Episodic memory in healthy aging: Role of the prefrontal cortex and medial temporal lobes

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Introduction

Background:

- Healthy aging comes with a decline in episodic memory – the ability to retrieve spatial and temporal details about past events *(Tulving, 1972; Reuter-Lorenz and Cappell, 2008).*
- The medial temporal lobes (MTL) and prefrontal cortex make-up a key circuit that supports episodic memory *(Eichenbaum, 2017).*
- Changes to the structural integrity and functional efficiency of this circuit occur across the lifespan *(Raz et al., 2005; Langnes et al., 2020)*
- Distinct structures within this circuit may differentially support distinct episodic memory processes in aging *(Spencer and Raz, 1995; Snytte et al., 2022)*

Research questions:

1. Are age differences in episodic memory consistent across memory tasks?
2. Do the same structures support episodic memory in younger and older adults?
3. What is the relationship between brain structure, memory performance and functional connectivity within this circuit, and across the cortex?

Methodology

Cohort:

- N = 208: 127 young adults (YA; 57% female), 81 older adults (OA; 57% female)
- Completed episodic memory battery, structural and resting state MRI scans

Table 1. Demographics and episodic memory performance

	Young adults	Older adults
Age	22.20 ± 3.19	67.28 ± 5.58
Education	15.16 ± 1.90	17.62 ± 3.05
PSMT	119.69 ± 13.32	98.38 ± 10.46
iRAVLT	32.29 ± 5.03	24.31 ± 4.89
VPA paired delay	13.03 ± 1.46	9.98 ± 2.73
VPA free delay	21.38 ± 3.60	15.90 ± 4.63
VPA immediate	43.62 ± 7.37	32.17 ± 9.21
VPA recog	39.73 ± 0.66	38.58 ± 1.90
Associative recall	184.23 ± 35.78	115.91 ± 48.61

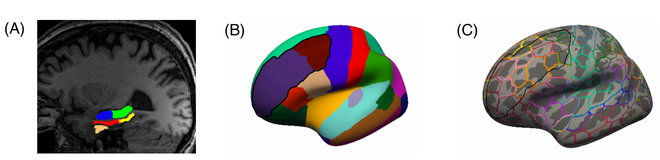
Image acquisition

- 1 mm isotropic T1 anatomical scan
- Two 10-minute multi-echo EPI resting state scans

Image processing:

- ME-ICA to classify BOLD signal and non-BOLD noise *(Kundu et al., 2013).*
- Participant specific functional parcellations using the Group Prior Individual Parcellation (GPIP) approach *(Chong et al., 2017).*
- Automated segmentation of the medial temporal lobes (MTL) using the Automatic Segmentation of Hippocampal Subfields (ASHS) pipeline (**Figure 1A;** *Yushkevich et al., 2014*)
  - BA35, BA36, ERC, PHC, antHC, postHC
- Cortical thickness of middle frontal gyrus (MFG) extracted with FreeSurfer from the DK atlas (**Figure 1B**).
- Resting state signal extracted from MTL regions of interest (ROIs) and from MFG parcels from Schaefer 400 cortical parcellation according to the Yeo17 network solution (**Figure 1C;** *Shaefer et al., 2018; Yeo et al, 2011*)

Figure 1. Segmentations of (A) MTL, (B) MFG thickness and (C) functional parcellation according to 17 network solution



Analyses:

- ANCOVA computed to measure group differences **(Figure 2)**
- Non-rotated partial-least-squares (PLS) analysis to measure group differences in connectivity **(Figure 3)**
- Behavioural-PLS analysis to assess associations between behaviour, brain structure and functional connectivity **(Figures 4-6)**

Results

Figure 2. Age differences in (a) episodic memory, (b) middle frontal gyrus thickness and (c) medial temporal lobe volumes

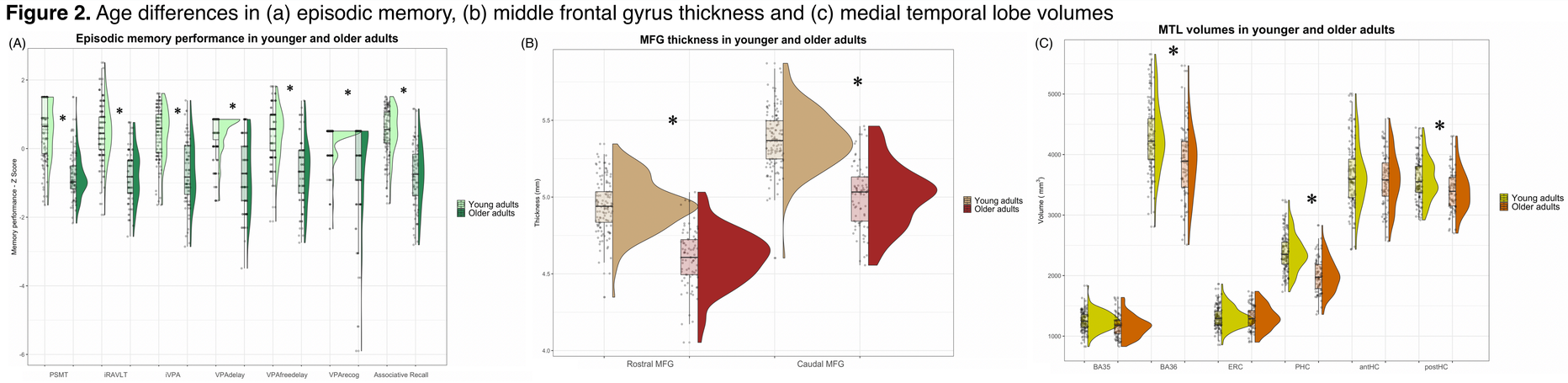


Figure 3. Age differences in functional connectivity in the MTL and MFG

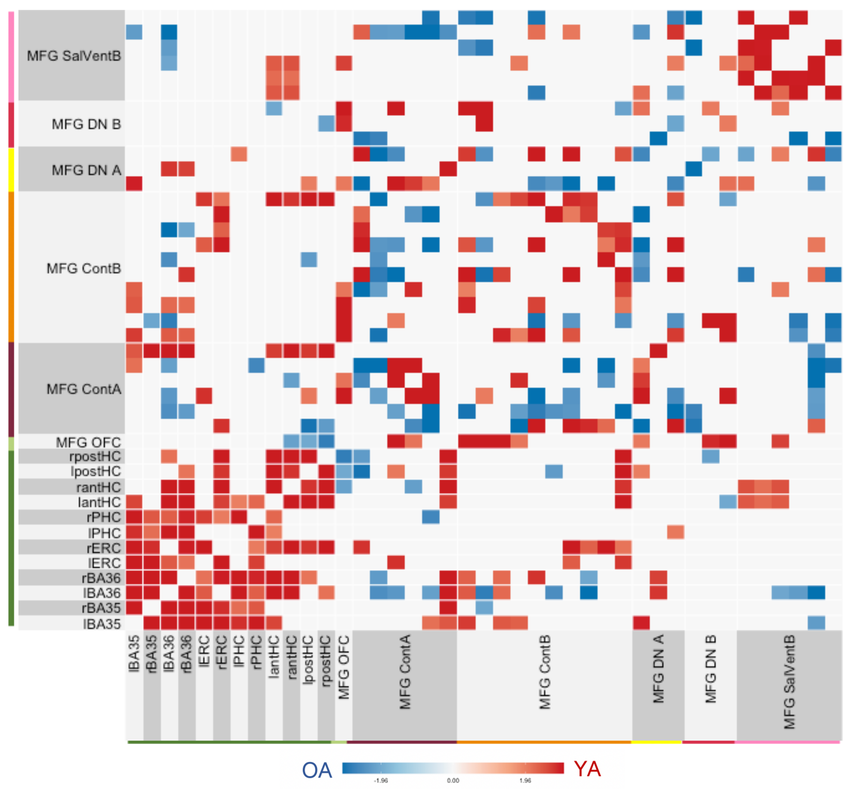


Figure 4. Episodic memory is supported by (A) the MFG in OA and (B) by the MTL in YA

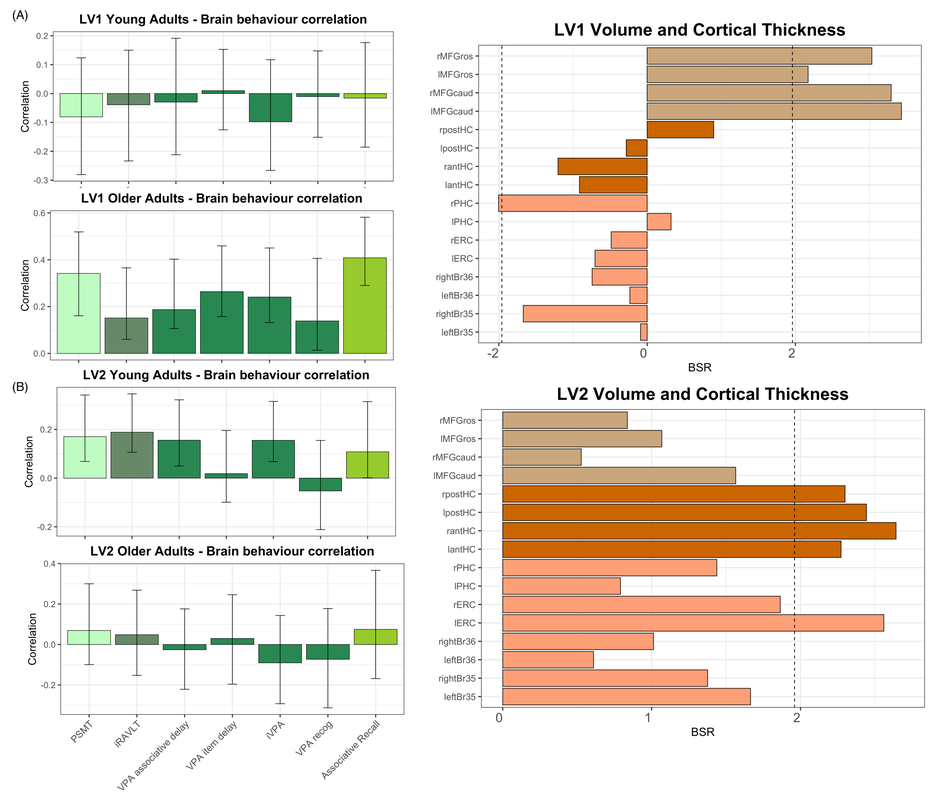


Figure 5. Episodic memory in older adults is related to MTL – MFG connectivity

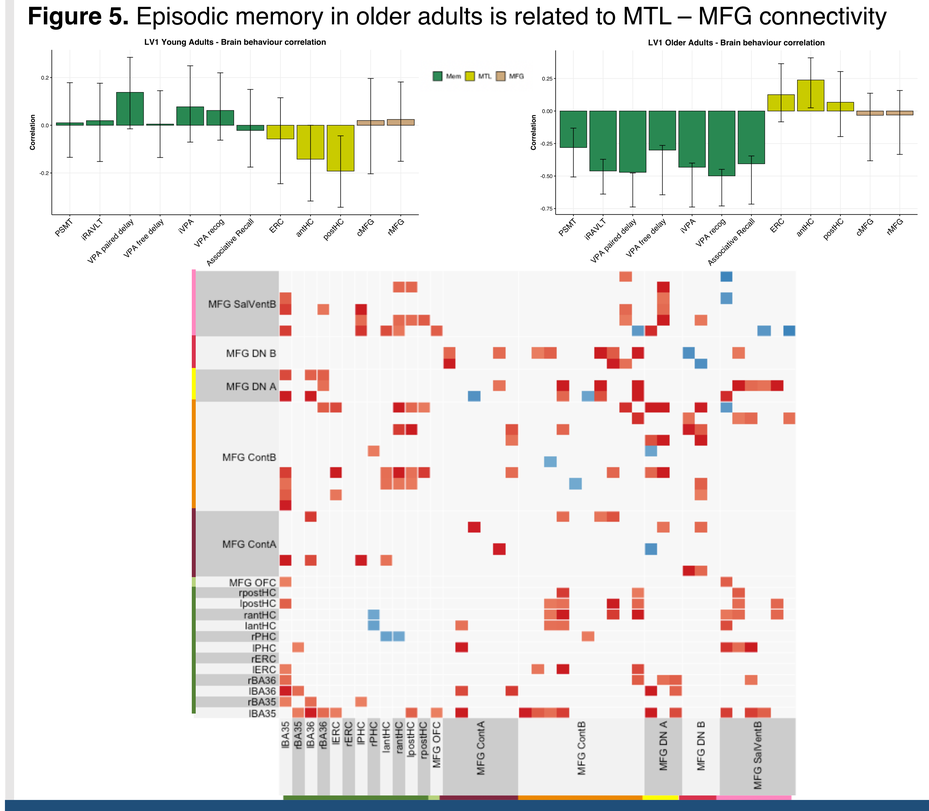
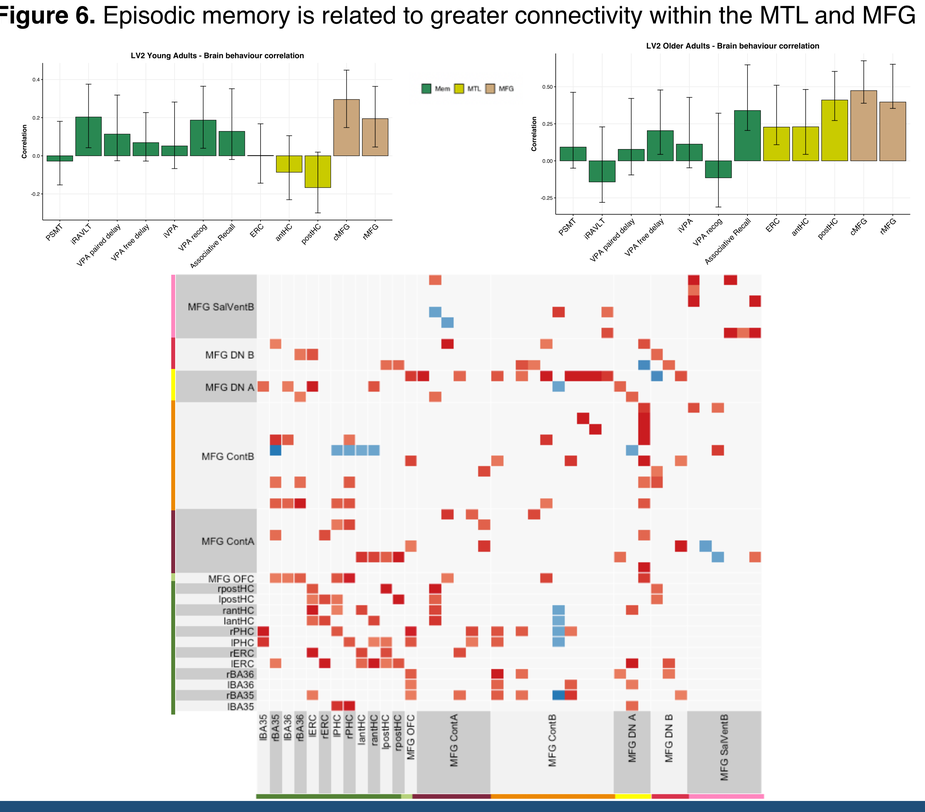


Figure 6. Episodic memory is related to greater connectivity within the MTL and MFG



Discussion

- Distinct brain structures support episodic memory in young (MTL) and older adults (PFC).
- Younger adults display greater connectivity within the MTL and within the MFG Control-A and Salience network parcels, compared to older adults, who display greater connectivity between the MTL and PFC, and within the DN and Control-A MFG parcels.
- Our analyses reveal connectivity patterns that support episodic memory in both younger and older adults.
- These observations highlight the importance of investigating structure-function interactions in healthy aging.
- Future work will examine how the brain dynamically shifts between distinct connectivity profiles across the lifespan.