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RESEARCH ARTICLE

Inflammation following childhood maltreatment is associated with episodic memory decline in older adults

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Abstract

Childhood maltreatment is recognized as a risk factor for cognitive decline in adulthood. However, the mechanisms underlying this association, particularly the role of systemic inflammation, remain understudied. To address this gap, this study investigated the indirect effects of inflammation on the associations between childhood maltreatment and both episodic memory (EM) and executive functioning (EF) performance 10 years after inflammatory measurement in older adults. We selected 590 participants (M_{age} = 65.5 years) from the Midlife in the United States Study based on available childhood maltreatment, inflammation, and composite cognitive data. Spearman's rank correlations were calculated to test associations among childhood maltreatment, cognition, and inflammation. The results informed follow-up analyses testing the indirect effects of inflammation on the associations between childhood maltreatment and cognition. Correlations demonstrated that inflammation was associated with overall childhood maltreatment as well as with specific domains of childhood maltreatment (i.e., physical abuse, sexual abuse, emotional abuse, and physical neglect), *p*s = .002–.010. Inflammation was negatively associated with EF, p = .001, and EM, p = .028. Follow-up analyses revealed significant indirect pathways linking overall childhood maltreatment, $\beta = -.0088$, $SE = 0.0058$, 95% CI [−0.0223, −0.00000], to EM performance through inflammation, but no specific domain of maltreatment drove this association. The results suggest that inflammation may help explain links between childhood maltreatment exposure and EM deficits in adulthood. These results elucidate the importance of evaluating childhood maltreatment as a risk factor for later-life cognitive decline, particularly within the context of heightened inflammatory biomarkers.

Early-life stress has been shown to be associated with an increased risk for a wide range of adverse health outcomes (Weleff & Potter, 2023), including diminished cognitive functioning in adulthood (Goodman et al., 2018; Hawkins et al., 2021). Various forms of abuse and neglect experienced in childhood can have lasting cognitive effects into adulthood, potentially serving as risk factors for Alzheimer's disease and other dementias later in

life (Huang et al., 2023). As of 2020, an estimated 64% of adults in the United States reported experiencing some form of maltreatment before the age of 18 years (Swedo et al., 2023). With the number of U.S. adults aged 65 years or older projected to nearly double by 2050 (U.S. Census Bureau, 2023), the high prevalence of childhood maltreatment exposure coupled with a rapidly aging population highlights a crucial need to understand how early life adversity influences later-life cognitive health.

Childhood maltreatment is associated with multiple mechanisms that can lead to cognitive decline later in life. An increasingly recognized pathway involves chronic inflammation (Walker et al., 2019), which has been associated with both peripheral tissue damage and breach of the blood–brain barrier, affecting the central nervous system (Nettis et al., 2019). Notably, the hypothalamic–pituitary–adrenal (HPA) axis, which modulates inflammatory activity (Silverman et al., 2005), may exhibit aberrant reactivity in the context of childhood maltreatment, contributing to a proinflammatory state over time (Cohen et al., 2012). Studies have demonstrated a link between early-life exposure to maltreatment and altered stress responses, including elevated levels of circulating cortisol and a blunted release of cortisol in response to acute stressors (Marques-Feixa et al., 2021), that persist into adulthood (Carpenter et al., 2007). Consequently, increased inflammatory burden may accumulate across the lifespan and, through cortical alterations (Marsland et al., 2015), contribute to global cognitive decline (Beydoun et al., 2018; Ashraf-Ganjouei et al., 2020) as well as an increased risk for neurodegenerative disease (Leonardo & Fregni, 2023); however, cognitive deficits following childhood maltreatment are not uniformly found across studies (Kirova et al., 2015; Silva et al., 2022). A meta-analysis by Irigaray and colleagues (2013) underscores these inconsistencies, noting that although some included studies found significant changes in episodic memory (EM) and/or executive functioning (EF) following childhood maltreatment, others reported no differences. Inflammation could serve as a key mediator in these associations. To date, studies that have explored the links between childhood maltreatment, inflammation, and cognition suggest that systemic inflammation is a key pathway connecting early-life adversity to cognitive health in adulthood (D'Amico et al., 2022; Davis et al., 2018). The current study builds upon these prior findings by examining the roles of childhood maltreatment and inflammation in cognition measured 10 years following inflammation biomarker measurement in a cohort of older adults (aged 50 years and above). This extended timeframe allowed us to assess the long-term impacts on specific cognitive domains, particularly executive functioning (EF) and episodic memory (EM), and understand their progression as this population ages. We hypothesized that higher levels of exposure to overall childhood maltreatment would be associated with elevated levels of proinflammatory cytokines and concomitant impairments in EM and EF performance in later life.

Additionally, we explored whether specific domains of maltreatment, such as physical and emotional abuse and neglect, were differentially associated with cognition. Prior work suggests that the effects of childhood maltreatment on inflammation and cognitive functioning may vary depending on the specific domain of maltreatment experienced (Brown et al., 2021). The Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998) provides a measure of childhood maltreatment across five domains: physical abuse (PA), emotional abuse (EA), sexual abuse (SA), emotional neglect (EN), and physical neglect (PN). Scores from the CTQ can be operationalized as total scores, representing cumulative exposure to childhood maltreatment (CTQ–COMP), or as domain-specific scores, representing exposure to specific forms of abuse and neglect. Indeed, studies have linked specific forms of neglect or abuse to later cognitive decline, but these findings have been inconsistent. Though some studies have demonstrated no link between overall CTQ scores and adult cognition (Grainger et al., 2019), others have identified domain-specific effects. For instance, PN was associated with poorer cognitive outcomes (Geoffroy et al., 2016), and exposure to multiple abuse types was linked to an increased risk of late-life dementia (Xie et al., 2023); however, in one longitudinal study, the authors found no significant overall cognitive decline related to maltreatment but observed improved scores within specific neglect domains (Lynch & Widom, 2022). These findings underscore the need for further research to clarify the nuanced impacts of different maltreatment types on cognitive decline and inflammation.

METHOD

Participants

Data were obtained from the Survey of Midlife in the United States (MIDUS) project. Established in 1995, the MIDUS is a longitudinal cohort study aimed at examining biopsychosocial factors that impact health and well-being in mid-to-late life adults. To be eligible for the MIDUS, participants must be English-speaking, noninstitutionalized adults. Additional information can be found elsewhere on the study's website (University of Wisconsin–Madison, Institute on Aging, 2022). Beginning at the second wave of data collection (MIDUS II), which took place in 2004–2006 ($N = 4{,}889$; Ryff et al., 2021), a cognitive battery (Cognitive

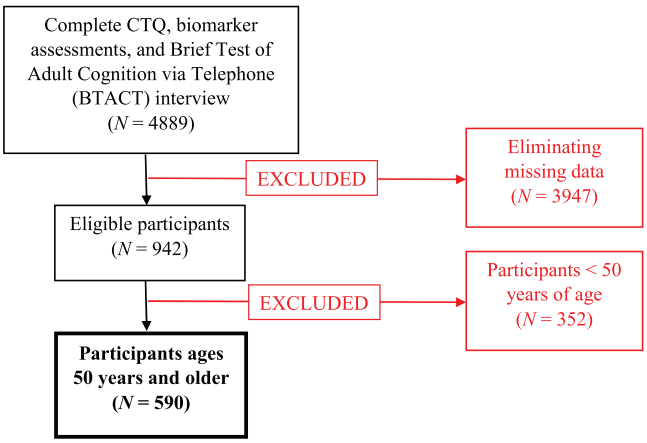

FIGURE 1 Study inclusion and exclusion criteria
Note: Inclusion and exclusion criteria were utilized to gather the total number of participants in the study ($N = 590$). CTQ = Childhood Trauma Questionnaire.

Project; $N = 4{,}512$) and blood assay (Biomarkers Project; $N = 1{,}255$) were administered to subgroups of the core sample. The MIDUS II Biomarkers Project also collected a battery of self-report questionnaires, including the CTQ. At the third wave of data collection (MIDUS III), which took place in 2013–2014 ($N = 3{,}294$; Ryff et al., 2019), cognitive assessment was repeated in a subgroup of participants ($N = 2{,}693$), providing measurements of later cognitive outcomes. In the current study, CTQ and biomarker data were obtained from the MIDUS II dataset, and cognitive data were obtained from the MIDUS III follow-up.

Procedure

Figure 1 outlines the inclusion criteria used to generate our final sample of older adults from the MIDUS cohort. Inclusion criteria were the completion of the CTQ and a blood draw at MIDUS II in addition to the completion of the Brief Test of Adult Cognition via Telephone (BTACT; Tun & Lachman, 2006) at MIDUS III ($N = 942$). Participants under 50 years of age at the time of the cognitive assessment (MIDUS III) were excluded. Individuals with missing data were removed ($N = 352$), leaving a final sample of 590 participants. Data collection was approved by the Institutional Review Board (IRB) at MIDUS testing sites (i.e., University of California–Los Angeles, University of Wisconsin–Madison, Georgetown University), and informed consent was obtained from all participants. Analyses were conducted at The Ohio State University, and the IRB deemed it exempt from review given the use of a publicly available dataset.

Measures

Childhood maltreatment

To assess exposure to childhood maltreatment, participants completed the CTQ, a 70-item self-report measure indexing the severity of five categories of childhood maltreatment (PA, SA, EA, PN, EN; Bernstein et al., 1994). Items are scored on a 5-point Likert scale ranging from 1 (*never true*) to 5 (*very often true*). An overall maltreatment score was calculated by summing all 70 items (range: 25–125). Domain-specific subscale scores were also obtained (range: 5–25), representing different severity classifications as outlined by Bernstein et al. (1994). Overall, the CTQ has demonstrated moderately strong internal reliability for both the full scale (Cronbach's $\alpha = .852$) and the five domain-specific subscales (Cronbach's αs = .491–.857; Peng et al., 2023). In the MIDUS sample, internal reliability for each of the five domains of maltreatment was very strong, Cronbach's αs = .698–.942 (see also University of Wisconsin–Madison, Institute on Aging, 2024).

Cognitive performance

At MIDUS III, participants were administered the BTACT (Tun & Lachman, 2006), a remote means of measuring cognitive performance in healthy adults that is composed of subtests across multiple cognitive domains. The BTACT has demonstrated good concurrent validity with other cognitive assessments (Lachman et al., 2013). Factor analysis in the MIDUS dataset found evidence supporting a two-factor model of the BTACT, with underlying factors representing EF and EM (Lachman et al., 2021). The MIDUS provides composite measures of EF and EM, obtained by averaging the z scores of included subtests. An EM composite was composed of summed scores for the Word List Immediate and Word List Delayed tasks, and an EF composite was composed of summed scores for the Digits Backward, Category Fluency, Number Series, and Backward Counting tasks. These composites have demonstrated good internal consistency in the MIDUS sample (Cronbach's $\alpha = .712$; Lachman et al., 2021) and have been used widely (Hughes et al., 2018; Karlamangla et al., 2014; Lee et al., 2014). For additional information regarding the subtests and composite calculations, see Lachman et al. (2021).

Inflammatory biomarkers

In accordance with prior work (Hostinar et al., 2015; Jurgens et al., 2023), systemic inflammation was indexed

using a composite score composed of five biomarkers markers known for their proinflammatory properties: C-reactive protein (CRP), interleukin-6 (IL-6), E-selectin, fibrinogen, and intercellular adhesion molecule-1 (ICAM-1). The composite measure was used to indicate an individual's baseline inflammatory state (Furman et al., 2020; Pahwa et al., 2023). This approach reflects the understanding that these inflammatory biomarkers collectively contribute to inflammation through a process termed the "cytokine cascade" (Cavaillon & Adib-Conquy, 2002). Additionally, composite inflammation scores have shown superiority to individual biomarker assessment within the context of inflammation and childhood maltreatment (Hostinar et al., 2015).

IL-6 is a proinflammatory cytokine released in response to tissue damage and infection (Tanaka et al., 2014), and CRP is an acute-phase reactant protein released in response to increased levels of IL-6 (Nehring et al., 2023). E-selectin is a molecule expressed on endothelial cells that is upregulated by other proinflammatory molecules (Timmerman et al., 2016), and fibrinogen is a glycoprotein involved in blood clotting (Kaur & Jain, 2023). ICAM-1 is another glycoprotein expressed on endothelial cells that aids in leukocyte recruitment during inflammation (Bui et al., 2020).

Serum IL-6, E-selectin, and ICAM-1 concentrations were measured via enzyme-linked immunosorbent assay (ELISA) kits. CRP was assayed via a particle-enhanced immunonephelometric assay. Immunochemical reactions determined fibrinogen levels. Specific information regarding collection and processing protocols for each biomarker can be found elsewhere (University of Wisconsin–Madison Institute on Aging, 2011). Prior to analysis, raw values of each biomarker were log-transformed to correct for nonnormality. Log-transformed values were then standardized and averaged to generate the inflammation composite score.

Covariates

The analyses were statistically adjusted for demographic factors including age, sex, and socioeconomic status (SES). T-tests and Mann–Whitney *U* tests were conducted to assess mean differences in the variables of interest across demographic groups (i.e. sex, chronic physical health status, depression; Supplementary Tables S1–S3). SES was measured using a composite score of three SES indicators collected at MIDUS II: occupational prestige, highest educational degree, and household income (Elliot & Chapman, 2016). Occupational prestige was assessed via the Duncan Socioeconomic Index (SEI; Duncan, 1961) calculated through the MIDUS. Educational attainment was operationalized on a 12-point scale, with a score of 1 reflecting no formal schooling or the completion of some grade school and a score of 12 reflecting the completion of a professional degree. Household income was calculated based on participants' responses to a question regarding total pretax household income from wages, pension, social security government assistance, and other monetary sources.

Analyses also included a binarized variable representing whether participants endorsed any given number of various chronic physical health symptoms or conditions (0 = no symptoms/conditions, 1 = endorsement of symptoms/conditions), as numerous health factors are independently associated with heightened inflammation (Alfaddagh et al., 2020; Arnson et al., 2010; Tsalamandris et al., 2019).

Given the extensive body of work linking psychopathology to inflammation (Su, 2012), cognitive deficits (Abramovitch et al., 2021), and childhood maltreatment (Humphreys et al., 2020; Nelson et al., 2017), depression was also included as a covariate. Participants completed the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), a 20-item self-report measure of depressive symptom severity. Scores on the CES-D range from 0 to 60, with scores higher than 17 considered as clinical threshold for depression. A binarized depression variable from CES-D scores at MIDUS II was used, with a cutoff score distinguishing no depression (0) from probable clinical depression (1). This distinction was based on evidence that only severe cases of depression are associated with elevated levels of inflammation (Jia et al., 2019). Consequently, the analysis was limited to clinical depression to avoid the variability introduced by subclinical depressive scores.

Data analysis

All analyses were conducted using R statistical software (Version 4.2.3; Dalthorp, 2021). Two-tailed ($\alpha = .05$) Shapiro–Wilk tests indicated that CTQ and EM data were normally distributed after log transformation, but inflammation and EF scores were not, $ps = .326–.864$.

Main analyses were conducted in a two-step process. First, Spearman's rank correlations were calculated to test the associations among CTQ scores, cognitive variables, and inflammation across the entire cohort. The results obtained from these comparisons informed follow-up analyses of indirect effects, which were conducted using Model 4 of the PROCESS macro with bootstrapping ($N = 10{,}000$) and standardization (Hayes, 2017). For each iteration of the indirect effect analyses, the dependent variable represented a cognitive domain (EF or EM), whereas the independent variable was either the CTQ–COMP or a CTQ domain-specific subscale score. For any given domain-specific analysis, the other CTQ domains were included as

covariates in the model. For example, when analyzing the indirect effect of PA on cognition through inflammation, EA, SA, PN, and EN were all included as covariates in the model. The intermediate variable for each iteration was the inflammation composite score.

RESULTS

Demographic and sample characteristics

Table 1 provides demographic characteristics and descriptive statistics of inflammatory markers for the full sample (N = 590). Participants were older adults (M_{age} = 65.5 years, SD = 9.75, range: 50–94 years), and there was a relatively equal proportion of male and female participants (43.9% male, 56.1% female). Most participants were middle-class based on reports of household income (M = $84,631.63 [USD], SD = $62,776.13). Regarding health variables, 6.8% of the sample endorsed chronic conditions or symptoms. According to the CES-D, 11.7% of the sample met the clinical threshold for probable depression.

CTQ variables, inflammation, and cognition

Correlation values between observed variables are reported in Table 2. A significant positive correlation was found between childhood maltreatment (CTQ–COMP) and the inflammation composite, $p < .001$. The inflammation composite was also significantly negatively associated with EF, $p = .001$, and EM performance, $p = .028$. In addition, exploratory analyses showed significant positive correlations between each CTQ domain (i.e., SA, PA, EA, and PN scores) and inflammation, ps < .001. These correlation results informed subsequent analyses testing the indirect effects of inflammation on the associations between CTQ–COMP, SA, PA, EA, and PN scores and both EM and EF performance.

Covariates

Correlation values between age, SES, and observed variables are also reported in Table 2. As expected, age was significantly negatively associated with both EF and EM. Age was also significantly negatively associated with CTQ–COMP and domain-specific scores for PA, EA, and EN. Age was positively associated with the inflammation composite. SES was not significantly associated with cognition, CTQ–COMP or domain-specific CTQ scores, or the inflammation composite. Differences based on sex, probable depression diagnosis, and chronic physical health conditions or symptoms are found in Supplementary Tables S1–S3.

Analyses of indirect effects: EM

CTQ-COMP

Path coefficients for this model are presented in Figure 2. There was a significant indirect effect of CTQ–COMP scores on EM through inflammation, $\beta = -.0088$, SE = 0.0058, 95% confidence interval (CI) [−0.0223, −0.0000]. Higher levels of childhood maltreatment were associated with elevated inflammatory biomarkers (a path), $\beta = .0049$, SE = 0.0019, 95% CI [0.0012, 0.0085], which, in turn, predicted worse EM performance (b path), $\beta = -.1286$, SE = 0.0602, 95% CI [−0.2469, −0.0103]. In total, the indirect effect explained 8.3% of the total variance in the association between CTQ–COMP scores and EM. The direct effect of CTQ–COMP scores on EM was also significant, 95% CI [−0.0116, −0.0009].

Domain-specific maltreatment

As part of the exploratory analyses, we investigated whether specific domains of maltreatment were driving the observed indirect effect of inflammation on the negative association between overall childhood maltreatment exposure and EM performance. When examining CTQ domains separately, only PA showed an indirect effect on EM through inflammation, $\beta = -0.0098$, SE = 0.0061, 95% CI [−0.0239, −0.0005]. Higher levels of PA were associated with elevated inflammatory biomarkers (a path), β = 0.0244, SE = 0.0087, 95% CI [0.0073, 0.0416], which, in turn, predicted worse EM performance, (b path), $\beta = -0.1391$, SE = 0.0605, 95% CI −0.258, −0.0203]. In total, the indirect effect explained 28.6% of the total variance in the association between PA scores and EM. However, this association was no longer significant when adjusting for all other domains in the model.

Analyses of indirect effects: EF

When including age, sex, SES, chronic health status, and depression as covariates in the model, neither CTQ–COMP nor any domain-specific scores had significant indirect effects of childhood maltreatment exposure on EF performance through inflammation.

DISCUSSION

This study investigated the role of inflammation as an indirect pathway linking childhood maltreatment to EM and EF performance in a large sample of older adults. There were three primary findings. First, childhood maltreat-

TABLE 1 Demographic data and summary statistics for the overall sample

Variable	*M*	*SD*	*n*	%
Demographic variables				
Age (years)	65.5	9.75		
Sex				
Male			259	43.9
Female			331	56.1
Race				
White			493	83.6
African American			70	11.9
Native American or Alaskan Islander			9	1.5
Asian			1	0.2
Other			17	2.9
Hispanic/Latino ethnicity			24	4.1
Educational attainment				
Less than a high school diploma			20	3.4
High school diploma/GED			111	18.8
1–3 years of college (no degree)			116	19.7
Graduated from 2-year college or vocational school/associate's degree			50	8.5
Bachelor's degree/graduated from a 4- or 5-year college			138	23.4
Some graduate school			27	4.6
Master's degree			93	15.8
Professional degree			35	5.9
Income (USD)	$84,631.63	$62,776.13		
Clinical characteristics and trauma variables				
Chronic conditions/symptoms			40	6.8
Clinical depression (CES-D)			69	11.7
Childhood maltreatment				
Total (CTQ–COMP)			371	62.9[a]
Physical abuse			136	23.1[b]
Sexual abuse			152	25.8[b]
Emotional abuse			169	28.6[b]
Physical neglect			153	25.9[b]
Emotional neglect			255	43.2[b]
Inflammation variables				
IL-6 (pg/mL)	1.03	0.86		
Fibrinogen (mg/nL)	346.84	85.55		
E-selectin (ng/mL)	40.25	20.04		
CRP (ug/mL)	2.79	4.07		
ICAM-1 (ng/mL)	283.63	101.88		
Cognitive variables				
Episodic memory	−0.021	0.974		
Executive functioning	−0.136	0.714		

Note: $N = 590$. CES-D = Center for Epidemiological Studies Depression Scale; CTQ-COMP = Childhood Trauma Questionnaire composite score; IL-6 = interleukin-6; CRP = C-reactive protein; ICAM-1 = intercellular adhesion molecule-1.

[a]Proportion of participants who had total CTQ composite scores greater than 0.

[b]Proportion of maltreatment-exposed participants who had a relevant domain score greater than 0.

TABLE 2 Correlations among childhood maltreatment variables, inflammation, cognition, age, and socioeconomic status (SES)

Variable	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. EF	.336***	−.050	−.023	−.109**	.026	.016	−.155***	−.133**	−.416***	−.013
2. EM	–	−.030	−.010	−.063	.034	−.024	−.072	−.091*	−.339***	.014
3. CTQ-COMP		–	−.780***	.634***	.868***	.831***	.764***	.126**	−.148***	.016
4. Physical abuse			–	.403***	.654***	.526***	.547***	.107**	−.143***	.019
5. Sexual abuse				–	.394***	.296***	.363***	.106*	−.065	−.031
6. Emotional abuse					–	.696***	.572***	.108**	−.150***	.012
7. Emotional neglect						–	.610***	.069	−.142***	.024
8. Physical neglect							–	.113**	−.061	.048
9. Inflammation composite score								–	.119	−.026
10. Age									–	.032
11. SES										–

Note: EF = executive functioning; EM = episodic memory; CTQ-COMP = Childhood Trauma Questionnaire composite score.
*$p < .05$. **$p < .01$. ***$p < .001$.

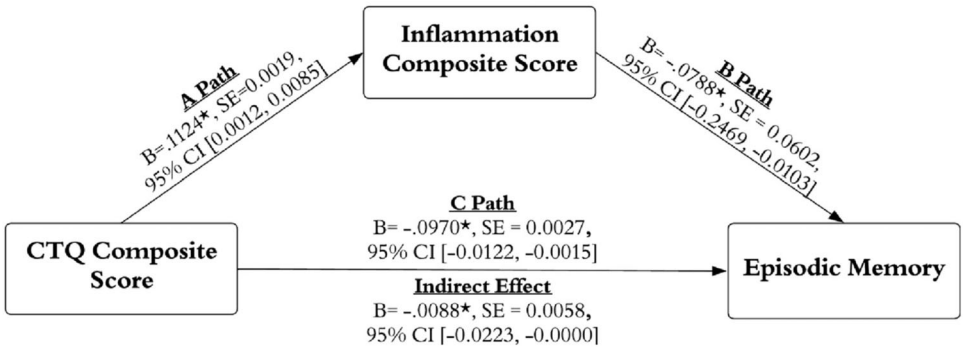

FIGURE 2 Intermediate pathways in the association between overall childhood maltreatment and episodic memory (EM)
Note: Pathways of the indirect effect of Childhood Trauma Questionnaire composite score (CTQ–COMP) on EM performance through inflammation composite score, covarying for age, sex, socioeconomic status, depression status, and physical health condition/symptom status. *a* Path: $R^2 = .0573$, *b* Path: $R^2 = .2527$, *c* Path: $R^2 = .2468$. CI = confidence interval.
*$p < .05$.

ment overall, as well as specific domains of maltreatment (i.e., PA, EA, SA, PN, and EN), were all associated with higher levels of systemic inflammation. Second, there was an indirect effect of inflammation on the association between childhood maltreatment and memory performance. Specifically, we found that higher levels of maltreatment were associated with an elevated inflammatory state, which, in turn, predicted poorer EM performance a decade later. Third, we found that although there was a nominal indirect effect of inflammation on the specific domain of PA and memory, it did not reach statistical significance after adjusting for EA and SA, and PN and EN. This suggests that the specific type of maltreatment an individual experiences may not distinctly influence the observed effects on inflammation and cognitive decline. Contrary to earlier studies (D'Amico et al., 2022; Nikulina & Widom., 2013), we observed no significant direct or indirect associations between childhood maltreatment and later-life EF performance. These results underscore the critical role of inflammation in the cognitive sequelae of childhood maltreatment, particularly affecting memory rather than EF in older age.

Our results suggest that childhood maltreatment may have a lasting inflammatory burden. Elevated levels of proinflammatory biomarkers, such as CRP, tumor necrosis factor (TNF), and IL-6, have been widely documented among adults exposed to childhood maltreatment (Baumeister et al., 2015) and may contribute to the increased inflammatory burden seen with aging (Franceschi et al., 2000). Results from this study confirm this positive association between childhood maltreatment and inflammation, suggesting that inflammation could be a key mechanism linking early-life stress to adverse cognitive outcomes in later life.

In contrast to our original hypothesis, EM, but not EF, demonstrated associations with childhood maltreatment through inflammation. This discrepancy may be explained in part by the neural pathways underlying these cognitive domains. It has been widely documented that the hippocampus—which is traditionally associated with EM (Tulving & Markowitsch, 1998)—is particularly sensitive to the physiological consequences of stress. Smaller hippocampi have been observed in populations exposed to chronic stress (Logue et al., 2018), including adults with a history of childhood maltreatment (Teicher et al., 2012). Though associations between stress and the hippocampus are commonly attributed to glucocorticoid vulnerability in this brain region (Mirescu & Gould, 2006), emerging work also suggests a role for inflammation in hippocampal alterations. Increased levels of proinflammatory biomarkers have been associated with decreased hippocampal volume in humans (Walker et al., 2017). Animal models have further demonstrated that neuroinflammatory responses may be particularly exaggerated in the hippocampus with age, potentially due to the high density of neural immune cells that inhabit this region (Barrientos et al., 2015). When activated, these immune cells indirectly suppress hippocampal neurogenesis (Chesnokova et al., 2016) and alter synaptic plasticity (Di Filippo et al., 2013; Riazi et al., 2015). Given the role of the hippocampus in memory functioning specifically, reduced hippocampal volume coupled with suppressed hippocampal neuronal production may contribute to the selective EM impairments seen with aging in the current study. Future work should further explore how brain structure may be implicated in the associations between childhood maltreatment exposure, inflammation, and EM in older adulthood.

Consistent with prior work, we found significant associations between inflammation and domain-specific maltreatment scores (i.e., PA, SA, EA, and PN; Brown et al., 2021); however, there were no significant indirect effects of inflammation on the association between domain-specific scores and cognition. This aligns with a meta-analysis conducted by Baumeister and colleagues (2015), which showed that although overall childhood maltreatment was linked to elevated levels of inflammatory markers such as CRP, IL-6, and TNF-a, the effects were not significantly driven by specific domains of maltreatment. Our results support the notion that exposure to childhood maltreatment is associated with elevated inflammatory levels, although individual domains do not solely drive this association.

There are several limitations that should be considered when interpreting the results of the present study. Despite assessing inflammatory biomarkers at baseline and cognitive variables 10 years later, the cross-sectional design limits causal interpretations. This design allows for the exploration of indirect effects, offering a starting point for understanding these complex relationships (Hayes & Rockwood, 2017). To enhance causal and temporal clarity, future research should adopt a longitudinal approach and include classic mediation analyses (Cole & Maxwell, 2003). Second, the cognitive assessments used were derived from the BTACT, a brief telephone cognitive screening instrument. More comprehensive neuropsychological evaluations are recommended for a deeper understanding of cognitive outcomes. Additionally, the lack of direct measures for PTSD or anxiety disorders due to the limitations of the measures provided by MIDUS (e.g., the Mood and Anxiety Questionnaire; MASQ; Buckby et al., 2007) underscores the need for gold-standard assessments in future studies Additionally, the CTQ was administered retrospectively and may be susceptible to recall bias, as participants were late-life adults at the time of assessment. Although depression was included as a covariate in our analyses, the retrospective nature of the study may still be prone to negative attentional biases in participants with clinical mental health conditions, potentially leading to an overestimation of childhood maltreatment experiences. Furthermore, although inflammation was measured using a composite score, it reflects peripheral rather than cerebral inflammation, which does not fully represent biomarker activity across the blood–brain barrier (Giridharan et al., 2019). This suggests caution should be used when interpreting how inflammation affects cognitive functions. Finally, the study did not account for health behaviors, such as diet and exercise, which can influence both inflammation (Woods et al., 2012) and cognition (Hillman et al., 2008). As childhood maltreatment also increases the risk of engaging in negative health behaviors (Abajobir et al., 2017), additional work is needed to clarify the role of lifestyle choices in shaping adult health outcomes among populations with exposure to early-life adversity.

Despite the aforementioned limitations, the present study offers several strengths. First, the results expand upon previous work examining inflammation as a pathway linking childhood maltreatment to cognition (D'Amico et al., 2022; Lynch & Lachman, 2020) by assessing cognition in older adulthood. Our novel findings demonstrate how overall childhood maltreatment exposure may drive later-life cognitive performance through inflammation. Though the indirect effect of inflammation on the association between childhood maltreatment and cognitive decline was small, the effect was still statistically significant, supporting the biopsychosocial model of childhood maltreatment on cognition. However, there are likely other factors that contribute to this association, such as metabolic health, cardiovascular burden, and psy-

chopathology (Weleff & Potter, 2023), that account for additional variance; future studies should consider these additional variables in determining the underlying mechanisms behind the observed negative association between childhood maltreatment and cognitive decline in older adults. The results add to the limited body of research investigating childhood maltreatment as a risk factor for cognitive decline in older adults and expand upon extant work by examining specific cognitive domains of EM and EF instead of global cognition alone (Feeney et al., 2013; Ritchie et al., 2010). Thus, these findings shed light on how early adversity may be a predisposing factor for later negative cognitive outcomes in older adults.

In conclusion, the findings indicate that childhood maltreatment experiences are linked to increased systemic inflammation, which is associated with decreased EM in older adults. These results elucidate the critical need to consider the long-term impacts of maltreatment on inflammatory and cognitive health in later life. Understanding these connections can guide the development of targeted interventions aimed at mitigating the risk factors for adverse cognitive outcomes in this population.

AUTHOR NOTE

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OPEN PRACTICES STATEMENT

Data were provided by the Midlife in the United States (MIDUS) study (https://www.midus.wisc.edu/index.php). Investigators within the MIDUS study contributed to the design and implementation of MIDUS and/or provided data but did not participate in the analysis or writing of this report. We analyzed archival data that are not under our direct control; requests to access the data should be directed to the relevant archive. Requests for our complete analysis scripts can be sent via email to the lead author at hayes.1075@osu.edu

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REFERENCES

Abajobir, A. A., Kisely, S., Williams, G., Strathearn, L., & Najman, J. M. (2017). Childhood maltreatment and high dietary fat intake behaviors in adulthood: A birth cohort study. *Child Abuse & Neglect*, *72*, 147–153. https://doi.org/10.1016/j.chiabu.2017.08.002

Abramovitch, A., Short, T., & Schweiger, A. (2021). The C factor: Cognitive dysfunction as a transdiagnostic dimension in psychopathology. *Clinical Psychology Review*, *86*, Article 102007. https://doi.org/10.1016/j.cpr.2021.102007

Alfaddagh, A., Martin, S. S., Leucker, T. M., Michos, E. D., Blaha, M. J., Lowenstein, C. J., Jones, S. R., & Toth, P. P. (2020). Inflammation and cardiovascular disease: From mechanisms to therapeutics. *American Journal of Preventive Cardiology*, *4*, Article 100130. https://doi.org/10.1016/j.ajpc.2020.100130

Arnson, Y., Shoenfeld, Y., & Amital, H. (2010). Effects of tobacco smoke on immunity, inflammation and autoimmunity. *Journal of Autoimmunity*, *34*(3), J258–J265. https://doi.org/10.1016/j.jaut.2009.12.003

Ashraf-Ganjouei, A., Moradi, K., Bagheri, S., & Aarabi, M. H. (2020). The association between systemic inflammation and cognitive performance in healthy adults. *Journal of Neuroimmunology*, *345*, Article 577272. https://doi.org/10.1016/j.jneuroim.2020.577272

Barrientos, R. M., Kitt, M. M., Watkins, L. R., & Maier, S. F. (2015). Neuroinflammation in the normal aging hippocampus. *Neuroscience*, *309*, 84–99. https://doi.org/10.1016/j.neuroscience.2015.03.007

Baumeister, D., Akhtar, R., Ciufolini, S., Pariante, C. M., & Mondelli, V. (2015). Childhood trauma and adulthood inflammation: A meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor-α. *Molecular Psychiatry*, *21*(5), 642–649. https://doi.org/10.1038/mp.2015.67

Bernstein, D. P., Fink, L., Handelsman, L., Foote, J., Lovejoy, M., Wenzel, K., Sapareto, E., & Ruggiero, J. (1994). Initial reliability and validity of a new retrospective measure of child abuse and neglect. *American Journal of Psychiatry*, *151*(8), 1132–1136. https://doi.org/10.1176/ajp.151.8.1132

Bernstein, D., & Fink, L. (1998). *Manual for the Childhood Trauma Questionnaire*. The Psychological Corporation.

Beydoun, M. A., Dore, G. A., Canas, J.-A., Liang, H., Beydoun, H. A., Evans, M. K., & Zonderman, A. B. (2018). Systemic inflammation is associated with longitudinal changes in cognitive performance among urban adults. *Frontiers in Aging Neuroscience*, *10*, Article 313. https://doi.org/10.3389/fnagi.2018.00313

Brown, M., Worrell, C., & Pariante, C. M. (2021). Inflammation and early life stress: An updated review of childhood trauma and inflammatory markers in adulthood. *Pharmacology Biochemistry and Behavior*, *211*, Article 173291. https://doi.org/10.1016/j.pbb.2021.173291

Buckby, J. A., Yung, A. R., Cosgrave, E. M., & Killackey, E. J. (2007). Clinical utility of the Mood and Anxiety Symptom Questionnaire (MASQ) in a sample of young help-seekers. *BMC Psychiatry*, *7*(1), Article 50. https://doi.org/10.1186/1471-244x-7-50

Bui, T. M., Wiesolek, H. L., & Sumagin, R. (2020). ICAM-1: A master regulator of cellular responses in inflammation, injury resolution, and tumorigenesis. *Journal of Leukocyte Biology*, *108*(3), 787–799. https://doi.org/10.1002/jlb.2mr0220-549r

Carpenter, L. L., Carvalho, J. P., Tyrka, A. R., Wier, L. M., Mello, A. F., Mello, M. F., Anderson, G. M., Wilkinson, C. W., & Price, L. H. (2007). Decreased adrenocorticotropic hormone and cortisol responses to stress in healthy adults reporting significant childhood maltreatment. *Biological Psychiatry*, *62*(10), 1080–1087. https://doi.org/10.1016/j.biopsych.2007.05.002

Cavaillon, J. M., & Adib-Conquy, M. (2002). The pro-inflammatory cytokine cascade. In *Immune response in the critically ill* (Vol. 31, pp. 37–66), Springer-Verlag Berlin Heidelberg. https://doi.org/10.1007/978-3-642-57210-4_4

Chesnokova, V., Pechnick, R. N., & Wawrowsky, K. (2016). Chronic peripheral inflammation, hippocampal neurogenesis, and behavior. *Brain, Behavior, and Immunity*, *58*, 1–8. https://doi.org/10.1016/j.bbi.2016.01.017

Cohen, S., Janicki-Deverts, D., Doyle, W. J., Miller, G. E., Frank, E., Rabin, B. S., & Turner, R. B. (2012). Chronic stress, glucocorticoid receptor resistance, inflammation, and disease risk. *Proceedings of the National Academy of Sciences*, *109*(16), 5995–5999. https://doi.org/10.1073/pnas.1118355109

Cole, D. A., & Maxwell, S. E. (2003). Testing mediational models with longitudinal data: Questions and tips in the use of structural equation modeling. *Journal of Abnormal Psychology*, *112*(4), 558–577. https://doi.org/10.1037/0021-843x.112.4.558

D'Amico, D., Amestoy, M. E., & Fiocco, A. J. (2022). The mediating role of allostatic load in the relationship between early life adversity and cognitive function across the adult lifespan. *Psychoneuroendocrinology*, *141*, Article 105761. https://doi.org/10.1016/j.psyneuen.2022.105761

Dalthorp, D. (2021). *GenEst–R installation. Generalized mortality estimator*. https://cran.r-project.org/web/packages/GenEst/readme/README.html

Davis, M. C., Lemery-Chalfant, K., Yeung, E. W., Luecken, L. J., Zautra, A. J., & Irwin, M. R. (2018). Interleukin-6 and depressive mood symptoms: Mediators of the association between childhood abuse and cognitive performance in middle-aged adults. *Annals of Behavioral Medicine*, *53*(1), 29–38. https://doi.org/10.1093/abm/kay014

Di Filippo, M., Chiasserini, D., Gardoni, F., Viviani, B., Tozzi, A., Giampà, C., Costa, C., Tantucci, M., Zianni, E., Boraso, M., Siliquini, S., de Iure, A., Ghiglieri, V., Colcelli, E., Baker, D., Sarchielli, P., Fusco, F. R., Di Luca, M., & Calabresi, P. (2013). Effects of central and peripheral inflammation on hippocampal synaptic plasticity. *Neurobiology of Disease*, *52*, 229–236. https://doi.org/10.1016/j.nbd.2012.12.009

Duncan, O. D. (1961). A socioeconomic index for all occupations. In A. J. Reiss, Jr. (Ed.), *Occupations and social status* (pp. 109–138). Free Press.

Elliot, A. J., & Chapman, B. P. (2016). Socioeconomic status, psychological resources, and inflammatory markers: Results from the MIDUS study. *Health Psychology*, *35*(11), 1205–1213. https://doi.org/10.1037/hea0000392

Feeney, J., Kamiya, Y., Robertson, I. H., & Kenny, R. A. (2013). Cognitive function is preserved in older adults with a reported history of childhood sexual abuse. *Journal of Traumatic Stress*, *26*(6), 735–743. https://doi.org/10.1002/jts.21861

Franceschi, C., Bonafè, M., Valensin, S., Olivieri, F., De Luca, M., Ottaviani, E., & de Benedictis, G. (2000). Inflamm-aging: An evolutionary perspective on immunosenescence. *Annals of the New York Academy of Sciences*, *908*(1), 244–254. https://doi.org/10.1111/j.1749-6632.2000.tb06651.x

Furman, D., Campisi, J., Verdin, E., Carrera-Bastos, P., Targ, S., Franceschi, C., Ferrucci, L., Gilroy, D. W., Fasano, A., Miller, G. W., Miller, A. H., Mantovani, A., Weyand, C. M., Barzilai, N., Goronzy, J. J., Rando, T. A., Effros, R. B., Lucia, A., Kleinstreuer, N., & Slavich, G. M. (2019). Chronic inflammation in the etiology of disease across the life span. *Nature Medicine*, *25*(12), 1822–1832. https://doi.org/10.1038/s41591-019-0675-0

Geoffroy, M.-C., Pinto Pereira, S., Li, L., & Power, C. (2016). Child neglect and maltreatment and childhood-to-adulthood cognition and mental health in a prospective birth cohort. *Journal of the American Academy of Child & Adolescent Psychiatry*, *55*(1), 33–40.e3. https://doi.org/10.1016/j.jaac.2015.10.012

Giridharan, V. V., Masud, F., Petronilho, F., Dal-Pizzol, F., & Barichello, T. (2019). Infection-induced systemic inflammation is a potential driver of Alzheimer's disease progression. *Frontiers in Aging Neuroscience*, *11*, Article 122. https://doi.org/10.3389/fnagi.2019.00122

Goodman, J. B., Freeman, E. E., & Chalmers, K. A. (2018). The relationship between early life stress and working memory in adulthood: A systematic review and meta-analysis. *Memory*, *27*(6), 868–880. https://doi.org/10.1080/09658211.2018.1561897

Grainger, S. A., Crawford, J. D., Kochan, N. A., Mather, K. A., Chander, R. J., Draper, B., Brodaty, H., Sachdev, P. S., & Henry, J. D. (2019). An investigation into early-life stress and cognitive function in older age. *International Psychogeriatrics*, *32*(11), 1325–1329. https://doi.org/10.1017/s1041610219001583

Hawkins, M. A. W., Layman, H. M., Ganson, K. T., Tabler, J., Ciciolla, L., Tsotsoros, C. E., & Nagata, J. M. (2021). Adverse childhood events and cognitive function among young adults: Prospective results from the National Longitudinal Study of Adolescent to Adult Health. *Child Abuse & Neglect*, *115*, Article 105008. https://doi.org/10.1016/j.chiabu.2021.105008

Hayes, A. F. (2017). Partial, conditional, and moderated moderated mediation: Quantification, inference, and interpretation. *Communication Monographs*, *85*(1), 4–40. https://doi.org/10.1080/03637751.2017.1352100

Hayes, A. F., & Rockwood, N. J. (2017). Regression-based statistical mediation and moderation analysis in clinical research: Observations, recommendations, and implementation. *Behaviour Research and Therapy*, *98*, 39–57. https://doi.org/10.1016/j.brat.2016.11.001

Hillman, C. H., Erickson, K. I., & Kramer, A. F. (2008). Be smart, exercise your heart: Exercise effects on brain and cognition. *Nature Reviews Neuroscience*, *9*(1), 58–65. https://doi.org/10.1038/nrn2298

Hostinar, C. E., Lachman, M. E., Mroczek, D. K., Seeman, T. E., & Miller, G. E. (2015). Additive contributions of childhood adversity and recent stressors to inflammation at midlife: Findings from the MIDUS study. *Developmental Psychology*, *51*(11), 1630–1644. https://doi.org/10.1037/dev0000049

Huang, Z., Jordan, J. D., & Zhang, Q. (2023). Early life adversity as a risk factor for cognitive impairment and Alzheimer's disease. *Translational Neurodegeneration*, *12*(1), Article 25. https://doi.org/10.1186/s40035-023-00355-z

Hughes, M. L., Agrigoroaei, S., Jeon, M., Bruzzese, M., & Lachman, M. E. (2018). Change in cognitive performance from midlife into old age: Findings from the Midlife in the United States (MIDUS) study. *Journal of the International Neuropsychologi-*

cal Society, *24*(8), 805–820. https://doi.org/10.1017/s1355617718000425

Humphreys, K. L., LeMoult, J., Wear, J. G., Piersiak, H. A., Lee, A., & Gotlib, I. H. (2020). Child maltreatment and depression: A meta-analysis of studies using the Childhood Trauma Questionnaire. *Child Abuse & Neglect*, *102*, Article 104361. https://doi.org/10.1016/j.chiabu.2020.104361

Irigaray, T. Q., Pacheco, J. B., Grassi-Oliveira, R., Fonseca, R. P., Leite, J. C., & Kristensen, C. H. (2013). Child maltreatment and later cognitive functioning: A systematic review. *Psicologia: Reflexão e Crítica*, *26*(2), 376–387. https://doi.org/10.1590/s0102-79722013000200018

Jia, Y., Liu, L., Sheng, C., Cheng, Z., Cui, L., Li, M., Zhao, Y., Shi, T., Yau, T. O., Li, F., & Chen, L. (2019). Increased serum levels of cortisol and inflammatory cytokines in people with depression. *Journal of Nervous & Mental Disease*, *207*(4), 271–276. https://doi.org/10.1097/nmd.0000000000000957

Jurgens, S. M., Prieto, S., & Hayes, J. P. (2023). Inflammatory biomarkers link perceived stress with metabolic dysregulation. *Brain, Behavior, & Immunity–Health*, *34*, Article 100696. https://doi.org/10.1016/j.bbih.2023.100696

Karlamangla, A. S., Miller-Martinez, D., Lachman, M. E., Tun, P. A., Koretz, B. K., & Seeman, T. E. (2014). Biological correlates of adult cognition: Midlife in the United States (MIDUS). *Neurobiology of Aging*, *35*(2), 387–394. https://doi.org/10.1016/j.neurobiolaging.2013.07.028

Kaur, J., & Jain, A. (2023). Fibrinogen. StatPearls [Internet]. https://pubmed.ncbi.nlm.nih.gov/30725869

Kirova, A.-M., Bays, R. B., & Lagalwar, S. (2015). Working memory and executive function decline across normal aging, mild cognitive impairment, and Alzheimer's disease. *BioMed Research International*, *2015*, Article 748212. https://doi.org/10.1155/2015/748212

Lachman, M. E., Agrigoroaei, S., Tun, P. A., & Weaver, S. L. (2013). Monitoring cognitive functioning. *Assessment*, *21*(4), 404–417. https://doi.org/10.1177/1073191113508807

Lachman, M. E., Tun, P. A., & Murphy, C. L. (2021). *MIDUS 2, Project 3: Data file notes–cognitive test battery*. https://midus-study.github.io/public-documentation/M2P3/Documentation/M2_P3_BTACT_DataFile_Notes_20211122.pdfRelease—Updates—Dec2021—Documentation—M2_P3_BTACT_DataFile_Notes_20211122.docx

Lee, P.-L. (2014). Cognitive function in midlife and beyond. *International Journal of Aging and Human Development*, *79*(4), 263–278. https://doi.org/10.1177/0091415015574190

Leonardo, S., & Fregni, F. (2023). Association of inflammation and cognition in the elderly: A systematic review and meta-analysis. *Frontiers in Aging Neuroscience*, *15*, Article 1069439. https://doi.org/10.3389/fnagi.2023.1069439

Logue, M. W., van Rooij, S. J. H., Dennis, E. L., Davis, S. L., Hayes, J. P., Stevens, J. S., Densmore, M., Haswell, C. C., Ipser, J., Koch, S. B. J., Korgaonkar, M., Lebois, L. A. M., Peverill, M., Baker, J. T., Boedhoe, P. S. W., Frijling, J. L., Gruber, S. A., Harpaz-Rotem, I., Jahanshad, N., … Morey, R. A. (2018). Smaller hippocampal volume in posttraumatic stress disorder: A multisite Enigma-PGC study: Subcortical volumetry results from posttraumatic stress disorder consortia. *Biological Psychiatry*, *83*(3), 244–253. https://doi.org/10.1016/j.biopsych.2017.09.006

Lynch, K. S., & Lachman, M. E. (2020). The effects of lifetime trauma exposure on cognitive functioning in midlife. *Journal of Traumatic Stress*, *33*(5), 773–782. https://doi.org/10.1002/jts.22522

Lynch, K. S., & Widom, C. S. (2022). Childhood maltreatment and cognitive functioning in middle adulthood. *Child Abuse & Neglect*, *132*, Article 105791. https://doi.org/10.1016/j.chiabu.2022.105791

Marques-Feixa, L., Palma-Gudiel, H., Romero, S., Moya-Higueras, J., Rapado-Castro, M., Castro-Quintas, Á., Zorrilla, I., José Muñoz, M., Ramírez, M., Mayoral, M., Mas, A., José Lobato, M., Blasco-Fontecilla, H., Fañanás, L., & the EPI-Young Stress GROUP. (2021). Childhood maltreatment disrupts HPA-axis activity under basal and stress conditions in a dose–response relationship in children and adolescents. *Psychological Medicine*, *53*(3), 1060–1073. https://doi.org/10.1017/s003329172100249x

Marsland, A. L., Gianaros, P. J., Kuan, D. C., Sheu, L. K., Krajina, K., & Manuck, S. B. (2015). Brain morphology links systemic inflammation to cognitive function in midlife adults. *Brain, Behavior, and Immunity*, *48*, 195–204. https://doi.org/10.1016/j.bbi.2015.03.015

Mirescu, C., & Gould, E. (2006). Stress and adult neurogenesis. *Hippocampus*, *16*(3), 233–238. https://doi.org/10.1002/hipo.20155

Nehring, S. M., Patel, B. C., & Goyal, A. (2023). *C-reactive protein*. StatPearls [Internet]. https://pubmed.ncbi.nlm.nih.gov/28722873/

Nelson, J., Klumparendt, A., Doebler, P., & Ehring, T. (2017). Childhood maltreatment and characteristics of adult depression: Meta-analysis. *British Journal of Psychiatry*, *210*(2), 96–104. https://doi.org/10.1192/bjp.bp.115.180752

Nettis, M. A., Pariante, C. M., & Mondelli, V. (2019). Early-life adversity, systemic inflammation and comorbid physical and psychiatric illnesses of adult life. *Neuroinflammation and Schizophrenia*, *44*, 207–225. https://doi.org/10.1007/7854_2019_89

Nikulina, V., & Widom, C. S. (2013). Child maltreatment and executive functioning in middle adulthood: A prospective examination. *Neuropsychology*, *27*(4), 417–427. https://doi.org/10.1037/a0032811

Pahwa, R., Goyal, A., & Jialal, I. (2023). *Chronic inflammation*. StatPearls [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK493173/

Peng, C., Cheng, J., Rong, F., Wang, Y., & Yu, Y. (2023). Psychometric properties and normative data of the Childhood Trauma Questionnaire–Short Form in Chinese adolescents. *Frontiers in Psychology*, *14*, Article 1130683. https://doi.org/10.3389/fpsyg.2023.1130683

Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*(3), 385–401. https://doi.org/10.1177/014662167700100306

Riazi, K., Galic, M. A., Kentner, A. C., Reid, A. Y., Sharkey, K. A., & Pittman, Q. J. (2015). Microglia-dependent alteration of glutamatergic synaptic transmission and plasticity in the hippocampus during peripheral inflammation. *Journal of Neuroscience*, *35*(12), 4942–4952. https://doi.org/10.1523/jneurosci.4485-14.2015

Ritchie, K., Jaussent, I., Stewart, R., Dupuy, A.-M., Courtet, P., Malafosse, A., & Ancelin, M.-L. (2010). Adverse childhood environment and late-life cognitive functioning. *International Journal of Geriatric Psychiatry*, *26*(5), 503–510. https://doi.org/10.1002/gps.2553

Ryff, C. D., Almeida, D. M., Ayanian, J. Z., Carr, D. S., Cleary, P. D., Coe, C., Davidson, R. J., Krueger, R. F., Lachman, M. E., Marks, N. F., Mroczek, D. K., Seeman, T. E., Seltzer, M. M., Singer, B.

H., Sloan, R. P., Tun, P. A., Weinstein, M., & Williams, D. R. (2021). *Midlife in the United States (MIDUS 2), 2004–2006*. Inter-university Consortium for Political and Social Research. https://doi.org/10.3886/ICPSR04652.v8

Ryff, C., Almeida, D., Ayanian, J., Binkley, N., Carr, D. S., Coe, C., Davidson, R., Grzywacz, J., Karlamangla, A., Krueger, R., Lachman, M., Love, G., Mailick, M., Mroczek, D., Radler, B., Seeman, T., Sloan, R., Thomas, D., Weinstein, M., & Williams, D. (2019). *Midlife in the United States (MIDUS 3), 2013–2014*. Inter-university Consortium for Political and Social Research. https://doi.org/10.3886/ICPSR36346.v7

Silva, P. C., de Oliveira, L. L., Teixeira, R. L., Brito, M. L., & Filippe, A. R. (2022). Executive functions in Alzheimer's disease: A systematic review. *Journal of Alzheimer's Disease Reports*, *6*(1), 81–99. https://doi.org/10.3233/adr-210059

Silverman, M. N., Pearce, B. D., Biron, C. A., & Miller, A. H. (2005). Immune modulation of the hypothalamic-pituitary-adrenal (HPA) axis during viral infection. *Viral Immunology*, *18*(1), 41–78. https://doi.org/10.1089/vim.2005.18.41

Su, K.-P. (2012). Inflammation in psychopathology of depression: Clinical, biological, and therapeutic implications. *BioMedicine*, *2*(2), 68–74. https://doi.org/10.1016/j.biomed.2012.03.002

Swedo, E. A., Aslam, M. V., Dahlberg, L. L., Niolon, P. H., Guinn, A. S., Simon, T. R., & Mercy, J. A. (2023). *Prevalence of adverse childhood experiences among U.S. adults–behavioral risk factor surveillance system, 2011–2020*. Centers for Disease Control and Prevention. https://www.cdc.gov/mmwr/volumes/72/wr/mm7226a2.htm

Tanaka, T., Narazaki, M., & Kishimoto, T. (2014). IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspectives in Biology*, *6*(10), Article a106295. https://doi.org/10.1101/cshperspect.a016295

Teicher, M. H., Anderson, C. M., & Polcari, A. (2012). Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum. *Proceedings of the National Academy of Sciences*, *109*(9), e563–e572. https://doi.org/10.1073/pnas.1115396109

Timmerman, I., Daniel, A. E., Kroon, J., & van Buul, J. D. (2016). Leukocytes crossing the endothelium: A matter of communication. *International Review of Cell and Molecular Biology*, *322*, 281–329. https://doi.org/10.1016/bs.ircmb.2015.10.005

Tsalamandris, S., Antonopoulos, A. S., Oikonomou, E., Papamikroulis, G.-A., Vogiatzi, G., Papaioannou, S., Deftereos, S., & Tousoulis, D. (2019). The role of inflammation in diabetes: Current concepts and future perspectives. *European Cardiology Review*, *14*(1), 50–59. https://doi.org/10.15420/ecr.2018.33.1

Tulving, E., & Markowitsch, H. J. (1998). Episodic and declarative memory: Role of the hippocampus. *Hippocampus*, *8*(3), 198–204. https://doi.org/10.1002/(sici)1098-1063(1998)8:3⟨198::aid-hipo2⟩3.0.co;2-g

Tun, P. A., & Lachman, M. E. (2006). Telephone assessment of cognitive function in adulthood: The Brief Test of Adult Cognition by Telephone. *Age and Ageing*, *35*(6), 629–632. https://doi.org/10.1093/ageing/afl095

University of Wisconsin–Madison Institute on Aging. (2011). *Midlife in the United States Study: Project 4–Biomarker project*. https://midus.wisc.edu/midus2/project4/

University of Wisconsin–Madison Institute on Aging. (2022). *Midlife in the United States Study: History & overview of MIDUS*. https://midus.wisc.edu/scopeofstudy.php

University of Wisconsin–Madison Institute on Aging. (2024). *Documentation for psychosocial constructs and composite variables in MIDUS 2 Biomarkers Project*. https://midus-study.github.io/public-documentation/M2P4/Documentation/M2_P4_Documentation_for_PsychoSocialConstructs_and_CompositeVariables_20240408.pdf

U.S. Census Bureau. (2023). 2023 *national population projections tables: Main series*. https://www.census.gov/data/tables/2023/demo/popproj/2023-summary-tables.html

Walker, K. A., Gottesman, R. F., Wu, A., Knopman, D. S., Gross, A. L., Mosley, T. H., Selvin, E., & Windham, B. G. (2019). Systemic inflammation during midlife and cognitive change over 20 years. *Neurology*, *92*(11), e1256–e1267. https://doi.org/10.1212/wnl.0000000000007094

Walker, K. A., Hoogeveen, R. C., Folsom, A. R., Ballantyne, C. M., Knopman, D. S., Windham, B. G., Jack, C. R., & Gottesman, R. F. (2017). Midlife systemic inflammatory markers are associated with late-life brain volume. *Neurology*, *89*(22), 2262–2270. https://doi.org/10.1212/wnl.0000000000004688

Weleff, J., & Potter, D. (2023). Key updates to understanding roles of childhood trauma in overall health. *AMA Journal of Ethics*, *25*(2), E116–E122. https://doi.org/10.1001/amajethics.2023.116

Woods, J. A., Wilund, K. R., Martin, S. A., & Kistler, B. M. (2012). Exercise, inflammation and aging. *Aging and Disease*, *3*(1), 130–140.

Xie, Z., Li, M., Sun, H., Zhou, C., Fu, C., Wang, Q., Dong, C., Hao, W., Zhen, X., & Zhu, D. (2023). Childhood, adulthood, and cumulative traumatic events experienced from childhood to adulthood and dementia risk: A population-based cohort study. *Journal of Public Health*, Advance online publication. https://doi.org/10.1007/s10389-023-02140-8

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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