

1. Background

- We know up to 40% of dementia cases could be prevented through addressing modifiable risk factors<sup>1</sup>
- We also know Alzheimer’s disease (AD) is preceded by up to decades of silent pathological change<sup>2</sup>
- This window of early biological change is a window of opportunity for early detection and intervention
- Blood-based biomarkers offer cost-effective, scalable and minimally invasive ways to measure the impact of an intervention
- Plasma phosphorylated (p-tau) 181 is emerging as a front runner blood-based biomarker for AD
- AD biomarkers are known to be influenced, sometimes differentially, by covariates such as age, sex, ethnicity, apolipoprotein E epsilon 4 (APOE-ε4), renal disease, cardiovascular disease, body mass index (BMI) and hypertension<sup>3,4</sup>
- Several of these covariates are known modifiable risk factors for dementia<sup>1</sup> so in order to provide confidence in the interpretation of p-tau 181 in detecting *pre-clinical* AD, we need to understand how both modifiable and non-modifiable risk factors are associated with plasma p-tau 181 in the general population

2. Methods

- Participants recruited from the ISLAND Study Linking Ageing and Neurodegenerative Disease (ISLAND)<sup>5</sup>
- ISLAND is a prospective public health initiative in Tasmania, Australia’s southernmost island state<sup>5</sup>
- ISLAND participants were invited to complete a set of surveys online: a questionnaire on dementia risk factor adherence, demographic surveys<sup>5</sup>
- Cognitive tests administered online via the Cambridge Neuropsychological Test Automated Battery (CANTAB); Paired Associates Learning (PAL) and Spatial Working Memory (SWM)
- At four clinics across the state, participants also provided blood samples for measurement of plasma phosphorylated tau 181 (p-tau 181) and genotyping for APOE

3. Results I

- 738 ISLAND participants took part in the study. Almost half of ISLAND participants (49.2%, n = 348) reported a family history of dementia and 26.4% (n = 194) had at least one APOE-ε4 allele
- Participants with a family history of dementia were significantly more likely to possess an ε4 allele. Non-modifiable risk factors were not associated with plasma p-tau 181 after adjustment for covariates
- We found impaired learning (CANTAB PAL) was associated with higher plasma concentrations of phosphorylated p-tau 181
- Increasing age, being female, having less education and possessing the APOE-ε4 allele were significantly associated with worse strategy scores in CANTAB SWM

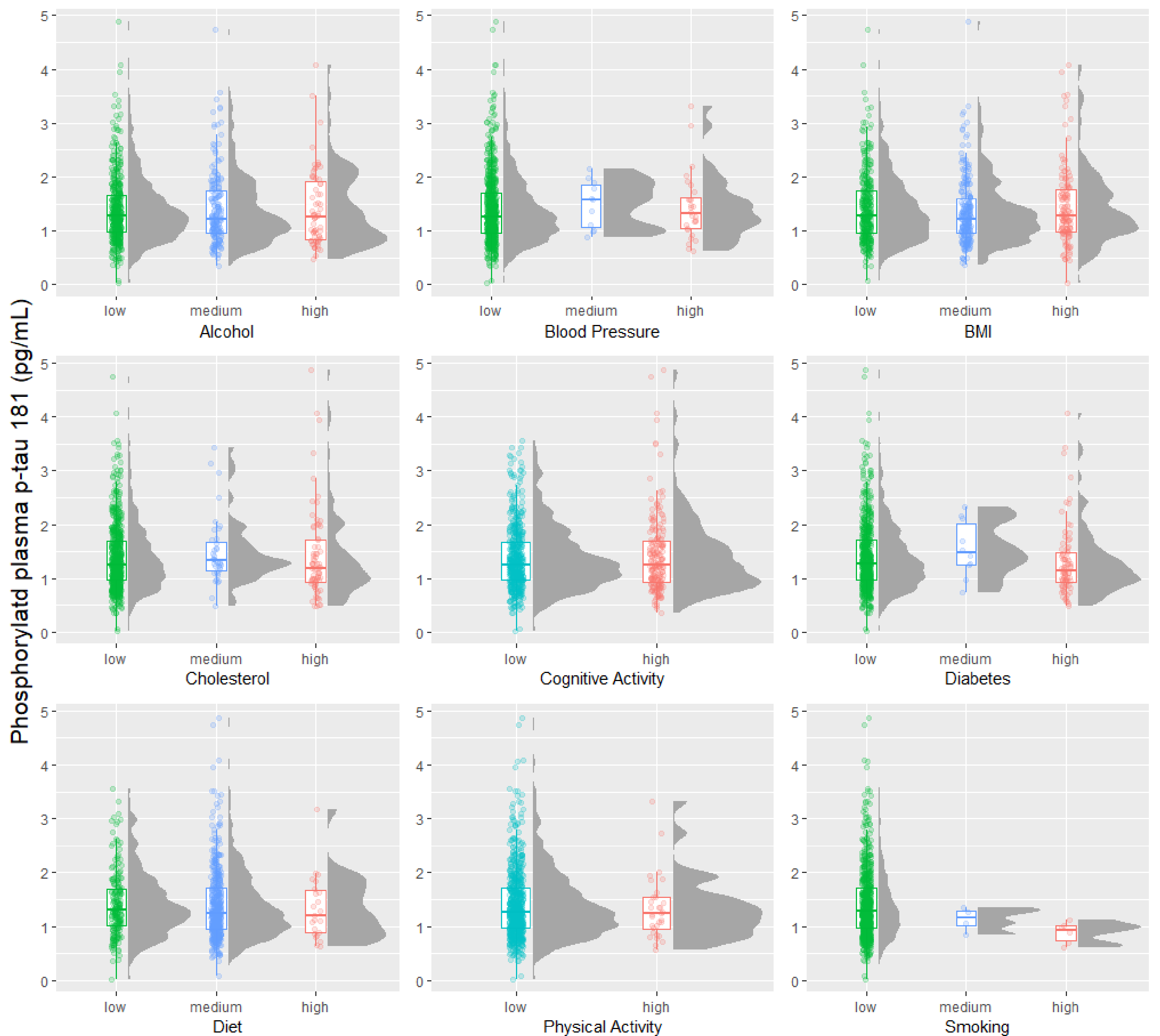


Figure 1: Modifiable risk factors and plasma concentrations of p-tau 181 (pg/mL)

4. Results II

	Total	Female	Male	p-value
N (%)	738	530 (71.8)	208 (28.2)	
Age at baseline (mean [SD])	65.41 (6.89)	65.02 (6.65)	66.40 (7.40)	0.015*
Total school years (mean [SD])	17.36 (3.13)	17.27 (3.07)	17.59 (3.26)	0.319
Employed (%)	277 (38.0)	212 (40.5)	65 (31.6)	0.030*
Family history of dementia (%)	358 (49.2)	267 (51.0)	91 (44.6)	0.145
APOE-ε4 genotype				0.297
e2e2	3 (0.4)	3 (0.6)	0 (0.0)	
e2e3	88 (12.0)	59 (11.2)	29 (14.0)	
e2e4	15 (2.0)	10 (1.9)	5 (2.4)	
e3e3	418 (56.9)	312 (59.1)	106 (51.2)	
e3e4	159 (21.6)	112 (21.2)	47 (22.7)	
e4e4	20 (2.7)	14 (2.7)	6 (2.9)	
CANTAB PAL (mean [SD])	15.87 (13.27)	14.88 (12.44)	18.41 (14.91)	0.001**
CANTAB SWM (mean [SD])	14.45 (4.94)	14.73 (4.73)	13.74 (5.36)	0.015*
Plasma p-tau pg/mL (mean [SD])	1.40 (0.64)	1.34 (0.60)	1.55 (0.72)	0.001**

Table 1: Demographic statistics for included ISLAND participants (n = 738)

5. Conclusions

- In a cognitively healthy cohort recruited from the general population in Tasmania, Australia, we found modifiable risk factors were not associated with plasma levels of p-tau 181, a key biomarker in AD
- Further, given the sex and genetic differences in plasma p-tau 181, we may expect to see sex-specific impacts of modifiable risk on blood-based biomarkers for dementia over time.
- Longitudinal biomarker collection in ISLAND is underway, we will be investigating how positive behaviour change may result in a change in biomarkers for AD, such as plasma p-tau 181

References

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