Virtual Reality for Assessment of Episodic Memory in Normal and Pathological Aging

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Episodic Memory

Memory is one of the most important cognitive functions in a person's life. Memory is essential for recalling personal memories and for performing many everyday tasks, such as reading, playing music, returning home, and planning future actions, and, more generally, memory is crucial for interacting with the world. Determining how humans encode, store, and retrieve memories has a long scientific history, beginning with the classical research by Ebbinghaus in the late 20th century (Ebbinghaus, 1964). Since this seminal work, the large number of papers published in the domain of memory testifies that understanding memory is one of the most important challenges in cognitive neurosciences. With population growth and population aging, understanding memory failures both in the healthy elderly and in neurological and psychiatric conditions is a major societal issue.

A substantial body of evidence, mainly from double dissociations observed in neuropsychological patients, has led researchers to consider memory not as a unique entity but as comprising several forms with distinct neuroanatomical substrates (Squire, 2004). With reference to long-term memory, e*pisodic memory* may be described as the conscious recollection of personal events combined with their phenomenological and spatiotemporal encoding contexts, such as recollecting one's wedding day with all the contextual details (Tulving, 2002). Episodic memory is typically opposed to *semantic memory,* which is viewed as a system dedicated to the storage of facts and general decontextualized knowledge (e.g., Paris is the capital of France), including also the mental lexicon. Episodic memory was initially defined by Tulving as a memory system specialized in storing specific experiences in terms of what happened and where and when it happened (Tulving, 1972). Later, phenomenological processes were associated with the retrieval of memories (Tulving, 2002). Episodic memory is assumed to depend on the self, and involves mental time travel and a sense of reliving the original encoding context that includes autonoetic awareness (i.e., the awareness that this experience happened to oneself, is not happening now, and is part of one's personal history). More recently, the multiple components of memory (central and contextual information) that together form a complete episodic memory are thought to be linked through a process known as "binding" (Kessels, Hobbel, & Postma, 2007; Shimamura & Wickens, 2009). The neuronal substrates of episodic memory are widely distributed in the brain, from the medial temporal lobe, including the hippocampus (Davachi, 2006; Eichenbaum, Sauvage, Fortin, Komorowski, & Lipton, 2012), to the frontal lobe (Habib, Nyberg, & Tulving, 2003) and the parietal cortex (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008).

Due to its large neuronal distribution, episodic memory is highly vulnerable. While episodic memory is considered to be the form of long-term memory that displays the greatest degree of age-related decline (Bäckman, Small, & Fratiglioni, 2001), its impairment is the most important deficit in Alzheimer's disease (AD) and constitutes a hallmark of early clinical manifestations (Hodges, 2006). Impairments in episodic memory function have also been described in individuals with mild cognitive impairment (MCI), Huntington's disease, Parkinson's disease, and psychiatric diseases, including schizophrenia, major depression, and dissociative disorders.

For decades, extensive research has been conducted on memory. While this research has led to a better understanding of memory, the majority of studies do not correspond to realistic situations close to daily life.

To further our understanding of memory, a sophisticated assessment is required, and hence the tools used to measure memory become crucial. The present chapter demonstrates how a new technology—virtual reality (VR)—can offer a relevant tool for the fundamental and clinical evaluation of memory. The discussion particularly focuses on episodic memory for two reasons: episodic memory is highly vulnerable to disease, and due to its complexity (what, where, when, and binding) it is the form of memory for which an ecological evaluation is of prime importance. The notion of *ecological validity* refers to the extent to which behavior indicative of cognitive functioning measured in one environment can be taken as characteristic of an individual's cognitive processes in a range of other environments (Barker, 1978; Bronfenbrenner, 1979). The discussion first addresses why VR provides features relevant for episodic memory assessment. Second, studies using VR for the fundamental comprehension of episodic memory are presented. Third, research on normal aging and on pathology is described. Finally, in conclusion some future perspectives are outlined.

Contribution of Virtual Reality to Memory Assessment

To respect the need to work with well-controlled laboratory paradigms, the majority of studies have used verbal material. As pointed out by Tulving: "Words to the memory researcher are what fruit flies are to the geneticist: a convenient medium through which the phenomena and processes of interest can be explored and elucidated" (1983, p. 146). In verbal paradigms, participants typically study a list of words and are then tested on that list. Each word is assumed to constitute an event. In this traditional conception, the focus is placed on the number of items remaining in the store and accessible to memory. Neisser (1976) pointed out discontinuities between the spatial, temporal, and intermodal continuities of real objects and events characteristic of laboratory-based research, suggesting that: "It is almost as if ecological invalidity were a deliberate feature of the experimental design" (1976, p. 34).

A more naturalistic approach to memory has led to studies focusing on the quality of memory, giving rise to work on false memory and to studies assessing self-relevant and everyday life material. In particular, research on autobiographical memory tries to remain very close to everyday memory: a typical method is to provide participants with a verbal cue (e.g., *a journey*) and ask them to recall a personal memory from this cue (Piolino, Desgranges, & Eustache, 2009). These different approaches have advantages and disadvantages—while the former can be criticized for its weak ecological validity, the latter can be criticized for its weak experimental control (Koriat & Goldsmith, 1996).

We claim that different criteria have to be respected for episodic memory evaluation, in accordance with other views (McDermott, Szpunar, & Christ, 2009; Pause et al., 2013). To guarantee the best experimental control, episodic memories have to be induced in the laboratory; the encoding of memories must be incidental, in order to prevent semantic processes from taking place, and must remain totally episodic; the test should preferably involve a one-trial learning event, as is the case in real life; and, last, the episodic memory measure must include measures of what, where, and when (i.e., feature binding)

Tests based on VR represent an acceptable compromise between the experimental control required by all laboratory research and an everyday-memory-like assessment of episodic memory. Much of what people remember in everyday life refers to complex events, including visual information and actions that have been performed. Consequently, when we remember an event, typically we remember what happened, where and when it happened, and the multimodal details associated with it. Due to the infinite possibilities afforded by VR, one can investigate the memory of complex events, i.e., the memory for central and perceptual details, spatiotemporal contextual elements, and binding of the multidimensional information.

In a clinical neuropsychological approach, the assessment of cognition in an ecological fashion is crucial. During a rehabilitation program, if patients observe a difference between the forms of memory targeted by memory rehabilitation techniques and memory for general life experiences, the program won't offer patients meaningful forms of improvement, which might decrease their motivation. Because tests are sometimes far removed from patients' daily life experiences, it has also been observed that performance on standard neuropsychological tests does not predict patients' behavior in the real world (Bowman, 1996; Farias, Harrell, Neumann, & Houtz, 2003; Sbordone & Long, 1996; Schultheis, Himelstein, & Rizzo, 2002). In addition, a number of studies evaluating subjects' complaints of everyday memory problems have found weak associations with results on verbal memory tests (Jacoby, Jennings, & Hay, 1996; Pearman & Storandt, 2004; Plancher, Tirard, Gyselinck, Nicolas, & Piolino, 2012; Reid & Maclullich, 2006).

The ecological validity of studies conducted in neuropsychology has been criticized and the need for a neuropsychological assessment 3.0 has been formulated (Bohil, Alicea, & Biocca, 2011; Bowman, 1996; Farias et al., 2003; Parsons, 2015; Sbordone & Long, 1996; Schultheis et al., 2002). The lack of technological progress in the standardized testing industry has been pointed out by Sternberg (1997), and current standardized tests differ weakly from tests used throughout the last century. It is probably time to move from traditional paper-and-pencil batteries toward more ecologically valid tools, such as virtual environments (VEs; Parsons, 2015).

Classical neuropsychological tools used to assess episodic memory are far from encompassing its complexity (Table 9.1). In traditional neuropsychological assessment, the memory measure focuses most of the time on the core content (what) of episodic memory and uses verbal material, such as words or sentences (Grober & Buschke, 1987; Logical Memory Test, Wechsler, 1997). For visuospatial memory evaluation, the material used generally concerns abstract or concrete figures (e.g., Rey-Osterrieth Complex Figure, Meyers & Meyers, 1995; Family Pictures Test, Weschler, 1997), which bear little resemblance to everyday visuospatial memory.

TABLE 9.1 Comparison Between Standard Neuropsychological Tests and Virtual Reality Regarding Episodic Memory

Criteria for episodic memory tests	Standard neuropsychological tests	Virtual reality tests
Controlled laboratory studies	+++	+++
Recollection	+	+++
Self-relevant events	–	++
Multimodality	+	+++
Phenomenological context	+	++
Spatiotemporal context	+	+++
Binding	–	+++
Motivation	+	+++
Transfer to reality	+	+++
Predictive power in daily life	+	+++

+++: very high; ++: high; +: medium; –: low.

VR is gaining popularity as a tool in cognitive psychology and neuropsychology because it enables researchers and clinicians to create naturalistic and controlled situations with different levels of immersion (Bohil et al., 2011; Mueller et al., 2012; Zawadzki et al., 2013). According to Fuchs and colleagues (Fuchs, Moreau, Berthoz, & Vercher, 2006), the purpose of VR is to allow users to carry out cognitive and sensorimotor activities in an artificial world, i.e., a person immersed in the virtual world perceives and acts physically through the intermediary of sensory and motor interfaces. The virtual world is based on computer-generated three-dimensional (3D) images. It can be imaginary or symbolic, or it can simulate aspects of the real world.

When participants are immersed in the virtual world, they control their own displacements in the environment and they can have a real feeling of immersion (Mestre & Fuchs, 2006). A sensation of presence, or "being there," in the environment is important, as memory performance has been correlated with presence ratings for the experience in the VE (Schomaker, Roos, & Meeter, 2014). While the feeling of presence does not necessarily depend on the degree of realism or details of the VE, in order to achieve a VR experience, it is important to truly represent a real-world situation, instead of a simple video experience. Different levels of immersion can be achieved depending on the system (García-Betances, Arredondo Waldmeyer, Fico, & Cabrera-Umpiérrez, 2015). The non-immersive system involves a conventional computer, keyboard, and mouse; joysticks or gamepads may replace the mouse. Semi-immersive VR systems involve more sophisticated graphics, typically with a larger flat surface. A fully immersive VE consists of large surrounding projection surfaces, or 3D displays, such as head-mounted displays (HMDs), that place the patient inside the VE (e.g., a city, an apartment, a kitchen, a garden, etc.).

Neuropsychology as a discipline clearly stands to benefit from VR techniques. VR is flexible: an infinity of environments and experimental tasks can be created. Furthermore, VR offers the possibility of creating multimodal environments that stimulate all of the senses (vision, audition, olfaction, proprioception, tactile sensation, etc.). Lastly, it offers an alternative to rehabilitation in real-life situations that could be dangerous, costly, and hard to control. By creating rich multimodal environments and letting participants interact with them, memory assessment with VR can allow experiences closer to those of daily life than standard computer interfaces or paper-and-pencil tests.

Virtual Reality Studies Assessing Memory in Young Adults

With an approach geared toward clinical neuropsychology, Parsons and Rizzo (2008) designed an experimental VR-based object memory and learning test (the Virtual Reality Cognitive Performance Assessment Test). Participants were asked to learn and recall objects across three free recall trials as a learning measure.

Subsequently, they navigated through five zones of a virtual city and for each zone, two items previously presented in the learning phase were presented again. Then the participants performed a delayed free recall task. The authors observed that performance on the VR test was consistent with that recorded by traditional paper-and-pencil measures involving learning and memory, thus validating the reliability of the virtual assessment of memory.

Because a main characteristic of VR is the possibility of creating a large-scale environment, many studies using VR have investigated spatial memory and navigation (Aguirre & D'Esposito, 1997; Brooks, Attree, Rose, Clifford, & Leadbetter, 1999; Gras, Gyselinck, Perrussel, & Orriols, 2013; Tlauka, Keage, & Clark, 2005; Wallet et al., 2011; Weniger, Ruhleder, Wolf, Lange, & Irle, 2009). These investigations show great rehabilitation promise, as it has been demonstrated for example that immersion in the virtual version of a city helped participants to transfer their spatial knowledge from the VE to the real world (Wallet et al., 2011). In addition, because it is convenient with this technology to directly compare active and passive exploration by keeping all other things equal, the question of how active learning enhances memory quickly arose. This kind of question fits with the framework of embodied cognition theories, for which "the mind must be understood in the context of its relationship to a physical body that interacts with the world" (Wilson, 2002). Memory should then be comprehended as a way to create meaning in the service of action (Glenberg, 1997).

Brooks and colleagues (1999) used a VE to compare the effects of active and passive conditions on recall of spatial layout, virtual objects, and their correct locations. Active participants used a joystick to navigate through a set of rooms. Passive participants watched the active participants' progress. At the same time, all participants had to look for an object. Active participants recalled the spatial layout better than passive participants. The authors attributed this benefit to an additional motor trace that increases the specificity of the memory. Different empirical findings suggest that active learning is important for memory (Nilsson, 2000; Carassa, Geminiani, Morganti, & Varotto, 2002; Nilsson, 2000; Zimmer et al., 2001). However, research using VR has yielded inconsistent results. Action is a complex cognitive construct; in a complex environment, action depends on the degree of interaction with the environment and freedom in the planning of an itinerary. Indeed, action has been defined as an intention to interact with the environment, rather than just a movement (Berthoz, 2003). The notion of planning thus appears as important as motion when investigating the effect of action on memory.

These hypotheses were tested by disentangling the interaction and planning components of action to examine whether each enhances factual and spatial memory (Plancher, Barra, Orriols, & Piolino, 2013). Participants explored a virtual town in one of three experimental conditions: a passive condition where participants were immersed as the passenger of the car (no interaction, no planning); a planning-only condition (the subject chose the itinerary but did not drive the car); and an interaction-only condition (the subject drove the car but the itinerary was fixed by the experimenter) (see Figure 9.1). The virtual

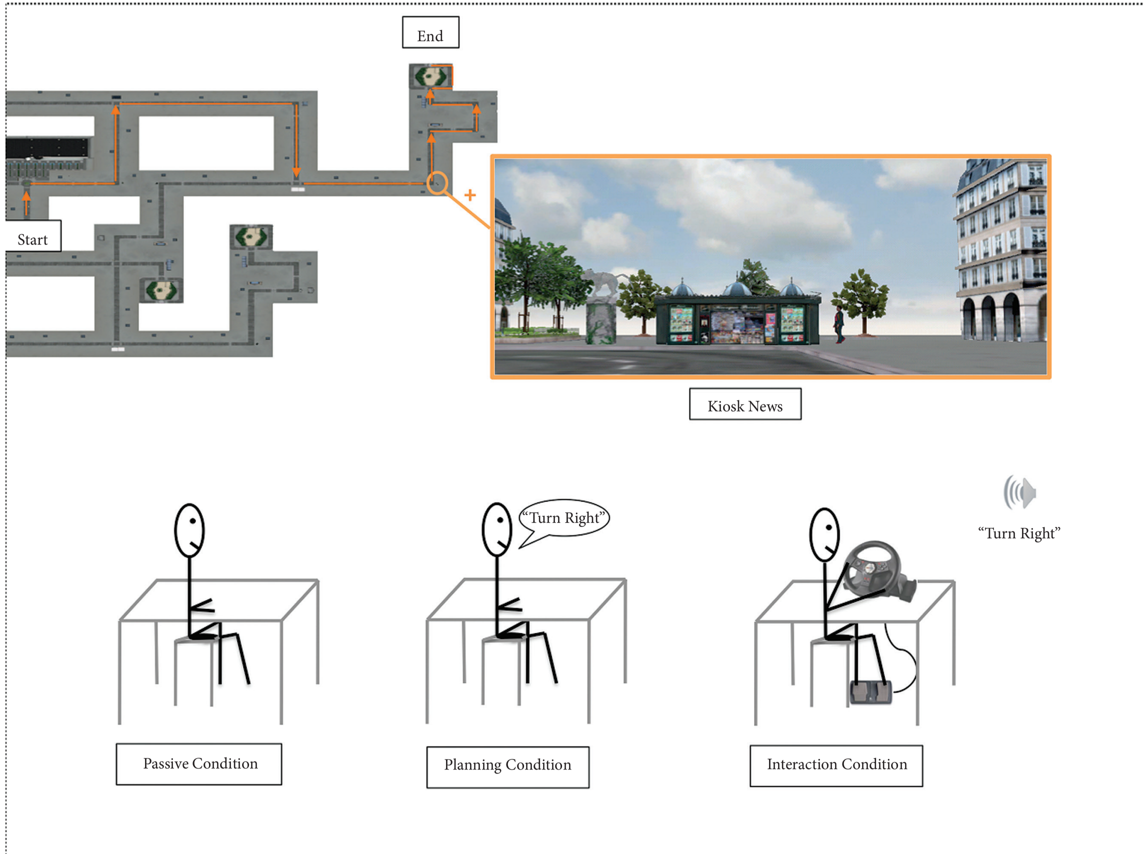

FIGURE 9.1 *TK*

AQ: Please provide caption for Fig 9.1

equipment consisted of a computer-generated 3D model of an artificial environment built with novel in-house 3D software to create virtual urban environments and scenarios (Editomem & Simulamem, Memory and Cognition lab., Paris Descartes University; for an example, see https://www.youtube.com/watch?v=KfF7fv4L7pc). The program was run on a PC laptop computer and the VE was explored with a virtual car using a "real" steering wheel, gas pedal, and brake pedal. The VE was projected using a video projector onto a screen 85 cm high and 110 cm wide. Participants were seated in a comfortable chair and the VE was projected 150 cm in front of them. Free recall of the elements of the scenes (e.g., a girl, the train station, a no-entry sign) and a visuospatial memory test (drawing a map and locating elements on it; locating elements on a prepared map) were recorded. While itinerary choice and motor control both enhanced spatial memory, factual memory was impaired by online motor control. The benefit of action for spatial memory is here attributable to both interaction with the environment and route planning. The action enhancement previously observed in some VR studies could be due to the fact that the participants were able to navigate freely in the environment and to plan their itinerary. The negative impact of motion on factual memory can be explained by the costly attentional demands of motor control in VR environments.

Sauzéon and collaborators also investigated the differences between active and passive navigation on different measures of memory (Sauzéon et al., 2011). Using a 3D simulated apartment (HOMES test: Human Object Memory for Everyday Scenes), they aimed to investigate robust laboratory-based memory effects that provide clinically relevant information relative to learning, proactive interference, strategic processing, and false recognitions (as in a neuropsychological reference test, the California Verbal Learning Test (CVLT); Delis, Kramer, Kaplan, & Ober, 2000), and to study the possible influence of sensorimotor activity on these effects. They observed the expected effects of the four memory components classically obtained on standard paper-and-pencil memory tests (i.e., learning, proactive interference, memory strategies, and false memories). They also showed an active superiority effect on three measures (learning, retrieval strategy, and false memories) but not on active forgetting, encoding strategies, and gist-based false recognitions. According to the authors, their results demonstrate the important role of active navigation in strengthening distinctive memory traces and enriching source memory, but not in memory measures influenced by relational processing.

VR has also been used to determine the neural bases of episodic memory by discriminating factual and spatial components. Burgess and collaborators (Burgess, 2002; Burgess, Maguire, & O'Keefe, 2002; Burgess, Maguire, Spiers, & O'Keefe, 2001; King, Hartley, Spiers, Maguire, & Burgess, 2005) as well as Rauchs et al. (2008) used a VE to investigate the substrates of episodic memory with fMRI. In the study by Burgess et al. (2001), young participants followed a route with a joystick, in the course of which they encountered a number of people in different locations. Each person handed them an object. The memory of the objects, and of where and from whom they were received, was then assessed under functional neuroimaging. The authors observed that parahippocampal areas were specifically involved in the retrieval of spatial information, but not in the retrieval of object information, which involves more the parietal and prefrontal areas implicated by neuroimaging of retrieval of conventional laboratory stimuli. Recently, Park and collaborators (2014) directly measured neural oscillations involved in encoding novel environments in the human hippocampus during spatial navigation in a VE. Epileptic patients with implanted intracranial hippocampal depth electrodes performed a VE navigation and were instructed to remember the location of the objects during different blocks. The researchers observed that delta, theta, and low-gamma oscillations were associated with environmental novelty but that high-gamma oscillations were crucial for the successful encoding of the environmental novelty.

The above-mentioned studies have demonstrated that VR is relevant for the fundamental comprehension of memory in young adults. Because of the large-scale environment it offers, it enables an interesting investigation of the different components of episodic memory and the binding between the components; in addition, it makes it possible to examine the effect of action on episodic memory.

Virtual Reality Studies Assessing Memory in Normal Aging

Due to its complexity, episodic memory is very sensitive to normal aging and neurodegenerative disorders (Aggleton & Pearce, 2001). In normal aging, the memory measures showing the highest effect are typically those involving strategic components requiring auto-initiated processes, such as free recall (Luo & Craik, 2008; Old & Naveh-Benjamin, 2008). When the core and contextual components of episodic memory are assessed, it is found that a decrease in memory performance affects mainly the spatiotemporal context and binding, indicating a source memory deficit (e.g., Chalfonte & Johnson, 1996; Kessels et al., 2007; Spencer & Raz, 1995). Episodic memory performance declines early in normal aging and this process is accentuated in AD. It is thus necessary to have sensitive tools for the cognitive stimulation of declining memory, to slow down the autonomy and cognition loss in elderly people and to improve well-being and quality of life during the aging process. The quality of the tools used to assess memory is also essential for diagnosis of a potential pathology. The prevention of cognitive and memory deficiencies could also be directed toward AD, particularly in older adults who have already begun to experience cognitive decline, namely, those with MCI, a category of persons who represent a preferential target of preventive interventions. We used VR to investigate episodic memory in normal aging (Plancher, Gyselinck, Nicolas, & Piolino, 2010; Plancher, Nicolas, & Piolino, 2008). We explored the effects of normal aging on the main aspects of episodic memory—what, where, and when—and on feature binding in an urban VE. Participants explored the virtual town via simulation of driving a car and saw several distinctive elements during their immersion (e.g., a fountain, the train station, a car accident). After a delay, participants were asked to freely recall and then recognize as much of the information encountered during the encoding phase as possible, specifying the perceptual details, the spatial and the temporal context of each factual element recalled. The main findings were that memory for spatiotemporal contexts decreases with aging, in accordance with previous studies (Chalfonte & Johnson, 1996; Kessels et al., 2007; Spencer & Raz, 1995), while memory for elements and perceptual details does not. In addition, we explored the influence of the mode of learning, intentional versus incidental. The majority of memory operations in daily life are incidental as opposed to intentional. However, neuropsychological tests seldom use incidental learning because it can be difficult to measure recall when encoding is not controlled. Previous experimental studies have demonstrated that participants perform better in memory tasks when they intentionally learn items, that is, when they make a conscious effort to memorize them, than when they learn the items incidentally and are not informed that their memory will be tested (Greene, 1986; Neill, Beck, Bottalico, & Molloy, 1990; Old & Naveh-Benjamin, 2008). We confirmed this finding with young adults, but found that older adults did not benefit as much as younger adults from effortful strategies. The fact that the deficit of memory with aging appeared mainly under intentional encoding is consistent with studies suggesting that deficits are observed in the context of tasks involving effortful processing, leaving more automatic processing unaffected (Hasher & Zacks, 1979; Old & Naveh-Benjamin, 2008).

We also tried to benchmark VE findings collected with older adults against data recorded in classical verbal memory tests, as well as clinical assessment of memory complaints. The subjective Cognitive Difficulties Scale (CDS; McNair & Kahn, 1983) was used to assess memory complaints in daily life. The CDS is a 39-item self-report measure of memory and general cognitive complaints using a Likert-type scale. For each item (e.g., Do you have difficulties in remembering the names of the people you know?), the participants have to choose among five responses, from “never” to “very often.” We found that correlations existed between the score on the CDS and the following scores captured by our VR test: binding scores, detail recalls, and recognitions, whereas no correlation was observed between the CDS and the verbal memory test. This suggests that scores on our VR test are especially sensitive to everyday memory complaints in normal aging. The VR test reflects both objective and subjective cognitive deficits, in contrast to the classical verbal learning test. By testing rarely explored aspects of memory and by testing memories formed without deliberate memorization, VR-based assessment can contribute to the search for an ecological neuropsychology (Parsons, 2015; Schultheis et al., 2002).

One way to improve episodic memory in aging is to give older participants encoding instructions that favor the link between content and its context (Glisky & Kong, 2008; Naveh-Benjamin et al., 2004, 2005). It is also possible to add an environmental support at encoding that can serve as a compensatory strategy for deficient memory processing (for reviews, see Naveh-Benjamin et al., 2002, and Luo & Craik, 2008). As already demonstrated, an encoding strategy considered one of the most effective consists of enhancing memory by linking the information to be remembered with personal actions (Madan & Singhal, 2012; Zimmer et al. 2001). Using the enactment paradigm, comparison of active encoding (the encoding of action sentences by subject-performed tasks) with verbal encoding, showed a benefit of active encoding in both young and older adults (Feyereisen, 2009).

Using the virtual HOMES test, Arvind-Pala et al. (2014) investigated memory with several measures. They confirmed poor recall, but better recognition, and intact clustering and proactive interference effects for item memory in older adults. In a second study in young and older adults, they looked at the effect of active exploration on learning, proactive interference, semantic clustering, recognition hits, and false recognitions (Sauzéon, N'Kaoua, Arvind Pala, Taillade, & Guitton, 2015). Participants either actively navigated or passively followed the computer-guided tour of an apartment. The researchers observed in both groups that active exploration increased recognition hits, consistent with their previous result (Sauzéon et al., 2011), even if they did not replicate the effect on all scores. According to the authors, this indicates that active encoding strengthens distinctive memory traces and enriches source memory even in aging. However, a differential effect of active navigation was observed for young and older adults: while it reduced false recognitions in younger adults, it increased those made by older adults. Older adults are typically more prone to false memories (Plancher, Guyard, Nicolas, & Piolino, 2009; Rémy, Taconnat, & Isingrini, 2008), which is consistent with a source-monitoring deficit with aging.

The benefit of active navigation was assumed to result from the enrichment of item-specific processing (Plancher et al., 2013; Sauzéon et al., 2011), and the addition of perceptive-motor traces at encoding for a specific memory task (Brooks et al., 1999; Wallet et al., 2011), while the detrimental effect could depend on the level of complexity of the active navigation (Gaunet, Vidal, Kemeny, & Berthoz, 2001; Wilson & Peruch, 2002; Wolbers & Hegarty, 2010). Indeed, active navigation may sometimes require additional cognitive resources that are not fully available for the encoding process, leading to a detrimental effect on some aspects of memory (Plancher et al., 2013).

Jebara, Orriols, Zaoui, Berthoz, and Piolino (2014) tested in an urban VE how different components of action (active navigation and decision) may influence episodic memory performance (item plus context) and the effect of aging. They compared a passive condition (where the subject was just immersed as the passenger of a car, i.e., no active navigation, no decision); an itinerary condition (the subject was immersed as a passenger and chose the itinerary but did not drive the car); a low active navigation condition (the subject moved the car on rails, but the itinerary was fixed); and a high active navigation condition (the subject drove the car using a steering wheel and pedals, but the itinerary was fixed). The latter two navigation conditions differed in the degree of interactive sensorimotor engagement, but also in the degree of attentional load. Higher navigation control adds sensorimotor interaction, which could help memory, but it also makes driving more complex in the VE, requiring a higher level of attentiveness (Blankertz et al., 2010) and thus could be detrimental for memory, especially in older adults. It has been shown that age-related memory differences after active navigation are mediated by executive functions (Taillade et al., 2013). The findings showed that both the low active navigation condition and the choice of the itinerary enhanced the central component and the binding between the what–where–when components in young and older participants. These results can be explained by the fact that the conditions engage a lower amount of cognitive resources at encoding than the high active condition, but involve a higher environmental support than the passive condition. This study provides new evidence for the positive influence of decision making on feature binding (Bakdash et al., 2008; Plancher et al., 2013).

How can we explain this benefit? Integrating multimodal codes is important for binding, and applies not only to sensorimotor processing but also to action planning (Hommel, 2004). Voss, Gonsalves, Federmeier, Tranet, and Cohen (2011) also suggested that "volitional control" may improve the performance in memory thanks to the interplay between distinct neural systems related to planning, attention, and item processing. They argued that such control improves episodic memory performance because the hippocampus is not only concerned with relational feature binding (Eichenbaum, 2000; Ergorul & Eichenbaum, 2004), but also with planning (Bird & Burgess, 2008; Viard, Doeller, Hartley, Bird, & Burgess, 2011). The study by Jebara et al. (2014) suggests that navigational and decisional activity during real-life events should be useful in aging to boost memory. Encouraging older adults to use their own actions, both via active navigation and decisional control, could improve memory performance. A new challenge is to use VR to assess episodic memory to differentiate healthy older adults from pathological aging.

Virtual Reality Studies Assessing Episodic Memory in Pathological Aging

Numerous studies have demonstrated that episodic memory impairment is one of the hallmarks of early clinical manifestations of AD (Hodges, 2006) and amnesic mild cognitive impairment (aMCI) (Petersen et al., 2001, 1999). This deficit has been explained by a reduced volume in the neural substrates of episodic memory, the hippocampus and in other brain regions, such as the parahippocampal gyrus and cingulate cortex, in both AD and aMCI patients (Chételat et al., 2002; De Leon et al., 2006; Dickerson et al., 2001; Fox and Schott, 2004; Gerardin et al., 2009; Risacher et al., 2009). Notably, 50% of older adults with a focal mild episodic memory impairment compared to normal aging will develop AD in the following 4 years (Trojanowski et al., 2010). This subgroup of older adults has been shown to present intermediate brain characteristics between those of AD patients and healthy controls (Chételat et al., 2009; Evans et al., 2010; Gerardin et al., 2009). Reliable diagnosis of dementia as early as possible is thus crucial for treatment and rehabilitation of patients with suspected AD, such as the aMCI patients. Yet, the neurological tests used for early diagnosis are often time-consuming and expensive (e.g., amyloid plaques measured by PET scan, hippocampus volume measured by MRI, cephalorachidian fluid puncture) and the cognitive tests often present a weak sensitivity for early forms of the disease (Pike & Savage, 2008).

Various clinical memory tests used in dementia generally measure only one aspect of episodic memory in isolation, rather than offering a complete measure of its components, such as memory for what, where, and when, and binding between components. To improve the diagnosis and the rehabilitation of aMCI and AD patients, studies took advantage of VR to develop paradigms capable of early detection of functional changes in cognitive abilities and of presenting conditions that resemble daily life. Some studies with aMCI patients (Cushman, Stein, & Duffy, 2008) have found a close relationship between performance in virtual and real environments. Moreover, other studies with AD patients (Burgess, Trinkler, King, Kennedy, & Cipolotti, 2006; Drzezga et al., 2005; Zakzanis, Quintin, Graham, & Mraz, 2009) have specifically found allocentric spatial impairments. Widmann, Beinhoof, and Riepe (2010) immersed AD patients and healthy participants in a VE, a virtual version of Philadelphia, to assess the learning of verbal material in situations that imitate natural conditions. Participants sat passively and watched the film of the VE. The experimenter instructed participants that they were going on a shopping trip through the city. While jewelry shops were presented on the left and on the right sides of the street, participants were asked to read the shops' names out loud and to try to remember them. They were also told to remember the path they took. There were a total of 12 shop names to remember and the route consisted of seven virtual city blocks and three turns. AD patients were found to be impaired in free memory recall of shop names and in spatial memory compared to healthy participants, and the impairment was more marked than that observed with classical list learning. The authors concluded that classical list-learning paradigms wrongly estimate the memory capacities of patients in everyday situations.

We used a VE similar to that used in studying normal aging (Plancher et al., 2010) to characterize episodic memory profiles in an ecological fashion. The constructs researched included memory for central and perceptual details, spatiotemporal contextual elements, and binding (Plancher et al., 2012). Three different populations were contrasted: healthy older adults, patients with aMCI, and patients with early to moderate AD. The participants were successively immersed in two VEs: the first, as the driver of a virtual car (active exploration), and the second, as the passenger in that car (passive exploration). We sought to determine whether environmental factors that can affect encoding (active vs. passive exploration) influence memory performance also in pathological aging. Subjects were instructed to intentionally encode all the elements of the environment as well as the associated spatiotemporal contexts. Following each immersion (see Figure 9.2), we assessed the patient's recall and recognition of central information (i.e., the elements of the environment), contextual information (i.e., temporal, egocentric, and allocentric spatial information), and lastly, the quality of binding (number of types of contextual information associated to central elements, i.e., what-where-when). We found that the AD patients' performances were poorer than those of the aMCI group and even more so than those of the healthy aged group, in line with the progression of hippocampal atrophy reported in the literature.

Binding recall administered 20 minutes after the immersion and spatial allocentric memory assessments were found to be particularly useful for distinguishing aMCI patients from healthy older adults, a result that has been since confirmed (see Serino, Cipresso, Morganti, & Riva, 2014, for a review). In particular, Morganti, Riva, and Stefanini (2013), using a VR-Maze and a VR-Road

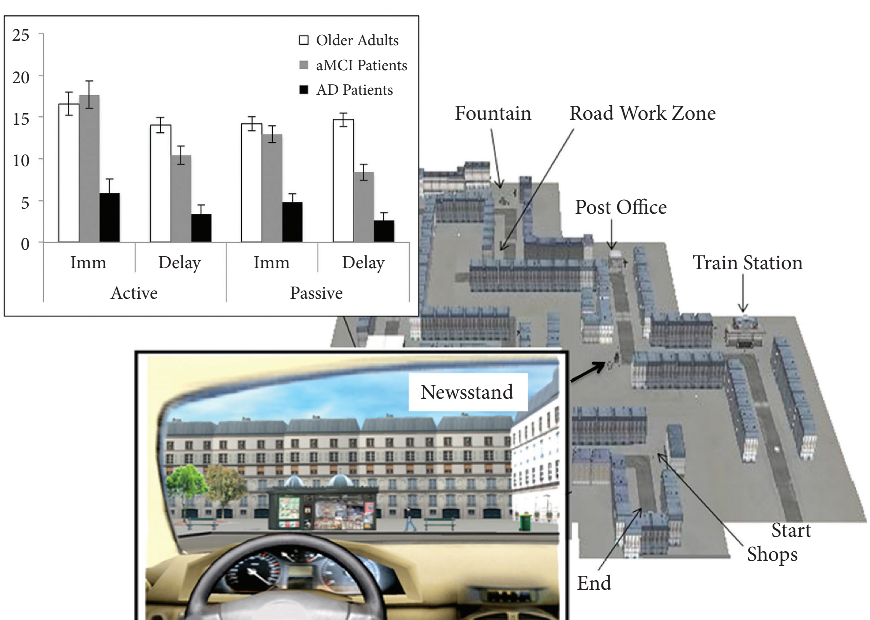

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FIGURE 9.2 *TK*

Map task, found a specific reduction in performing allo- to egocentric spatial tasks in AD, which is consistent with the early degeneration of the hippocampus and retrosplenial cortex underlying the ability to move between allocentric and egocentric reference frames. In addition, VR paradigms are able to discriminate pathological populations. Lee et al. (2014) observed that a significant spatial reference memory impairment was found in the aMCI group that converted to AD as compared to the nonconverter group, and Tu et al. (2015) found that spatial orientation performance assessed with a virtual supermarket task discriminated AD and frontotemporal dementia patient groups. We extended these results, revealing the relevance of the long-term feature binding assessment in ecological conditions for early detection of AD.

Confirming other VR studies in young and healthy older persons (Jebara et al., 2014; Plancher et al., 2013; Sauzéon et al. 2011, 2015), Plancher et al. (2012) observed that active exploration yielded enhanced recall of central and allocentric spatial information, as well as binding, in healthy aging but also in pathological populations (aMCI and AD). The beneficial effect of active encoding on populations showing a strong decline in episodic memory could be explained by relatively well-preserved frontal and motor brain functions implicated in procedural abilities or self-referential effects. Typically, AD patients exhibit a normal nondeclarative memory, at least when the disease is not too advanced (Lipinska & Bäckman, 1997; Van Halteren-van Tilborg, Scherder, & Hulstijn, 2007), as they can still play the piano or ride a bicycle and even can learn a new procedure. In addition, it has been demonstrated that AD patients can still experience some self-reference effects (Gutchess, Kensinger, & Schacter, 2010; Lalanne, Rozenberg, Grolleau, & Piolino, 2013). Interestingly, the patients' daily memory complaints were more highly correlated with their performance on the virtual test than with their performance on the classical memory test.

With a view to assessing multiple processes of episodic memory functioning embedded within contexts closely related to real life, Sauzéon and collaborators (2014) likewise investigated everyday memory from their VR apartment (HOMES test) in aging and in AD. As expected, they observed that AD patients exhibited poorer clustering, learning, and recognition performance than healthy older participants. They also observed that the HOMES indices were related to mnesic complaint, supporting the fact that the VR-based memory test is an appropriate device to capture the AD effect with respect to both in situ and laboratory settings. Taken together, these studies highlight specific cognitive differences found between AD and healthy populations that may provide additional insight into the early diagnosis and rehabilitation of pathological aging. In particular, neuropsychological studies would benefit from using virtual tests and a multicomponent approach to assess episodic memory, and to encourage the active encoding of information in patients suffering from mild or severe age-related memory impairment.

Conclusion

In summary, in recent years, several criticisms have been leveled at the validity of neuropsychological tests for measuring episodic memory dysfunctions and predicting decline in daily life. With current developments and the decreasing cost of VR technology, an ecologically valid but nonetheless objective and well-controlled assessment of episodic memory has become possible. This noninvasive, nonpharmacological cognitive evaluation has gained increasing attention in recent years (Cotelli, Manenti, Zanetti, & Miniussi, 2012; García-Betances et al., 2015), addressing the challenge of MCI and AD diagnosis, as well as starting to assess pathology in pediatric patients (Abram, Cuny, Picard, & Piolino, 2014; Picard, Abram, Orriols, & Piolino, 2015), epileptic patients (Grewe et al., 2014; Rosas, Parrón, Serrano, & Cimadevilla, 2013), and schizophrenic patients (Spieker, Astur, West, Griego, & Rowland, 2011; Weniger & Irle, 2008).

VR provides an excellent opportunity for investigating memory in the context of embodied and situated cognition, especially the links between memory, perception, and action (Hommel, 2004). The domain needs to be developed in future research and extended to other types of memory, such as prospective memory (Canty et al., 2014; Debarnot et al., 2015; Kalpouzos et al., 2010; Sweeney, Kersel, Morris, Manly, & Evans, 2010) and interactions between working and long-term memory systems (Gras et al., 2013). The results indicating an improvement in episodic memory with active exploration of VE (at least when it is not too effortful) suggest that sensorimotor and decisional activity during real-life events should be useful to boost episodic memory. It could encourage older adults and patients with early dementia to use their own actions, both via active navigation and decisional control, to boost the encoding of complex events in their daily life or with VR training programs. Overall, this recent research opens up new avenues in the fundamental understanding of memory and clinical neuropsychology.

Even if VR offers a vast number of possibilities in clinical neuropsychology, improvements are still possible. Studies sometimes do not take full advantage of VEs with high levels of immersion and interaction. Increasing the immersion level induces a higher intensity of the subjective sense of presence experienced by patients and affects their behavioral responses (Slobounov, Ray, Johnson, Slobounov, & Newell, 2015). However, some devices, such as HMDs, can provoke cyber-sickness, a visually induced motion sickness, which should be avoided in clinical settings (Bohil et al., 2011). Finally, in clinical neuropsychology, it is important that VR applications be normed in large healthy populations as current standard tests. It is also crucial that this technic becomes easily and affordably transferable to clinical structures but also to home to transform the patient's environment in a place where cognitive training can be performed in an intensive and properly controlled way, and potentially open it to social networks.

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