Physical activity and blood-based biomarkers of neurodegeneration in community dwelling Australians from ISLAND

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1. Background

- Three *Lancet* Commissions have found an increasing proportion of dementia cases could be prevented through lifestyle modification[1,2,3]
- Physical activity, a key modifiable risk factor, has been associated with biomarkers of Alzheimer's disease (AD) in the central nervous system; but less is known about blood-based biomarkers[4]

Research Question: How does physical activity associate with blood-based biomarkers of AD?

2. Methods

- Participants recruited from the ISLAND Study Linking Ageing and Neurodegenerative Disease (ISLAND)[5]; a prospective public health initiative in Tasmania, Australia's southernmost island state
- Participants completed a battery of online surveys, including background health, medications, demographics[6]
- Physical activity was assessed based on daily metabolic equivalent (MET) of task, eg: light (walking for transport/leisure), moderate (bicycling/dancing) and vigorous (running/swimming) intensity
- Generalized linear regression models were used to investigate the association of the physical activity matrix score (Total MET) and blood-based biomarkers of AD: serum neurofilament light (NfL), serum glial fibrillary acidic protein (GFAP) and plasma phosphorylated tau 181 (p-tau 181)
- Sub-group analysis looked at the moderating effect of APOE-ε4, whilst post-hoc testing investigated the intensity of physical activity (light, moderate, vigorous)
- All analyses were adjusted for age, gender, APOE-ε4 presence and body mass index (BMI) as covariates

3. Results I

- 739 participants included (72% female, 27% APOE-ε4)
- When compared to males, female participants displayed significantly younger ages, lower levels of physical activity (Total MET) and lower BMI. They also had higher levels of serum GFAP and lower levels of plasma p-tau 181 (Table 1)

3. Results II

- Greater physical activity (in MET) was significantly associated with serum GFAP (in pg/mL). This remained after covariate adjustment
- Sub-group analysis revealed this association was moderated by presence of APOE-ε4: APOE-ε4 negatives had a significant association between MET and serum GFAP, but APOE-ε4 positives did not (Figure 1)
- Post-hoc intensity testing revealed that participants self-reported levels of vigorous activity had the strongest association with serum GFAP, whilst light and moderate activity were not significant
- There was no relationship between physical activity (in MET) and p-tau 181 or NfL. We also did not observe an association with p-tau 181 or NfL when physical activity was stratified by intensity

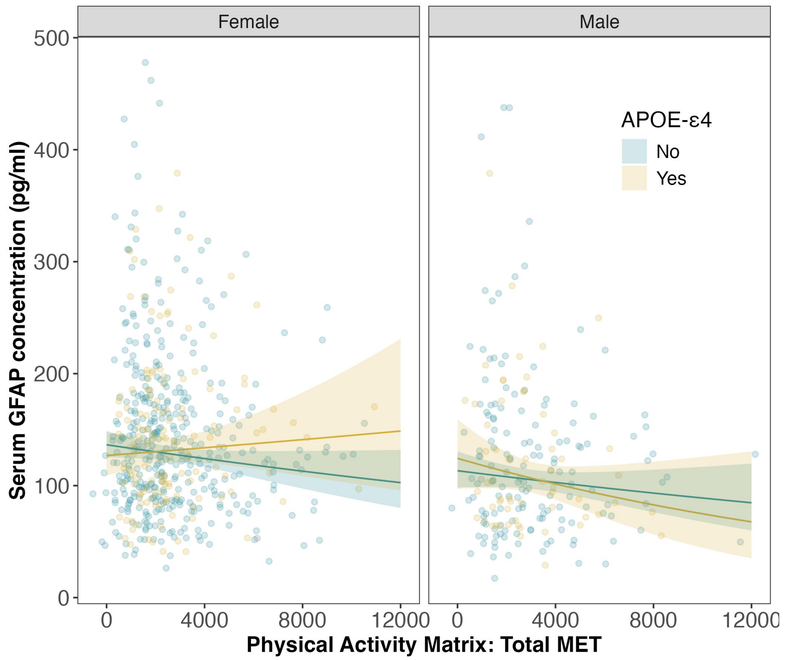

Figure 1: ISLAND participants physical activity matrix (Total metabolic equivalent [MET]) against serum glial fibrillary acidic protein (GFAP) concentration stratified by APOE-ε4 presence and gender

4. Results II

Variable	N	Female	Male	P
		n = 529	n = 210	
Age (in years)	**739**	63.96 (6.59)	65.50 (7.41)	**0.007**
Physical Activity Matrix: Total MET	**739**	2,685.67 (1,897.07)	3,052.25 (2,085.86)	**0.022**
What is the highest level of education you have obtained?	**737**			0.3
Bachelor's Degree		137 (26%)	51 (24%)	
Certificate or Apprenticeship		49 (9.3%)	26 (12%)	
Diploma / Associate Degree		97 (18%)	28 (13%)	
High School		44 (8.3%)	21 (10%)	
Higher University degree		189 (36%)	81 (39%)	
Other		12 (2.3%)	2 (1.0%)	
Body Mass Index (kg/m^2)	**738**	25.99 (4.99)	26.59 (4.04)	**0.006**
APOE4 Present	**735**	136 (26%)	59 (28%)	0.5
Serum GFAP (pg/mL)	**735**	144.74 (72.55)	122.44 (71.70)	**<0.001**
Serum NfL (pg/mL)	**735**	14.82 (8.17)	14.78 (7.14)	0.8
Plasma p-tau181 (pg/mL)	**724**	1.35 (0.60)	1.56 (0.72)	**<0.001**

Table 1: Demographic statistics for included ISLAND participants (n = 739)

5. Conclusions

Greater physical activity was associated with lower levels of serum GFAP in adults over 50 years of age

- APOE-ε4 and physical activity intensity impacted this association
- This study highlights the importance of targeted longitudinal interventions for reducing the risk of AD, and potentially the blood-based biomarkers that precede disease course.

References

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Acknowledgements

- We acknowledge and deeply thank the contributions made by our study participants, the Wicking Centre data managers (Alex Kitsos and Timothy Saunder), Wicking laboratory team (Graeme McCormack), ISLAND Portal web development team (Joshua Eastgate, Chris Parker) the ISLAND Project Team (Florence Sward and Adam Kane) and ISLAND's Community Advisory Group
- This was a sub-study of the ISLAND Project, which is supported by the Medical Research Futures Fund Keeping Tasmanians out of Hospital, the University of Tasmania, St Lukes Health, and the Masonic Centenary Medical Research Foundation.
- Attendance at this conference was supported by an AAIC 2025 Conference Fellowship