

The impact of pro-inflammatory cytokines on learning and memory in late-life depression and healthy older adults.

Rebecca A. Charlton^{1,2}, Melissa Lamar², Aifeng Zhang², Xinguo Ren³, Olusola Ajilore², Ghanshyam N. Pandey^{2,3} & Anand Kumar²

¹ Department of Psychology, Goldsmiths University of London; ² Department of Psychiatry, University of Illinois at Chicago; ³ Department of Pharmacology, University of Illinois at Chicago .

Background

- Learning and memory problems are common in healthy ageing and late-life depression (LLD).
- There is growing evidence that pro-inflammatory cytokines may also affect learning and memory.
- Pro-inflammatory markers are often elevated in ageing, age-related vascular disease and depression.
- The impact of pro-inflammatory cytokines may be exacerbated in LLD versus healthy older adults (HOA).

Hypotheses

- Pro-inflammatory cytokines will be higher in LLD compared to HOA.
- Pro-inflammatory cytokines will be associated with learning and memory, particularly in LLD.

Methods

- Participants: 34 HOA, 24 LLD (aged ≥ 60 years)
- Depression rating: HDRS (LLD, range=15-27; HOA, range=0-6) and GDS.
- Cognitive Assessment: Learning, immediate free recall from CVLT; Logical Memory & Visual Reproduction. Memory, long delay free recall from the above measures.

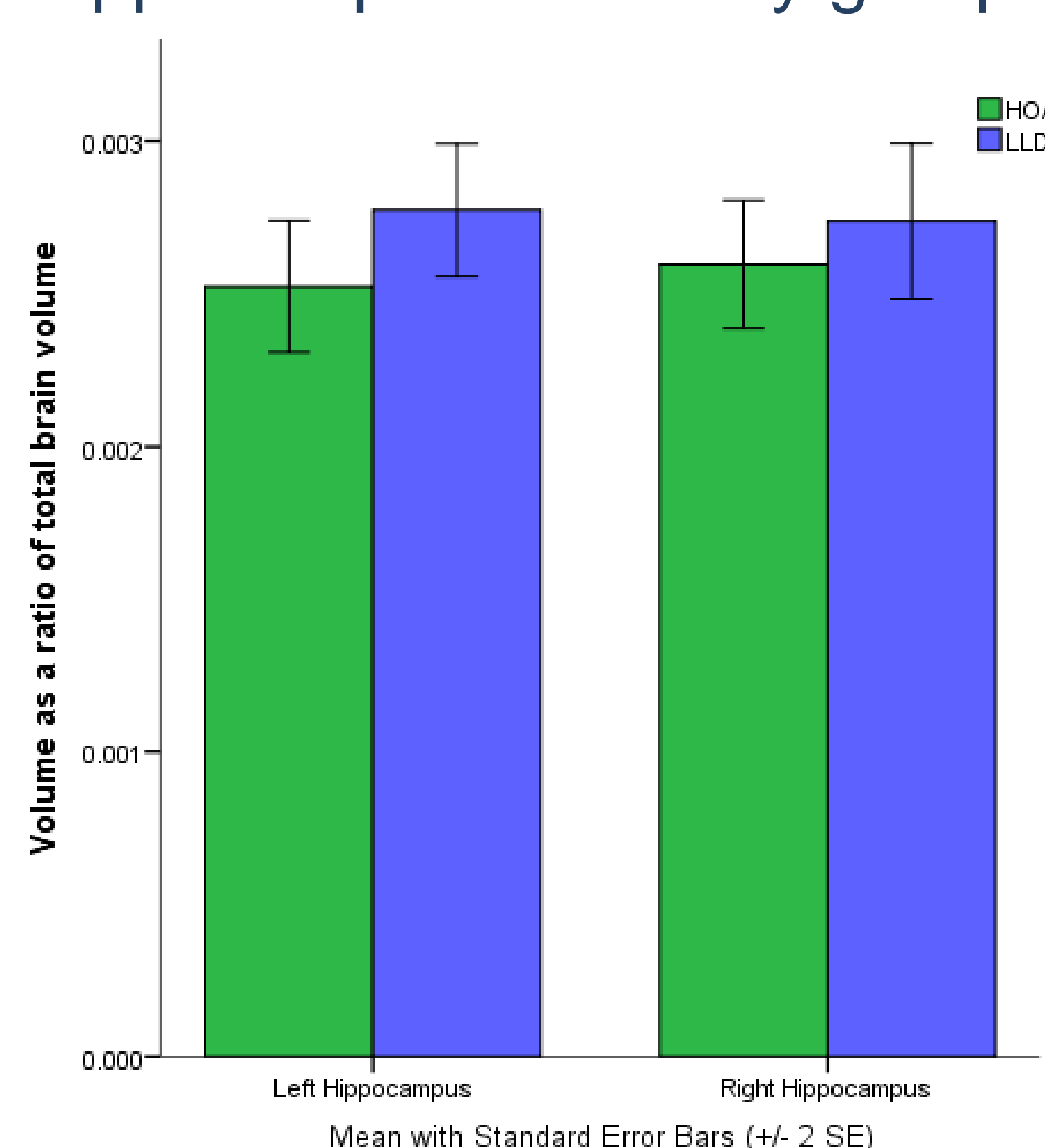
Table 1: Group demographics, mean (standard deviation)

	HOA (n=34)	LLD (n=24)	Group differences
Age	70.15 (6.07)	67.21 (9.09)	$F=2.18, p=.145$
Sex (m,f)	13,21	8,16	$\chi^2=.146, p=.786$
Highest Ed.	16.41 (3.01)	15.92 (2.75)	$F=.409, p=.525$
GDS	2.10 (2.78)	18.86 (5.80)	$F=186.50, p<.001$
Learning	-.046 (.816)	.065 (.807)	$F=.260, p=.612$
Memory	-.096 (.717)	.136 (.882)	$F=1.22, p=.274$

- Pro-inflammatory cytokines: Interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α) and Interleukin-6 (IL-6) were measured in plasma/serum, ELISA Quantakine kits.
- MRI, acquisition: Philips Achieva 3T. T1-w high resolution 3D MPRAGE; FOV=240mm;134 contiguous axial slices TR/TE= 8.4/3.9ms; flip angle=8 $^\circ$; voxel size=1.1X1.1X1.1mm).
- MRI, image analysis: Left and Right hippocampal volumes extracted with Freesurfer image analysis suite.

Results, Group differences

Figure 1: No hippocampal volume by group differences



Results, Group Differences

- Health measures: no differences in stroke risk, BMI, or HA1c (not shown)

Table 2: Pro-inflammatory Cytokines by Group

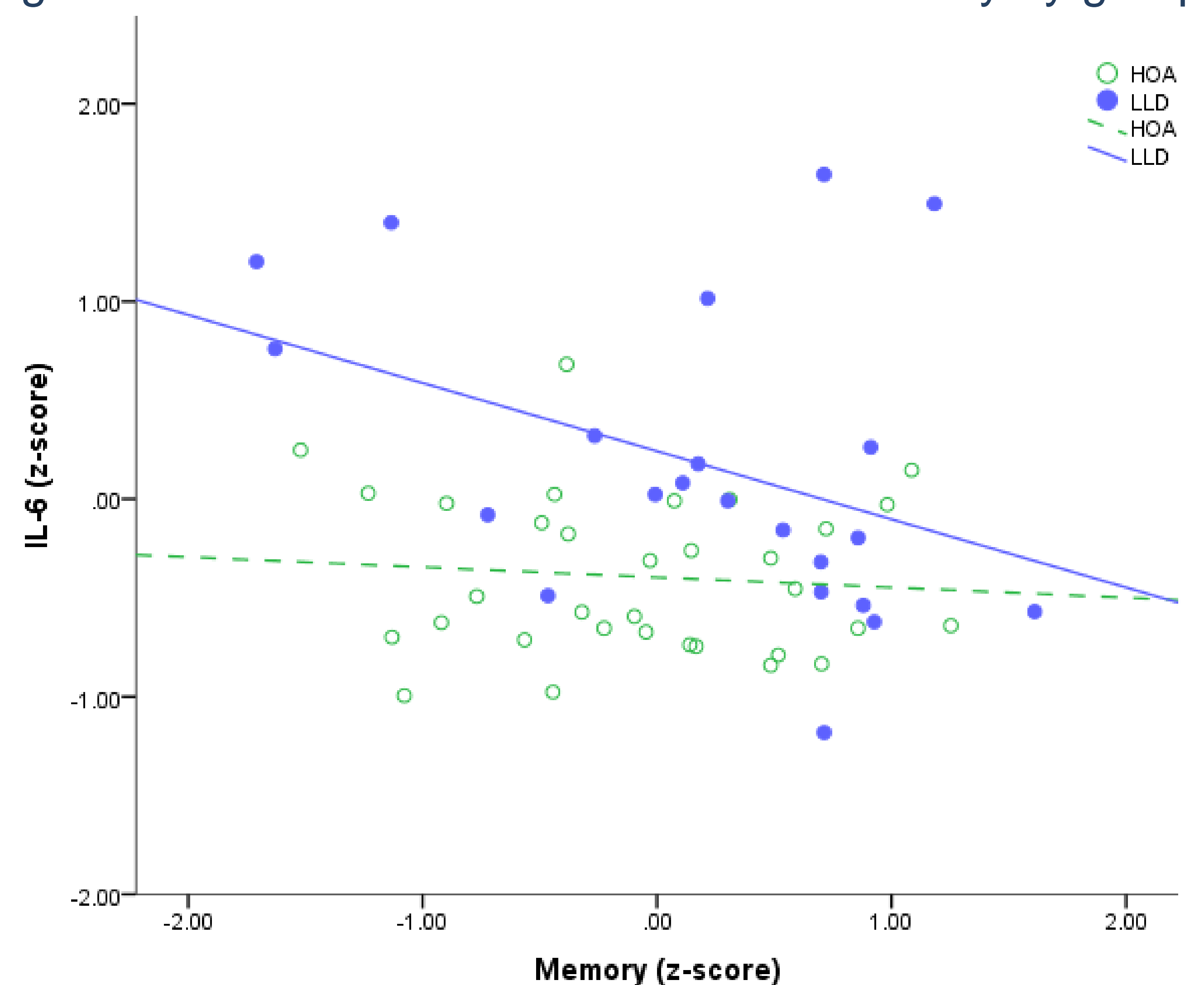
	HOA	LLD	Group differences
IL-1 β	1.52 (.699)	2.38 (1.03)	$F(1,56)=14.49, p<.001$
TNF- α	3.09 (1.40)	4.05 (2.16)	$F(1,56)=4.18, p=.046$
IL-6	1.24 (.443)	2.03 (1.22)	$F(1,56)=11.73, p=.001$

- GDS (across whole sample) correlated significantly with:
 - IL-1 β ($r=.379, p=.017$)
 - IL-6 ($r=.390, p=.014$)
 - NOT with TNF- α ($r=.121, p=.461$)

Results, Logistic Regression Analyses

- Learning (41.4%; $F=13.05, p<.001$) explained by:
 - Education level (21.2%)
 - Right hippocampal volume (20.2%)
- Memory (40.7%; $F=9.92, p<.001$) explained by:
 - Education level (21.4%),
 - Right hippocampal volume (17.1%),
 - Grp x IL-6 interaction term (6.7%)

Figure 2: Association between IL-6 and Memory by group



Conclusion

- IL-1 β , TNF- α and IL-6 were higher in LLD versus HOA.
- IL-1 β and IL-6 correlated significantly with severity of depression across the whole sample.
- High levels of IL-6 seem to impact Memory in LLD group but not HOA.
- Results suggest that the impact of high pro-inflammatory cytokines may be different in LLD versus HOA.
- Pro-inflammatory cytokines may significantly impact cognition in "at-risk population", but have a lesser impact in healthy ageing.

Acknowledgments

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