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

Eddy Roccati[1], Jessica Collins[1], Michele Callisaya[1], Jane Alty[1,2], Anna King[1], James Brady[1], James Vickers[1]

1: Wicking Dementia Research and Education Centre, University of Tasmania – Health, Hobart, Tasmania, Australia 2: Royal Hobart Hospital, Hobart, Tasmania, Australia
eddy.roccati@utas.edu.au - @eddy_roccati - utas.edu.au/wicking

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 mid-life modifiable risk factor for dementia, has been associated with biomarkers of Alzheimer's disease (AD) in the central nervous system, however less is known about blood-based biomarkers[4]
- Here we aimed to investigate whether physical activity was associated with the hallmark blood-based biomarkers of AD (serum neurofilament light [NfL], serum glial fibrillary acidic protein [GFAP], plasma phosphorylated tau 181 [p-tau 181]), and whether presence of apolipoprotein E epsilon 4 (APOE-ε4) moderated this relationship

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 deployed to investigate the association of the physical activity matrix score (Total MET) and blood-based biomarkers of AD (GFAP, NfL and p-tau 181). Sub-group analysis looked at the moderating effect of APOE-ε4, whilst post-hoc testing investigated the intensity (light, moderate, vigorous)
- All analyses were adjusted for age, gender, APOE-ε4 presence and body mass index (BMI)

3. Results I

- Included were 739 participants (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)**
- 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
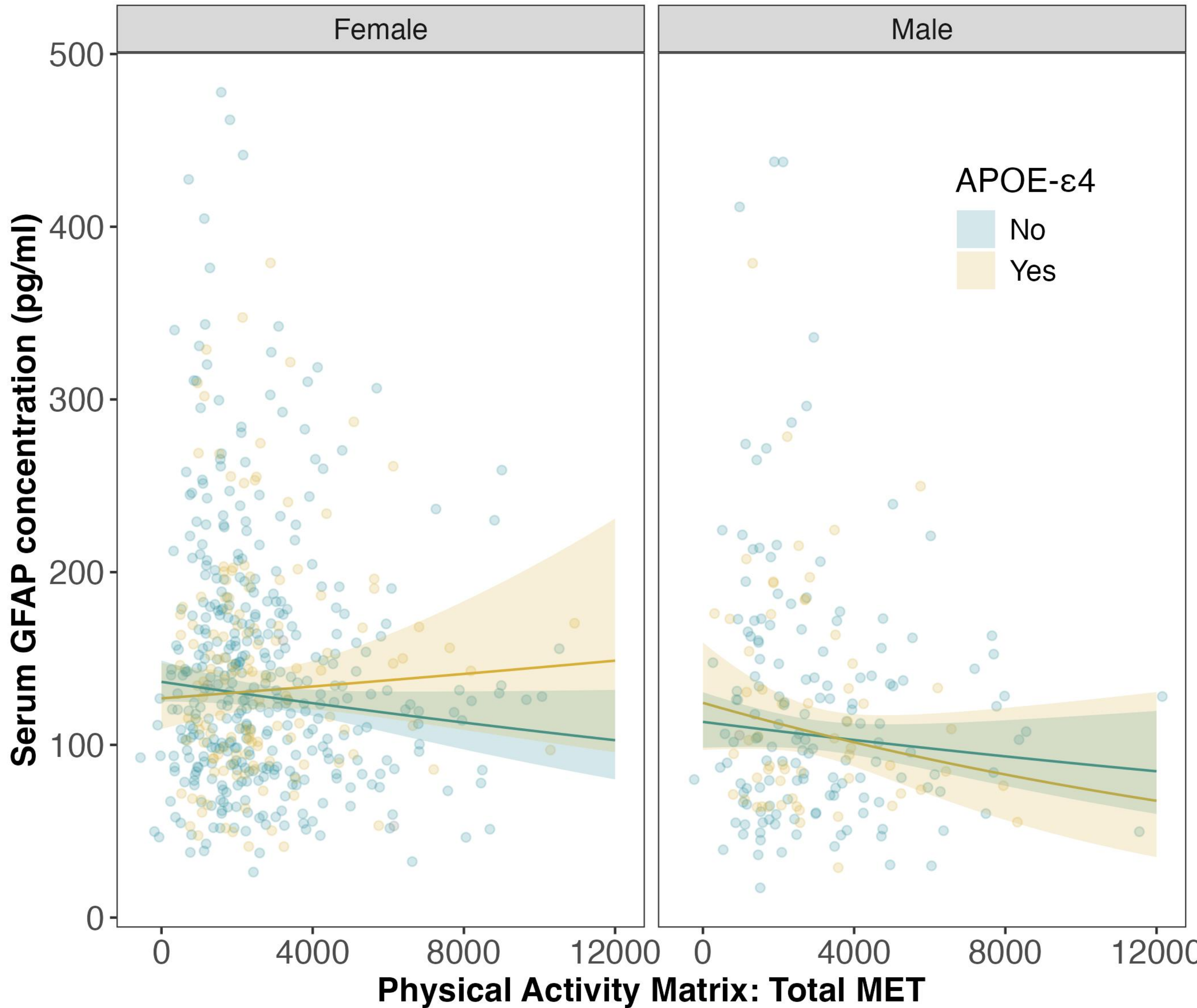

Figure 1: ISLAND participants physical activity matrix (Total metabolic equivalent [MET]) against serum glial fibrillary acidic protein (GFAP) concentration stratified by APOE-ε4 presence and gender.

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 community-dwelling Australian 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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