

Hippocampal viscoelasticity and episodic memory performance in cognitively healthy older adults

Lucy Hiscox^{1,2}, Curtis Johnson³, Hillary Schwarb⁴, Matt McGarry⁵,
Edwin van Beek², Neil Roberts², John Starr¹

¹ Alzheimer Scotland Dementia Research Centre, University of Edinburgh, UK

² Edinburgh Imaging facility QMRI, University of Edinburgh, UK.

³ Department of Biomedical Engineering, University of Delaware, USA.

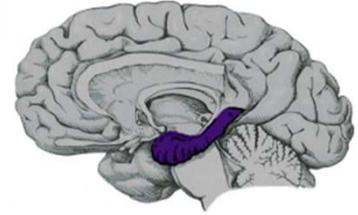
⁴ Beckman Institute, University of Illinois at Urbana-Champaign, USA.

⁵ Thayer School of Engineering, Dartmouth College, Hanover, USA.





Background

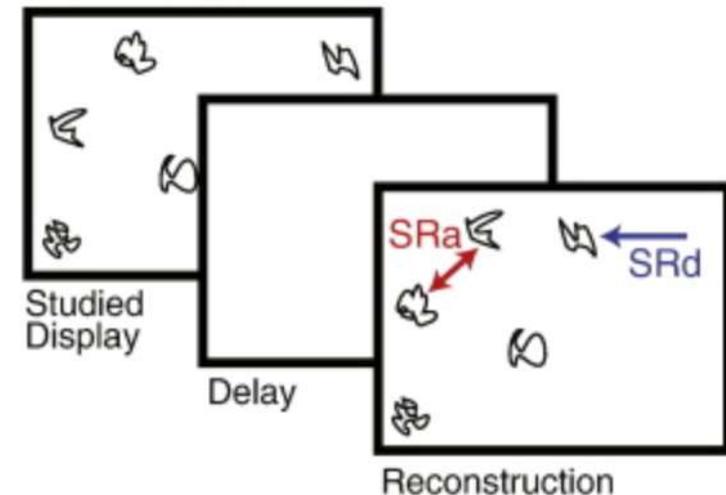
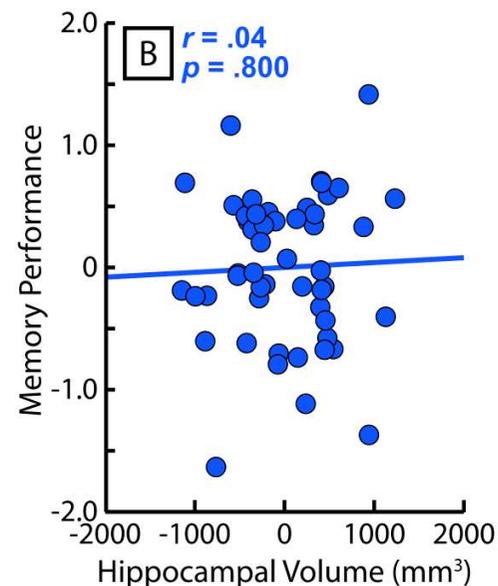
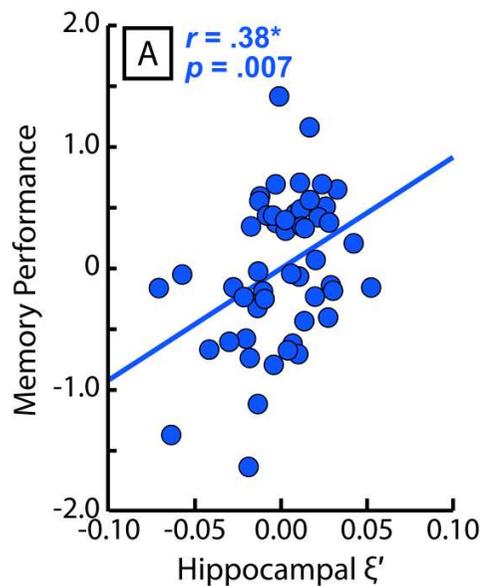


- Disruptions to episodic memory (EM) is one of the first signs and symptoms of Alzheimer's disease (AD).
- Cognitive test of EM have shown its ability to predict MCI to AD conversion.
- Issues with neuropsychological measures, however, necessitate the use of an alternative biomarker.
- Consensus that the hippocampus supports episodic memory.
- In particular, the left hippocampi has been implicated in **verbal** episodic memory, whereas the right is responsible for **visuospatial** associations.
- Well established relationship between hippocampal volume and cognitive decline in ageing.



MRE of the Hippocampus

- Hippocampal viscoelasticity correlates with relational memory performance in young adults¹
- In particular, greater viscous-to-elastic behaviour (i.e. increase in damping ratio, ξ), is associated with poorer memory performance.
- Better aerobic fitness was associated with hippocampal ξ which mediated the benefits of fitness on memory function²



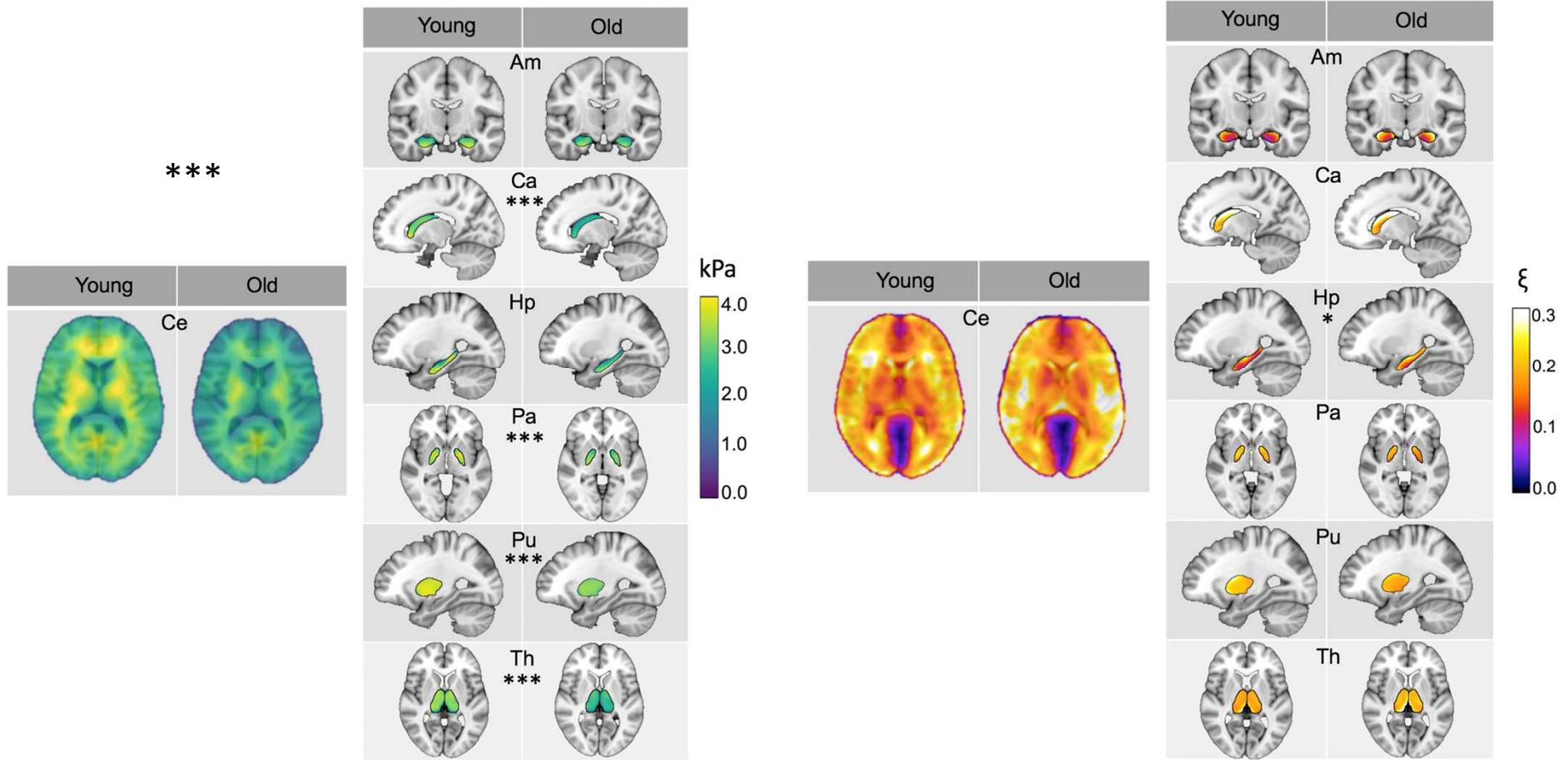
¹Schwarb et al. 2016, *NeuroImage*; ²Schwarb et al. 2017, *NeuroImage*



MRE of the ageing brain

Young = 18-30 years, n = 12

Old = 65-75 years, n = 12



No significant differences in hippocampal stiffness, $p > 0.5$

Significant difference in hippocampal damping ratio, $p = .041$

Hiscox et al., *in sub*



Study aims

- To investigate the relationship between episodic memory performance and hippocampal MRE measures in *cognitively healthy older* adults.
- To assess whether a verbal memory task (i.e. verbal-paired associates subtest) would illicit a specific association with the left hippocampi, as opposed to the right hippocampi, due its known role in verbal memory.

Methods

Subjects

- 12 older participants
- Mean age: 69.4 ± 2.5 years.
- 6 female, 6 male

Cognitive assessment

- Montreal Cognitive Assessment (MoCA) (score $> 26/30$)

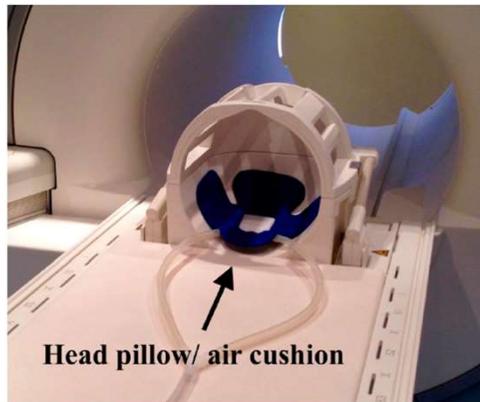
Test of episodic memory

- Verbal paired associates subtest from the Wechsler memory scale: a widely used instrument for assessing explicit episodic memory.
- Participant read a list of words, and ask to remember their associations. Paired word items can be either semantically related (apple-fruit), or not related (obey-inch).

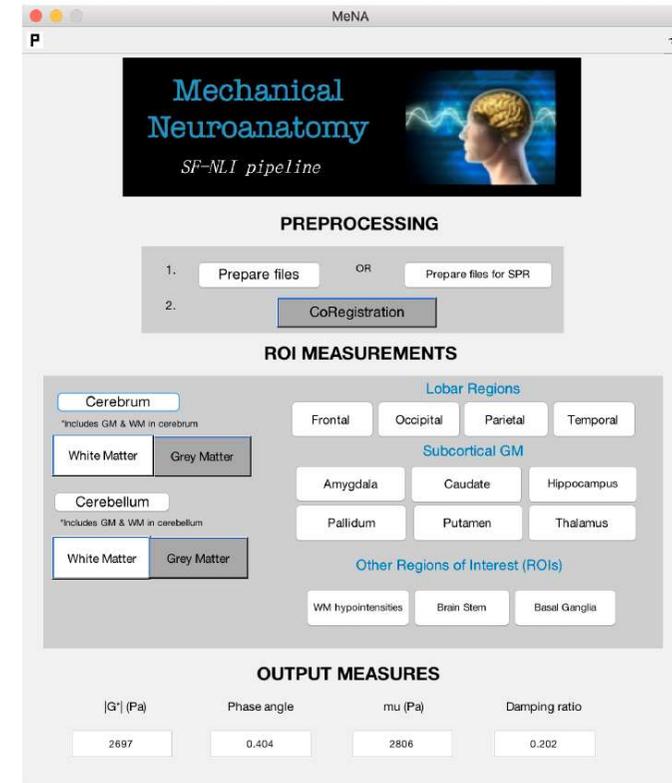


Methods - MRE

- 3T Siemens Verio MRI scanner
- Resoundant actuator and head pillow¹
- Single frequency 50Hz vibrations
- MRE multi-shot spiral 1.6mm acquisition²
- 3D subzone FEM non-linear inversion³
- Soft Prior Regularisation (SPR)⁴
- Freesurfer for ROI segmentations
- Output parameters: shear stiffness μ and damping ratio ξ



GUI



¹ resoundant.com; ² Johnson et al. 2014, Magn Res Med; ³McGarry et al. 2012, Med. Phys; ⁴ McGarry et al. 2013, Med.



Hypotheses

- Consistent with findings in young adults, we predicted that hippocampal ξ would be associated with memory performance in older adults. i.e. greater viscous-to-elastic behaviour = poorer performance.
- That memory performance would be associated with MRE measures of the left hippocampi due to its known role in verbal memory.

Statistical analyses

- Pearson partial correlation coefficients
- Age (years), sex, ROI volume and full-scale IQ were controlled for within the analyses.
- Amygdala (Am) and global cerebrum (Ce) were used as control ROIs.

Bilateral results

- Strong negative correlation between hippocampal ξ and memory performance ($r = -.779, p = .036$).
- No correlation between hippocampal volume ($r = -.191, p = .651$), or hippocampal stiffness ($r = -.181, p = .697$) with memory performance.

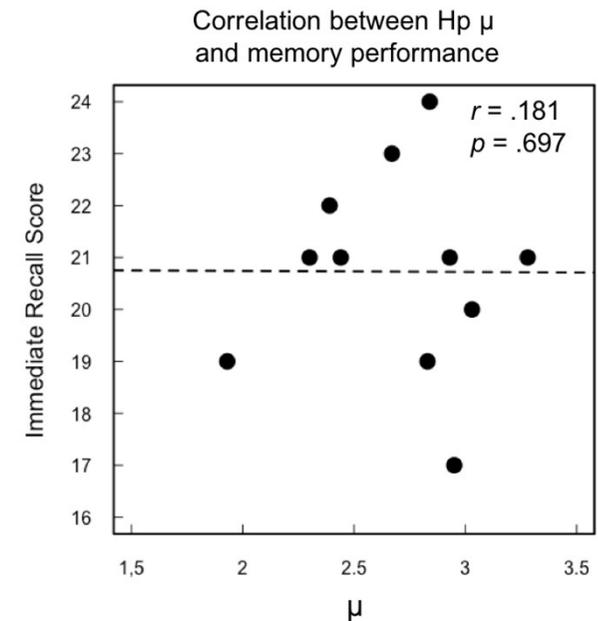
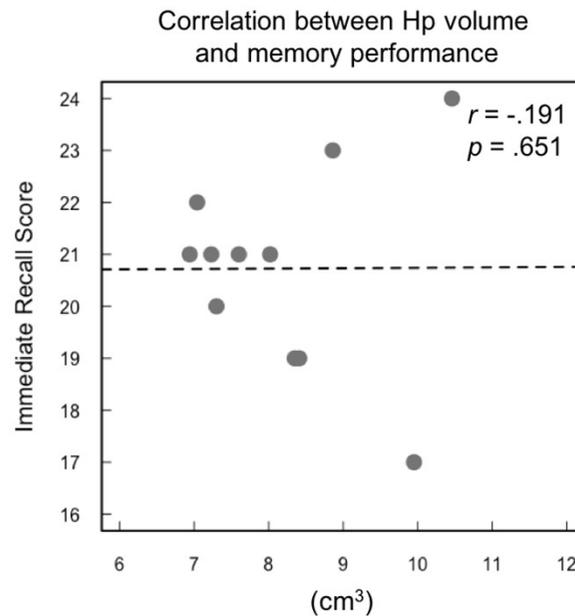
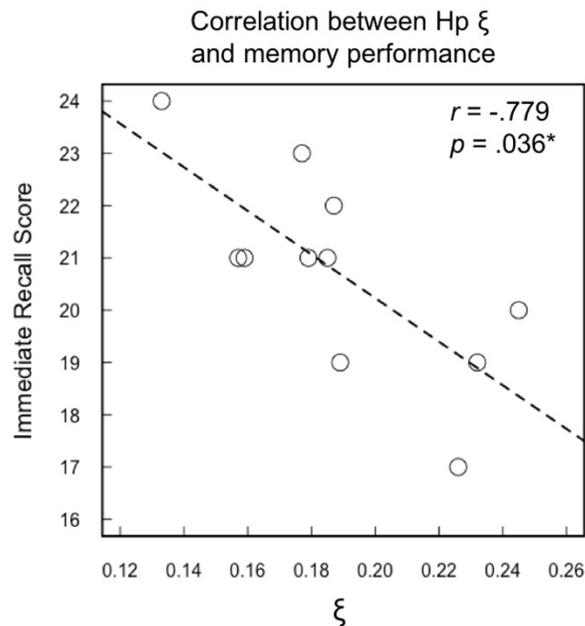




Table 1: Mean values of bilateral ROI analysis with VPA correlation coefficient, r .

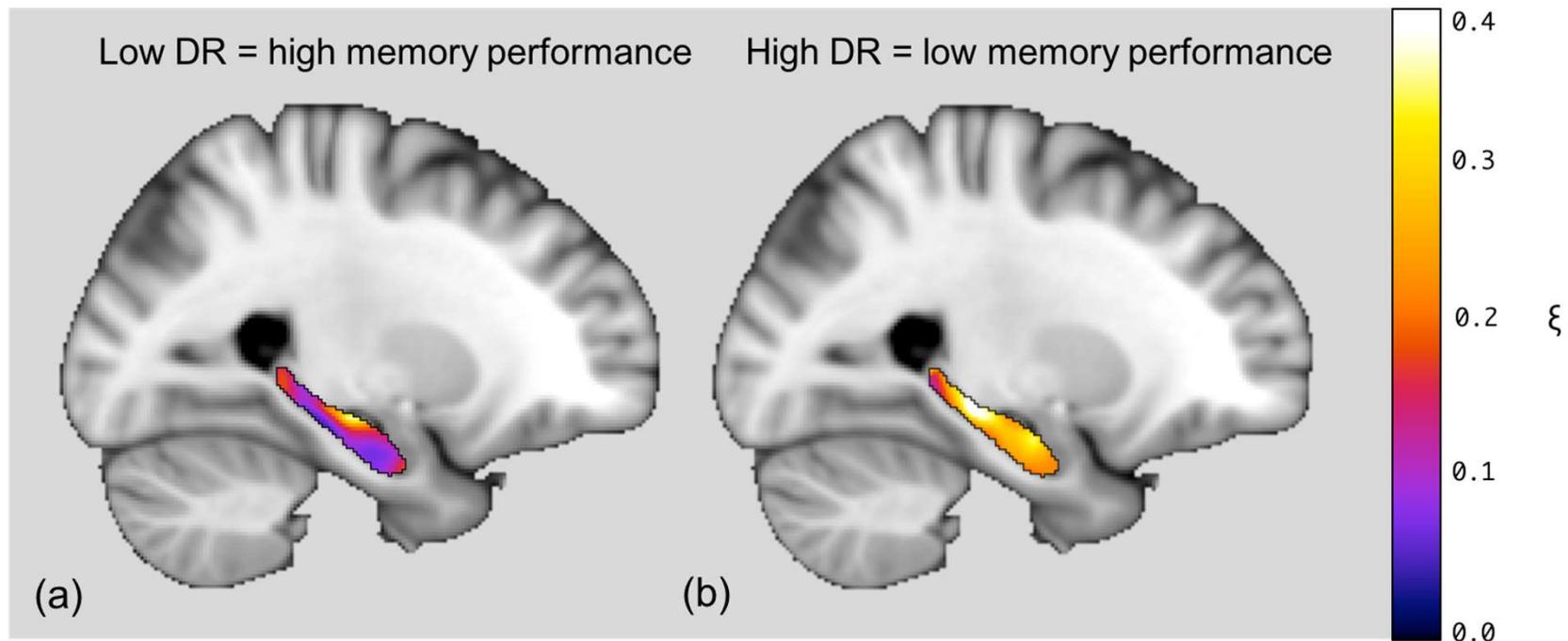
	Mean	SD	CV (%)	VPA score, r	p -value
Hippocampal measures					
μ (kPa)	2.69	0.39	13.8%	.181	.697
ξ	.188	.034	18.2%	-.779	.039*
Volume (cm ³)	8.19	1.17	14.3%	-.191	.651
Amygdala measures					
μ (kPa)	3.05	0.40	13.2%	-.077	.870
ξ	.183	.023	12.6%	-.742	.056
Volume (cm ³)	3.13	0.39	12.6%	.079	.852
Cerebral measures					
μ (kPa)	2.70	0.15	5.7%	-.035	.941
ξ	.259	.017	6.7%	.128	.784
Volume (cm ³)	1076	89.2	8.3%	.419	.302
Memory performance measure					
VPA	20.7	1.95	9.4%	-	-



Unilateral results

Table 8.2: Unilateral Hp ξ mean scores and VPA correlation coefficients, r .

	Mean	SD	CV	VPA score, r	p -value
Left Hp ξ (kPa)	.183	.050	27.4%	-.863	.012*
Right Hp ξ (kPa)	.200	.036	18.3%	-.599	.155





Conclusions

- Episodic memory is associated with hippocampal damping ratio ξ in older subjects, as measured with MRE.
- Greater relative viscous to elastic behaviour correlated with poorer memory scores - consistent with findings in young adults.
- Association was stronger in the left hippocampi – a region known for its role in verbal memory - suggesting MRE could assist with studies investigating unilateral specialization.
- **HOWEVER**, results very preliminary due to the small sample size. Our aim is to recruit a larger number of subjects to support these initial findings.



Acknowledgements

Prof John Starr
Prof Neil Roberts
Prof Edwin van Beek
Dr Curtis Johnson
Dr Matt McGarry
Mike Perrins
Helen Marshall
Annette Cooper
Aimee Littlejohn



And many thanks to all the participants who took part in the study.