

Openness, plasma biomarkers, and time to dementia: independent effects and interactions

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Background

- Several personality traits are associated with dementia risk, potentially via behaviours and lifestyle patterns that confer cognitive resilience or increase vulnerability to neuropathology.
- Current evidence is inconsistent and largely confined to conscientiousness and neuroticism in postmortem studies.
- This study extends the research to plasma biomarkers, using trait × plasma biomarker interactions to prospectively examine cognitive resilience and vulnerability to neurodegeneration and Alzheimer's pathology.

Methods

Sample: 712 Sydney MAS participants without dementia at baseline (48% male, aged 71–91).

Personality: Neuroticism, openness and conscientiousness scales from the NEO-FFI; standardised to z-scores.

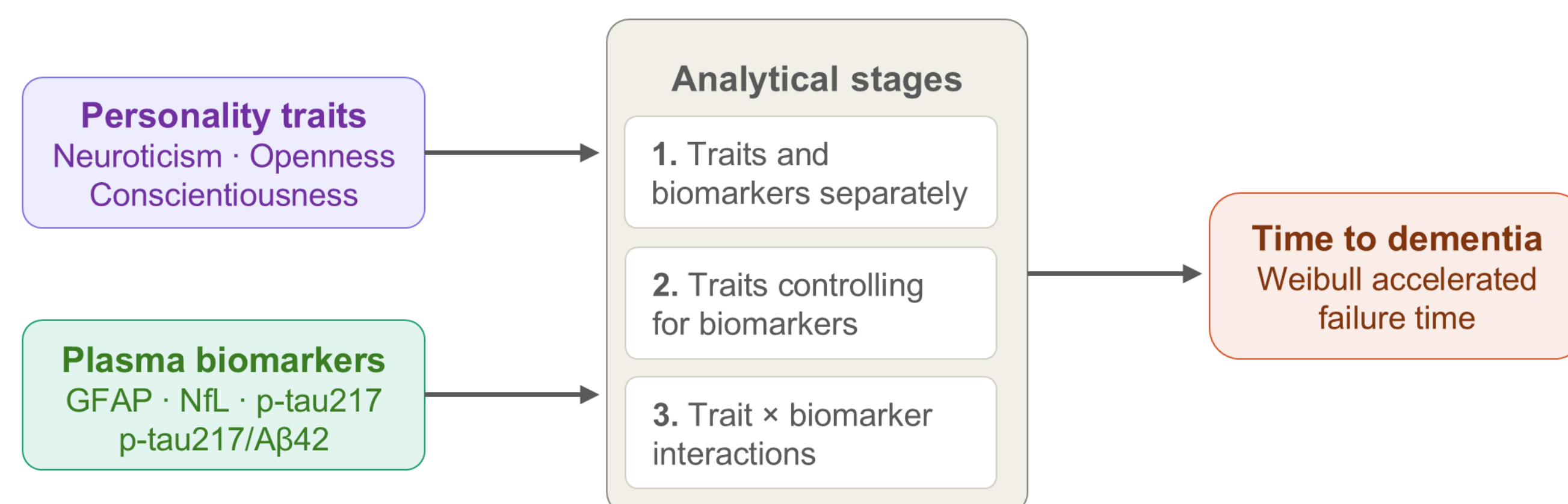
Plasma biomarkers: Measured from baseline blood samples (University of Gothenburg); all log-transformed and z-scored.

- Aβ42, NfL, GFAP (Simoa 4-Plex E assay, Quanterix)
- p-tau217 (ALZpath)
- p-tau217/Aβ42 ratio calculated

Dementia: Neuropsychological battery every two years (waves 2–7); consensus diagnosis using DSM-IV criteria (DSM-5 also applied in waves 5–7).

Analyses: Weibull accelerated failure time models (3 stages; Fig. 1); time ratios (TR >1 = longer, TR <1 = shorter time to dementia).

Fig. 1.



- Stages 2 and 3: biomarker block (GFAP, NfL, p-tau217) and p-tau217/Aβ42 separately.
- Moderation by cognitive status (MMSE ≥28 vs 24–27) tested via interaction terms.
- Models adjusted for age, sex, education, and assay batch (Model 1) and additionally for language background, APOE ε4 carriage, depression, MMSE, BMI, smoking, hypertension, diabetes, eGFR and physical activity (Model 2).

Results

- 222 incident dementia cases over 7.4 (± 3.5) years of follow-up (42.2 per 1000 person-years).
- Higher biomarker levels were associated with shorter time to dementia (Fig. 2A, Model 2).
- Openness was the only trait significantly associated with time to dementia (Fig. 2A, Model 2).
- This protective effect was maintained when controlling for biomarkers (Fig. 2B) but present only in the higher cognitive status subgroup (MMSE ≥28; Fig. 2C, Model 2).
- Openness × p-tau217/Aβ42 interaction shows the protective effect at low but not at high p-tau217/Aβ42 levels (Fig. 3, Model 2).

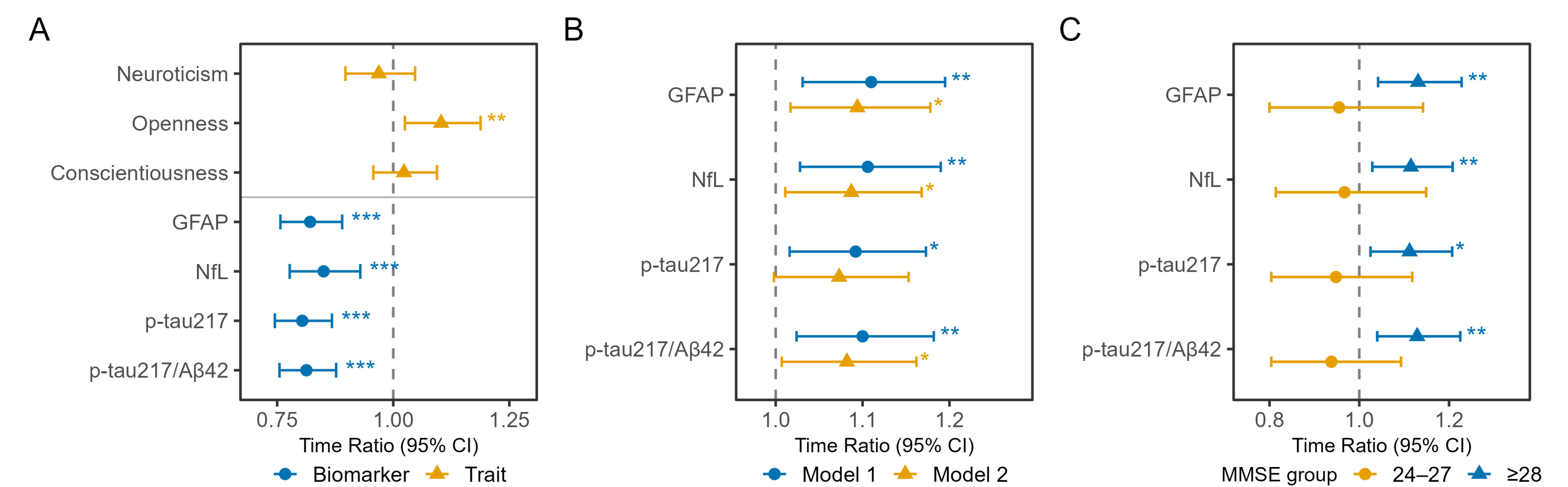


Fig. 2. Time to dementia. **A:** Traits and biomarkers; **B and C:** Openness when controlling for biomarkers.

Conclusions

- Higher openness predicted a longer time to dementia.
- Consistent with openness being associated with greater levels of brain and cognitive reserve.
- In a novel application of plasma biomarkers, we also found that higher openness appeared to confer cognitive resilience to Alzheimer's pathology, but this protective effect diminished as pathology advanced (Fig. 3).

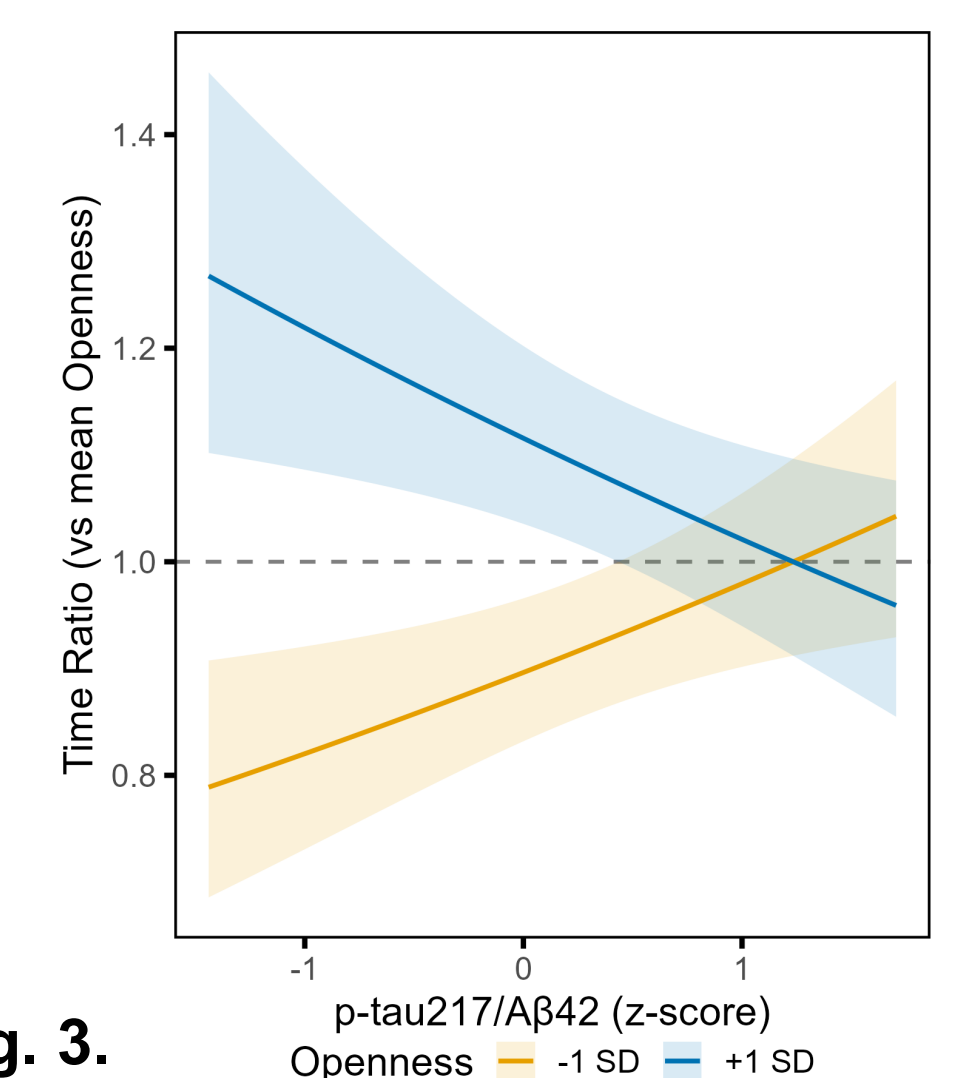


Fig. 3.

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