Biopsychosocial Science and Medicine Publish Ahead of Print
DOI:10.1097/PSY.0000000000001490

The Compounding Risks of Early Life Adversity and Couples' Later Life Conflicts in Biological Aging

M. Rosie Shrout, PhD (1), Stephanie J. Wilson, PhD (2), Megan E. Renna, PhD (3), Annelise A. Madison, PhD (4), MiKaila J. Leonard, MS (5), Lisa M. Christian, PhD (6,7), Elissa S. Epel, PhD (8), Christin E. Burd, PhD (9), Jue Lin, PhD (10), Samuel H. Molli, MA (2), Kelsi Broich, BS (3), Khiara Cardoza Brown, MS (1), Allison Swarens (5), and Janice K. Kiecolt-Glaser, PhD (6,7)

(1) Department of Psychology, The University of British Columbia, Vancouver, Canada
(2) Department of Psychology, University of Alabama at Birmingham, Birmingham, Alabama
(3) Department of Psychology, The Ohio State University, Columbus, Ohio
(4) Department of Psychology, University of Michigan, Ann Arbor, Michigan
(5) Department of Human Development and Family Science, Purdue University, West Lafayette, Indiana
(6) Department of Psychiatry & Behavioral Health, The Ohio State University Wexner Medical Center, Columbus, Ohio
(7) The Institute for Behavioral Medicine Research, The Ohio State University Wexner Medical Center, Columbus, Ohio
(8) Department of Psychiatry & Behavioral Sciences, University of California San Francisco, San Francisco, California
(9) Departments of Molecular Genetics, Cancer Biology and Genetics, The Ohio State

(10) University, Columbus, Ohio
(11) Department of Biochemistry and Biophysics, University of California San Francisco, San Francisco, California

Address correspondence to M. Rosie Shrout, PhD, University of British Columbia, 6200 University Blvd, Vancouver, BC V6T 1Z4. E-mail: rosie.shrout@psych.ubc.ca

Total Number of Tables: 2; Total Number of Figures: 1; Total Supplemental Digital files: 1
Article Editor: Bert Uchino

Source of Funding and Conflicts of Interest: This study was supported by the National Institute on Aging (R01 AG057032, PI: Kiecolt-Glaser). Costs for DNA methylation assays were partially offset by TruDiagnostic, and we thank Dr. Varun Dwaraka and Ryan Smith at TruDiagnostic. The authors declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

Acknowledgements: We thank Dr. Bill Malarkey for his contributions to this work.

Transparency and Openness: This study was not preregistered, nor was the data analysis plan. The study protocol, materials, data, and analytic code are available upon request.

Abstract

Objective: Abuse in both childhood and adult romantic relationships is linked to age-related health problems. Positive marital dynamics, however, can buffer stress and protect health, particularly as couples grow older. In this longitudinal study, we applied dyadic and life-course stress theories to examine how couples' destructive, abusive conflicts exacerbate biological aging associated with early life adversity, while constructive conflicts temper adversity's biological aging toll.

Methods: Married couples (n=107 couples, 214 individuals, ages 40–87 years) in mixed-sex relationships completed two visits, two years apart. Partners completed the Childhood Adversities scale, Childhood Trauma Questionnaire, and the Revised Conflict Tactics Scale short form. Blood-based measurements of biological aging included telomere length, T cell $p16^{INK4a}$ expression, and epigenetic age acceleration (EAA; PhenoAgeEAA, GrimAgeEAA, HannumEAA, Horvath2EAA, DunedinPACE).

Results: Linear mixed models showed those with greater childhood family adversities had shorter telomeres and accelerated epigenetic aging (PhenoAgeEAA, GrimAgeEAA, DunedinPACE). Over two years, childhood family adversities or maltreatment predicted larger rises in $p16^{INK4a}$ and accelerated epigenetic aging (Horvath2EAA, PhenoAgeEAA, DunedinPACE). Couples' destructive conflicts moderated concurrent effects: spouses who experienced adversity or maltreatment in both childhood and the past year of their marriage aged 10 months faster in GrimAgeEAA and DunedinPACE. Constructive conflicts were not related to biological aging nor helped offset adversity's biological aging toll.

Conclusions: Couples' destructive, abusive conflict tactics exacerbate the harmful effects of early life adversity on the rate of biological aging in mid-to-late life.

Adverse and abusive relationships in both early and later life show synergistic effects to accelerate biological aging.

Keywords: aging, marriage, relationships, stress, abuse

EAA=epigenetic age acceleration, CTQ=Childhood Trauma Questionnaire, TL=telomere length

Introduction

Although relationships often provide health benefits, adverse or abusive relational ties have significant health costs. Individuals who experience adversity in childhood or adult romantic relationships have an increased risk for metabolic disorders, chronic disease and pain, immune dysregulation, and heightened inflammation (1–4). More than 60% of adults in the United States and Canada have experienced early life adversity (5,6). These adversities often include childhood maltreatment (emotional, sexual, and physical abuse and emotional or physical neglect) and broader childhood family adversity, such as parental death, family alcoholism or psychiatric problems, not having a close relationship with any parent, and parental marital problems. Additionally, 1 in 4 women and 1 in 7 men have experienced at least one type of abuse (emotional, physical, or sexual) in romantic relationships, often referred to as intimate partner violence (7). The prevalence and severity of adversity in childhood and abuse in adult romantic relationships pose serious public health concerns, particularly with aging populations whose adverse exposures threaten their health and longevity. In this study of middle-aged and older couples, we examined how experiencing relational adversities in both early and later life interact to accelerate biological aging. Addressing these compounding effects reveals biological pathways through which adversity and abuse in childhood and adult relationships hasten morbidity and mortality.

Initial evidence and theoretical models suggest that both early and later life adverse experiences have the potential to accelerate biological aging, an important mechanism implicated in early age-related disease and death (2,8). Dyadic and life-course stress theories, including the stress responsiveness model, biological embedding hypothesis, and the dyadic biobehavioral stress model, suggest that

adverse relational experiences increase and exacerbate biological health risks throughout the lifespan (3,9,10). These frameworks propose that adverse experiences during early life occur within developmentally sensitive periods and alter the regulation of multiple physiological systems, thereby compromising long-term health. Chronic stress associated with adversity can drive poor health effects through sustained activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system, leading to over-release of glucocorticoids and catecholamines, and long-term changes in glucocorticoid receptor sensitivity (11). Over time, this stress-related activation promotes cellular stress, mitochondrial dysfunction, and systemic inflammation—processes implicated in biological aging. DNA methylation-based biomarkers of aging (epigenetic clocks) provide integrative estimates of biological age that predict morbidity and mortality risk and may be particularly responsive to relational stressors (12,13). As discussed in dyadic and life-course stress frameworks, adversity in intimate relationships, including emotional and physical abuse, are especially harmful in mid-to-late life when age-related disease risks are elevated (8). Consequently, adversity experienced in both early and later life relationships may especially exacerbate biological aging and foreshadow health decline.

Several studies have documented the toll of early life adversity on the speed of biological aging. Data from UK Biobank studies showed adults with childhood maltreatment had shorter telomere lengths, indicative of cell senescence, and older biological ages as measured by HannumAge, GrimAge, and PhenoAge DNA methylation-based epigenetic clocks (14,15). Likewise, in a representative sample of Americans over age 50, greater childhood family adversities predicted older GrimAge and a faster pace of aging as measured by the DunedinPoAm38 clock, increasing risks for early disease onset and shorter healthspans (16). Though the effects of early life

adversity on $p16^{INK4a}$ expression, a robust indicator of cellular senescence and key predictor of age-related disease (17), remain largely unaddressed, similar patterns may emerge. For instance, a study on mid-life parents showed chronic stress-related increases in $p16^{INK4a}$ expression over two months (18).

Initial examinations of adversity and abuse in intimate relationships have found associations with biological aging among middle-aged adults. Longitudinal data from the Dunedin Study showed adults who had been in romantic relationships at different points of the study had a slower PACE of aging, as measured by the DunedinPACE epigenetic clock, than those who were less relationally involved (19). However, among those in relationships, adults who experienced intimate partner violence had an accelerated PACE of aging. These findings parallel research using the UK Biobank and a community sample of young-to-midlife women showing shorter telomere length among those with a history of intimate partner violence (20,21). Though not equivalent to intimate partner violence, mid-life parents' arguing or fighting correlated with increased $p16^{INK4a}$ expression (11). Similarly, older adults' greater spousal strain was associated with an older HannumAge (22). In contrast, positive or supportive spousal relationships predicted longer telomere length (23) and younger epigenetic age (PhenoAge, GrimAge, DunedinPoAm38) in older adults (22).

The dyadic and life-course stress theories propose a compounding effect of relational adversities across the lifespan (3,9,10). For example, exposure to multiple relational adversities can contribute to cumulative stress that threatens health and accelerates age-related risks (24,25). Data from a representative population-based health survey showed that adults who experienced adversities in both childhood and adulthood had more health problems than those without either type of adversity (25). Likewise, several couples studies highlight that stress and conflict have harsher

effects on several age-related biomarkers if couples used negative or hostile behaviors (26–28). Hostile exchanges heighten inflammatory responses, enhancing disease and accelerated aging risks (2). In contrast, couples' positive or constructive behaviors help reduce or offset the biological toll of conflict. In a daily diary study of midlife parents, positive relationship dynamics buffered chronic stress-related biological aging: chronic stress predicted increased *CDKN2A* expression (encompassing $p16^{INK4a}$ and $p14^{ARF}$), only for parents who felt less close with their spouse (29). In contrast, greater relationship closeness helped protect parents from chronic stress-related *CDKN2A* increases. In addition, in a study of middle-aged and older couples, older couples showed lower inflammation in association with more constructive conflict tactics (2). These findings illustrate the compounding ill-effects of chronic stress and adversity, along with the buffering health benefits of couples' positive dynamics; however, the effects on accelerated biological aging remain untested despite the implications for serious chronic disease development and premature mortality (12,13,30). Research is needed to address how experiencing adversity and abuse across important and trusted relationships during pivotal life periods accelerates biological aging and undermines health.

In this study, we examined how adversities in early and later life compound to accelerate the rate of biological aging over two years. Investigating the far-reaching biological effects of early and later life relational adversity will help explain how abusive relationships across the life course foreshadow poor health in adulthood. We focused on middle-aged and older couples because, despite their age-related health risks, they remain an understudied group whose relationships are central to health. We tested effects across both established and cutting-edge biomarkers, including epigenetic age acceleration (EAA; PhenoAgeEAA, GrimAgeEAA, HannumEAA,

Horvath2EAA, and DunedinPACE), telomere length, and T cell $p16^{INK4a}$ expression, leading to a comprehensive picture of the consequences of early-to-later life adversity on biological aging. In particular, DNA methylation (DNAm)-based clocks estimated epigenetic age acceleration with first-generation clocks Horvath (31) and Hannum (32) predicting chronological age, second-generation clocks PhenoAge (33) and GrimAge (34) predicting healthspan and time-to-death, and third-generation DunedinPACE foreshadowing multiorgan system deterioration (35). Each of these clocks were of interest due to their predictive validity for clinically relevant aging outcomes in healthy populations, including chronic disease onset and mortality. Telomeres, composed of repetitive DNA elements that cap and protect the ends of chromosomes, were included because of the well-established relationship between shortened telomeres, morbidity, and mortality (36). Lastly, $p16^{INK4a}$ was of interest because it foreshadows age-related disease, including cardiovascular disease, arthritis, and Alzheimer's disease (12,30). These biomarkers reflect distinct age-related biological processes responsive to social factors and chronic stress (12,13,30).

Consistent with dyadic and life-course stress perspectives, we hypothesized that those with greater childhood family adversities, a history of childhood maltreatment, more frequent destructive (abusive) conflict tactics, and less frequent constructive conflicts would show faster biological aging cross-sectionally and two years later. We also expected that couples' destructive, abusive conflict tactics would exacerbate the rate of biological aging due to early life adversity, both concurrently and over two years. In contrast, we expected that constructive conflict tactics would temper biological aging tied to early life adversity, given positive marital dynamics can buffer stress and protect health (8,10).

Methods

Participants and Procedures

Mixed-sex couples in middle and older adulthood (N = 214 individuals in 107 couples) were recruited for a longitudinal study examining couple relationships and molecular aging. We used multiple recruitment mechanisms for a broad reach in the greater Columbus, Ohio region, including local newspaper advertisements, print and e-mail announcements in local community and work-place newsletters, and referrals from other participants. To reach and encourage couples with high conflict, recruitment materials also stated that we were interested in relationships that were going well and those that were having difficulties. Interested couples in a marriage or marriage-like relationship completed online and in-person screens to determine eligibility. Couples were excluded if they were cohabiting for fewer than three years, were younger than 40 years old, and had sensory or cognitive impairments that would interfere with study completion. To reduce bias in biological data, couples were excluded if either partner reported a range of chronic health problems (e.g., autoimmune conditions, cancer, chronic obstructive pulmonary disease, diabetes [Hba1c > 6.5], liver failure), smoked, abused substances, or took an immunomodulatory prescription medication. In total, 412 individuals were excluded for not meeting the health criteria.

The parent study's sample size was planned based on the expected power for hypothesized two-way interactions, which suggested that 220 individuals nested within 110 couples would be sufficient. The calculations used two-tailed tests, □=.05, and assumed a 10% attrition rate. They also relied on sample size adjustment for a couple-level intraclass correlation coefficient (ICC) of 0.10, resulting in an effective sample size of 200. Given the parent study's adequate power for similarly sized effects for the current study, it was concluded that the primary hypotheses for the

present study were powered.

At baseline, participants were primarily non-Hispanic white (92.1%), held a bachelor's degree or higher (86.9%), worked full-time (57%), had household incomes over $100,000 (57.5%), and were married and cohabiting with an average relationship duration of 28.62 years (*SD*=14.06 years, range = 3–63 years). The average age was 56.52 years (*SD*=11.22 years, range=40–87 years). A majority of the 107 couples who completed a baseline visit returned two years later for their second visit (*n*=92, 86.0%). A select few couples elected to complete surveys without collecting a blood sample (*n*=4, 3.7%), and 11 couples did not return for their second visit (10.3%). Those couples who did not return or provide blood samples at follow-up did not differ in demographics, relationship metrics, or health dimensions (age, education, comorbidities, years together as a couple).

Participants completed an in-person screen, followed by two identical study visits, two years apart, at a hospital research unit. The in-person screens were on average 3 months (*SD*=1.65) before each couple's Visit 1. The self-report measures for childhood family adversities, childhood maltreatment, and conflict tactics were assessed once per person at the initial in-person screen, and the blood samples were taken at the subsequent two study visits. Partners did not need to complete the screen together but were required to complete the two study visits together as a couple. If partners completed the initial screen as a couple, they completed the measures separately in different rooms. As part of the consent form and study website, provided before the initial screen, participants were told that during the screen and study visits, they would complete psychological questionnaires of a personal nature regarding their mood, health behaviors, health, feelings about their partner, and relationship; they were told that the questions may make them uncomfortable or produce stress. They

were provided with a list of psychological counseling services and were told that efforts would be made to keep their study-related information confidential. Prior to the subsequent two study visits, eligible couples were told to avoid alcohol and strenuous physical activity 2 days before each study visit. They began a 12-hour fast at 7:30 PM the evening before the visits and then arrived at 7:30 AM the next day. Each person was fitted with a venous catheter. Following a brief relaxation period, participants provided baseline blood samples, from which biological aging assays were performed. Data collection occurred between November 2017 and June 2022. Study procedures were approved by the Ohio State University Institutional Review Board and participants provided written informed consent.

Self-Report Measures

The Childhood Trauma Questionnaire (CTQ) was used to measure childhood maltreatment, a widely used self-report questionnaire that retrospectively measures abuse and neglect experienced prior to age 18 (37). Questions were related to physical (5 items; e.g., “people in my family hit me so hard that is left me with bruises or marks”), emotional (5 items; e.g., “people in my family said hurtful or insulting things to me”), and sexual (5 items; e.g., “someone tried to touch me in a sexual way or tried to make me touch them”) abuse, as well as emotional (e.g., “I felt loved” [reverse coded]) and physical (e.g., “I didn’t have enough to eat”) neglect. Participants responded on a 5-point Likert scale ranging from “never true” to “very often true” about childhood experiences. Consistent with previous research on childhood maltreatment’s implications for age-related outcomes (1,14,38), high-sensitivity CTQ cut-off scores were used to identify individuals reporting emotional (10+), physical (8+), and sexual abuse (8+) and physical (8+), and emotional (15+) neglect (39). These cut-scores are well-established and represent a clinically meaningful threshold

of severe maltreatment (39). Individuals were classified as reporting a history of any childhood maltreatment if they scored above the threshold on one or more types of abuse or neglect (yes/no if someone experienced maltreatment). Sensitivity analyses using the CTQ as a continuous variable (i.e., an overall average of all abuse and neglect items) to examine effects of maltreatment severity on biological aging were conducted and reported in the Supplemental Digital Content S1, https://links.lww.com/PSY/A1. The CTQ demonstrates strong internal consistency and reliability across a range of samples worldwide (40).

Data on childhood family adversity were obtained from the Childhood Adversities scale (41,42). Questions related to the presence or absence (yes/no) of experiencing parental death, family alcoholism, family psychiatric problems, not having a close relationship with any parent, and parental marital problems. Items were summed to create a variable in which higher scores indicated greater childhood family adversity.

The Revised Conflict Tactics Scale short form (CTS2S) provided data on couple-level constructive and destructive conflict tactics in the past year (43). The short form has comparable validity to the full scale and is a useful screening instrument for intimate partner violence (43). Half of the items assessed an individual's own behavior during conflicts, and the other half assessed their partner's behavior. Destructive conflict tactics included psychological aggression (4 items; e.g., "My partner insulted or swore or shouted or yelled at me"; "I destroyed something belonging to my partner or threatened to hit my partner") and physical aggression (4 items; e.g., "I pushed, shoved, or slapped my partner"; "My partner punched or kicked or beat me up") subscales. Constructive conflict tactics included cognitive and emotional negotiation subscales (4 items; e.g., "My partner explained his or her side

or suggested a compromise for a disagreement with me"; "I showed respect for, or showed that I cared about, my partner's feelings about an issue we disagreed on"). Response options ranged from "Once in the past year", "Twice in the past year", "3–5 times in the past year", "6–10 times in the past year", "11–20 times in the past year", "More than 20 times in the past year", "Not in the past year, but it has happened before", and "This has never happened." Consistent with past scoring and to index past-year frequency, answers were scored at their midpoint if there was a range (e.g., 4 for 3–5 times in the past year); if participants reported that it had never happened or had not happened in the past year, they received a score of zero; if participants reported that it occurred more than 20 times in the past year, they received a score of 25 in line with convention (44). For each subscale, items were aggregated such that higher total scores reflected a greater occurrence of the conflict tactic in the past year. The ceiling score for the eight-item destructive conflict aggregate was 200, whereas the highest possible score for the four-item constructive conflict aggregate was 100. Cronbach α is not computed for this scale, given that there is no total score, and each subscale consists of two items assessing own behavior and two items assessing partner behavior (43). We created separate composite scores for destructive and constructive conflict, each including individuals' rating of themselves and their partners, due to the high correlations between these ratings (r values 0.65 to 0.88). This composite is in line with prior studies that have used a composite of self and partner hostile behavior (44).

Biological Aging Marker Assays

Human CD3+ T cells were isolated from density gradient derived peripheral blood mononuclear cells (PBMCs) using the EasySep Human T Cell Enrichment kit (StemCell Technologies, Vancouver, Canada). The DNA and RNA were extracted

from the T cells using the Quick DNA/RNA Miniprep Plus kit (Zymo Research, Irvine, CA). The concentration and purity of the DNA/RNA was assessed on a NanoDrop One (Fisher Scientific, Pittsburgh, PA).

DNA from PBMCs was aliquoted and sent to TruDiagnostic (Lexington, KY) for methylation analysis using Illumina Infinium MethylationEPICv1 BeadChips. TruDiagnostic applied established epigenetic clock algorithms along with combinatorial normalization processing (Funnorm procedure) and RCP (ENmix package) to reduce sample variation as described (45). Horvath2EAA, HammumEAA, GrimAgeEAA, PhenoAgeEAA, and DunedinPACE were analyzed in the current study due to their predictive validity for clinically relevant aging outcomes. GrimAge and PhenoAge, second-generation epigenetic clocks, are trained models using blood-based measures to predict mortality and disease burden, respectively, and build on earlier-generation Horvath2EAA and HammumEAA clocks that predicted chronological age (31–34). EAA was calculated via the residuals of models that regressed each clock on chronological age to enable interpretation of how much older a person's biological age is compared to their chronological age. We used principal component (PC) corrected Horvath2EAA, HannumEAA, GrimAgeEAA, and PhenoAgeEAA clocks to improve reliability of epigenetic clocks. DunedinPACE, a third-generation clock, was developed using 20-year trajectories of physiological and biological changes in a young-adult cohort, reducing conflation of chronic disease incidence with normative aging processes (35). Acceleration across these biological clocks has predicted earlier morbidity and mortality (12,13,30).

Telomere length was measured in DNA from PBMC-derived T cells using quantitative polymerase chain reaction (qPCR). Results represent the ratio of telomeres versus single copy gene (human beta-globin) abundance (T/S). The T/S

ratio for each sample were measured twice, each in triplicate wells. When the duplicate T/S value and initial value varied by more than 7%, the sample was run a third time, and the two closest values were reported. Details of the telomere length assay protocol can be found at https://trn.tulane.edu/wp-content/uploads/sites/72/2021/07/Lin-qPCR-protocol-01072020.pdf, and these procedures follow the gold standard methods recommended by the Telomere Research Network (46,47). The inter-assay coefficient of variation was 2.1±1.5% for this study. The intra-class correlation (ICC) of duplicate DNA extractions from 29 samples was 0.976 (95% CI: 0.948-0.988).

A custom Nanostring nCounter Gene Expression Codeset (OSU_Senescence) was used to measure $p16^{INK4a}$ expression (48). The integrity and concentration of all RNA samples run on the OSU_Senescence platform was confirmed on an Illumina Tapestation. Post-run analysis included automated quality control procedures to ensure measurement linearity and quality. Samples not meeting quality controls were examined for irregularities and removed from further analyses if it was deemed that RNA clean-up and/or re-analysis could not correct for these issues.

Analytical Plan

We first conducted descriptive statistics, such as frequencies, means, SDs, correlations, and sex differences in study variables. We also examined test-retest correlations in the biological aging measures. Linear mixed models were then used to test the study hypotheses, which accounted for within-person and couple-level correlations. Models included random intercepts using a variance components covariance structure to account for the similarity in spouses' outcomes; we also accounted for the similarity in the residuals of the spouses' variables at the two time points using an unstructured covariance matrix. A strength of mixed models is that

they account for missing data by maximizing the use of existing values. Mixed model analyses were performed using the MIXED MODELS procedure with restricted maximum likelihood estimation in SPSS version 30. Covariates included sex and comorbidities, with models predicting telomere length and $p16^{INK4a}$ also controlling for chronologic age. Visit was controlled for in concurrent models. Covariate effects are reported in the Supplemental Digital Content S1, https://links.lww.com/PSY/A1. Before the primary analyses, the continuous independent variables (destructive conflict, constructive conflict) and continuous covariates (comorbidities, chronologic age) were grand mean-centered to improve the interpretability of the intercepts. Childhood maltreatment (no maltreatment = 0, maltreatment = 1) and dichotomous covariates entered as categorical variables (sex: male = 0, female = 1; visit: Visit 1 = 0, Visit 2 = 1). Telomere length and $p16^{INK4a}$ were log-transformed to correct for skewed residuals.

To examine hypotheses that early life adversity and couples' conflict tactics would predict biological age concurrently, we specified models examining biological aging markers at both visits as a function of concurrent childhood family adversity, childhood maltreatment, destructive conflict tactics, and constructive conflict tactics in separate models. Then, to test prospective associations, we used the same process but predicted changes in each Visit 2 aging biomarker while controlling for the respective Visit 1 biomarker. To test moderation hypotheses that early life adversity and conflict tactics would interact to predict biological aging, we examined two-way interactions with each early-life adversity and conflict tactics variable in separate models. Significant interacting effects were probed at one standard deviation above and below the means for each continuous interacting variable. We used the Benjamini–Hochberg false discovery rate method to account for multiple comparisons

(Benjamini & Hochberg, 1995); this method controls the error rate of false positives by considering the number of significant results in a family of tests. As discussed by McDonald (49), a false discovery rate (FDR) of 0.05 is likely too low for the Benjamini–Hochberg correction, and a rate of up to 0.20 is suggested. All associations reported held after FDR adjustments and fell below an FDR of 0.15. Code and data are available upon request from the first author; this study was not preregistered.

Results

Descriptive Statistics

Overall, 43% of the sample (92 people) had a history of childhood maltreatment. This included 26% of the sample reporting a history of emotional abuse, 21% reporting physical abuse, and 11% reporting sexual abuse, as well as 18% reporting emotional neglect and 21% reporting physical neglect. Sixty-one percent of the sample also reported at least one childhood family adversity, with most people reporting one adverse event (29%), followed by two (19%), three (9%), and four (4%) adverse events. People most commonly reported parental marital problems (29%) and family member psychiatric problems (29%), followed by not having a close relationship with at least one parent (28%), having a family member with alcoholism (21%), and their father (5%) or mother (1%) passing before age 17.

For conflict tactics, 99% of the sample reported that their marital conflicts included a constructive tactic negotiation in the past year, including emotional (98%) and cognitive (98%) negotiation. As for destructive tactics, a total of 66% of participants reported that their marital conflicts included psychological aggression, and 5% indicated physical assault and 7% indicated sexual coercion occurred. For questions related to these behaviors occurring at some point in their relationship, all but one participant (99.5%) reported the constructive tactic negotiation had occurred,

86% reported psychological aggression occurred, 20% reported physical assault occurred, and 13% reported sexual coercion occurred. Among those who reported that these tactics occurred in the past year, the average number of conflicts in which constructive tactics (emotional or cognitive negotiation) occurred was 38.97 (27.29), and 6.65 (10.65) conflicts for psychological aggression or physical assault.

Females had greater childhood family adversities ($M_{females}$= 1.39, SD = 1.24, M_{males}= 0.85, SD = 0.98, t(385) = -4.85, p < .001), were more likely to experience childhood maltreatment (χ^2(1, 406) = 4.48, p = .036), and reported more frequent destructive conflicts ($M_{females}$= 7.82, SD = 12.94, M_{males}= 5.63, SD = 8.12, t(342) = -2.05, p = .041). Females also showed younger biological aging across HannumEAA ($M_{females}$= -0.74, SD = 4.62, M_{males}= 0.74, SD = 4.30, t(385) = 3.25, p = .001), PhenoAgeEAA ($M_{females}$= -0.57, SD = 5.16, M_{males}= 0.58, SD = 4.80, t(383) = 2.26, p = .024), GrimAgeEAA ($M_{females}$= -1.19, SD = 2.09, M_{males}= 1.20, SD = 2.11, t(383) = 11.17, p < .001), DunedinPACE ($M_{females}$= 0.81, SD = 0.09, M_{males}= 0.84, SD = 0.09, t(383) = 3.47, p = .001), and telomere length ($M_{females}$= 1.95, SD = 0.04, M_{males}= 1.94, SD = 0.03, t(383) = 0.06, p < .001). There were no sex differences in constructive conflicts, Horvath2EAA, or $p16^{INK4a}$ expression (ps > .530).

Test-retest correlations showed good reliability for each index of biological aging across the two years: Horvath2EAA (r = 0.84, p < .001), HannumEAA (r = 0.83, p < .001), PhenoAgeEAA (r = 0.84, p < .001), GrimAgeEAA (r = 0.85, p < .001), DunedinPACE (r = 0.84, p < .001), telomere length (r = 0.96, p < .001), and $p16^{INK4a}$ (r = 0.63, p < .001). As shown in Table 1, correlations between chronological age and the non-EAA biological aging variables, telomere length and $p16^{INK4a}$, were moderate to large at each visit. Correlations were significant between baseline age and two-year changes in telomere length (r = -0.18, p = 0.019) but not $p16^{INK4a}$ (r = -0.07,

$p = 0.375$).

Concurrent Effects of Early Life Adversity and Couples' Conflicts on the Rate of Biological Aging

As shown in Table 2, those with greater childhood family adversities had shorter telomeres ($p = .023$) and faster epigenetic aging (PhenoAgeEAA, GrimAgeEAA, DunedinPACE; ps $< .05$). According to GrimeAgeEAA, for each additional childhood family adversity, adults aged another 2.16 months (Estimate = 0.18), meaning they were biologically ~2.16 months older than their chronological age. For PhenoAgeEAA, adults aged ~2.04 months biologically (Estimate = 0.17) with each additional childhood family adversity. For DunedinPACE, each additional childhood family adversity corresponded to another ~3.3 days per chronological year; for example, adults with one childhood family adversity aged 9.90 months per chronological year (Estimate for one adversity = 0.825), and those with two adversities aged 10.01 months per chronological year (Estimate for two adversities = 0.834). Effects of childhood family adversities on Horvath2EAA, HannumEAA, and $p16^{INK4a}$ expression were not significant, nor were associations between childhood maltreatment and biological aging.

There were no significant main effects of constructive and destructive conflict tactics on biological aging; however, destructive conflict tactics moderated the effects of childhood family adversity on GrimAgeEAA ($B = 0.15$, $SE = 0.06$, $p = .025$) and DunedinPACE ($B = 0.21$, $SE = 0.06$, $p < .001$, as well as a history of childhood maltreatment on DunedinPACE ($F(1, 275) = 7.15$, $p = .008$). As shown in Figure 1a-1b, greater family childhood adversities predicted accelerated epigenetic aging only among those with highly destructive couple conflicts (GrimAgeEAA: $B_{\text{high destructive conflicts}} = 0.31$, $SE = 0.09$, $p = .001$; $p_{\text{low destructive conflicts}} = .86$; DunedinPACE: $B_{\text{high destructive}}$

$_{\text{conflicts}}$= 0.30, *SE* = 0.08, $p < .001$; $p_{\text{low destructive conflicts}}$= .14). Likewise, couples' destructive conflicts predicted faster epigenetic aging only among those with more childhood family adversities (GrimAgeEAA: $B_{\text{high adversities}}$= 0.21, *SE* = 0.09, $p = .03$; $p_{\text{low adversities}}$=.382; DunedinPACE: $b_{\text{high adversities}}$= 0.20, *SE* = 0.09, $p = .038$; $p_{\text{low adversities}}$ = .053). Thus, the combination of childhood family adversities and destructive conflicts predicted faster epigenetic aging. That is, those with higher levels of both childhood family adversities and destructive, abusive conflicts showed age acceleration in their GrimAgeEAA (Estimate = 0.87) of ~10.4 months older biologically than their chronological age. In contrast, those with lower levels of childhood adversities or destructive conflicts showed GrimAgeEAA deceleration (Estimates = -0.07 to -.26), ~3 weeks to 3.1 months younger biologically than their chronological age. For DunedinPACE, adults with higher levels of both childhood family adversities and destructive conflicts aged 10.1 months per chronological year (Estimate = 0.85). Those with fewer childhood adversities or destructive conflicts aged 9.6 to 9.7 months per chronological year (Estimates = 0.80 to 0.81), reflecting a slower PACE of aging.

As shown in Figure 1c, findings were similar for childhood maltreatment: couples' destructive conflicts predicted faster DunedinPACE only among those with a history of childhood maltreatment ($b_{\text{maltreatment history}}$= 0.21, *SE* = 0.07, $p = .005$; $p_{\text{no maltreatment history}}$ = .377). The effects of childhood maltreatment at both low and high destructive conflicts were not significant (*p*s > .062). Thus, adults who experienced childhood maltreatment and higher levels of destructive conflicts aged 10.1 months per chronological year (Estimate = 0.85); those without a history of childhood maltreatment or fewer destructive conflicts aged 9.6 to 9.7 months per chronological year (Estimates = 0.81 to 0.82), a slower PACE of aging.

Prospective Effects of Early Life Adversity and Couples' Conflicts on the Rate of Biological Aging

Longitudinal associations showed those with greater childhood family adversities had larger rises in Horvath2EAA (p = .049), DunedinPACE (p = .041), and $p16^{INK4a}$ (p = .015) two years later. For each additional childhood family adversity, adults aged about 1 week faster over time in Horvath2EAA (Estimate = 0.02, meaning they were biologically ~1 week older than their chronological age with each adversity). They also developed a faster PACE of aging, ~ 1.7 months additional biological aging per chronological year for each childhood family adversity (change Estimate for 1 childhood family adversity = 0.13; change Estimate for 2 childhood adversities = 0.27).

For those with a history of childhood maltreatment, they showed greater rates of change in Horvath2EAA (p = .017), PhenoAgeEAA (p = .043), and DunedinPace (p = .038) two years later than those without such a history. Accordingly, compared to those without such a history, those with a history of childhood maltreatment aged ~4.3 months faster in Horvath2EAA over the two years (Estimate = 0.36), 3.6 months faster in PhenoAgeEAA (Estimate = 0.30), and showed 3.6 months of additional biological aging per chronological year in their PACE of aging. Contrary to hypotheses, associations with GrimAgeEAA (ps > .160) and telomere length (ps > .352) were not significant; the main (ps > .142) and moderating (ps > .183) effects of constructive and destructive conflict tactics were also not significant.

Discussion

Consistent with dyadic and life-course stress theories, this study demonstrated the compounding effects of early and later life adversities on accelerated biological aging among middle-aged and older couples. Those with greater adversities or maltreatment

in childhood had faster epigenetic aging in mid-to-late life, most notably if they engaged in destructive conflicts with their spouse in the past year. Contrary to hypotheses, these effects were not shown for constructive conflicts, suggesting that aging biomarkers may be particularly sensitive to couples' hostile interactions. Childhood family adversity was consistently related to accelerated aging across biomarkers concurrently and over two years, while the toll of childhood maltreatment on biological age occurred over time. These findings illustrate the combined accelerated aging risks of adverse and abusive relationships in both early and later life, revealing potential biological pathways to adversity-related increases in morbidity and mortality.

Concurrently, childhood family adversity, including parental or family death, family problems, parental alcohol abuse, and psychiatric issues, was linked to shorter telomere length and older epigenetic age as measured by PhenoAgeEAA, GrimAgeEAA, and DunedinPACE. Thus, for each additional childhood family adversity, adults aged 2 to 2.2 months faster in GrimeAgeEAA and PhenoAgeEAA and ~3.3 days in their PACE of aging per chronological year. Prospectively, those with greater childhood family adversities aged faster in Horvath2EAA and DunedinPACE and experienced increased $p16^{INK4a}$ expression over two years compared to their counterparts with fewer childhood family adversities. Though childhood maltreatment, including emotional, sexual, and physical abuse as well as emotional and physical neglect, was not associated with biological aging concurrently, those who experienced childhood maltreatment aged faster as measured by Horvath2EAA. PhenoAgeEAA, and DunedinPACE over the two-year study period than those without such a history. To illustrate, adults with a history of childhood maltreatment or family adversities aged 1 week to 4.3 months faster over the next two

years in Horvath2EAA, 1.7 to 3.6 months in their PACE of aging, and 3.6 months faster in PhenoAgeEAA compared to those without such histories.

These findings are consistent with previous research linking early life adversity to shorter telomere length and faster epigenetic aging (11-13); importantly, the findings extend prior work by demonstrating greater adversity-related changes across an array of aging biomarkers over time. While previous research suggested stress-sensitive effects on cellular senescence (18), the current study identified childhood family adversities as a key predictor of increased $p16^{INK4a}$ expression over time. These findings highlight the importance of taking a life course perspective and investigating longitudinal changes in biological aging, particularly among middle-aged and older adults who are susceptible to rapid health declines. Even in mid-to-later life, early life adversity may accelerate biological aging and threaten long-term health. Interestingly, childhood maltreatment's prospective effects were not shown in the sensitivity analyses when using the continuous CTQ score, a more gradient-like measure of childhood maltreatment severity, and instead were evident only when using the high-sensitivity cut-score. The cut-score was designed to identify clinically meaningful thresholds of severe maltreatment (37). It is possible that only people with clinically-relevant and severe levels of childhood maltreatment show accelerated biological aging. Thus, childhood maltreatment may have more of a threshold than continuous, gradient-like effect on biological aging over time.

Moderation results identified couples' destructive or abusive conflict tactics as particularly harmful for those who also experienced early life adversity. Indeed, spouses with greater childhood family adversities had a greater GrimAgeEAA and faster DunedinPACE of aging than those with fewer adversities, but only if couples engaged in more frequent destructive conflicts in the past year. Likewise, among those

who experienced greater childhood family adversities, spouses with more destructive conflicts had an accelerated GrimAgeEAA and faster PACE of aging than those with fewer destructive conflicts. Accordingly, the combination of childhood family adversities and destructive conflicts predicted faster biological aging. For those who experienced childhood maltreatment, they had a faster DunedinPACE of aging if they also engaged in more frequent destructive conflicts in the past year. To illustrate, adults with a history of childhood maltreatment or family adversities and had destructive, abusive conflicts with their spouse in the past year aged 10.4 months faster in GrimAgeEAA and 10.1 months in their PACE of aging per chronological year than those without such histories or destructive conflicts. Sensitivity analyses showed moderation effects were similar when assessing childhood maltreatment using the continuous, gradient-like CTQ score. In addition to a faster DunedinPACE of aging, adults with higher levels of childhood maltreatment had greater GrimAgeEAA if they also had more frequent destructive conflicts, a marginal effect using the CTQ cut-score. Thus, faster epigenetic aging may occur for individuals with high levels of childhood maltreatment and for those who meet a high sensitivity threshold of maltreatment, but only if they also experience frequent destructive, abusive conflicts with their spouse. In contrast, if spouses experienced childhood family adversities or childhood maltreatment, couples' less frequent destructive conflicts may have helped reduce early life adversity's biological aging costs.

These findings reveal the cumulative biological impact of relational adversities experienced across both childhood and adulthood. Aligning with, and extending, dyadic and life-course stress theories (3,9,10), this study highlights how relational adversity and abuse during developmentally sensitive periods—childhood and mid-to-older adulthood—pose unique biological risks. Models of stress

responsiveness and biological embedding suggest that early life adversity can dysregulate physiological systems, setting the stage for long-term health problems (3,9). Adversity in later life may compound these effects, further taxing dysregulated systems and increasing vulnerability to age-related disease. From a relational life-course perspective, this study identified both early and later life relational adversities—particularly within family/parental and spousal relationships—as key predictors of accelerated biological aging. Biologically, it may be especially harmful to experience adversity in both family/parental and spousal relationships because these are often people's most important and trusted bonds in each respective stage of life. This is particularly salient in later life when couples' relationships are central to health, yet they face heightened risks for chronic disease and age-related decline (50,51). These age-related risks are significant, given that accelerated biological aging underlies the onset and worsening of serious chronic conditions and premature mortality (12,13,30). Adversities across core relationships during pivotal periods of life may accelerate biological aging and undermine long-term health.

Although early life adversity and destructive conflicts interacted to predicted faster biological aging at each visit, their interactive effects did not predict changes in the pace of biological aging over time. It is possible that the combination of early and later relational adversities may amplify physiological burden, resulting in elevated biological aging levels without changing the rate of biological aging over two years. In contrast, given that childhood family adversity and maltreatment predicted prospective changes in biological aging over the two-year period, a decades-long history of adversity may become biologically embedded in ways that promote continued acceleration of biological aging over time (3,11). Concurrent levels of biological aging may therefore be particularly sensitive to the combined effects of

early and later life adversity. In contrast, changes in the rate of biological aging over two years may be less responsive to proximal adversity in later life and more reflective of long-standing biological embedding associated with early life adversity.

Unexpectedly, constructive conflicts were not related to biological aging nor helped offset adversity's biological aging toll. These non-significant effects were surprising given that middle-aged and older couples' positive relationship dynamics are linked to better health and lower risks across the hallmarks of aging (8,52,53). However, negative relationship dynamics often have a stronger and longer-lasting health impact than the positive dynamics (54,55). Since nearly all couples endorsed using constructive strategies, there be restricted variance on this measure in this sample. It is also possible that constructive conflict tactics over the past year might not be time-sensitive enough to influence biological aging markers. Measures capturing greater variability and range of positive conflict behaviors, along with more recent positive relational interactions, may exert stronger biological effects.

In the current study, a large proportion of the sample experienced early life adversity: 61% reported family adversity and 43% reported childhood maltreatment. Likewise, two-thirds of the sample indicated that their marital conflicts included psychological aggression the past year, with an average of seven times. Most spouses (86%) also reported psychological aggression ever occurring, along with one in five reporting physical assault and one in ten reporting sexual ever occurring in their current relationship. Though these percentages are consistent with past research and national estimates (5–7), they are alarming. This research provides evidence for age-related biological consequences associated with both childhood and adult relationship adversity and abuse. Investing in programming to prevent such troubled relational dynamics and help support those with current or past abuse may help slow biological

aging and improve the healthspan. Prevention and intervention programming should be a priority at both individual and systemic levels, including providing access to trauma-informed services, holding abusers accountable, and challenging societal norms that normalize violence in family and intimate relationships (56,57).

Strengths of this study include a relational life-course course perspective that identified both early and later life relational adversities as key biological aging risk factors. Importantly, this approach revealed accelerated biological aging among those who experienced adversity or abuse in both family/parental and spousal relationships. This study also provided evidence for adversity's lasting health effects on middle-aged and older couples, an understudied group whose relationships are central to their health (8,50). Following up with couples two years later allowed us to test prospective associations and demonstrate adversity-related increases in biological aging over time. The inclusion of multiple biological markers also demonstrated early and later life adversity's biological toll across an array of established and cutting-edge aging biomarkers that foreshadow chronic disease onset, functional decline, and premature mortality (12,13,30). Taken together, these findings highlight the far-reaching biological health effects of early and later life relational adversity, helping explain how abusive relationships across the life course contribute to morbidity and mortality.

A limitation of this study was that the sample may not be representative of all middle-aged and older couples. The couples were all different-sex and comprised of primarily White and highly educated partners in good health. It is important for research to include same-sex couples to understand how relational adversities influence biological aging among those who may have also experienced sexuality-based discrimination. Likewise, although couples were recruited for their good health to reduce bias in biological data, avoid disease- and medication-confounds, and to

foreshadow significant health changes more accurately, the sample was relatively healthy. It is important to assess adversity's long-term health effects across samples with greater diversity in health challenges. It would be meaningful to examine associations in a larger sample that recruits adults specifically with a range of early life adversities and conflict levels. Likewise, investigations in an age-diverse sample would further address how current IPV and age exacerbate the negative health effects of childhood family adversity and maltreatment. The early life adversity measures are widely used instruments for evaluating childhood family adversity and maltreatment, though they rely on retrospective reports that are subject to memory and recall bias. Findings should be replicated using prospective reports of adversity and maltreatment. Sensitivity analyses showed concurrent effects were similar using the continuous CTQ and its high-sensitivity cut-score, however, prospective effects were only shown in the cut-score models. It is important for future research to test effects using both threshold and continuous measures to examine their unique associations with biological markers of health and aging. Such results have implications for practice and policy, including using certain measures for determining eligibility for social and health-related services.

In sum, this longitudinal study demonstrated the combined accelerated biological aging risks of adverse and abusive relationships in both early and later life. Spouses who experienced childhood maltreatment or greater family adversities had older epigenetic ages and a faster pace of aging than those without such histories cross-sectionally and over time. Likewise, those with greater childhood adversities also had shorter telomeres and increased $p16^{INK4a}$ expression. Adversity-related biological aging was exacerbated by the additional presence of couples' destructive, abusive conflict tactics: spouses who experienced adversity or abuse in both

childhood and the past year of their marriage aged about 10 months faster in GrimAgeEAA and DunedinPACE. In contrast, spouses with fewer destructive conflicts were biologically younger, even if they experienced early life adversity. This work contributes to research and theory on the biological pathways through which adversity and abuse in people's closest relationships and across the life course foreshadow health in adulthood.

References

1. Renna ME, Peng J, Shrout MR, Madison AA, Andridge R, Alfano CM, et al. Childhood abuse histories predict steeper inflammatory trajectories across time. Brain, Behavior, and Immunity. 2021;91(November):541–5. doi:10.1016/j.bbi.2020.11.012 PubMed PMID: 33166662.

2. Madison AA, Wilson SJ, Shrout MR, Malarkey WB, Kiecolt-Glaser JK. Intimate Partner Violence and Inflammaging: Conflict Tactics Predict Inflammation Among Middle-Aged and Older Adults. Psychosom Med. 2024;86(5):379–86. doi:10.1097/PSY.0000000000001179

3. Miller GE, Chen E, Parker KJ. Psychological Stress in Childhood and Susceptibility to the Chronic Diseases of Aging: Moving Toward a Model of Behavioral and Biological Mechanisms. Psychological Bulletin. 2011;137(6):959–97. doi:10.1037/a0024768 PubMed PMID: 21787044.

4. Stubbs A, Szoeke C. The Effect of Intimate Partner Violence on the Physical Health and Health-Related Behaviors of Women: A Systematic Review of the Literature. Trauma, Violence, & Abuse. 2022 Oct;23(4):1157–72. doi:10.1177/1524838020985541

5. Swedo EA, Aslam MV, Dahlberg LL, Niolon PH, Guinn AS, Simon TR, et al. Prevalence of Adverse Childhood Experiences Among U.S. Adults — Behavioral Risk Factor Surveillance System, 2011–2020. MMWR Morb Mortal Wkly Rep. 2023 Jun 30;72(26):707–15. doi:10.15585/mmwr.mm7226a2

6. Joshi D, Raina P, Tonmyr L, MacMillan HL, Gonzalez A. Prevalence of adverse childhood experiences among individuals aged 45 to 85 years: a cross-sectional analysis of the Canadian Longitudinal Study on Aging. cmajo. 2021 Jan;9(1):E158–66. doi:10.9778/cmajo.20200064

7. Breiding MJ, Black MC, Ryan GW. Prevalence and Risk Factors of Intimate Partner Violence in Eighteen U.S. States/Territories, 2005. American Journal of Preventive Medicine. 2008 Feb;34(2):112–8. doi:10.1016/j.amepre.2007.10.001

8. Wilson SJ. Is age more than a number? Accounting for adult development and aging in the study of psychoneuroimmunology, stress, and health. Comprehensive Psychoneuroendocrinology. 2024 Nov;20:100266. doi:10.1016/j.cpnec.2024.100266

9. Kiecolt-Glaser JK, Renna ME, Shrout MR, Madison AA. Stress Reactivity: What Pushes Us Higher, Faster, and Longer—and Why It Matters. Current Directions in Psychological Science. 2020;29(5):492–8. doi:10.1177/0963721420949521

10. Shrout MR. The Health Consequences of Stress in Couples: A Review and New Integrated Dyadic Biobehavioral Stress Model. Brain, Behavior, & Immunity - Health. 2021;16. doi:10.1016/j.bbih.2021.100328

11. Polsky LR, Rentscher KE, Carroll JE. Stress-induced biological aging: A review and guide for research priorities. Brain, Behavior, and Immunity. 2022 Aug;104:97–109. doi:10.1016/j.bbi.2022.05.016

12. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. The Hallmarks of Aging. Cell. 2013 Jun;153(6):1194–217. doi:10.1016/j.cell.2013.05.039

13. Hillmann AR, Dhingra R, Reed RG. Positive social factors prospectively predict younger epigenetic age: Findings from the Health and Retirement Study. Psychoneuroendocrinology. 2023 Feb;148:105988. doi:10.1016/j.psyneuen.2022.105988

14. Zhang Z, Ren H, Han R, Li Q, Yu J, Zhao Y, et al. Impact of childhood maltreatment on aging: a comprehensive Mendelian randomization analysis of multiple age-related biomarkers. Clin Epigenet. 2024 Aug 5;16(1):103. doi:10.1186/s13148-024-01720-z

15. Wolf EJ, Maniates H, Nugent N, Maihofer AX, Armstrong D, Ratanatharathorn A, et al. Traumatic stress and accelerated DNA methylation age: A meta-analysis. Psychoneuroendocrinology. 2018 Jun;92:123–34. doi:10.1016/j.psyneuen.2017.12.007

16. Klopack ET, Crimmins EM, Cole SW, Seeman TE, Carroll JE. Accelerated epigenetic aging mediates link between adverse childhood experiences and depressive symptoms in older adults: Results from the Health and Retirement Study. SSM - Population Health. 2022 Mar;17:101071. doi:10.1016/j.ssmph.2022.101071

17. Martin N, Beach D, Gil J. Ageing as developmental decay: insights from p16INK4a. Trends in Molecular Medicine. 2014 Dec;20(12):667–74. doi:10.1016/j.molmed.2014.09.008

18. Rentscher KE, Carroll JE, Repetti RL, Cole SW, Reynolds BM, Robles TF. Chronic stress exposure and daily stress appraisals relate to biological aging marker p16INK4a. Psychoneuroendocrinology. 2019 Apr;102:139–48. doi:10.1016/j.psyneuen.2018.12.006

19. Bourassa KJ, Caspi A, Harrington H, Houts R, Poulton R, Ramrakha S, et al. Intimate partner violence and lower relationship quality are associated with faster biological aging. Psychology and Aging. 2020 Dec;35(8):1127–39. doi:10.1037/pag0000581

20. Chan KL, Lo CKM, Chen XY, Ip P, Leung WC, Shiels PG, et al. Association between intimate partner violence and leukocyte telomere length: a retrospective cohort study of 144 049 UK Biobank participants. Epidemiol Psychiatr Sci. 2023;32:e26. doi:10.1017/S2045796023000112

21. Humphreys J, Epel ES, Cooper BA, Lin J, Blackburn EH, Lee KA. Telomere Shortening in Formerly Abused and Never Abused Women. Biological Research For Nursing. 2012 Apr;14(2):115–23. doi:10.1177/1099800411398479

22. Rentscher KE, Klopack ET, Crimmins EM, Seeman TE, Cole SW, Carroll JE. Social relationships and epigenetic aging in older adulthood: Results from the Health and Retirement Study. Brain, Behavior, and Immunity. 2023 Nov;114:349–59. doi:10.1016/j.bbi.2023.09.001

23. Barger SD, Cribbet MR. Social support sources matter: Increased cellular aging among adults with unsupportive spouses. Biological Psychology. 2016 Mar;115:43–9. doi:10.1016/j.biopsycho.2016.01.003

24. McEwen BS, Gianaros PJ. Central role of the brain in stress and adaptation: Links to socioeconomic status, health, and disease. Annals of the New York Academy of Sciences. 2010 Feb;1186(1):190–222. doi:10.1111/j.1749-6632.2009.05331.x

25. Nurius PS, Green S, Logan-Greene P, Borja S. Life course pathways of adverse childhood experiences toward adult psychological well-being: A stress process analysis. Child Abuse & Neglect. 2015 Jul;45:143–53. doi:10.1016/j.chiabu.2015.03.008

26. Kiecolt-Glaser JK, Loving TJ, Stowell JR, Malarkey WB, Lemeshow S, Dickinson SL, et al. Hostile Marital Interactions, Proinflammatory Cytokine Production, and Wound Healing. Archives of General Psychiatry. 2005;62(12):1377. doi:10.1001/archpsyc.62.12.1377 PubMed PMID: 16330726.

27. Shrout MR, Renna ME, Madison AA, Jaremka LM, Fagundes CP, Malarkey WB, et al. Cortisol slopes and conflict: A spouse's perceived stress matters. Psychoneuroendocrinology. 2020;121:104839. doi:10.1016/j.psyneuen.2020.104839

28. Shrout MR, Renna ME, Madison AA, Malarkey WB, Kiecolt-Glaser JK. Marital negativity's festering wounds: The emotional, immunological, and relational toll of couples' negative communication patterns. Psychoneuroendocrinology. 2023;149:105989. doi:10.1016/j.psyneuen.2022.105989

29. Rentscher KE, Carroll JE, Cole SW, Repetti RL, Robles TF. Relationship closeness buffers the effects of perceived stress on transcriptomic indicators of cellular stress and biological aging marker p16INK4a. Aging. 2020 Jul 26;12(16):16476–90. doi:10.18632/aging.103739

30. Liu Y, Sanoff HK, Cho H, Burd CE, Torrice C, Ibrahim JG, et al. Expression of p16INK4a in peripheral blood T-cells is a biomarker of human aging. Aging Cell. 2009 Aug;8(4):439–48. doi:10.1111/j.1474-9726.2009.00489.x

31. Horvath S. DNA methylation age of human tissues and cell types. Genome Biol. 2013 Dec 10;14(10):3156. doi:10.1186/gb-2013-14-10-r115

32. Hannum G, Guinney J, Zhao L, Zhang L, Hughes G, Sadda S, et al. Genome-wide Methylation Profiles Reveal Quantitative Views of Human Aging Rates. Molecular Cell. 2013 Jan;49(2):359–67. doi:10.1016/j.molcel.2012.10.016

33. Levine ME, Lu AT, Quach A, Chen BH, Assimes TL, Hou L, et al. An epigenetic biomarker of aging for lifespan and healthspan. Aging. 2018;10(4):573–91.

34. Lu AT, Quach A, Wilson JG, Reiner AP, Aviv A, Raj K, et al. DNA methylation GrimAge strongly predicts lifespan and healthspan. Aging. 2019 Jan 21;11(2):303–27. doi:10.18632/aging.101684

35. Belsky DW, Caspi A, Arseneault L, Baccarelli A, Corcoran DL, Gao X, et al. Quantification of the pace of biological aging in humans through a blood test, the DunedinPoAm DNA methylation algorithm. eLife. 2020 May 5;9:e54870. doi:10.7554/eLife.54870

36. Epel ES, Lin J, Dhabhar FS, Wolkowitz OM, Puterman E, Karan L, et al. Dynamics of telomerase activity in response to acute psychological stress. Brain, Behavior, and Immunity. 2010 May;24(4):531–9. doi:10.1016/j.bbi.2009.11.018

37. Bernstein DP, Fink L, Handelsman L, Foote J, Lovejoy M, Wenzel K, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. The American Journal of Psychiatry. 1994;151(8):1132–6. doi:10.1176/ajp.151.8.1132

38. Widom CS, Do H (Heather), Miller QC, Javakhishvili M, Eckstein Indik C, Belsky DW. Childhood maltreatment and biological aging in middle adulthood: The role of psychiatric symptoms. Biological Psychiatry Global Open Science. 2024 Sep 1;4(5):100341. doi:10.1016/j.bpsgos.2024.100341

39. Walker EA, Gelfand A, Katon WJ, Koss MP, Von Korff M, Bernstein D, et al. Adult health status of women with histories of childhood abuse and neglect. The American Journal of Medicine. 1999 Oct;107(4):332–9. doi:10.1016/S0002-9343(99)00235-1

40. Viola TW, Salum GA, Kluwe-Schiavon B, Sanvicente-Vieira B, Levandowski ML, Grassi-Oliveira R. The influence of geographical and economic factors in estimates of childhood abuse and neglect using the Childhood Trauma Questionnaire: A worldwide meta-regression analysis. Child Abuse & Neglect. 2016 Jan 1;51:1–11. doi:10.1016/j.chiabu.2015.11.019

41. Kessler RC, Davis CG, Kendler KS. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. Psychol Med. 1997 Sep;27(5):1101–19. doi:10.1017/S0033291797005588

42. Kessler RC, Magee WJ. Childhood adversities and adult depression: basic patterns of association in a US national survey. Psychol Med. 1993 Aug;23(3):679–90. doi:10.1017/S0033291700025460

43. Straus MA, Douglas EM. A Short Form of the Revised Conflict Tactics Scales, and Typologies for Severity and Mutuality. Violence Vict. 2004 Oct;19(5):507–20. doi:10.1891/vivi.19.5.507.63686

44. Straus MA, Hamby SL, Boney-McCoy SUE, Sugarman DB. The revised conflict tactics scales (CTS2) development and preliminary psychometric data. Journal of Family Issues. 1996;17(3):283–316.

45. Rosko AE, Elsaid MI, Woyach J, Islam N, Lepola N, Urrutia J, et al. Determining the relationship of p16INK4a and additional molecular markers of aging with

clinical frailty in hematologic malignancy. J Cancer Surviv. 2024 Aug;18(4):1168–78. doi:10.1007/s11764-024-01591-6

46. Lin J, Epel E, Cheon J, Kroenke C, Sinclair E, Bigos M, et al. Analyses and comparisons of telomerase activity and telomere length in human T and B cells: Insights for epidemiology of telomere maintenance. Journal of Immunological Methods. 2010 Jan;352(1–2):71–80. doi:10.1016/j.jim.2009.09.012

47. Cawthon RM. Telomere measurement by quantitative PCR. Nucleic Acids Research. 2002 May 15;30(10):47e–47. doi:10.1093/nar/30.10.e47

48. Burd CE, Peng J, Laskowski BF, Hollyfield JL, Zhang S, Fadda P, et al. Association of Epigenetic Age and p16INK4a With Markers of T-Cell Composition in a Healthy Cohort. Le Couteur D, editor. The Journals of Gerontology: Series A. 2020 Nov 13;75(12):2299–303. doi:10.1093/gerona/glaa108

49. McDonald JH. Handbook of Biological Statistics. 3rd ed. Sparky House Publishing; 2014.

50. Hoppmann CA, Gerstorf D. Biobehavioral Pathways Underlying Spousal Health Dynamics: Its Nature, Correlates, and Consequences. Gerontology. 2014;60(5):458–65. doi:10.1159/000357671 PubMed PMID: 24776655.

51. Carstensen LL. Evidence for a life-span theory of socioemotional selectivity. Current Directions in Psychological Science. 1995;4(5):151–6. doi:10.1111/1467-8721.ep11512261

52. Shrout MR, Black AE, Wilson SJ, Renna ME, Madison AD, Kiecolt-Glaser JK, et al. How aging couples' emotional and physiological associations change across positive, supportive, and conflictual discussions: Roles of capitalization and responsive behaviors. Biological Psychology. 2023;177:108500. doi:10.1016/j.biopsycho.2023.108500

53. Shrout MR, Wilson S, Renna M, Madison A, Kiecolt-Glaser JK. "We've Got This": Middle-Aged and Older Couples' Satisfying Relationships and We-Talk Promote Better Physiological, Relational, and Emotional Responses to Conflict. Psychosom Med. 2023;85:154–64. doi:10.1097/PSY.0000000000001162

54. Kiecolt-Glaser JK, Wilson S. Lovesick: How couples' relationships influence health. Annual Review of Clinical Psychology. 2017;8(13):421–43. doi:10.1146/annurev-clinpsy-032816-045111 PubMed PMID: 17561440.

55. Shrout MR, Wilson SJ, Farrell AK, Rice TM, Weiser DA, Novak JR, et al. Dyadic, biobehavioral, and sociocultural approaches to romantic relationships and health: Implications for research, practice, and policy. Social and Personality Psychology Compass. 2024;18(2):e12943. doi:DOI: 10.1111/spc3.12943

56. George J, Stith SM. An Updated Feminist View of Intimate Partner Violence. Fam Proc. 2014 Jun;53(2):179–93. doi:10.1111/famp.12073

57. De Coster S, Heimer K. Unifying Theory and Research on Intimate Partner Violence: A Feminist Perspective. Feminist Criminology. 2021 Jul;16(3):286–303. doi:10.1177/1557085120987615

Table 1. Correlations Among Study Variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Childhood family adversity	-	0.54***	0.05	0.05	0.06	0.00	0.08	0.03	0.03	0.02	0.16*	0.23**	0.06	-0.14
2. Childhood maltreatment	0.55***	-	-0.03	0.01	-0.01	-0.02	0.08	0.05	-0.00	-0.03	0.21**	0.10	0.09	-0.02
3. Construct conflicts	0.08	0.00	-	0.34***	0.15	0.05	0.03	0.04	-0.10	0.01	-0.03	0.04	-0.01	-0.06
4. Destructive conflicts	0.04	0.00	0.33***	-	0.02	-0.07	-0.07	-0.04	0.01	0.16*	-0.08	0.11	-0.13	-0.11
5. Horvath2 EAA	0.06	-0.07	0.16*	0.09	-	0.76***	0.71***	0.44***	0.25***	-0.58***	0.08	-0.07	-0.05	0.03
6. HannumEAA	0.07	-0.08	0.03	-0.03	0.77***	-	0.87***	0.50***	0.38***	-0.58***	0.07	-0.21**	-0.08	0.06
7. PhenoAge EAA	0.16*	0.03	0.02	0.03	0.67***	0.85***	-	0.58***	0.42***	-0.57***	0.09	-0.17*	-0.02	0.05
8. GrimAge EAA	0.08	0.02	0.03	0.05	0.37***	0.46***	0.55***	-	0.56***	-0.40***	0.07	-0.52***	0.19*	-0.00
9. DunedinPACE	0.05	-0.05	-0.05	0.09	0.20**	0.32***	0.39***	0.57***	-	-0.47***	0.07	-0.24**	0.13	0.34***

10. Telomere length	0.02	-0.03	0.01	0.09	-0.49***	-0.49***	-0.48***	-0.40***	-0.40***		-0.33***	0.19**	-0.03	-0.67***
11. $p16^{IN}_{K4a}$	-0.06	0.02	-0.01	0.02	0.15*	0.10	0.11	0.04	0.04	-0.28***		0.07	0.07	0.27***
12. Sex	0.24**	0.11	0.02	0.10	0.03	-0.12	-0.07	-0.48***	-0.12	0.19**	-0.00		-0.03	-0.07
13. Comorbidities	0.05	0.15*	-0.03	-0.12	0.02	0.03	0.07	0.18*	0.03	-0.05	-0.08	-0.03		0.15*
14. Chronological age	-0.10	0.04	-0.06	-0.09	-0.03	-0.04	-0.04	0.01	0.28***	-0.66***	0.22**	-0.05	0.10	

Note. Results are from correlation analyses (N = 214 individuals in 107 couples). TL = telomere length. Childhood maltreatment coded: no maltreatment = 0, maltreatment = 1. Sex coded: male = 0, female = 1. Visit 1 correlations are below the diagonal, and Visit 2 are above the diagonal.
*p < .05. **p < .01. ***p < .001

Table 2. Results for Effects of Early Life Adversity and Conflict Tactics on Biological Aging

		Concurrent Associations			Prospective Associations		
Outcome	Predictor	Estimate	*SE*	*p*	Estimate	*SE*	*p*
Horvath2EAA	Childhood family adversity	0.09	0.06	0.143	0.02	0.07	0.049
	Childhood maltreatment	-0.04	0.12	0.749	0.36	0.15	0.017
	Constructive conflicts	0.16	0.08	0.058	0.04	0.07	0.565
	Destructive conflicts	0.10	0.06	0.107	-0.04	0.07	0.948
HannumEAA	Childhood family adversity	0.09	0.06	0.116	0.02	0.07	0.837
	Childhood maltreatment	-0.05	0.12	0.640	0.28	0.15	0.057
	Constructive conflicts	0.05	0.06	0.397	0.06	0.07	0.412
	Destructive conflicts	-0.02	0.06	0.639	-0.03	0.07	0.913
PhenoAgeEAA	Childhood family adversity	0.17	0.07	0.021	0.02	0.08	0.771
	Childhood maltreatment	0.13	0.12	0.266	0.30	0.15	0.043
	Constructive conflicts	0.04	0.06	0.492	0.06	0.07	0.403
	Destructive conflicts	0.02	0.06	0.636	-0.11	0.07	0.139
GrimAgeEAA	Childhood family adversity	0.18	0.05	<0.001	0.05	0.08	0.546
	Childhood maltreatment	0.12	0.12	0.328	0.20	0.15	0.164
	Constructive conflicts	0.05	0.05	0.327	0.07	0.07	0.369
	Destructive conflicts	0.08	0.05	0.124	-0.06	0.07	0.397
DunedinPACE	Childhood family adversity	0.11	0.06	0.049	0.14	0.07	0.041
	Childhood maltreatment	-0.01	0.11	0.909	0.30	0.15	0.038
	Constructive conflicts	-0.09	0.06	0.104	-0.10	0.07	0.166
	Destructive conflicts	0.09	0.06	0.472	-0.01	0.07	0.796
Telomere length	Childhood family adversity	-0.10	0.04	0.023	-0.07	0.08	0.358

	Childhood maltreatment	-0.06	0.09	0.494	-0.09	0.15	0.531
	Constructive conflicts	-0.05	0.04	0.230	-0.06	0.07	0.372
	Destructive conflicts	0.04	0.05	0.409	0.10	0.07	0.161
p16^{INK4a}	Childhood family adversity	0.05	0.05	0.352	0.18	0.07	0.015
	Childhood maltreatment	0.11	0.10	0.295	0.24	0.14	0.079
	Constructive conflicts	0.02	0.05	0.689	0.02	0.07	0.744
	Destructive conflicts	0.01	0.06	0.896	-0.07	0.07	0.367

Note. Results are from linear mixed models (N = 214 individuals in 107 couples); all effects held after a Benjamini–Hochberg false discovery rate correction of 0.15. All models controlled for sex and comorbidities; models for *p16*^{ink4a} expression and telomere length additionally controlled for age. Predictors were tested in separate models. Childhood maltreatment coded: no maltreatment = -1, maltreatment = 1. EAA = epigenetic age acceleration. p-values were FDR-corrected

Figure 1. Visual depictions of two-way interactions between: (A) childhood family adversity and destructive conflict tactics predicting GrimAgeEAA; (1B) childhood family adversity and destructive conflict tactics predicting DunedinPACE; and (1C) childhood maltreatment and destructive conflict tactics predicting DunedinPACE. *p<0.05; **p<0.01; ***p<0.001