

Provided for non-commercial research and education use.
Not for reproduction, distribution or commercial use.



This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

<http://www.elsevier.com/copyright>



Contents lists available at ScienceDirect

Behavioural Brain Research

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

Research report

Age differences in the formation and use of cognitive maps

Giuseppe Iaria^{a,*}, Liana Palermo^b, Giorgia Committeri^c, Jason J.S. Barton^a^a Human Vision and Eye Movement Laboratory, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada^b Psychology Department, University of Rome "La Sapienza", Rome, Italy^c Department of Clinical Sciences and Biomedicine, University G. D'Annunzio and ITAB, Foundation G. D'Annunzio, Chieti, Italy

ARTICLE INFO

Article history:

Received 1 July 2008

Received in revised form 26 August 2008

Accepted 28 August 2008

Available online 4 September 2008

Keywords:

Aging

Topographical orientation

Navigation

Virtual environment

ABSTRACT

Topographical orientation relies on the integrity of several cognitive functions and different strategies that individuals may adopt while navigating in the environment. Although previous studies have shown an age-related decline in navigational ability, these have not clarified the precise function or strategy that is affected. We hypothesized that aging may have an adverse effect on the ability to form and use a 'cognitive map', a mental representation of the environment. We had young and older participants solve a navigational task in a virtual environment designed to assess cognitive map use. Older participants required more time to form a cognitive map of the environment than young individuals and required more time and made more errors when subsequently using the cognitive map for orientation. These results suggest that decreased efficacy in both forming and using cognitive maps makes a significant contribution to the age-related decline in orientation skills.

© 2008 Elsevier B.V. All rights reserved.

1. Introduction

Several behavioural studies have documented an age-related decline in the human ability to orient and navigate in the environment [1–5]. In most studies, participants solve a virtual version of the Morris Water Maze task, in which they learn to reach a location hidden in the environment [6]. This task was originally designed to assess the use spatial information in the environment and shown to depend on hippocampal function. In other studies, orienting skills have been assessed with more ecological paradigms, such as mazes with hallways leading to target locations in virtual environments [4], or the performance of routes from memory in real surroundings [5]. These studies consistently report that elderly subjects take longer to reach a target location and make more errors than younger individuals. These behavioural results have parallels in neuroimaging findings. In a recent functional magnetic resonance imaging (fMRI) study [7], elderly volunteers performing a navigational task had less neural activity than young participants in the hippocampal complex, parietal cortex and retrosplenial cortex, regions involved in spatial navigation [8–13]. Another study [14] revealed that the age-related impairments while performing spatial and non-spatial hippocampus-dependent tasks were signif-

icantly correlated with both reduced volume and neurochemical properties of the hippocampus. Thus, with normal aging the brain may undergo structural and functional changes that impair cognitive components important for navigation and orientation.

While navigating in the environment, however, one may use different strategies that in turn may rely on different brain regions. Studies in human and non-human animals [15–19] have shown that at least two different memory systems with differing anatomic substrates are involved in orientation. The striatum subserves procedural memory, which individuals use when they navigate by following habitual paths in a fairly automatic manner [15,16]. On the other hand, the hippocampal complex subserves spatial memory, which individuals use when they orient by using landmarks in the environment and their spatial relationships [12,13,20,21]. When learning to navigate in a new environment, subjects may either over-learn a habitual route, thus relying on the procedural memory, or develop a "cognitive map" [22], a mental representation of the landmarks and paths in the environment, thus relying on spatial memory. (The latter strategy has the advantage of allowing individuals to reach any target location by any route available, not just a habitual one [18].)

Many elderly individuals develop a coping strategy of avoiding unfamiliar routes and places [23]. This raises suspicion that aging may have particularly adverse effects on the use of a cognitive map of the environment. Although several studies have shown that aging affects the ability to orient and navigate, it is not yet known whether aging specifically affects the ability to form and use cognitive maps.

In this report, we asked young and older participants to perform a virtual navigation task designed to assess both formation and use

* Corresponding author at: Human Vision and Eye Movement Laboratory Faculty of Medicine, University of British Columbia, VGH Eye Care Centre, Section D, 2550 Willow Street, Vancouver, BC, Canada V5Z 3N9. Tel.: +1 604 875 4111x62929; fax: +1 604 875 4302.

E-mail address: giaria@eyecarecentre.org (G. Iaria).

¹ Website: www.gettinglost.ca.

of cognitive maps, by limiting the utility of other strategies. The independent assessment of both formation and also usage of cognitive maps is also important since these two processes may have distinct anatomic substrates [10,24]; an fMRI study has shown that these may involve the left anterior and right posterior hippocampi differently [10]. We hypothesized that older participants would be impaired in both forming and subsequently using a cognitive map of the environment.

2. Methods

2.1. Participants

Participants were 55 healthy right-handed volunteers (30 young participants: 15 females and 15 males; 25 older participants: 10 females, 15 males). The mean age of the young participants was 23.9 years (range 19–30 years), and the mean age of the older participants was 55.8 years (range 50–69 years). Since the experimental tasks involved interaction with a computerized virtual environment, we included only older participants who have or had a job that required the use of computers. In both young and older samples, we included participants who had played video games only a few times in their lives. Thus we excluded both computer gaming experts and computer novices from the samples. At the time of testing, no participants were taking medications, and none had a history of mental illness or a neurological disorder. Older participants were questioned regarding memory skills and any change in cognitive function in the preceding months: none reported memory problems or change in the ability to perform their daily-life and work-related activities. This was done to exclude subjects with early dementia or mild cognitive impairment: the relatively low variance in the performance of the older group is also reassuring that the sample was not heterogeneous with respect to the presence or absence of cognitive dysfunction. The study conformed with The Code of Ethics of the World Medical Association (Declaration of Helsinki), printed in the British Medical Journal (18 July 1964), and all subjects gave informed consent.

2.2. Experimental protocol, procedure and tasks

The virtual environment, created with the editor of a three-dimensional game software (Game Studio A6, La Mesa, CA, USA), was composed of several buildings of different sizes and shapes, but the same texture: thus the buildings could not easily be distinguished from each other. However, there were six clearly identifiable landmarks: a cinema, a restaurant, a bar, a hotel, a pharmacy and a flower shop (Fig. 1). This virtual environment is not a large city but a relatively small neighborhood in which all routes can be traveled in about 2 min. This environment was presented on a 17-in. computer laptop display, and participants moved within it by using three

arrow keys on the computer keyboard, which corresponded to left-turn, forward-movement, and right-turn. Turning rate and movement velocity were constant and not under the control of participants. This ensured that all subjects navigated within the environment at the same velocity, excluding differences in performance that might arise from age-related differences in motor performance.

Before starting the experiment, the participants were required to navigate freely for 15 min within a "practice virtual environment" different from the experimental one. This allowed them to practice the motor and perceptual aspects of the task and familiarize themselves with a similar virtual environment. In this practice virtual environment, there were the same general buildings but no identifiable landmarks. After 15 min, subjects were administered three control trials that required them to navigate three routes defined by arrow signs present along the pathways. The training phase ended only when the participants performed the three control trials with 100% accuracy, i.e., following the defined pathways without interruptions, walking in the middle of the route, and reaching the end of the path without stopping along the way. If participants did not meet criteria in any of the three control trials, they were given extra training until they were able to achieve this. This training was designed to ensure that both young and older participants were equivalent in the basic motor and perceptual processes needed for navigating in the virtual environment during the experiment. This was particularly important since speed is known to decline with age [25,26]. Given the single constant velocity while navigating and the requirement to complete routes without stopping, accurate performance on the control trials helped ensure that, during the experiment, differences between groups in the time spent to perform the tasks reflected differences in the efficiency of solving the orientation tasks, rather than differences in the ability to control the experimental tools, or differences in motor or perceptual speed. After completion of the training phase, participants were given the instructions for the following tasks, shown the identity of the landmarks available within the environment, and the experiment was started.

The experimental design probed two functions, first learning and then retrieval of a cognitive map. During the learning task, participants were instructed to explore freely the virtual environment, and learn the locations of the six landmarks and their spatial relationships within the environment. They were told that they would need to create a mental representation of the environment including the locations of the six landmarks (i.e. a cognitive map), and that they would later need to use this mental representation to solve the retrieval task. Participants were also told that during their exploration the examiner would stop them every 2 min and ask them to report the locations of the landmarks on a schematic map representing the virtual environment from a top-view perspective (Fig. 1A). If they failed to indicate all six locations correctly, they continued in the learning task. In addition to the examiner's timed assessments, subjects could stop at any time if they felt that they had attained an accurate mental representation. At that "terminal moment" the examiner asked them to report the locations of the landmarks on the schematic map. The 2-min interval between assessments were chosen based on a pilot study using young participants that showed that this was enough time to visit all six landmarks.

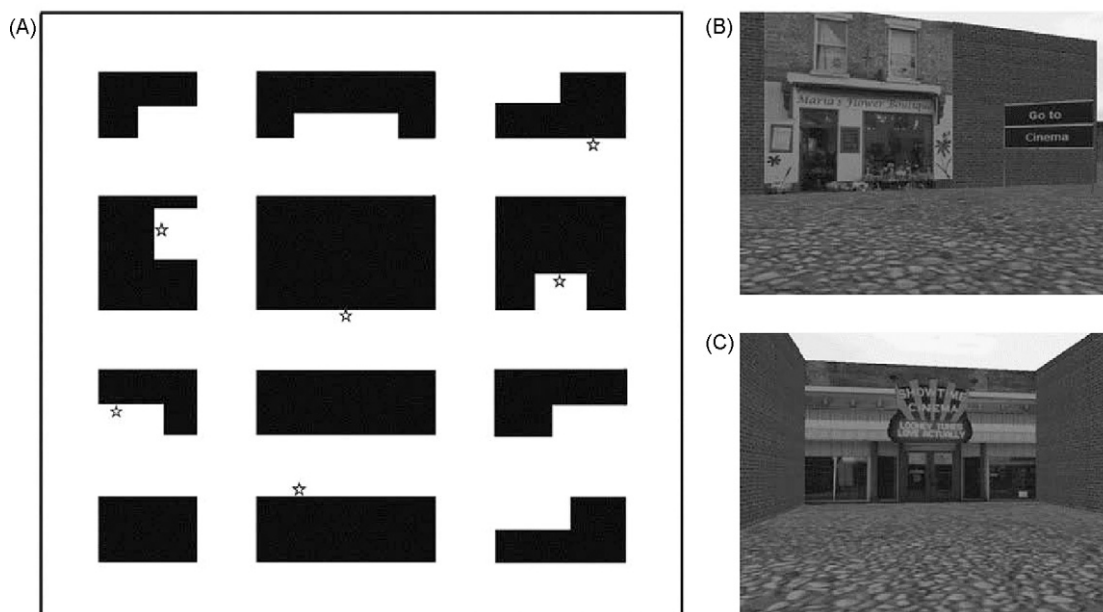


Fig. 1. Outline of the virtual environment. (A) Structure of the virtual city in which the participants performed both the learning and the retrieval tasks. (★) The locations of the six landmarks. Same map, but with no indications of landmarks' locations, was used to assess individuals' formation of the cognitive map. (B) View of the participants' starting position while performing one trial of the retrieval task: in this example, subjects were asked to reach the cinema (C) (target location) from the flower shop (starting position).

Given the standardized speed of movement, the older group would not differ in this respect. The learning task was considered complete when a participant was able to indicate the correct locations of all six landmarks, on either one of the every 2-min examiner-initiated assessment or at the subject-initiated terminal moment. The time to completion (not including the time used for the assessments) was considered the time required to form the cognitive map. After completion, subjects were given 3 min of rest, following which they performed the retrieval task.

The retrieval task consisted of 12 trials that required the subject to use the mental representation they had formed to reach the location of specific landmarks. On each trial, the subjects started by facing one of the six landmarks and a sign that indicated the target location they needed to reach as quickly as possible by the shortest path (Fig. 1B). Both starting places and target locations varied across trials, so that the only efficient way to perform the task correctly was to use the cognitive map that they had formed. Procedural memory would be of no assistance given that in each trial a new path was always required. Indexing the efficiency of performance needed to take into account the fact that the optimal route differed in length between trials. To do this, we determined the 'ideal time' to complete each path by using a computerized script that followed the shortest paths as quickly as possible without stopping. This ideal time was then subtracted from the time a participant actually used for that path, to give the 'additional time' they required for that trial. Averaging the 'additional time' across trials gave us each participant's 'mean time delay' in reaching target locations, which would inversely reflect their efficiency in using their cognitive map. Since the velocity of movement is kept constant, delay in reaching the target location may be due to either following a path that was not the shortest or by stopping along the way, both of which would reflect inefficient use of the cognitive map. In addition, we measured the number of errors made while solving the retrieval task, an error being a trial in which the participants made a detour to reach the target location, instead of following the most direct route.

At the end of the experiment, the examiner interviewed the participant for information regarding the strategies used during both the learning and the retrieval tasks.

3. Results

3.1. Learning task

Most of both young (27 out of 30) and older (20 out of 25) participants exhibited a similar systematic strategy in exploring the environment: they defined the northern, southern, western and eastern sides of the environment first, then navigated from one side to the opposite until all landmarks were found and all routes explored. The few subjects that did not define the sides of the environment followed a different but equally systematic strategy, moving around the perimeter first and then exploring the environment in the same fashion described above. These strategies were confirmed by the individuals' reports, indicating that they were conscious of the exploratory strategies they had adopted.

Analysis using *t*-test comparisons between the groups showed that older participants (mean time (S.D.)=1173.6 s (422.52)) required significantly more time than young participants (mean time (S.D.)=896 s (453.93)) to complete formation of a cognitive map of the environment ($t(1,53)=2.33, p=0.0237$) (Fig. 2A).

3.2. Retrieval task

All participants were able to reach the target locations (100% accuracy). Analysis of the 'mean time delay' using *t*-test comparisons between the groups showed that older participants (mean time (S.D.)=53.32 s (28.3)) needed more time than young individuals (mean time (S.D.)=9.6 s (9.4)) to reach the target locations ($t(1,53)=7.96, p<0.0001$). Thus, they were less efficient in making use of the cognitive map they had previously formed for the purpose of orientation (Fig. 2B). Similarly, *t*-test comparisons between groups of the number of errors made while performing the task (i.e. the number of trials in which participants deviated from the shortest route), showed that older participants made more errors (mean errors (S.D.)=7.28 (2.37)) than young participants (mean errors (S.D.)=1.3 (1.15)) ($t(1,53)=12.21, p<0.0001$) (Fig. 2C).

To determine if age-related differences in the ability to use the map in the retrieval phase could be accounted for solely by the efficiency of cognitive map formation in the learning phase, we performed an ANCOVAs, with mean time delay and error rate in the retrieval phase as dependent variables, time required to complete the cognitive map in the learning phase as a co-variate, and subject group as independent factor. The results showed that the main effect of group was still significant, with older participants spending more time ($F(1,51)=4.25, p=0.0443$) and making more errors ($F(1,51)=8.419, p=0.0055$) compared to young participants. Thus, even after the results are adjusted for the time to form a cognitive map, a significant age-related difference remains ($F(2,50)=4.436, p=0.0168$).

4. Discussion

Compared to young participants, older individuals both required more time to form a cognitive map of the environment and also were less efficient in using the map for orientation. This confirms our hypothesis that an effect of age on processing cognitive maps contributes to the age-related decline in navigational skill previ-

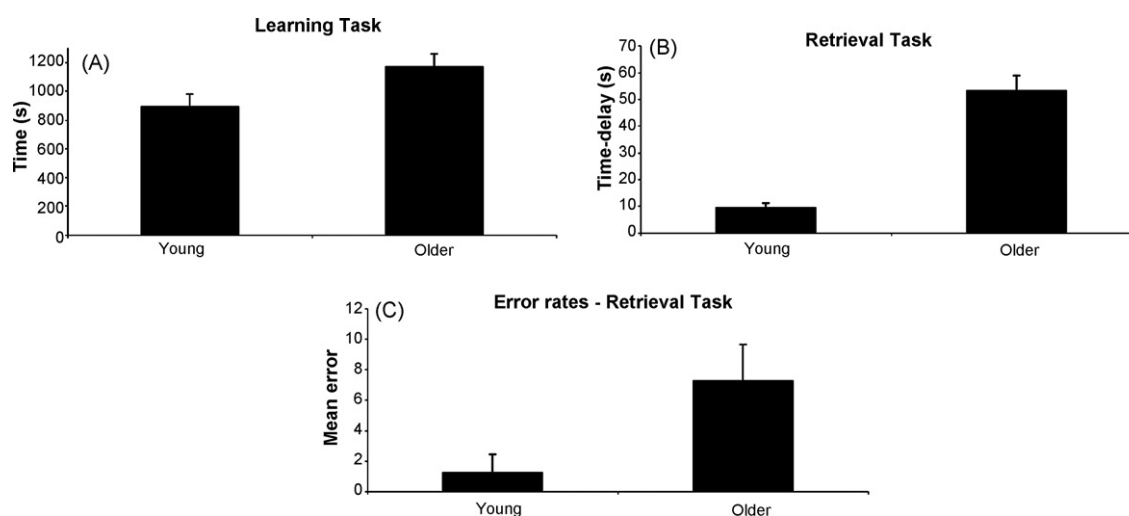


Fig. 2. The histogram displays the mean time (s) required by young and older participants to form the cognitive map of the environment (A) and their time-delay in reaching the target locations (B). Error bars indicate standard errors of the means. Panel C displays the mean errors (bars indicate standard deviations) made by young and older participants while reaching the target locations during the retrieval task.

ously shown in both human and non-human animals [3,4,7,27–29]. These prior studies, however, did not distinguish between the different strategies that individuals might adopt while navigating (see discussion in [7]). Our study used a paradigm designed to maximize reliance on a cognitive map and minimize the contribution of procedural memory, to show an age-related difference in one specific component of navigational ability, the formation and use of a cognitive map. Difficulty with cognitive map processing may explain why elderly individuals particularly report difficulties with learning to orient in new surroundings [23], a situation in which cognitive maps are more important than procedural memory.

Two prior studies have used a maze test to show similar age-related impairments in navigation. First, Newman and Kasznick [30] used a real environment (a large tent-like enclosure), and asked younger and older healthy participants to learn and remember the location of a target relative to a series of environmental cues—in essence, a human version of the Morris Water Maze used in rodents. Moffat and Resnick [28] used a virtual version of the Morris Water Maze, allowing greater control of the environmental stimuli and computerized measures of performance.

Both of these studies suggested that their results may reflect age-related declines in cognitive map use. However, there are several aspects of the Morris Water Maze task that limit such a conclusion. In the maze task, subjects learn to reach a hidden platform located in the environment, which also contains visual cues, usually coloured shapes, one of which is associated with the platform's location. During these learning trials, subjects repeatedly start from the same location, meaning that they could learn either a habitual route (procedural memory) and/or a cognitive map. Intermittently there are probe trials in which the subjects start from a different location and must reach the location of the platform, which has been removed, although the coloured shape associated with the platform is still present. The time spent in the correct location despite the absence of the platform is taken as an indirect measure of the ability to locate the target.

This type of maze protocol has several limitations. First, the time spent in the target vicinity does not directly measure the efficiency of the route followed to the target, and second, such an index may also reflect in part the strength of the learned association between the visual cue and the platform, which may reflect object memory rather than spatial memory. Third, while having the subjects start from a different location during these probe trials does emphasize cognitive map use rather than procedural memory, the fact that either procedural or spatial memory could have been used during the learning trials means that failures on probe trials could reflect either (a) inability to form a cognitive map or (b) a spontaneous bias in the choice of the subject to rely on a procedural strategy during learning [16], limiting the development of such a map. Finally, the alternation of probe and learning trials means that the measures on the probe trials reflect performance while the subject is still learning the environment, meaning that the processes of formation and use of navigational strategies are not assessed independently.

Our study attempted to address each of these issues. Our learning phase emphasized the memory of the location of a number of target locations, not a route between a single starting place and a single target location. Our assessment of use of the cognitive map did not begin until after subjects had demonstrated formation of an accurate cognitive map, allowing us to distinguish between learning and retrieval of such a map. During the retrieval phase, subjects were given different starting locations and different targets to reach, and our measure of performance was the time taken to travel, not the time spent at the target. For these reasons, we believe that our study provides stronger support for the conclusion that cognitive map formation and use are specifically affected by aging.

One limitation of our results is that it may be difficult to conclusively demonstrate that use of a cognitive map is affected independently of age-related effects on formation of a cognitive map. Although both young and older participants could reach the same criterion for successful formation of a cognitive map, we cannot exclude the possibility that the need for more time in the older group may be associated with a less robust mental representation of the environment. Allowing them more time to reach criterion was meant to compensate for any inefficiencies in cognitive map formation, but may have been only partially successful in doing so. Thus a difference in the quality of cognitive maps formed could have contributed to the reduced efficiency in map usage during the retrieval task. Qualitative inspection of performance during the task revealed that older participants sometimes headed in the wrong direction initially, detoured to other landmarks along the way, or stopped several times while getting to the target locations, all of which increased time they spent in solving the task. In contrast, young participants generally headed in the correct direction and reached targets by the shortest pathway. We conclude that retrieval difficulties can reflect either cognitive maps of limited quality or problems with accessing such maps.

It is worth noting that our finding of an age-related differences occurred with an older group of participants that is not usually defined as elderly, since their mean age was of 56.7 years. We selected this age because older individuals may lack familiarity and skills with the computer technology used in our task. Also, general motor, attention and perceptual skills decline at older ages [31–34], leading to slower reaction times and manual responses, which can confound temporal measures in any cognitive task. By using subjects who could attain similar measures of basic exploratory performance by the end of the training task, and by using a protocol that keeps velocity constant and under the control of the computer rather than the subject, we can be more confident that the age-related differences in our temporal parameters are related more to differences in the efficiency of cognitive map processing than to differences in motor skills, an inference that is supported by the difference in a non-temporal parameter, namely the number of errors made.

Of course, limiting the impact of low-level sensorimotor factors does not exclude a possible contribution of other higher-level cognitive functions to age-related declines in a complex task like cognitive map usage. Using functional magnetic resonance imaging, we have shown activation in the hippocampal complex, parietal lobe and retrosplenial cortex with the same tasks and stimuli used in this study [10]. These cortical regions have been implicated in functions such as attention, space-perception and memory [11,35–38], all of which likely contribute to efficient navigation. A functional neuroimaging study of aging effects on navigation [7] showed age-related reductions in the activation of these same regions. Hence the wide network of cortical regions recruited by navigation tasks supports assertions that other cognitive functions such as mental rotation [1,39] may be involved in cognitive map processing. If so, the age-related decline in forming and using cognitive maps we report may reflect a convergence of aging deficits in multiple cognitive abilities. Such a convergence may render tests of a complex phenomenon such as navigating in the environment particularly sensitive to the effects of age. Thus, while we provide evidence that aging affects the formation and use of cognitive maps, we do not exclude the possibility that a decline in other cognitive functions also contributes to a deterioration in navigational and orientation skills with age. Cognitive map use is only one of several orientation strategies that individuals can adopt in navigation. Following routes in both familiar and unfamiliar surroundings can also be accomplished by remembering either a sequence of motor displacements or a series of behavioural responses (right or

left turns) related to the recognition of single familiar landmarks. In a taxonomy of topographical orientation disorders, Aguirre and D'Esposito [40] showed that these different orientation strategies may be affected by lesions to different brain regions. For instance, the ability to remember and derive directional information (left and right) from a specific landmark is affected by lesion in the retrosplenial cortex, resulting in "egocentric disorientation". Since aging may affect the functional and structural organization of different brain regions at different stages, it is reasonable to believe that the cognitive strategies available for orienting may be affected at different times in life. Further studies are needed to shed more light on the development and decline of the complex and fascinating cognitive skill of spatial orientation.

In summary, our findings suggest that decreased efficiency in the formation and use of cognitive maps occurs with aging, which likely contributes to difficulties in navigation among the elderly. Given a recent report that cognitive map processing is correlated with the microstructural properties of the hippocampus [24], this age-related decline in navigational skills may in part reflect degenerative changes in the hippocampal complex. This, however, remains a speculation for future studies to verify. Deficits in the use of cognitive maps may be relevant to work in age-related conditions such as Alzheimer's disease and mild cognitive impairment, particularly since the anatomic structures implicated in navigation are affected by such disorders [41–43], and complaints of navigational difficulties may occur early in the course of dementia [44].

Acknowledgments

This study was supported by grants from the Canadian Institutes for Health Research (MOP77615, JJSB), and the European Community FPS-Streep-Wayfinding (LP). GI is supported by the Alzheimer Society of Canada and the Michael Smith Foundation for Health Research. We thank Graziana Virgilio, Alessandro Natali, Angelo Iorio and Mauro Mastrilli for their help in collecting some of the data.

References

- [1] Driscoll I, Hamilton DA, Yeo RA, Brooks WM, Sutherland RJ. Virtual navigation in humans: the impact of age, sex, and hormones on place learning. *Horm Behav* 2005;47:326–35.
- [2] Kirasic KC. Spatial cognition and behavior in young and elderly adults: implications for learning new environments. *Psychol Aging* 1991;6:10–8.
- [3] Kirasic KC, Allen GL, Haggerty D. Age-related differences in adults' macrospatial cognitive processes. *Exp Aging Res* 1992;18:33–9.
- [4] Moffat SD, Zonderman AB, Resnick SM. Age differences in spatial memory in a virtual environment navigation task. *Neurobiol Aging* 2001;22:787–96.
- [5] Wilkniss SM, Jones MG, Korol DL, Gold PE, Manning CA. Age-related differences in an ecologically based study of route learning. *Psychol Aging* 1997;12:372–5.
- [6] Morris RG, Garrud P, Rawlins JN, O'Keefe J. Place navigation impaired in rats with hippocampal lesions. *Nature* 1982;297:681–3.
- [7] Moffat SD, Elkins W, Resnick SM. Age differences in the neural systems supporting human allocentric spatial navigation. *Neurobiol Aging* 2006;27:965–72.
- [8] Aguirre GK, Detre JA, Alsop DC, D'Esposito M. The parahippocampus subserves topographical learning in man. *Cereb Cortex* 1996;6:823–9.
- [9] Epstein R, Harris A, Stanley D, Kanwisher N. The parahippocampal place area: recognition, navigation, or encoding? *Neuron* 1999;23:115–25.
- [10] Iaria G, Chen JK, Guariglia C, Ptito A, Petrides M. Retrosplenial and hippocampal brain regions in human navigation: complementary functional contributions to the formation and use of cognitive maps. *Eur J Neurosci* 2007;25:890–9.
- [11] Maguire EA, Burgess N, Donnett JG, Frackowiak RS, Frith CD, O'Keefe J. Knowing where and getting there: a human navigation network. *Science* 1998;280:921–4.
- [12] Maguire EA, Burgess N, O'Keefe J. Human spatial navigation: cognitive maps, sexual dimorphism, and neural substrates. *Curr Opin Neurobiol* 1999;9:171–7.
- [13] Mellet E, Briscogne S, Tzourio-Mazoyer N, Ghaem O, Petit L, Zago L, et al. Neural correlates of topographic mental exploration: the impact of route versus survey perspective learning. *Neuroimage* 2000;12:588–600.
- [14] Driscoll I, Hamilton DA, Petropoulos H, Yeo RA, Brooks WM, Baumgartner RN, et al. The aging hippocampus: cognitive, biochemical and structural findings. *Cereb Cortex* 2003;13:1344–51.
- [15] Hartley T, Maguire EA, Spiers HJ, Burgess N. The well-worn route and the path less traveled: distinct neural bases of route following and wayfinding in humans. *Neuron* 2003;37:877–88.
- [16] Iaria G, Petrides M, Dagher A, Pike B, Bohbot VD. Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: variability and change with practice. *J Neurosci* 2003;23:5945–52.
- [17] McDonald RJ, White NM. Parallel information processing in the water maze: evidence for independent memory systems involving dorsal striatum and hippocampus. *Behav Neural Biol* 1994;61:260–70.
- [18] O'Keefe J, Nadel L. *The hippocampus as a cognitive map*. Oxford: Clarendon; 1978.
- [19] Packard MG, McGaugh JL. Inactivation of hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning. *Neurobiol Learn Mem* 1996;65:65–72.
- [20] Maguire EA. Hippocampal involvement in human topographical memory: evidence from functional imaging. *Philos Trans R Soc Lond B Biol Sci* 1997;352:1475–80.
- [21] Maguire EA, Frackowiak RS, Frith CD. Learning to find your way: a role for the human hippocampal formation. *Proc Biol Sci* 1996;263:1745–50.
- [22] Tolman EC. Cognitive maps in rats and men. *Psych Rev* 1948;55:189–208.
- [23] Burns PC. Navigation and the mobility of older drivers. *J Gerontol B Psychol Sci Soc Sci* 1999;54:S49–55.
- [24] Iaria G, Lanyon LJ, Fox CJ, Giaschi D, Barton JJ. Navigational skills correlate with hippocampal fractional anisotropy in humans. *Hippocampus* 2008;18:335–9.
- [25] Salthouse TA, Berish DE, Siedlecki KL. Construct validity and age sensitivity of prospective memory. *Mem Cogn* 2004;32:1133–48.
- [26] Salthouse TA, Schroeder DH, Ferrer E. Estimating retest effects in longitudinal assessments of cognitive functioning in adults between 18 and 60 years of age. *Dev Psychol* 2004;40:813–22.
- [27] Barnes CA, Suster MS, Shen J, McNaughton BL. Multistability of cognitive maps in the hippocampus of old rats. *Nature* 1997;388:272–5.
- [28] Moffat SD, Resnick SM. Effects of age on virtual environment place navigation and allocentric cognitive mapping. *Behav Neurosci* 2002;116:851–9.
- [29] Tanila H, Shapiro M, Gallagher M, Eichenbaum H. Brain aging: changes in the nature of information coding by the hippocampus. *J Neurosci* 1997;17:5155–66.
- [30] Newman MC, Kaszniak AW. Spatial memory and aging: performance on a human analog of the Morris Water Maze. *Aging, Neuropsychol Cogn* 2000;7:86–93.
- [31] Lorenzo-Lopez L, Amenedo E, Pazo-Alvarez P, Cadaveira F. Visual target processing in high- and low-performing older subjects indexed by P3 component. *Neurophysiol Clin* 2007;37:53–61.
- [32] Lovden M, Schellenbach M, Grossman-Hutter B, Kruger A, Lindenberger U. Environmental topography and postural control demands shape aging-associated decrements in spatial navigation performance. *Psychol Aging* 2005;20:683–94.
- [33] Sullivan S, Ruffman T, Hutton SB. Age differences in emotion recognition skills and the visual scanning of emotion faces. *J Gerontol B Psychol Sci Soc Sci* 2007;62:P53–60.
- [34] Taniwaki T, Okayama A, Yoshiura T, Togao O, Nakamura Y, Yamasaki T, et al. Age-related alterations of the functional interactions within the basal ganglia and cerebellar motor loops in vivo. *Neuroimage* 2007.
- [35] Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 2002;3:201–15.
- [36] Ekstrom AD, Kahana MJ, Caplan JB, Fields TA, Isham EA, Newman EL, et al. Cellular networks underlying human spatial navigation. *Nature* 2003;425:184–8.
- [37] Mesulam MM. A cortical network for directed attention and unilateral neglect. *Ann Neurol* 1981;10:309–25.
- [38] Posner MI, Walker JA, Friedrich FJ, Rafal RD. Effects of parietal injury on covert orienting of attention. *J Neurosci* 1984;4:1863–74.
- [39] Palermo L, Iaria G, Guariglia C. Mental imagery skills and topographical orientation in humans: a correlation study. *Behav Brain Res* 2008.
- [40] Aguirre GK, D'Esposito M. Topographical disorientation: a synthesis and taxonomy. *Brain* 1999;122(Pt 9):1613–28.
- [41] Fellgiebel A, Wille P, Muller MJ, Winterer G, Scheurich A, Vucurevic G, et al. Ultrastructural hippocampal and white matter alterations in mild cognitive impairment: a diffusion tensor imaging study. *Dement Geriatr Cogn Disord* 2004;18:101–8.
- [42] Huang J, Auchs AP. Diffusion tensor imaging of normal appearing white matter and its correlation with cognitive functioning in mild cognitive impairment and Alzheimer's disease. *Ann NY Acad Sci* 2007;1097:259–64.
- [43] Medina D, DeToledo-Morrell L, Urresta F, Gabrieli JD, Moseley M, Fleischman D, et al. White matter changes in mild cognitive impairment and AD: a diffusion tensor imaging study. *Neurobiol Aging* 2006;27:663–72.
- [44] Hort J, Laczó J, Vyhnalek M, Bojar M, Bures J, Vlcek K. Spatial navigation deficit in amnesic mild cognitive impairment. *Proc Natl Acad Sci USA* 2007;104:4042–7.