Behavioural Brain Research 307 (2016) 150–158

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Real-space path integration is impaired in Alzheimer's disease and mild cognitive impairment

I. Mokrisova[a,b], J. Laczo[a,b,*], R. Andel[b,c], I. Gazova[a,b], M. Vyhnalek[a,b], Z. Nedelska[a,b], D. Levcik[d], J. Cerman[a,b], K. Vlcek[b,d,**], J. Hort[a,b]

[a] Memory Clinic, Department of Neurology, Charles University in Prague, 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic
[b] International Clinical Research Center, St. Anne's University Hospital Brno, Brno, Czech Republic
[c] School of Aging Studies, University of South Florida, Tampa, FL, USA
[d] Department of Neurophysiology of Memory, Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic

HIGHLIGHTS

- Path integration (PI) depends on structures affected early in Alzheimer's disease (AD).
- We examined PI in patients with mild AD and amnestic mild cognitive impairment (aMCI) and assessed the role of the hippocampus, entorhinal and inferior parietal cortices in this association.
- We used a novel real space Arena Path Integration Task.
- AD and aMCI subjects were impaired in PI accuracy.
- Hippocampal volume and thicknesses of entorhinal and parietal cortices partially explained differences in PI between controls, aMCI and AD subjects.

ARTICLE INFO

Article history:
Received 27 October 2015
Received in revised form 7 March 2016
Accepted 29 March 2016
Available online 30 March 2016

Keywords:
Alzheimer disease
Mild cognitive impairment
Spatial navigation
Hippocampus
Path integration

ABSTRACT

Introduction: Path integration (PI) is an important component of spatial navigation that integrates self-motion cues to allow the subject to return to a starting point. PI depends on the structures affected early in the course of Alzheimer's disease (AD) such as the medial temporal lobe and the parietal cortex.
Objectives: To assess whether PI is impaired in patients with mild AD and amnestic mild cognitive impairment (aMCI) and to investigate the role of the hippocampus, entorhinal and inferior parietal cortex in this association.
Methods: 27 patients with aMCI, 14 with mild AD and 18 controls completed eight trials of Arena Path Integration Task. The task required subjects with a mask covering their eyes to follow an enclosed triangle pathway through two previously seen places: start–place1–place2–start. Brains were scanned at 1.5T MRI and respective volumes and thicknesses were derived using FreeSurfer algorithm.
Results: Controlling for age, education, gender and Mini-Mental State Examination score the aMCI and AD subjects were impaired in PI accuracy on the pathway endpoint ($p = 0.042$ and $p = 0.013$) compared to controls. Hippocampal volume and thickness of entorhinal and parietal cortices explained separately 36–45% of the differences in PI accuracy between controls and aMCI and 28–31% of the differences between controls and AD subjects.
Conclusions: PI is affected in aMCI and AD, possibly as a function of neurodegeneration in the medial temporal lobe structures and the parietal cortex. PI assessment (as a part of spatial navigation testing) may be useful for identification of patients with incipient AD.

* Corresponding author at: Memory Clinic, Department of Neurology, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, V Uvalu 84, Praha 5, 150 06, Czech Republic.
** Corresponding author at: Department of Neurophysiology of Memory, Institute of Physiology, Academy of Sciences of the Czech Republic, Videnska 1083, Praha 4, 142 00, Czech Republic.
E-mail addresses: janlaczo@seznam.cz (J. Laczo), kamil@biomed.cas.cz (K. Vlcek).

http://dx.doi.org/10.1016/j.bbr.2016.03.052
0166-4328/

1. Introduction

Spatial navigation is the process of determining and maintaining a course or trajectory from one place to another [1] and its impairment is seen mainly in older adults, limiting considerably independence and quality of life [2–5]. Spatial navigation difficulties may also be a first hallmark of Alzheimer's disease (AD) evident at the stage of amnestic mild cognitive impairment (aMCI) [6–9]. Most of the studies dealing with spatial navigation used tests under visual control [3,4,6,8–10]. However, impairment of vision among older adults may adversely influence, or even prevent, spatial navigation testing. Thus testing of a specific type of spatial navigation, path integration (PI), that is independent of vision control and depends on the brain structures affected very early in patients with AD, on the medial temporal and parietal lobe [11–13] may be more specific for early AD changes.

PI is a strategy of spatial navigation that uses cues from different sensory sources that are entirely self-generated during locomotion to estimate position relative to a known starting point without reference to visual or external landmarks [14]. The cues are derived from vestibular system (translational and rotational accelerations), proprioception (feedback from muscles, tendons, and joints) [15] or visual system (linear and radial optic flow) [16]. PI is an unconscious process that happens automatically whenever an individual is moving around its environment. It allows an individual to keep track of its own position in space, in relation to its home base or a fixed starting point. The information about homeward direction and distance is maintained by a continuous integration of moment-to-moment changes to update the position [17]. This allows one to return to the starting point along the shortest path without any external (e.g. visual) cues [18]. Signals from vestibular system, proprioception and optic flow in mammals are integrated in specific brain structures, in which neural cells encode information about position and movement in space. The most important brain structures for PI in animals are the hippocampus with place cells [19,20], entorhinal cortex with grid cells [20,21] and posterior parietal cortex [22]. Lesions of these brain structures may impair the ability of animals to integrate path [22,23].

The medial temporal lobe structures and parietal cortex are further important for PI in humans. PI deficits were found in patients after medial temporal lobe resections, who were impaired in reproducing a complex route [24] or walking without vision toward a previously seen goal [25], and in patients with hippocampal atrophy, who were impaired in reproducing rotational displacements [26]. However, more recent reports suggested that in tasks with spatial working memory demands, medial temporal lobe structures may not be necessary for successful return to the starting place after short outward paths [27,28]. Other studies suggested that the medial temporal lobe structures may be essential for preliminary estimates of the target path and that patients with medial temporal lobe lesions are not impaired in PI tasks, which do not require trajectory prediction (e.g. in the experimenter-guided walking tasks) [29]. In contrast, patients with posterior parietal cortex lesions are not impaired at walking to the previously seen targets [30], however, inhibition of this brain area by repetitive transcranial magnetic stimulation disrupts perception of angular displacements [31].

Impairment of medial temporal lobe structures and parietal cortex has been demonstrated even in the early stages of AD and also in aMCI and may help to explain why spatial navigation deficits are commonly observed in patients with AD and aMCI [6–9]. To the best of our knowledge, none of the studies examined PI in aMCI and AD patients as a potentially important type of spatial navigation. There are several studies which examined PI in cognitively normal older subjects [32–35] and demonstrated that older adults, compared to younger individuals, were less successful in returning to the starting point on triangle completion task. However, most of these studies shared the limitation of using virtual space [33,35],

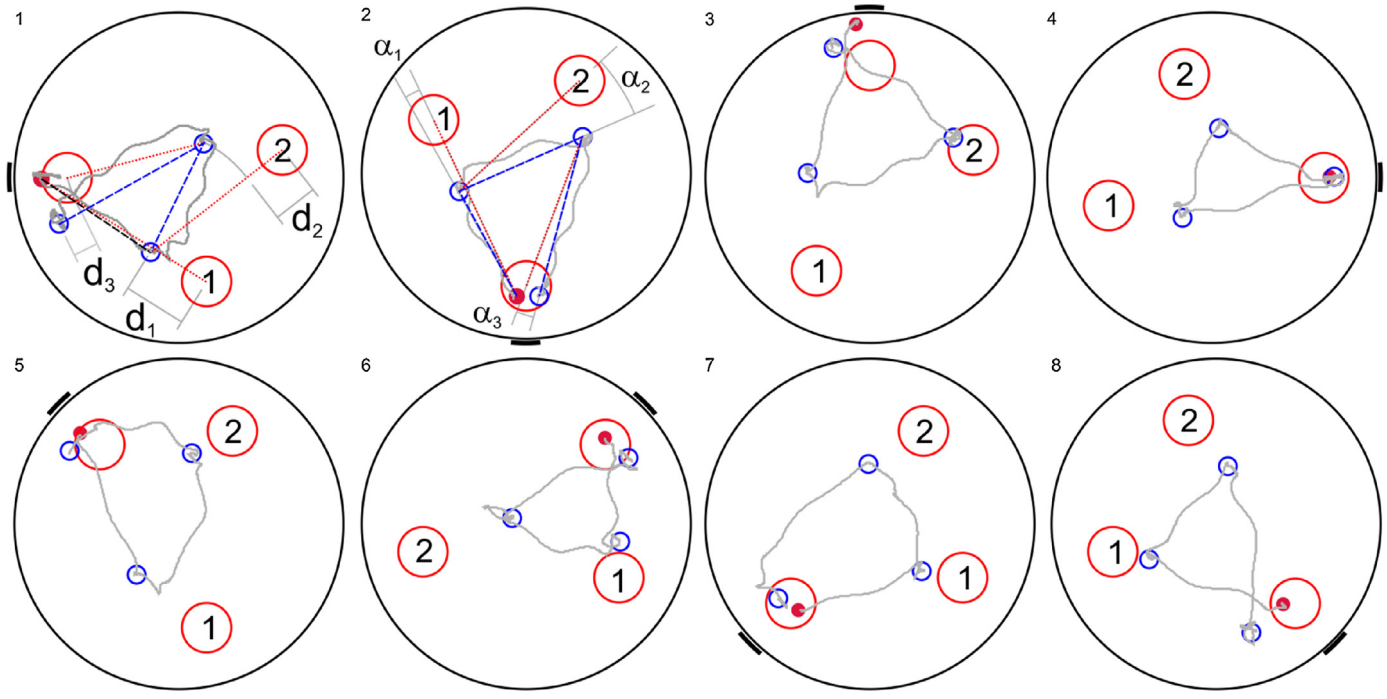

Fig. 1. Example of the recorded path of a hypothetical median control subject in eight trials of APIT. The large red circles with numbers inside indicate the correct start and goal positions, the small open blue circles indicate the goal positions as estimated by the subject. Each path begins at the small filled red circle, near to the short line sign on the arena wall that indicates start position. The first and the second trial further demonstrate the way of computation of the absolute distance (d1–d3) and absolute angular (α1–α3) errors, respectively. For explanation see the Methods section in the body of the manuscript. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)