

# The association between diabetes and severity of mild behavioural impairment symptoms was not mediated or moderated by AD-related biomarkers

The association between diabetes mellitus and mild behavioural impairment in older adults

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## Background & Method

### What we know:

- Neuropsychiatric symptoms (NPS), such as those that are persistent and later-life emergent (mild behavioural impairment [MBI]), can predict the development and progression of dementia.<sup>1</sup>
- Diabetes mellitus (DM) has been linked to MBI.<sup>2</sup>
- DM is also linked to AD biomarkers, including alterations in hippocampal volume, amyloid, and tau.<sup>3-5</sup>
- Less is known of the mechanisms linking DM and MBI

Sample: 508 participants from COMPASS-ND



| n                        | 508         |
|--------------------------|-------------|
| Age (years)              | 70.5±7.4    |
| Sex (female)             | 254 (50.0%) |
| Education (years)        | 15.2±2.7    |
| DM+ status               | 59 (11.6%)  |
| Cognitive Status         |             |
| Unimpaired               | 237 (46.7%) |
| MCI                      | 98 (19.3%)  |
| Dementia                 | 173 (34.0%) |
| APOE ε4 Status (carrier) | 177 (34.5%) |
| MBI-C Severity           | 8.2±11.2    |

**Table 1. Demographic information for the sample.** Numeric variables are shown as mean ± standard deviation . Categorical variables are shown as n (%).

### Moderator & Mediator variables:

- Amyloid-beta 42/40
- P-tau181
- GFAP
- NfL
- Hippocampal volume

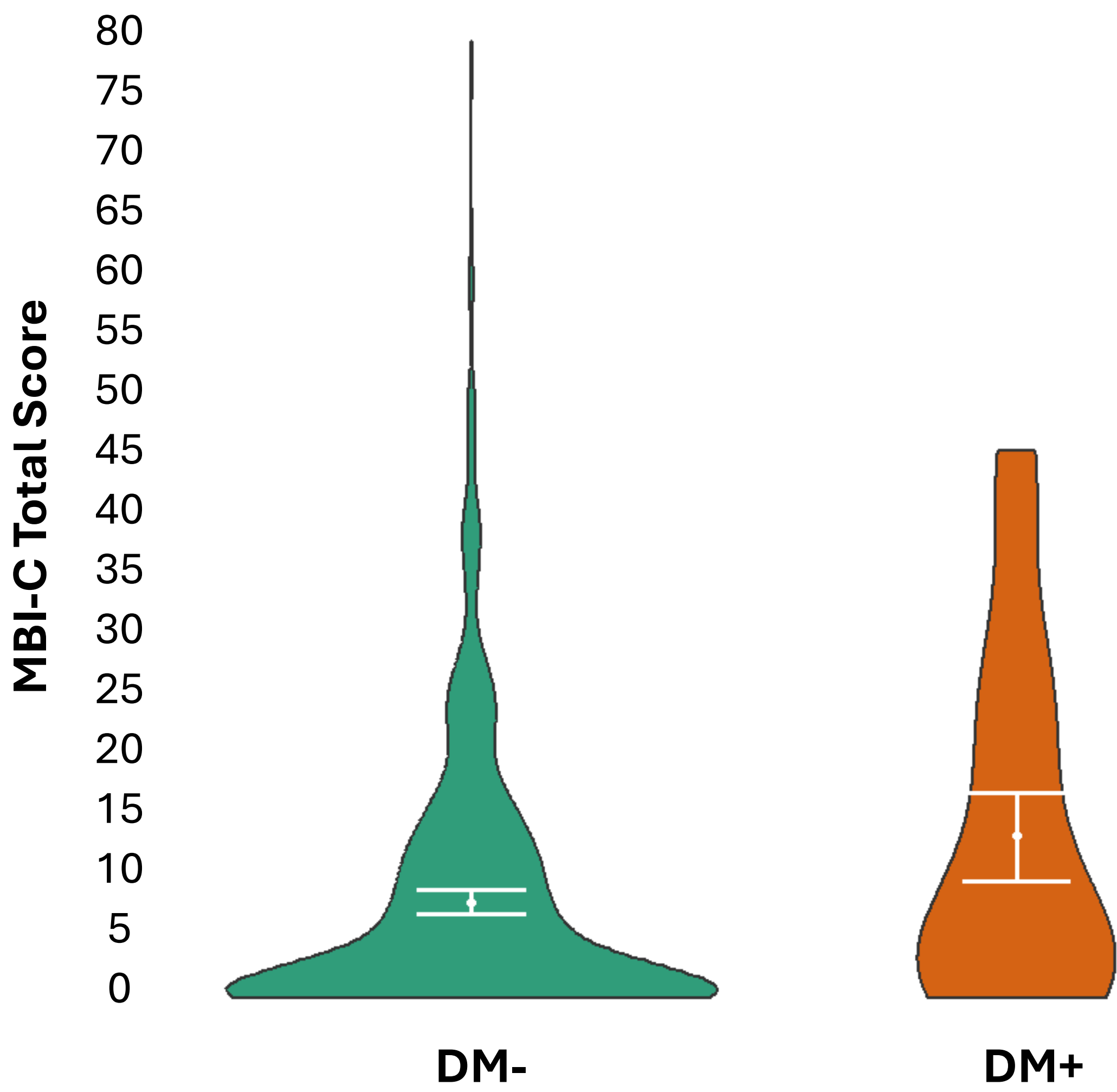
GFAP, glial fibrillary acidic protein; NfL, neurofilament light

### Modelling:

Zero-inflated negative binomial regression

\*Adjusted for age, sex, education, APOE ε4 allele carrier status, and cognitive status.

## Result



**Exp(b)=1.48, 95%CI[1.02, 2.15], p=0.04\***  
DM was associated with 1.48x greater MBI symptom severity

### Moderation: Non-significant biomarker interactions

| Biomarker          | b     | 95% CI          | p-value |
|--------------------|-------|-----------------|---------|
| Amyloid-beta 42/40 | -1.06 | [-20.55, 18.43] | .92     |
| P-tau181           | -0.12 | [-0.34, 0.10]   | .30     |
| GFAP               | 0.00  | [0.00, 0.01]    | .58     |
| NfL                | -0.01 | [-0.03, 0.01]   | .38     |

**Table 2.** Moderation of the association between diabetes mellitus and MBI-C severity by AD-related plasma biomarkers. Unstandardized coefficient (b) represents the DM\*biomarker interaction term.

### Mediation: Non-significant indirect effect

| Biomarker          | b    | 95% CI        | p-value |
|--------------------|------|---------------|---------|
| Hippocampal volume | 0.04 | [-0.31, 0.38] | .78     |

**Table 3.** Mediation of the association between diabetes mellitus and MBI-C severity by hippocampal volume. Unstandardized coefficient (b) represents the indirect (mediated) effect.

## Conclusion

- DM was associated with greater MBI symptom severity, independent of cognition
- This association was not explained by, or dependent on AD-related biomarkers in this cohort
- Mechanisms linking DM and MBI may occur earlier in the disease course
- Future studies should investigate potential vascular and upstream inflammatory mechanisms underlying these associations.

## References & Contact



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