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Hippocampal region-specific contributions to memory performance in normal elderly

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ABSTRACT

To investigate the relationship between regional hippocampal volume and memory in healthy elderly, 147 community-based volunteers, aged 55–83 years, were evaluated using magnetic resonance imaging, the Groton Maze Learning Test, Visual Reproduction and the Rey Auditory Verbal Learning Test. Hippocampal volumes were determined by interactive volumetry. We found greater age-related reduction in the volume of the hippocampal head relative to the tail. Right hippocampal tail volume correlated with spatial memory on the Groton Maze Learning Test while left hippocampal body volume was associated with delayed verbal memory. These associations were independent of age, sex, education and speed of processing and support the notion of functional differentiation along the long axis of the hippocampus.

1. Introduction

The hippocampus is vital to declarative memory as evidenced by the finding of reduced hippocampal volume in neurological conditions where declarative memory deficits are prominent (de Toledo-Morrell et al., 2000; Petersen et al., 2000; van der Flier et al., 2005). These observations lead one to predict that hippocampal volume and declarative memory will be correlated in healthy persons. However, morphometric studies in healthy elderly have not consistently borne out this expectation (Van Petten, 2004), causing some to question the generalizability of the link between memory and hippocampal volume (de Toledo-Morrell et al., 2000; Kohler et al., 1998; Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998). A possible reconciliation between the two sets of observations is that the relationship between hippocampal volume and memory may depend on the locus of volume loss (Hackert et al., 2002) and/or the sensitivity of the tasks used to evaluate memory (Golomb et al., 1993; Walhovd et al., 2004).

Regarding the locus of volume loss, the left hippocampus has been associated with verbal memory (Milner, 1965; Nunn, Graydon, Polkey, & Morris, 1999; Nunn, Polkey, & Morris, 1998; Smith & Milner, 1981; Spiers et al., 2001; Strange, Fletcher, Henson, Friston, & Dolan, 1999) while the right posterior hippocampus appears to be more involved in spatial memory (Maguire et al., 2000). Along the anterior–posterior direction, the anterior hippocampus is thought to contribute to encoding and the posterior hippocampus to retrieval (e.g., Greicius et al., 2003; Henson, 2005; Lepage, Habib, & Tulving, 1998; Moser & Moser, 1998). Additionally, the anterior hippocampus appears to be more vulnerable to age-related atrophy in both healthy (Hackert et al., 2002; Jack et al., 1997) and neurologically-abnormal elderly persons (Bouchard et al., 2008; Whitwell et al., 2007).

Given these observations, we predicted that regional hippocampal volume would correlate with memory performance in a region- and task-specific manner, whereby left hippocampal volume would correlate with verbal delayed memory (Golomb et al., 1993; Walhovd et al., 2004) and right posterior hippocampal volume would correlate with spatial memory. To test the second part of this hypothesis, we used a newer and possibly more 'hippocampal specific' test in addition to more established neuropsychological measures. We assessed spatial learning and memory using the Groton Maze Learning Test (GMLT)©, a recently developed computerized maze learning test (Snyder, Bednar, Cromer, & Maruff, 2005) reported to be sensitive to impairment of spatial memory and executive function in normal elderly (Pietrzak, Cohen, & Snyder, 2007). Verbal and visual immediate, as well as delayed memory, were evaluated using the Rey Auditory Verbal Learning Test (RAVLT) and Visual Reproduction (VR) from the Weschler Memory Scale (WMS-III).

We also predicted that age-related atrophy would be more prominent in the anterior hippocampus, a finding supported by some (Hackert et al., 2002; Jack et al., 1997) but not other studies (Kalpouzos et al., 2009; Malykhin, Bouchard, Camicioli, & Coupland, 2008) on healthy elderly.

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2. Methods

2.1. Participants

Participants in this study represent a subset ($N = 147$) of participants in the Singapore Longitudinal Aging Brain Study (Chee et al., 2009). Participants were persons aged 55 years and above with no known active medical conditions other than treated, uncomplicated diabetes mellitus or hypertension (Table 1). Participants met strict recruitment criteria (see Chee et al., 2009). Briefly, they were excluded if they had any chronic medical condition or any active medical or psychiatric condition that impaired cognition, scored <26 on the Mini Mental state Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) or >9 on a modified 15-point Geriatric Depression Scale (Yesavage et al., 1982). The study was approved by the Singapore General Hospital IRB and informed consent was obtained from all participants.

2.2. MR imaging

Detailed information on participants, imaging methods and analytical protocols had been documented earlier (Chee et al., 2009), and will only be briefly described here. Magnetic resonance imaging (MRI) was conducted using a 3T Siemens Allegra (Siemens, Erlangen, Germany). The T1-weighted Magnetization Prepared Rapid Acquisition Gradient Echo (MPRAGE) sequence used for morphometric analyses was similar to that used by the Alzheimer's Disease Neuroimaging Initiative (ADNI) consortium (Jack et al., 2008); TR = 2300 ms, T1 = 900 ms, flip angle = 9°, BW 240 Hz/pixel, FOV = 256 × 240 mm, matrix = 256 × 256; resulting voxel dimensions: 1.0 × 1.0 × 1.1 mm.

2.2.1. MR image analysis

Total intracranial and hippocampal volumes were manually measured by two trained researchers using Analyze 7.0 (Mayo Clinic, Rochester, MN). For the purpose of computing inter- and intra-rater reliability, the two raters traced 10 randomly selected brains on two different occasions separated by at least 4 weeks. Both inter- and intra-rater reliability coefficients were calculated using intra-class correlation coefficients and separately determined for all hippocampal volumes of interest (see Supplementary data Table 1). The reliabilities were high and comparable to other studies (e.g., Hackert et al., 2002).

2.2.1.1. Total intracranial volume (TIV). TIV was determined by tracing the margin of the inner table of the calvarium across sagittal 3D T1-weighted images. Sections were traced every 6.6 mm starting from the right, totaling 17–22 measured slices per volunteer. The volumes were summed across all traced slices (Jack et al., 1989). The most lateral slice on which the cerebral cortical gyri were visible was traced first. The inferior limit was the region across the foramen magnum.

2.2.1.2. Hippocampus measurement. Coronal images of the hippocampus were traced every 2 mm, moving in the posterior–anterior direction, resulting in 18–23 measured slices per person. The first slice traced was one in which the crura of the fornices could be seen enface, and the most anterior slice was determined retrospectively as the last slice on which the hippocampus was visible. Total hippocampal volume was computed by summing the cross-sectional areas from each slice and multiplying by slice thickness. Separate volumes were computed for the head, body and tail of the hippocampus (Fig. 1): the anterior 35% of slices constituted the anterior hippocampus (head), the intermediate 45% of slices represented the hippocampus middle/body and the remaining posterior 20% of traced slices the posterior hippocampus (tail) (Hackert et al., 2002). Hippocampal volumes were normalized to the total intracranial volume using an analysis of covariance approach (Buckner et al., 2004; Mathalon, Sullivan, Rawles, & Pfefferbaum, 1993; Raz et al., 2003): $Vol_{adj} = Vol_{raw} - b(\text{TIV} - \text{mean TIV})$, where b represents the slope of the regression line for volume against age.

2.3. Assessments

Participants completed two standardized measures of memory; the Rey Auditory Verbal Learning Test (RAVLT) (Lezak, Howieson, & Loring, 2004) and the Visual Reproduction (VR) subtest from the third edition of the Wechsler Memory Scale (Wechsler, 1997). The Groton Maze Learning Test (GMLT) and Simple Reaction Time test (SRT) were administered as part of the CogHealth© neuropsychological test battery (CogHealth Research version 3.4.5; CogState Ltd, Melbourne, Australia). The computerized tasks were presented on a pen-based interactive display (Wacom DTU-710, Wacom Saitama, Japan). Participants responded by tapping on the tablet using a stylus-pen for the GMLT or by pressing a key on the keyboard for the SRT.

2.3.1. Rey Auditory Verbal Learning Test

The RAVLT was administered in a standardized manner (Lezak et al., 2004). A list of 15 words (List A) was read consecutively for five trials and participants verbally listed as many words as they could recall after each presentation. Following this, another list of 15 words (List B) was presented, and recall was tested. Immediately after, participants were asked to recall List A. Thirty minutes later, without forewarning, participants were again asked to recall as many words they could remember from List A. We summed the words recalled across the five learning trials to provide a measure of immediate memory. Delayed memory performance was quantified as the total number of words recalled following the 30-min delay.

2.3.2. Visual Reproduction

Participants viewed a series of five designs for 10 s each and attempted to reproduce each design from memory immediately following each presentation. Following a 30-min delay, participants were asked, without warning, to reproduce all five designs from

Table 1
Demographic and neuropsychological data of study participants ($N = 147$).

Age (years)	64.7 (6.32)
Age range (years)	55–83
Sex, M/F	74/73
Education (years)	11.1 (3.02)
Mini mental state examination score (0–30)	28.6 (1.09)
Modified geriatric depression scale score (0–15)	1.54 (1.77)
Body mass index (kg/m^2)	23.2 (2.86)
Systolic blood pressure (mm Hg)	130.8 (14.0)
Diastolic blood pressure (mm Hg)	80.8 (8.89)
Hypertension (%)	56.5
Diabetes (%)	11.6
APOE-ε4 heterozygotes[a] (%)	15.6
Neuropsychological tests	
Rey Auditory Learning Test (RAVLT)	
Immediate recall	46.9 (8.39)
Delayed recall	10.2 (2.77)
Visual Reproduction (VR)	
Immediate recall	71.1 (12.4)
Delayed recall	46.4 (17.3)
Groton Maze Learning Test (GMLT)	
Maze efficiency index (MEI)	.59 (.12)
Total errors	72.7 (21.8)
CogHealth Simple Reaction Time (ms)	501 (180)

All values, except for sex, are means (SD) or n (%).
[a] There were no APOE-ε4 homozygotes in this cohort.

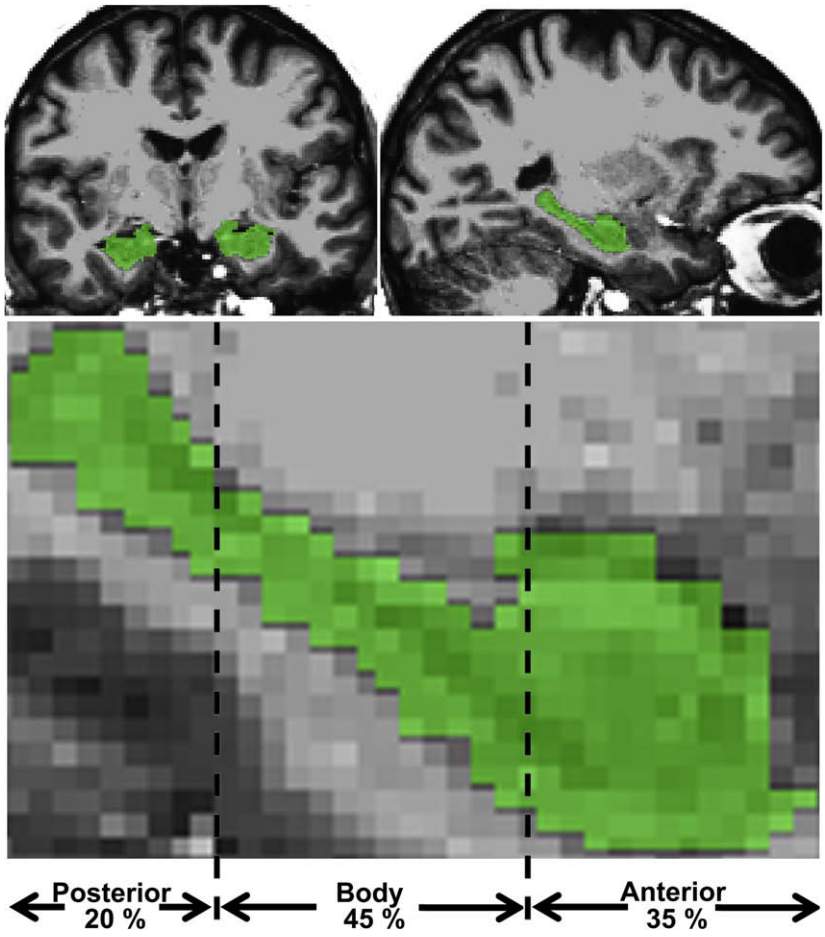

Fig. 1. Manual segmentation of the hippocampus. Top: coronal (left) and sagittal (right) brain slices through the hippocampus. Bottom: the hippocampus was segmented into three sections, anterior/head, middle/body and posterior/tail as described by Hackert et al. (2002).

memory. Total scores (summed across five designs) were computed separately for both immediate (VR-IR) and delayed recall (VR-DR).

2.3.3. Groton Maze Learning Test

The GMLT is a brief computerized neuropsychological task designed to measure spatial memory and executive function (Snyder et al., 2005). A practice trial was first administered to allow participants to familiarize themselves with the task. Participants were instructed to navigate through the 10×10 grid of grey tiles (28 steps, 11 turns) by following a hidden pathway through the grid from the top left corner to bottom right corner by tapping one tile at a time while adhering to two rules: they were not allowed to make diagonal moves and could move only one square at a time (Fig. 2). The start and end points of the pathway were indicated on the grid. Participants received feedback on every move. A correct move was accompanied by a tone and the appearance of a green tick on the tapped tile. If the move was incorrect, a red cross was displayed on the tapped tile and participants moved back to the last known correct tile and chose a different tile to advance forward. A trial ended when the end point of the pathway at the bottom right was reached.

During the test phase, participants navigated a different maze (28 steps, 11 turns), using the same 10×10 grid of tiles, for a total of five successive trials. Each subject completed one of 20 well-matched alternate forms. Each trial was timed and timing started automatically when the participant made his or her first move on each trial.

The maze efficiency index (MEI), the primary outcome measure of the GMLT, was the ratio of the number of correct moves to total time. The MEI was computed separately for every trial and then averaged across the five trials to provide an average MEI. Secondary outcome measures were the number of errors made during each trial and the total number of errors made over the five learning trials (the Error Monitoring Index).

2.3.4. Simple Reaction Time

A single card was presented face-down in the center of the computer screen and participants pressed the "K" key with their right index finger as soon as the card flipped over. A beep sounded when participants failed to make a response or pressed the response key before the card turned face-up. This test was presented twice (35 trials at each test), at the beginning and at the end of the battery and an averaged reaction time (in ms) was obtained across both tests.

2.4. Statistical analyses

The data was analyzed using SPSS version 13.0 (SPSS Inc., Chicago, IL). Annualized percentage change (APC: $\frac{vol_b - vol_a}{vol_a \times (b-a)} \times 100$) (Raz et al., 2003) was computed for all neuroanatomical volumes of interest – a being the lowest age in the sample and b the highest age. Vol_a and Vol_b represent the brain volumes at each age, estimated by regressing brain volume on age in our sample. The effects of sex were investigated using independent samples t-tests. Pearson correlation coefficients were computed to evaluate

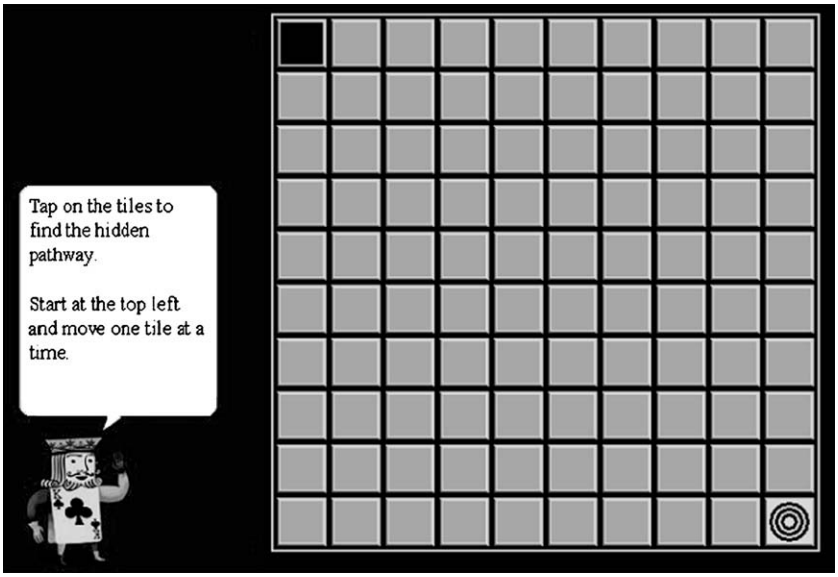

Fig. 2. Monochromatic illustration of the Groton Maze Learning Test. Participants were instructed to navigate through the 10 × 10 grid of grey tiles by following a hidden pathway through the grid from the top left corner to bottom right corner by tapping one tile at a time. The start is indicated by the tile at the top left and the finish location is the tile with the circles at the bottom right of the grid.

pairwise relationships between age, years of education, memory performance and hippocampal volumes. Significant bivariate correlations between hippocampal volumes and indices of memory performance were further investigated using standard multiple regression to partial out the effects of age, education, sex and SRT. These latter variables were also associated with memory performance and age and we wished to ensure that the relationships we report between memory, hippocampal volumes and age are independent of these potentially confounding variables.

3. Results

3.1. Effects of sex and age on neuroanatomical volumes and memory performance

Prior to normalization, males had significantly larger volumes in all hippocampal volumes of interest (largest $p = 0.04$), except the hippocampal tail, bilaterally. Sex differences were not significant following head size adjustment (smallest $p = .20$). For all subsequent analyses, only adjusted brain volumes were reported (Table 2).

There were significant age-related decrements in all measured brain volumes (Table 2). The age–volume correlations support an anterior to posterior gradient of age-related hippocampal atrophy, evidenced by the higher annual percent volume change in the hippocampal head relative to the tail (Table 2). Education did not significantly correlate with any hippocampal volumes ($r = -.15$ to .07, all $p > .05$).

With the exception of immediate and delayed recall RAVLT, age correlated significantly with all other indices of memory performance (Table 3); older individuals scored lower on these tests compared to their younger counterparts. There were significant effects of sex on the MEI of the GMLT; males performed better on the task consistent with previous literature demonstrating a sex advantage favoring males on tests of spatial route learning, navigation and mental rotation (Astur, Tropp, Sava, Constable, & Markus, 2004; Driscoll, Hamilton, Yeo, Brooks, & Sutherland, 2005; Moffat, Hampson, & Hatzipantelis, 1998; Rizk-Jackson et al., 2006). In contrast, females performed better on the immediate and delayed components of the RAVLT.

3.2. Neuropsychological performance and neuroanatomical correlates

3.2.1. Groton Maze Learning Test

Across all subjects, maze navigation efficiency improved significantly across trials, $F(4, 584) = 175.96$, $p < 0.001$ (Supplementary data Table 2), while errors were reduced, $F(4, 584) = 118.27$, $p < 0.001$ (Supplementary data Table 3).

Table 2
Adjusted mean volumes (and SD) and annualized percentage change (%) of hippocampal regions and their correlations with age.

Hippocampal regions	Adjusted volume (cm^3)	APC (%)	r_{age}	$r_{HC\text{-}middle}$	$r_{HC\text{-}posterior}$
Left hippocampus					
Total	3.21 (.31)	−.57	−.31**		
Head	1.43 (.17)	−.73	−.33**	.54**	.39**
Body	1.23 (.12)	−.42	−.21*	–	.53**
Tail	.55 (.07)	−.42	−.20*	–	–
Right hippocampus					
Total	3.34 (.31)	−.61	−.36**		
Head	1.52 (.17)	−.74	−.39**	.54**	.32**
Body	1.27 (.14)	−.51	−.22**	–	.55**
Tail	.55 (.07)	−.45	−.19*	–	–

* $p < .05$.
** $p < .01$.

Table 3
Univariate associations between demographic variables and volumes of hippocampal regions and performance on the cognitive tests.

Variables	Cognitive tests						
	RAVLT		VR		GMLT		SRT
	IR	DR	IR	DR	MEI	Errors	
Age	−.15	−.05	−.32**	−.21*	−.26**	.23**	.27**
Sex	.32**	.24**	.05	.11	−.30**	.16	.07
SRT	−.03	−.08	−.18*	−.21*	−.19*	.19*	−−
Years of education	.17*	.06	.23**	.11	.21**	−.27**	−.35**
HC regions							
Left HC							
Total	.06	−.05	.15	.13	.14	.03	−.04
Head	.07	−.01	.14	.15	.15	−.04	−.10
Body	−.02	−.17*	.09	.04	.14	.08	.04
Tail	.07	.06	.12	.09	.08	.09	.01
Right HC							
Total	.16	.03	.19*	.10	.17*	.05	−.01
Head	.15	.08	.14	.12	.15	−.01	−.04
Body	.11	−.05	.15	.07	.06	.10	.06
Tail	.15	.07	.20*	.05	.18*	.08	−.04

Abbreviations: RAVLT: Rey Auditory Verbal Learning Test; IR: Immediate Recall; DR: Delayed recall; VR: Visual Reproduction Test; GMLT: Groton Maze Learning Test; MEI: maze efficiency index; SRT: Simple Reaction Time; HC: hippocampal.
* $p < .05$.
** $p < .01$.

Averaged MEI correlated significantly with the total hippocampal and right hippocampal tail volume (Table 3). When effects associated with age, education, sex, and SRT performance were partialled out, a significant association remained between averaged MEI and right hippocampal tail volume (Table 4, Model 2). There were no correlations between total errors and any hippocampal volume of interest (largest $r = .10$, $p = .23$).

3.2.2. Visual Reproduction

There were significant correlations between VR-Immediate Recall, total right hippocampal volume and right hippocampal tail volume (Table 3). However, these relationships were not significant after accounting for the effects of age, sex, education and SRT (Table 4).

3.2.3. Rey Auditory Verbal Learning Test

A significant correlation was present between left hippocampal body and delayed recall (Table 3). This relationship remained significant even after partialling out the effects of age, sex, education and SRT (Table 4).

4. Discussion

We found that the anterior hippocampus showed greater age-related atrophy. Additionally, we observed that right hippocampal tail volume correlated with spatial memory and learning, while left hippocampal body volume correlated with delayed verbal memory.

4.1. Locus of age-related hippocampal atrophy

Consistent with studies (Hackert et al., 2002; Jack et al., 1997) that recruited large samples, our findings support greater age-related reduction in hippocampal head volume relative to tail volume. This stands in contrast to smaller, contrary studies (e.g., Kalpouzos et al., 2009; Malykhin et al., 2008).

Differences in the anatomical landmarks used to define the hippocampal sub-regions could contribute to the disparity between studies (Hackert et al., 2002; Jack et al., 1997; Malykhin et al., 2008). However, it is also noted that studies that reported a differential age-related vulnerability of the posterior hippocampus had involved individuals aged between 20 and 80 years (Kalpouzos

Table 4
Variance in memory performance accounted for by hippocampal volumes and other demographic variables using multiple regression. In Model 1, total right hippocampal volume was included as an independent variable, while in Model 2, right hippocampal tail volume was included as an independent variable.

Predictors	RAVLT-DR		VR-IR				GMLT			
	Model 1		Model 1		Model 2		Model 1		Model 2	
	β	p	β	p	β	p	β	p	β	p
Age	−.07	.42	−.26	<.01	−.27	<.01	−.18	<.05	−.19	<.05
Sex	.25	<.01	.09	.23	.08	.29	−.27	<.01	−.28	<.001
Education	.04	.62	.22	<.01	.21	<.05	.14	.09	.13	.11
SRT	−.06	.49	−.41	.69	−.03	.73	−.07	.43	−.06	.47
Right THC	–	–	.10	.21	–	–	.11	.20	–	–
Left HB	−2.06	<.05	–	–	–	–	–	–	–	–
Right HT	–	–	–	–	.13	.09	–	–	.15	<.05
R^2	.10		.16		.17		.19		.20	

Abbreviations: RAVLT-DR: Rey Auditory Verbal Learning Test Delayed Recall; VR-IR: Visual Reproduction Test Immediate Recall; GMLT: Groton Maze Learning Test; THC: Total hippocampal volume; HB: Volume of hippocampal body; HT: Volume of hippocampal tail.

et al., 2009; Malykhin et al., 2008). In contrast, studies restricted to normal elderly (Hackert et al., 2002; Jack et al., 1997), as well as elderly with neurodegenerative conditions like Alzheimer's disease (Jack et al., 1997; Whitwell et al., 2007) and Parkinson's disease (Bouchard et al., 2008), reported greater reduction of anterior hippocampal volume. Within-group (old only) and inter-group (young and old) findings relating to age-related changes in brain volume can differ depending on who, among the sample, is carrying the variance (Buckner, 2004).

4.2. Spatial memory and learning and the right posterior hippocampus

The present finding of an association between larger right hippocampal tail volume and better spatial memory is concordant with previous animal (Colombo, Fernandez, Nakamura, & Gross, 1998; Moser, Moser, & Andersen, 1993) and human (Maguire et al., 2000) studies. Hippocampal damage in rats and non-human primates results in deficits in spatial learning and memory (Jarrard, 1993; Rolls, 1991) while volumetric studies in animals have linked an enlarged hippocampus with advantageous behavioral adaptations related to better spatial memory (Biegler, McGregor, Krebs, & Healy, 2001; Jacobs, Gaulin, Sherry, & Hoffman, 1990; Sherry, Jacobs, & Gaulin, 1992).

Maguire et al. (2000) reported an *experience-driven* association between right posterior hippocampal volume and spatial memory; London taxi drivers, with extensive navigation experience, had significantly larger posterior hippocampal volumes compared to controls. This relationship was not present in individuals who were not taxi drivers (Maguire et al., 2003). A selective reduction of posterior right hippocampal volume was reported in early-blind individuals who have reduced opportunities to develop spatial memories (Chebat et al., 2007). While these findings point to some form of experience-driven modulation of right posterior hippocampal volume, none of the elderly participants in the present study engaged in occupations that made particularly high demands on spatial ability.

The GMLT purportedly taps two dissociable cognitive constructs: spatial memory, measured by the maze efficiency index, and executive control, reflected in the number of errors committed during the task (Pietrzak et al., 2008). In the present study, the right posterior hippocampal volume was associated with maze learning efficiency but not error monitoring, the latter being a function of the frontal cortex (Shallice, 1982) lending support to a two-factor structure of the GMLT (Pietrzak et al., 2008).

Hippocampal volumes were also not significantly associated with performance on Visual Reproduction over and above age. This is in line with our hypothesis that GMLT may be a more sensitive measure of spatial memory while Visual Reproduction may tap visual memory. Dissociations have been drawn between these memory modalities (Smith & Jonides, 1997).

4.3. Verbal delayed memory and left hippocampus

Delayed verbal memory correlated with left hippocampal body volume while no such association was present for immediate memory. This finding is consistent with studies suggesting that memory retrieval shows increased dependence on the hippocampus as a function of increasing delay between encoding and test (Golomb et al., 1993, 1994; Walhovd et al., 2004).

At present, only a limited number of studies have investigated correlations between regional hippocampal volume and verbal memory. Our finding of a correlation between verbal delayed memory and left hippocampal body volume contrasts with Hackert et al. (2002), who reported correlations between verbal memory and bilateral hippocampal head volumes. The reasons underlying this difference in findings are uncertain. One possible reason may be differences in methods of hippocampal volume normalization (Lye et al., 2006). Hackert et al. (2002) had reported correlations between verbal memory and non-adjusted hippocampal volumes, removing variance associated with intracranial volume, age, sex, and education. To investigate this issue, we conducted a supplementary analysis where we regressed verbal delayed memory on unadjusted left hippocampal volume (separately for head and body), age, total intracranial volume, sex and education (Supplementary data Table 4). The pattern of our reported findings was unchanged.

4.4. Study limitations

The current study has a few methodological limitations. We did not control for participants' day-to-day familiarity with computers. Although practice trials were administered, we cannot exclude the possibility that inter-individual differences in computer familiarity may have contributed to the age and sex effects in GMLT performance. The Simple Reaction Time task used was not matched to the GMLT. A newer version of the CogState employs the Timed-Chase Task, which is matched to the GMLT in all respects except the requirement to learn the hidden maze path.

While the present study focused on the hippocampus, performance on our memory tasks might not be solely dependent on hippocampal integrity. Other relevant brain regions may include the prefrontal cortex (Cabeza et al., 1997; Kessels, Postma, Wijnalda, & de Haan, 2000; Shallice et al., 1994), posterior parietal regions (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Kesner, 2008), parahippocampal cortex (Maguire, Frith, Burgess, Donnett, & O'Keefe, 1998) and perirhinal/entorhinal cortex (Schmidt-Wilcke, Poljansky, Hierlmeier, Hausner, & Ibach, 2009; Strange, Otten, Josephs, Rugg, & Dolan, 2002).

5. Conclusions

In summary, the present findings demonstrate an anterior–posterior gradient of vulnerability to aging in the hippocampus of healthy elderly persons and support the notion that there is functional differentiation along the long axis of the hippocampus. In particular, right posterior hippocampal volume was associated with spatial memory while left hippocampal body volume was related to delayed verbal memory.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bandc.2009.11.007.

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