

Systemic inflammation and blood-based biomarkers of Alzheimer's Disease

Grace Austin¹, Shaun Eslick¹, Jessica J A Ferguson², Christopher Oldmeadow³, Manohar L Garg¹, Ralph Martins¹

¹. Macquarie Medical School, Macquarie University, Macquarie Park, NSW, Australia
². School of Biomedical Sciences & Pharmacy, UoN, Callaghan, NSW, Australia
³. Clinical Research Design, Information Technology and Statistical Support Unit, HMRI, New Lambton, NSW, Australia

INTRODUCTION

- Systemic inflammation is increasingly implicated in Alzheimer's disease (AD) pathogenesis.¹
- Chronic low-grade inflammation may contribute to neuroinflammation, neuronal injury and early AD pathology.²
- The relationship between inflammation markers and blood-based AD biomarkers remain less established, particularly in midlife adults.

AIM

- This study examined **associations between systemic inflammation markers and blood-based AD biomarkers** in dementia-free adults.

METHODS

- **237-person cross-sectional cohort study.**
- Stored plasma (-80 °C) samples were analysed for **hs-CRP, IL-6 and TNF-α** using enzyme-linked immunosorbent assays.
- Plasma AD biomarkers **Aβ1-40, Aβ1-42, GFAP, and NFL** and **pTau181** were measured using ultra-sensitive Single Molecule Array (SIMOA) assay platform.
- **Multivariable regression analysis** were used to adjust for confounders age and sex.

SIGNIFICANCE

- **Systemic inflammation may represent a modifiable target for dementia prevention** and supports the utility of blood biomarkers for early detection
- Longitudinal RCTs examining associations between inflammation and AD biomarkers are warranted.

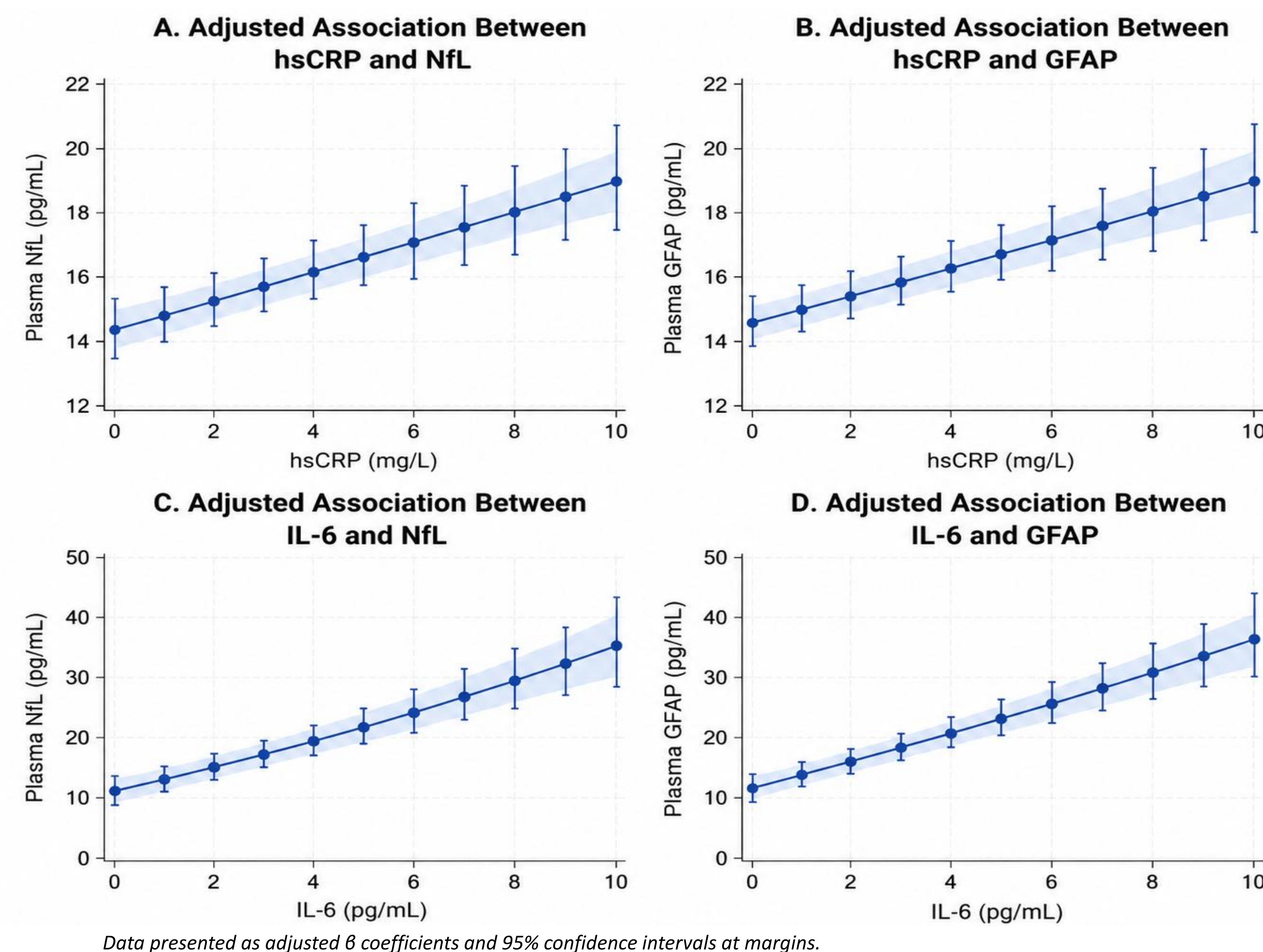
RESULTS

Participant Characteristics:

- Mean age 54±10.2yrs, 78% female, mean BMI 24.4kg/m²

Adjusted association between systemic inflammation and Alzheimer's Disease blood biomarkers

- ✓ **Hs-CRP** was associated with significantly increased **NfL** (0.44, 95% CI 0.14, 0.74, P < 0.004) and **GFAP** (2.77, 95% CI, 1.10, 4.43, P < 0.001)
- ✓ **IL-6** was associated with significantly increased NfL (and 2.61, 95% CI 1.72 ,3.49, P < 0.0001,) and **GFAP** (and 9.41, 95% CI, 3.64, 15.19, P < 0.002, respectively).
- Significant confounders adjusted for were age and sex
- In a crude analysis, TNF-α was significantly associated with NfL only.
- There was no significant association between any systemic inflammation markers and Aβ1-42/Aβ1-40 and p-tau181.



CONCLUSION

- Findings suggest a **pro-inflammatory profile in midlife is associated with blood-based biomarkers of neurodegeneration and astrocyte activation**
- There were no association between pro-inflammatory markers and AD biomarkers Aβ1-42/Aβ1-40 and p-tau181.

SUMMARY

Higher hs-CRP and IL-6 were associated with increased NfL and GFAP, suggesting systemic inflammation may contribute to early neurodegenerative processes in midlife adults.

CONTACT

Grace Austin

PhD, B&D (Hons I), APD
 Post Doctoral Research Fellow,
Email: grace.austin@mq.edu.au
 Macquarie Medical School, Macquarie University, Sydney, Australia

REFERENCES

1. Xie et al. *Front. Immunol.* 2022.
2. Walker et al. *ACS Chem. Neurosci.* 2019.