

Child maltreatment, adulthood adversities, and grey matter volume by biological sex and age in the UK Biobank

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Exposure to ≥ 2 types of adulthood adversity, but not child maltreatment alone, was associated with lower sex-specific, age-adjusted residual total grey matter volume (GMV), of the largest magnitudes in mid-life (ages 47 to <65 years) males and females, compared to participants who reported no adversities. Findings support adversity-informed, sex- and age-stratified models of residualised GMV that distinguish mid-life (before age 65), consistent with young-onset dementia susceptibility, from later-life (after age 65).

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES																							
- Child maltreatment (CM) associated with lower grey matter volume (GMV) in cognition and stress-regulation regions,¹⁻³ and to young-onset dementia (YOD) risk,⁴ compared to the unexposed. - Adulthood adversities (violence, housing insecurity, socioeconomic inequity, life-threatening illness or accidents, and social isolation) also correlate with lower GMV,⁵ independently of CM.⁶ - Prior neuroimaging findings are inconsistent; studies rarely model CM and adulthood adversity jointly, and most omit residualisation of GMV and sex- and age-stratification, obscuring differences in females and males before versus after age 65. Aim - Test whether CM and levels of adulthood adversity are associated independently and jointly with sex-specific, age-adjusted residual whole-brain GMV, stratified by sex and age at MRI (47 to <65 vs ≥ 65 years).	Sample - UK Biobank sub-cohort: 28,298 adults with brain MRI + Mental Health Questionnaire (MHQ) data: 12,987 males (46%), 15,311 females (54%). Outcome - Total GMV (T1-weighted MRI, head-size normalised, 2015–2024), residualised on age and age² within females and males separately for sex-specific, age-adjusted residual total GMV. Exposures (from MHQ) - CM: 0 vs ≥ 1 type (5-item Childhood Trauma Screener). - Adulthood adversity: 0, 1, or ≥ 2 (11 types). Analysis - Linear regression stratified by sex $\times$ age group (4 strata); adjusted marginal means (Stata 18). Tested main effects and CM $\times$ adulthood adversities interaction. - Adjusted for ethnicity, Townsend Deprivation Index, education, maternal & paternal dementia, Alzheimer’s disease and schizophrenia polygenic risk scores. Complete-case analysis (~7% missing).	<table border="1"><thead><tr><th>Age Group</th><th>Sex</th><th>1 adulthood adversity (mm³)</th><th>≥ 2 adulthood adversities (mm³)</th><th>p-value</th></tr></thead><tbody><tr><td rowspan="2">Mid-life (47–65)</td><td>Males</td><td>-4,673</td><td>-4,673</td><td>p=0.001</td></tr><tr><td>Females</td><td>-3,437</td><td>-3,437</td><td>p=0.005</td></tr><tr><td rowspan="2">Later-life (≥ 65)</td><td>Males</td><td>-3,016</td><td>-3,016</td><td>p=0.011</td></tr><tr><td>Females</td><td>-2,782</td><td>-2,782</td><td>p=0.006</td></tr></tbody></table> 1-adversity contrasts all non-significant (p > 0.05)	Age Group	Sex	1 adulthood adversity (mm³)	≥ 2 adulthood adversities (mm³)	p-value	Mid-life (47–65)	Males	-4,673	-4,673	p=0.001	Females	-3,437	-3,437	p=0.005	Later-life (≥ 65)	Males	-3,016	-3,016	p=0.011	Females	-2,782	-2,782	p=0.006	- Exposure to ≥ 2 adulthood adversities, not CM alone, was associated with lower sex-specific, age-adjusted residual total GMV, particularly in mid-life. - Negative differences from the mean (–4,673 to –2,782 mm³) are comparable in magnitude to hippocampal volume, a marker of dementia risk.⁷ - Sex differences (mid-life males > females) may reflect sex-specific cardiometabolic and neuroendocrine ageing.⁸ - Supports adversity-informed, sex-age stratified models of residualised GMV suggesting potentially elevated YOD risk before age 65. - Hypothesis-generating: routine screening of asymptomatic adults is not currently indicated, but adulthood violence and adversity burden warrants attention in mid- and later-life brain health equity research.⁹ - Clinicians and patient support services may benefit from integrating violence survivor-centred practices into brain health promotion education and dementia early detection.	- Yang W, et al. Psychol Med. 2023;53:1681-99. - Orellana SC, et al. Proc Natl Acad Sci USA. 2024; 121(13):e2304704121. - Teicher MH, et al. Nat Rev Neurosci. 2016;17(10):652-66. - Schulte MC, et al. 2026. Under review. - Ringwald KG, et al. Hum Brain Mapp. 2022;43(11):3577-84. - See CRZ, et al. Eur Psychiatry. 2025;68(1):e18. - Foteno AF, et al. Neurology. 2005;64(6):1032-9. - Mosconi L, et al. Neurology. 2017;89(13):1382–90. - Murchland AR, et al. Alzheimers Dement. 2025;21(5):e70029.
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