

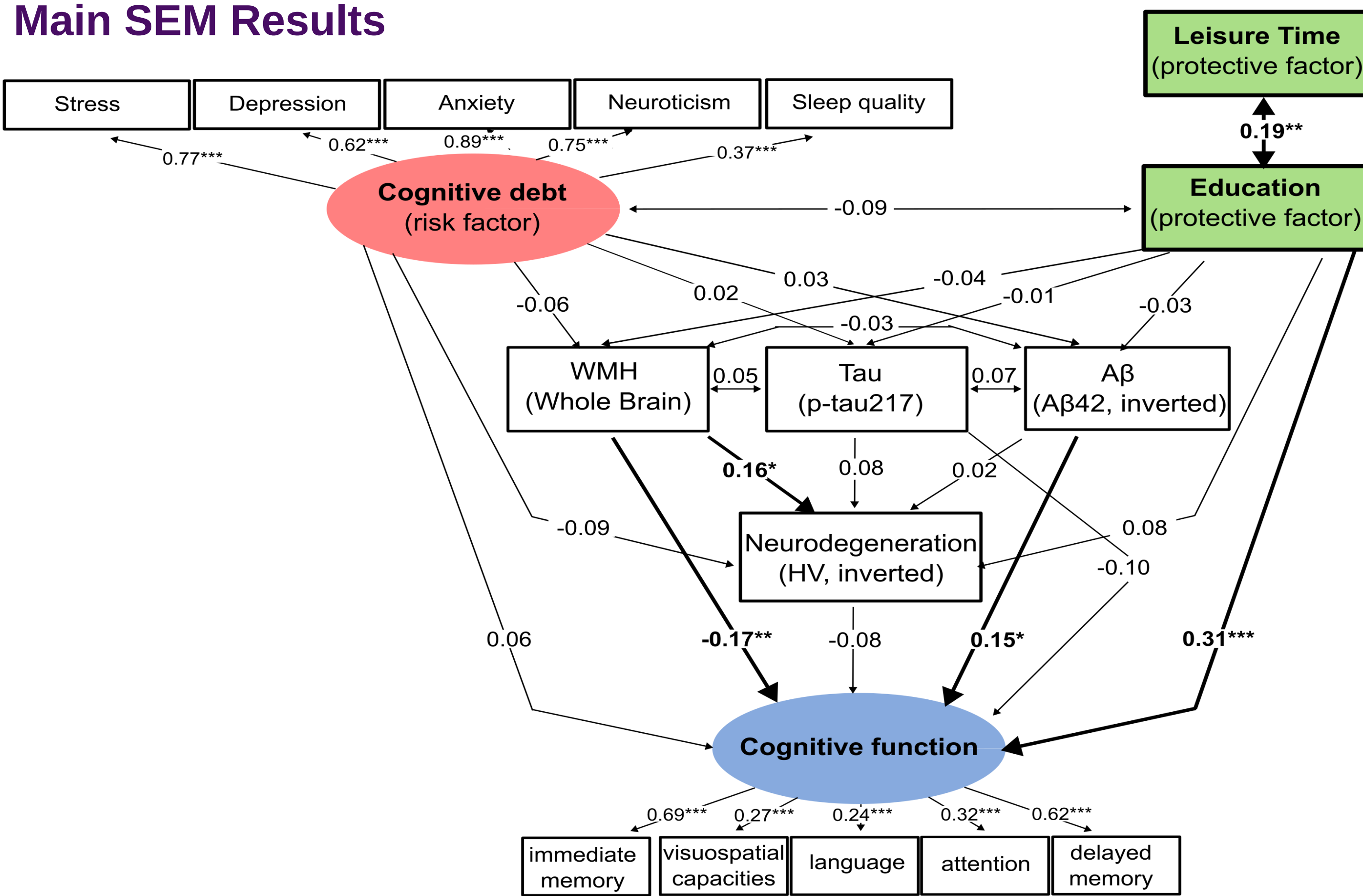
Targeting Alzheimer’s Risk: Modifiable Factors, Multimodal Biomarkers, and Cognitive Health in PREVENT-AD

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INTRODUCTION	METHODS	RESULTS	DISCUSSION																					
Modifiable lifestyle and psychological factors have an impact on Alzheimer’s disease (AD) pathology and cognition¹ Cognitive reserve and cognitive debt are, respectively, potential modifiable protective and risk factors for AD^{2,3,4} Research Goal: - to investigate cross-sectional pathways linking modifiable protective and risk factors, multimodal AD biomarkers, and cognitive function in the PREVENT-AD - to assess moderation effects of sex and apolipoprotein E (APOE) ε4 status <table><tr><th></th><th>Women</th><th>Men</th></tr><tr><td>n</td><td>241</td><td>96</td></tr><tr><td>Age (years)</td><td>63.6</td><td>63.5</td></tr><tr><td>Education (years)</td><td>15.2</td><td>15.9</td></tr></table>		Women	Men	n	241	96	Age (years)	63.6	63.5	Education (years)	15.2	15.9	Sample: 337 cognitively unimpaired older participants with a family history of AD from the PREVENT-AD cohort⁵ Baseline Measurements: <u>Biomarkers:</u> plasma amyloid beta 42 (Aβ42), plasma phosphorylated tau (p-tau) 217, white matter hyperintensities (WMH), hippocampal neurodegeneration (inverted hippocampal volume [HV]) <u>Self-reported questionnaires:</u> stress (DASS), depression (GDS), anxiety (GAI-SF), neuroticism (BFI-10), sleep quality (PSQI), leisure time activities, education <u>Cognitive Function:</u> Repeatable Battery for Assessment of Neuropsychological Status Statistical Analysis: Structural Equation Modeling (SEM) and multigroup analyses (after establishing measurement invariance), adjusted for age	Main SEM Results  <i>Note. Latent constructs are represented by ellipses and observed variables are represented by rectangles. Terms show standardized coefficients (β). Significant terms are indicated in bold fonts. Significant paths are indicated with bold lines.</i> ***p < .001, **p < .01, *p < .05. Multigroup Analyses Results <u>Significant differences among structural paths between men and women</u> <table><tr><th></th><th>Women (β)</th><th>Men (β)</th></tr><tr><td>Cognitive debt → neurodegeneration</td><td>0.000</td><td>-0.357***</td></tr><tr><td>Education → Aβ42 (inverted)</td><td>0.060</td><td>-0.231*</td></tr></table> No significant differences between APOE ε4 carriers vs non-carriers		Women (β)	Men (β)	Cognitive debt → neurodegeneration	0.000	-0.357***	Education → Aβ42 (inverted)	0.060	-0.231*	Educational attainment showed a direct positive association with cognition in women and men For cognitive debt, no significant associations were observed → might be due to sub-clinical symptom levels Observed sex differences further underscore the need for precision AD intervention and prevention strategies References ¹Livingston et al. (2024) https://doi.org/10.1016/s0140-6736(24)01296-0 ²Stern et al. (2020). https://doi.org/10.1016/j.jalz.2018.07.219 ³Marchant & Howard. (2015). https://doi.org/10.3233/JAD-141515 ⁴Boscheck & Luft et al. (2026). https://doi.org/10.1186/s13195-026-02054-z ⁵Tremblay-Mercier et al. (2021). https://doi.org/10.1016/j.nicl.2021.102733 Contact: dilan.barisan@dzne.de  AAIC 26
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