et al. Spatial navigation impairment is proportional to right hippocampal volume. Proc Natl Acad Sci 2012;109:2590–4.
[30] Weniger G, Ruhleder M, Lange C, Wolf S, Irle E. Egocentric and allocentric memory as assessed by virtual reality in individuals with amnestic mild cognitive impairment. Neuropsychologia 2011;49:518–27.
[31] Bellassen V, Igloi K, Cruz de Souza L, et al. Temporal order memory assessed during spatiotemporal navigation as a behavioral cognitive marker for differential Alzheimer's disease diagnosis. J Neurosci 2012;32:1942–52.
[32] Pengas G, Patterson K, Arnold RJ, Bird CM, Burgess N, Nestor PJ. Lost and found: bespoke memory testing for Alzheimer's disease and semantic dementia. J Alzheimer Dis 2010;21:1347.
[33] Caffò AO, De Caro MF, Picucci L, Notarnicola A, Settanni A, Livrea P, et al. Reorientation deficits are associated with amnestic mild cognitive impairment. Am J Alzheimers Dis Other Demen 2012;27:321–30.
[34] Tarnanas I, Laskaris N, Tsolaki M, Muri R, Nef T, Mosimann UP. On the comparison of a novel serious game and electroencephalography biomarkers for early dementia screening. GeNeDis 2015;821:63–77.
[35] Kessels R, Van Doormaal A, Janzen G. Landmark recognition in Alzheimer's dementia: spared implicit memory for objects relevant for navigation. PloS One 2011;6:e18611.
[36] Burgess N, Trinkler I, King J, et al. Impaired allocentric spatial memory underlying topographical disorientation. Rev Neurosci 2006;17:239–51.
[37] Drzezga A, Grimmer T, Peller M, Wermke M, Siebner H, Rauschecker JP, et al. Impaired cross-modal inhibition in Alzheimer disease. PLoS Med 2005;e288.
[38] Livingstone SA, Skelton RW. Virtual environment navigation tasks and the assessment of cognitive deficits in individuals with brain injury. Behav Brain Res 2007;185:21–31.
[39] Skelton RW, Ross SP, Nerad L, Livingstone SA. Human spatial navigation deficits after traumatic brain injury shown in the arena maze, a virtual Morris water maze. Brain Inj 2006;20:189–203.
[40] Morris RGM, Garrud P, Rawlins JNP, O'Keefe J. Place navigation impaired in rats with hippocampal lesions. Nature 1982;297:681–3.
[41] Astur RS, Taylor LB, Mamelak AN, Philpott L, Sutherland RJ. Humans with hippocampus damage display severe spatial memory impairments in a virtual Morris water task. Behav Brain Res 2002;132:77–84.
[42] Goodrich-Hunsaker NJ, Livingstone SA, Skelton RW, Hopkins RO. Spatial deficits in a virtual water maze in amnesic participants with hippocampal damage. Hippocampus 2010;20:481–91.
[43] Weniger G, Ruhleder M, Wolf S, Lange C, Irle E. Egocentric memory impaired and allocentric memory intact as assessed by virtual reality in subjects with unilateral parietal cortex lesions. Neuropsychologia 2009;47:59–69.
[44] Van der Ham IJ, van Zandvoort MJ, Meilinger T, Bosch SE, Kant N, Postma A. Spatial and temporal aspects of navigation in two neurological patients. NeuroReport 2010;21:685–9.
[45] Slobounov SM, Zhang K, Pennell D, Ray W, Johnson B, Sebastianelli W. Functional abnormalities in normally appearing athletes following mild traumatic brain injury: a functional MRI study. Exp Brain Res 2010;202:341–54.
[46] Buxbaum LJ, Palermo MA, Mastrogiovanni D, Read MS, Rosenberg-Pitonyak E, Rizzo AA, et al. Assessment of spatial attention and neglect with a virtual wheelchair navigation task. J Clin Exp Neuropsychol 2008;30:650–60.
[47] Buxbaum LJ, Dawson AM, Linsley D. Reliability and validity of the Virtual Reality Lateralized Attention Test in assessing hemispatial neglect in right-hemisphere stroke. Neuropsychology 2012;26:430.
[48] Claessen MH, van der Ham IJ, Jagersma E, Visser-Meily JM. Navigation strategy training using virtual reality in six chronic stroke patients: a novel and explorative approach to the rehabilitation of navigation impairment. Neuropsychol Rehabil 2015;4:1–25.
[49] Caglio M, Latini-Corazzini L, D'Agata F, Cauda F, Sacco K, Monteverdi S, et al. Virtual navigation for memory rehabilitation in a traumatic brain injured patient. Neurocase 2012;18:123–31.
[50] Weniger G, Irle E. Allocentric memory impaired and egocentric memory intact as assessed by virtual reality in recent-onset schizophrenia. Schizophr Res 2008;101:201–9.
[51] Wilkins LK, Girard TA, Konishi K, King M, Herdman KA, King J, et al. Selective deficit in spatial memory strategies contrast to intact response strategies in patients with schizophrenia spectrum disorders tested in a virtual navigation task. Hippocampus 2013;23:1015–24.
[52] Spieker EA, Astur RS, West JT, Griego JA, Rowland LM. Spatial memory deficits in a virtual reality eight-arm radial maze in schizophrenia. Schizophr Res 2012;135:84–9.
[53] Ledoux A-A, Phillips JL, Labelle A, Smith A, Bohbot VD, Boyer P. Decreased fMRI activity in the hippocampus of patients with schizophrenia compared to healthy control participants, tested on a wayfinding task in a virtual town. Psychiatry research. Neuroimaging 2013;211:47–56.
[54] Siemerkus J, Irle E, Schmidt-Samoa C, Dechent P, Weniger G. Egocentric spatial learning in schizophrenia investigated with functional magnetic resonance imaging. NeuroImage Clin 2012;1:153–63.
[55] Ekstrom AD, Arnold AEGF, Iaria G. A critical review of the allocentric spatial representation and its neural underpinnings: toward a network-based perspective. Front Hum Neurosci 2014;8:803.
[56] Wolbers T, Wiener JM. Challenges for identifying the neural mechanisms that support spatial navigation: the impact of spatial scale. Front Hum Neurosci 2014;8:571.
[57] Doeller CF, King JA, Burgess N. Parallel striatal and hippocampal systems for landmarks and boundaries in spatial memory. Proc Natl Acad Sci 2008;105: 5915–20.
[58] Gomez A, Cerles M, Rousset S, Rémy C, Baciu M. Differential hippocampal and retrosplenial involvement in egocentric-updating, rotation, and allocentric processing during online spatial encoding: an fMRI study. Front Hum Neurosci 2014;8:150.
[59] Chrastil E. Neural evidence supports a novel framework for spatial navigation. Psychon Bull Rev 2013;20:208–27.
[60] Hartley T, Lever C, Burgess N, O'Keefe J. Space in the brain: how the hippocampal formation supports spatial cognition. Philos Trans R Soc Lond B Biol Sci 2014;369. 2012.0510.
[61] Grant SC, Magee LE. Contributions of proprioception to navigation in virtual environments. J Hum Factors Ergon Soc 1998;40:489–97.
[62] Rose FD, Brooks BM, Attree EA. An exploratory investigation into the usability and usefulness of training people with learning disabilities in a virtual environment. Disabil Rehabil 2002;24:627–33.
[63] Williams B, Narasimham G, McNamara TP, Carr TH, Rieser JJ, Bodenheimer B. Updating orientation in large virtual environments using scaled translational gain. In: Proceedings of the 3rd symposium on applied perception in graphics and visualization; 2006;21–8.
[64] Wallet G, Sauzéon H, Pala PA, Larrue F, Zheng X, N'Kaoua B. Virtual/real transfer of spatial knowledge: benefit from visual fidelity provided in a virtual environment and impact of active navigation. Cyberpsychol Behav Soc Netw 2011;14:417–23.
[65] Ruddle RA, Volkova E, Mohler B, Bülthoff HH. The effect of landmark and body-based sensory information on route knowledge. Memory Cogn 2011;39:686–99.
[66] Larrue F, Sauzeon H, Wallet G, Foloppe D, Cazalets JR, Gross C, et al. Influence of body-centered information on the transfer of spatial learning from a virtual to a real environment. J Cogn Psychol 2014;26:906–18.
[67] Sangani S, Fung J, Kizony R, Koenig ST, Weiss PL. Navigating and shopping in a complex virtual urban mall to evaluate cognitive functions. Virtual Rehabil 2013;9–14.
[68] Chrastil ER, Warren WH. Active and passive contributions to spatial learning. Psychon Bull Rev 2012;19:1–23.
[69] Lloyd J, Persaud NV, Powell TE. Equivalence of real-world and virtual-reality route learning: a pilot study. Cyberpsychol Behav 2009;12:423–7.
[70] Sorita E, N'Kaoua B, Larrue F, Criquillon J, Simion A, Sauzéon H, et al. Do patients with traumatic brain injury learn a route in the same way in real and virtual environments? Disabil Rehabil 2013;35:1371–9.
[71] Mellet E, Laou L, Petit L, Zago L, Mazoyer B, Tzourio-Mazoyer N. Impact of the virtual reality on the neural representation of an environment. Hum Brain Mapp 2010;31:1065–75.
[72] Fuchs P. Les interfaces de la réalité virtuelle. Éditeur AJIIMD; 1996, 2-9509954-0-3.
[73] Darken RP, Sibert JL. Navigating large virtual spaces. Int J Hum Comput Interact 1996;8:49–71.
[74] Sjölinder M, Höök K, Nilsson L-G, Andersson G. Age differences and the acquisition of spatial knowledge in a three-dimensional environment: evaluating the use of an overview map as a navigation aid. Int J Hum Comput Stud 2005;63:537–64.
[75] Parush A, Berman D. Navigation and orientation in 3D user interfaces: the impact of navigation aids and landmarks. Int J Hum Comput Stud 2004;61:375–95.
[76] Burigat S, Chittaro L. Navigation in 3D virtual environments: effects of user experience and location-pointing navigation aids. Int J Hum Comput Stud 2007;65:945–58.
[77] Boggus M, Crawfils R. Distance field illumination: a rendering method to aid in navigation of virtual environments. ISVC 2010;6454:501–10.
[78] Andersen N, Dahmani L, Konishi K, Bohbot V. Eye tracking, strategies, and sex differences in virtual navigation. Neurobiol Learn Memory 2012;97:81–9.
[79] Broadbent HJ, Farran EK, Tolmie A. Sequential egocentric navigation and reliance on landmarks in Williams syndrome and typical development. Front Psychol 2015;25:216.
[80] Van der Brink D, Janzen G. Visual spatial cue use for guiding orientation in two-to-three-year-old children. Front Psychol 2015;4:904.

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[81] Fickas S, Sohlberg M, Hung P-F. Route-following assistance for travelers with cognitive impairments: a comparison of four prompt modes. Int J Hum Comput Stud 2008;66:876–88.
[82] Sohlberg MM, Fickas S, Hung PF, Fortier A. A comparison of four prompt modes for route finding for community travellers with severe cognitive impairments. Brain Inj 2007;21:531–8.
[83] Walker BN, Lindsay J. Using virtual environments to prototype auditory navigation displays. Assist Technol 2005;17:72–81.
[84] Degara N, Kuppanda T, Neate T, Yang J, Torres AV. Reproducible sonification for virtual navigation.In: lIEEE VR Workshop: sonic interaction in virtual environments. 07006288. 2014;p. 35–40.
[85] Sorkin A, Weinshall D, Modai I, Peled A. Improving the accuracy of the diagnosis of schizophrenia by means of virtual reality. Am J Psychiatry 2006;163:512–20.
[86] Ardito C, Costabile M-F, Angeli A, Pittarello F. Navigation help in 3D worlds: some empirical evidences on use of sound. Multimedia Tools Appl 2007;33:201–16.
[87] Smyth CC. Sensitivity of Subjective Questionnaires to cognitive loading while driving with navigation aids: a pilot study. Aviat Space Environ Med 2007;78 [No. 5 Section II May 2007].
[88] Viaud-Delmon I, Warusfel O. From ear to body: the auditory-motor loop in spatial cognition. Front Neurosci 2014;8:283.
[89] Sanchez J, Saenz M, Pascual-Leone A, Merabet L. Enhancing navigation skills through audio gaming. Ext Abstr Hum Factors Computing Syst 2010; 3991–4000.
[90] Afonso A, Blum A, Katz BFG, Tarroux P. Structural properties of spatial representations in blind people: Scanning images constructed from haptic exploration or from locomotion in a 3-D audio virtual environment. Memory Cogn 2010;38:591–604.
[91] Maidenbaum S, Levy-Tzedek S, Chebat D-R, Amedi A. Increasing accessibility to the blind of virtual environments, using a virtual mobility aid based on the ‘‘eyecane’’: feasibility study. Plos One 2013;8:0072555.
[92] Yi J, Lee HC, Parsons R, Falkmer T. The effect of the global positioning system on the driving performance of people with mild Alzheimer's disease. Gerontology 2015;61:79–88.
[93] Riley GA, Venn PA. Comparison of automatic and intentional instructions when using the method of vanishing cues in acquired brain injury. Neuropsychol Rehabil 2015;25:53–81.
[94] Lavie N, Hirst A, de Fockert JW, Viding E. Load theory of selective attention and cognitive control. J Exp Psychol Gen 2004;133:339–54.
[95] Stankiewicz BJ, Kalia AA. Acquisition of structural versus object landmark knowledge. J Expl Psychol Hum Percept Perform 2007;33:378–90.
[96] Caduff D, Timpf S. On the assessment of landmark salience for human navigation. Cogn Process 2008;9:249–67.
[97] Janzen G, Van Turennout M. Selective neural representation of objects relevant for navigation. Nat Neurosci 2004;7:673–7.
[98] Han X, Byrne P, Kahana M, Becker S. When do objects become landmarks? A VR study of the effect of task relevance on spatial memory. PLoS One 2012;7:e35940.