Review

The role of egocentric and allocentric abilities in Alzheimer's disease: A systematic review

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ABSTRACT

A great effort has been made to identify crucial cognitive markers that can be used to characterize the cognitive profile of Alzheimer's disease (AD). Because topographical disorientation is one of the earliest clinical manifestation of AD, an increasing number of studies have investigated the spatial deficits in this clinical population. In this systematic review, we specifically focused on experimental studies investigating allocentric and egocentric deficits to understand which spatial cognitive processes are differentially impaired in the different stages of the disease. First, our results highlighted that spatial deficits appear in the earliest stages of the disease. Second, a need for a more ecological assessment of spatial functions will be presented. Third, our analysis suggested that a prevalence of allocentric impairment exists. Specifically, two selected studies underlined that a more specific impairment is found in the translation between the egocentric and allocentric representations. In this perspective, the implications for future research and neurorehabilitative interventions will be discussed.

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1. Background

The cognitive profile of Alzheimer's disease (AD) is primarily characterized by episodic memory impairment in the context of more subtle language, attention, perceptive, and executive deficits

(Weintraub et al., 2012). In addition to episodic memory impairment, topographical disorientation distinguishes the first stages of AD (Guariglia and Nitrini, 2009; Henderson et al., 1989; Monacelli et al., 2003; Pai and Jacobs, 2004). Topographical disorientation is an "umbrella term" used for various visuo-spatial deficits that range from difficulties in using salient environmental features for orientation (*landmark agnosia*), representing the location of objects with respect to self (*egocentric disorientation*), and remembering the direction of orientation with respect to external stimuli (*heading disorientation*) to a difficulty in creating a new representation of the

environment (*anterograde disorientation*) (Aguirre and D'Esposito, 1999).

Topographical disorientation may reflect a deficit in spatial memory, which can be defined as the ability to encode, store and retrieve spatial information. In this perspective, the topographical orientation is successfully accomplished through the continuous construction of a more abstract representation, namely a "cognitive map" (Gallistel, 1990; O'Keefe and Nadel, 1978; Tolman, 1948).

First, it is crucial to define the two fundamental reference frames used to construct a cognitive representation of our space. On the basis of a reference point, i.e. the origin, individuals may use two reference frames for organizing spatial information in memory coding: the allocentric frame and the egocentric frame (Klatzky, 1998). In an egocentric reference frame constituted by subject-to-object relations, locations are represented by an individual's orientation (self-centered). Egocentric spatial representations derived from this process have the same perspective in which the spatial information was acquired. Alternatively, in an allocentric reference frame, constituted by object-to-object relations, locations are unrelated to the individual's orientation (world-centered). Therefore, the allocentric representations are centered on objects and/or environmental characteristics. These two fundamental reference frames form the basic structure of spatial memory and allow for spatial navigation. Spatial navigation is the cognitive function used to find and maintain a route from one place to another (Gallistel, 1990); in this manner, individuals are able to remember important locations and their mutual relations, as well as their relationships to themselves. Individuals may preferentially navigate in their surroundings using an allocentric survey map with specified directions and distances or using an egocentric route sequence with left-right turns (Morganti et al., 2007; Siegel and White, 1975). Different cognitive models have been proposed to explain how egocentric and allocentric representations work together to support spatial memory, and the consequent successful spatial orientation and navigation (for a review, see Avraamides and Kelly, 2008).

According to the "self-reference" model proposed by Sholl (Easton and Sholl, 1995; Sholl, 2001), a long-term allocentric representation is immediately available during navigation. In real-time, the self-reference system codes and updates egocentric relations to objects using the front–back and left–right axes of the body as a reference. At a representational level, the self-reference system interfaces with the allocentric maps from the long-term memory by providing location; the allocentric representation is itself orientation-free. Wang and Spelke proposed that individuals are able to successfully orient themselves and navigate by forming and updating several egocentric representations of their transient relations to significant spatial landmarks (Wang and Spelke, 2000, 2002). Only the geometric shape of the environment is stored in long-term allocentric representations; its function is to support orientations when the dynamic path integration system fails. Another model was proposed by Mou and colleagues (Mou et al., 2004), who stated that the spatial memory system is composed of two subsystems. The egocentric subsystem is responsible for computing the transient self-to-objects spatial relations necessary for immediate action. The environmental system is responsible for storing the spatial array of familiar environments with a specific preferred orientation.

Several neurobiological studies support the existence of both egocentric and allocentric representations (Burgess, 2006; Galati et al., 2010; Nadel and Hardt, 2004). Burgess described (Burgess, 2008) multiple egocentric representations that are integrated in the posterior parietal area 7a (Pouget and Sejnowski, 1997; Zipser and Andersen, 1988). On the other hand, the discovery of place cells in the hippocampus of rats (O'Keefe and Dostrovsky, 1971), primates (Ono et al., 1993) and humans (Ekstrom et al., 2003) have provided a basis for the allocentric representation of space. These hippocampal cells fire when an animal is in a specific location independent of its orientation within the environment, suggesting that they store a spatial location within an allocentric reference frame. Recently, Burgess and colleagues proposed a model that addresses the relationship between egocentric and allocentric spatial representations and their roles in supporting spatial navigation (Burgess et al., 2001; Byrne et al., 2007). Based on the reciprocal circuitry between the hippocampus and neocortical regions, their Boundary Vector Cells Model provides support for a crucial role of the hippocampal place cells in encoding and retrieving a spatially coherent scene. When prompted by a partial cue, the full spatial representation can be retrieved through the process of pattern completion (Byrne et al., 2007). Although allocentric, this representation is translated to an egocentric representation in the medial parietal areas via information from other cells. Place cells impose a viewpoint location (Ekstrom et al., 2003), and head-direction cells provide a viewing direction on the retrieved contents (Taube, 1998) to allow the generation of an egocentrically coherent representation in medial parietal areas. Grid cells support the process of updating a viewpoint in relation to self-motion signals (Boccara et al., 2010). More specifically, the retrosplenial cortex (RSC) transforms long-term hippocampal allocentric representations into egocentric parietal representations to compensate for the rotational offset between different coordinates (Maguire, 2001; Vann et al., 2009). With an fMRI study, Galati et al. (2010) have recently shown that the RSC and parahippocampal regions are selectively involved when an environmental object is not directly available to the senses, and it is located within a broader imagined spatial context. Whereas parahippocampal regions are engaged in processing the visuo-spatial structure of the scene, the RSC supports the process of orientation by retrieving references, allowing the scene to be localized within the wider spatial environment (Epstein et al., 2007).

An increasing number of studies have investigated the spatial deficits in AD patients (Gazova et al., 2012; Iachini et al., 2009; Lithfous et al., 2013; Vlček and Laczó, 2014). Indeed, the earliest AD-related neuropathological changes usually begin in the medial temporal lobe and related structures (Alafuzoff et al., 2008; Braak et al., 2006; Braak and Braak, 1991, 1996; Dickson, 1997; Morris et al., 1996; Thal et al., 2002). Whereas the role of the hippocampus in the episodic memory is well known, several neurocognitive have provided evidence that the hippocampus is also involved in spatial memory (Abrahams et al., 1997; Maguire et al., 1996, 1998; Morris et al., 1982; O'Keefe and Nadel, 1979; Spiers et al., 2001). Specifically, as noted above, an allocentric spatial map is encoded and stored in hippocampal place cells. Furthermore, medial temporal lobes are hypometabolic in early AD (e.g. De Santi et al., 2001), but when the metabolic rate of the medial temporal lobe and posterior cingulate cortex were compared with the same cohort, metabolic rate of the posterior cingulate lesion was significantly higher (Nestor et al., 2003).

Specifically, recent studies demonstrated that the RSC is as vulnerable to neurodegeneration as the hippocampus (Pengas et al., 2010; Scahill et al., 2002).

This neuropathological evidence supports to the hypothesis that in the early stages of AD, brain regions that are primarily affected are those involved in the neural circuit that supports the processing of allocentric and egocentric representations, and their mutual relations. On one hand, lesions in the hippocampus and related structures diminish the ability to construct and store a long-term allocentric-map. On the other hand, the neurodegeneration of the RSC seriously influences the allocentric-to-egocentric transformation: An impoverished egocentric representation useful for navigation could result from that process (for a review, see Cavanna and Trimble, 2006).

To the best of our knowledge, no systematic review has been performed that specifically focuses on the deficits in encoding and