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Associations between epigenetic age acceleration and longitudinal measures of psychosocioeconomic stress and status

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ABSTRACT

Relationships between epigenetic aging markers and psychosocial variables such as socioeconomic status and stress have been well-documented, but are often examined cross-sectionally or retrospectively, and have tended to focus on objective markers of SES or major life events. Here, we examined associations between psychosocial variables, including measures of socioeconomic status and social stress, and epigenetic aging markers in adulthood, using longitudinal data spanning three decades from the Midlife in the United States (MIDUS) study. The largest effects were observed for epigenetic markers of change in health, such as DunedinPACE and GrimAge, and for associations involving education, income, net assets, general social stress, inequality-related stress, and financial stress. Analyses of polygenic indices suggests that at least in the case of education, the link to epigenetic aging cannot be accounted for by common genetic variants.

Biological markers of aging — indicators of aging status independent of chronological age — have been an increasing focus of research in recent years, with the recognition that some individuals experience accelerated aging and shortened lifespan relative to others. A variety of biological markers of aging have been examined, such as telomere length (Aubert and Lansdorp, 2008; Blackburn et al., 2015) and metabolic, hormonal, and inflammatory markers of frailty (Cardoso et al., 2018; Saedi et al., 2019). Among the most researched, however, and among the most predictive of lifespan, are epigenetic markers (i.e., markers of epigenetic age acceleration or EAA). These markers reflect observed patterns of DNA methylation associated with chronological age, health (e.g., Hannum et al., 2013; Horvath, 2013), or aging-related changes in health status (e.g., Belsky et al., 2022), and are predictive of physiological and psychosocial functioning in a number of systems related to healthy aging, as well as the rate of change in functioning, independent of chronological age.

A substantial literature has documented associations between accelerated epigenetic aging and health-related variables such as sleep, BMI, smoking, and alcohol use (Kong, et al., 2023; Ryan et al., 2020). Psychosocial variables such as socioeconomic status and education are also predictive of epigenetic aging, with higher SES and greater levels of education associated with slower epigenetic aging (e.g., Kong et al., 2023; Oblak et al., 2021; Ryan et al., 2020).

Although psychosocial factors such as socioeconomic status and stress have been examined as predictors of epigenetic age acceleration, there is a need for them to be studied longitudinally, especially throughout adulthood. Many longitudinal studies have focused on childhood, adolescence, or young adult stressors (Colich et al., 2020; e.g., Oblak et al., 2021), with fewer studies of stress or socioeconomic variables over a longer timeframe in middle adulthood. Other studies have examined retrospectively recalled socioeconomic and stress variables (e.g., Graf et al., 2022; Zannas et al., 2015), such as childhood stressors and traumas, which are subject to recall biases and unreliability, or restricts focus to variables that can be more easily assessed through recall, such as major life events. Examining psychosocial variables longitudinally across adulthood reduces recall bias and affords a greater range of variables to be examined with reference to epigenetic age acceleration, including socioeconomic and psychosocial stressors as they unfold over time and possibly have cumulative effects over the lifespan.

Various lines of research and theory point to the need to consider psychosocial variables such as SES, education, and psychosocial stress

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within a common empirical framework. Research on socioeconomic status has demonstrated that objective and subjective socioeconomic status variables are dissociable and have distinct patterns of relationships with other variables. Objective socioeconomic status refers to objective socioeconomic resources, such as objective educational attainment and household income; subjective socioeconomic status refers to one's perceived (usually self-perceived) socioeconomic circumstances, possibly including one's position relative to others (Cundiff and Matthews, 2017; Tan et al., 2020). Subjective components of socioeconomic position have been shown to independently predict health, including biological as well as self-reported health (Cundiff and Matthews, 2017); psychological well-being similarly has been observed to be more strongly related to subjective socioeconomic position (Tan et al., 2020). Economic surveys similarly consistently point to phenomena such as the "regular rich", wherein individuals or households may be objectively high on indicators such as income or education, but nevertheless be stressed financially and report difficulties related to standards of living. Conversely, studies may examine more objective indicators of socioeconomic deprivation without assessing for coincident subjectively experienced stress (e.g., Simons et al., 2022). Focusing solely on objective SES indicators without considering other subjective indicators or psychosocial stress may provide an incomplete picture of overall functioning and its relationship with the aging process.

Similar research conversely points to the centrality of socioeconomic factors in psychosocial stress. Research has indicated that different forms of psychosocial stress, including different types of social and economic stress, are distinct but strongly associated, such that they can be understood empirically and theoretically as different components of general social stress within a unified model (Mann et al., 2021). Job stress, discrimination, inequality, relationship stress, and financial stress are all interrelated, and simultaneously act and are perceived jointly in terms of overall stress. Subjective socioeconomic position is instantiated in multiple forms of stress, such as financial stress, job stress, and inequality-related stress, which in turn act as components of general stress along with other forms of stress. Specific forms of stress such as financial stress may have spillover or distributed effects on other areas of functioning, or may be affected by other forms of stress. How these different forms of stress independently and jointly predict epigenetic age acceleration is poorly understood, however. Current studies, although critically informative, are often retrospective or cross-sectional, often focus on general stress or event-related stress (e.g., trauma or major life events) without considering other specific forms of psychosocial stress within a unified framework, and often partial out socioeconomic variables (e.g., Harvanek et al., 2021; Vetter et al., 2022).

Socioeconomic indicators are among the more robust predictors of epigenetic aging and related variables such as inflammation and mortality (e.g., Faul et al., 2023; Schmitz et al., 2021). How relatively objective indicators of SES compare to more subjective indicators in their prediction of EAA is currently unclear, however, as is how different objective forms of SES relate to epigenetic aging markers, or how different forms of subjective SES and stress, including financial and nonfinancial stress, comparatively relate to epigenetic aging markers.

Increased interested in epigenetic correlates of aging has led to a variety of EAA indicators or "clocks". The first EAA markers were derived by identifying methylation patterns predictive of chronological age (in blood or other tissues; Hannum et al., 2013; Hannum et al., 2013), with accelerated or deaccelerated aging defined as the deviation of chronological age from one's predicted age based on these methylation patterns. Later EAA markers were developed through the prediction of targets other than chronological age per se — such as a "phenotypic age" composite including blood biomarkers of aging and health (Levine, et al., 2018), a similar composite comprising mortality itself as a predictive target (Lu et al., 2022), or change in health and aging markers across time (Belsky et al., 2022).

As the number of epigenetic markers of aging has increased, so has interest in their relationships with one another, with processes underlying aging, and their relative ability to predict outcomes and mortality. If different epigenetic aging markers are indexing some shared aging process, they should correlate with one another in a way that is reflective of this shared process (Belsky et al., 2017). Along these lines, empirical findings suggest that relatively recent EAA markers indexed to change (decline in functioning indicators as with DunedinPACE, or death as with GrimAge for example) are relatively more highly correlated with one another and cluster together in that sense, and that earlier EAA markers indexed to age as a state per se also similarly cluster together (e.g., Graf et al., 2022; Simons et al., 2022). These clusters might reflect methylation patterns of different etiology (Yousefi et al., 2022), and some evidence suggests they might differentially predict significant outcomes such as mortality (e.g, Belsky et al., 2017). Not all studies observe these clusterings, however (e.g., Li et al., 2020); additional research is needed to quantify how diverse indicators of epigenetic age acceleration correlate with one another and other variables.

Genetic studies of EAA have provided varying estimates of overall heritability of EAA, from 0.15 for polymorphism-based heritability estimates in adults to 1.0 for twin-based heritability estimates in newborn twins (Gibson et al., 2019; Horvath, 2013; Lu et al., 2018), with most estimates roughly in the range of 0.15–0.40. Given that genetic influences on socioeconomic variables have also been identified (e.g., Okbay et al., 2022), it raises the possibility that at least some of the relationship between psychosocial variables such as SES and EAA might be due to genetic background.

The purpose of this study was to examine relationships between psychosocial variables, including measures of socioeconomic status and social stress, and epigenetic aging markers in adulthood, using data from the Midlife in the United States (MIDUS) program. The aim of this study was to examine associations with markers of epigenetic aging using longitudinally informative measures of socioeconomic and psychosocial stress, examining socioeconomic variables and psychosocial stress variables jointly, and epigenetic aging as reflected in a broad set of epigenetic aging markers (e.g., DunedinPACE, which reflects pace of change in aging rather than aging status per se; Belsky et al., 2022). We used the model of Mann et al. (2021) as a framework for social stress predictors of epigenetic aging. We also sought to characterize the role of genetic factors in associations between SES and epigenetic aging markers using a polygenic index for educational attainment (Lee et al., 2018).

1. Methods

1.1. Participants and general design

Participants from MIDUS (N = 1310) comprised individuals from two subsamples: participants from the MIDUS Core project (N = 511), and participants from the MIDUS Refresher project (N = 799). Among these participants were 148 twins constituting 74 complete pairs. Individuals from the MIDUS Core cohort completed surveys on three occasions, roughly 8–10 years apart (mean ages 43.35–60.71 years), and blood samples, additional surveys and physical measurements were obtained near the second occasion (mean age 55.15). Survey data and blood samples were collected at single timepoints from the MIDUS Refresher cohort (mean age 51.03 years for the survey; mean age 52.89 for the blood samples), as these were the initial waves of a project designed to replicate the MIDUS Core project with a new cohort. Characteristics of the overall sample are presented in Table 1; details regarding MIDUS are also available at the MIDUS website and in other publications (https://www.midus.wisc.edu; Ryff and Krueger, 2018).

With missing data, final Ns ranged from 479 (for variance in household income) to 1310 (that is, no missing data), with most measures in the range of 1300–1310 (Tables 2 and 3). Models predicting missingness from the remaining variables would only converge for home and work stress and variance in household income, perhaps because these were the only two variables with substantial amounts of

Table 1
Descriptive statistics of sample.

	Mean (sd)/Percent
Age	
T1	48.64 (13.22)
T2	52.47 (11.22)
T3	60.71 (10.53)
Biomarker Visit	53.77 (12.57)
Gender	
Female	0.60
Male	0.40
Race	
White	0.70
Black	0.23
Other	0.07
Education (Years)	14.93 (2.56)
Education (Highest Degree)	
Less than high school	0.05
GED	0.02
High school	0.15
Some college	0.20
College and above	0.58
Household Income	79389.26 (59777)
Variance In Household Income	2269638857 (4156770119)
Net Assets (Yes)	0.70

Note. Values are mean (sd) or percentage of sample; means reflect mean over the course of the study (income and ratings) or the highest attained value over the course of the study (education and assets) or variance over the course of the study (income variance). The item "current situation" was rated on a scale of 1–10; "Enough" was rated on a scale of 1–3, and "Difficult to pay" was rated on a scale of 1–4; greater values reflected fewer financial difficulties for each item.

missingness. Missingness in home and work stress was only significantly predicted by household income, such that lower income individuals were more likely to be missing (binomial GLM β = -1.35; p = 0.001); missingness in household income variance was predicted by more years of education (binomial GLM $\beta = 0.13$; $p < 0.001$), lack of assets (binomial GLM β = -1.23; $p < 0.001$), and higher household income (binomial GLM $\beta = 0.26$; $p = 0.001$).

1.2. Socioeconomic and psychosocial measures

Education, household income (both mean and variance over time), and assets were modeled as objective socioeconomic variables; general social stress and its five subfactors (job stress, discrimination, inequality, relationship stress, and financial stress; Mann et al., 2021) were modeled as subjective psychosocial variables. For state-like socioeconomic and psychosocial variables, mean level over the course of the study was used (household income and stress ratings); for cumulative variables, the highest attained value over the course of the study was used (education and net household assets); variance over the course of the study was used to examine variability in household income. Analyses used number of expected years of education given the highest degree attained, due to convergence difficulties with education coded categorically as degree (results where estimates converged were similar). Net household assets were coded as net positive assets or lack thereof due to changes in the method used to ask about assets over the course of the study.

Psychosocial stress variables were coded as mean scores on scales as have been previously described (Mann et al., 2021), using interview ratings on items related to five different forms of stress: job stress, discrimination, inequality, relationship stress, and financial stress. For example, financial stress was rated using three items: "Using a scale from 0 to 10 where 0 means "the worst possible financial situation" and 10 means "the best possible financial situation," how would you rate your financial situation these days?"; "In general, would you say you (and your family living with you) have more money than you need, just enough for your needs, or not enough to meet your needs?" (with responses options of "1, more money than you need" "2, just enough money", or "3, not enough money"), and "How difficult is it for you (and your family) to pay your monthly bills?" (with response options ranging from "1, very" to "4, not at all"). Responses were recoded such that higher values indicated fewer financial difficulties, and standardized and averaged to create an overall scale value. Details about the

Table 2
Effects on decline-predictive epigenetic age acceleration factor.

	N	R^2	β	se(β)	LR	p	q
Education	1309	0.015	−0.121	0.031	14.76	<0.001	0.005
Mean Household Income	1286	0.011	−0.103	0.030	11.73	<0.001	0.005
Variance Household Income	479	0.000	0.019	0.040	0.214	0.644	0.809
Assets	1265	0.011	−0.104	0.033	10.00	0.002	0.008
General Social Stress	1310	0.015	0.124	0.032	15.10	<0.001	0.005
Discrimination	1306	0.005	0.070	0.034	4.11	0.043	0.117
Home & Work	952	0.001	0.034	0.042	0.65	0.421	0.615
Inequality	1309	0.012	0.109	0.030	13.33	<0.001	0.005
Relationship	1305	0.002	0.041	0.034	1.45	0.229	0.435
Financial	1309	0.016	0.127	0.031	16.99	<0.001	0.005

Note. R^2 = percent of variance explained. β = standardized regression coefficient. *se* = standard error. *LR* = likelihood ratio. p = p-value, unadjusted for multiple testing. q = q-value (Storey, 2002), adjusted for multiple testing across Tables 2 and 3

Table 3
Effects on state-predictive epigenetic age acceleration factor.

	N	R^2	β	se(β)	LR	p	q
Education	1309	0.000	0.007	0.032	0.05	0.816	0.911
Mean Household Income	1286	0.000	−0.003	0.031	0.01	0.911	0.911
Variance Household Income	479	0.004	0.063	0.048	1.53	0.216	0.435
Assets	1265	0.001	−0.028	0.031	0.81	0.367	0.584
General Social Stress	1310	0.002	0.041	0.031	1.69	0.194	0.435
Discrimination	1306	0.000	−0.004	0.032	0.02	0.889	0.911
Home & Work	952	0.000	0.017	0.036	0.22	0.643	0.809
Inequality	1309	0.004	0.067	0.028	5.45	0.020	0.063
Relationship	1305	0.000	0.012	0.028	0.17	0.681	0.809
Financial	1309	0.001	0.028	0.031	0.81	0.369	0.584

Note. R^2 = percent of variance explained. β = standardized regression coefficient. *se* = standard error. *LR* = likelihood ratio. p = p-value, unadjusted for multiple testing. q = q-value (Storey, 2002), adjusted for multiple testing.

distributions of the psychosocial stress variables are also presented in Table S1.

1.3. Epigenetic markers

Fasting blood draws were obtained from the MIDUS Core sample from 2004 to 2009 and from the MIDUS Refresher sample from 2012 to 2016. Whole blood samples were collected using a BD Vacutainer Tube with EDTA anticoagulant and frozen in storage. In 2019, DNA methylation profiling was conducted on the whole blood DNA samples from both the Core and Refresher samples. After DNA was tested for suitable yield and integrity, it was subjected to genome-wide methylation profiling using Illumina Methylation EPIC microarrays. The resulting beta values were noob-normalized to control for technical sources of variance, registered onto the list of CpG sites assayed on the Illumina Methylation 450K microarray, and screened using standard quality control metrics. Raw methylation data was used to score the following markers: Horvath (2013), Hannum (Hannum et al., 2013), PhenoAge (Levine et al., 2018), GrimAge Version 2 (Lu et al., 2022), and DunedinPACE epigenetic pace of aging markers (Belsky et al., 2022). For more information on data collection and the derivation of epigenetic variables in MIDUS, reference the data documentation on the MIDUS Colectica Portal (https://midus.colectica.org/).

1.4. Analyses

Epigenetic age acceleration was modeled as a function of psychosocial and socioeconomic predictors, controlling for covariates using linear models; analyses were conducted using full-information maximum likelihood (ML) estimation. Twin pair ID was used as a clustering variable to account for dependence of observations in estimates of overall effects of predictors on EAA markers and factors, to avoid inflated estimates of statistical significance and confidence (although estimates of effects themselves remain unbiased in the presence of unmodeled dependency; Chatterjee and Hadi, 2012; Williams et al., 2013). In all analyses, estimated epigenetic age variables were adjusted for chronological age and age squared, gender, tobacco use frequency and amount, alcohol use frequency and amount, BMI, sleep quality (using the Pittsburgh Sleep Quality Index; Buysse et al., 1989), cognitive status (measured using the Brief Test of Adult Cognition by Telephone, BTACT; Lachman et al., 2014), methylation assay well plate, and race. Quadratic effects of age were included in addition to linear effects to control for nonlinear age trends (McGue and Bouchard, 1984); other covariates were included in models as potential methodological or demographic confounds, or well-documented known correlates of EAA markers (e.g., Kong et al., 2023; Ryan et al., 2020; models adjusting only for methodological and basic demographic covariates are also presented in the supplement in Tables S7 and S8). In addition, variance in income over the course of the study controlled for mean income over the same time period. Mean income and variability in income (i.e., within-participant variance) were standardized relative to the initial wave to avoid difficulties with model convergence due to widely different scales (magnitudes) of variables; models with raw income variables failed to converge unless they were rescaled.

Epigenetic markers were substantially correlated (Table S1), with Horvath, Hannum, and PhenoAge correlated more strongly with each other, and Grimage and DunedinPACE more strongly correlated with one another. Correlations between age-adjusted markers were smaller than the raw markers, but patterns were similar. Exploratory factor analysis of the age-adjusted markers using a 2-factor model with unweighted least squares estimation (using the psych R library; Revelle, 2024) produced estimates consistent with this clustering of variables (Table S2; RMSEA = 0.003; RMSR = 0.000). Factor scores from this two-factor model were used in the remainder of analyses in lieu of the original epigenetic marker variables as outcome variables in regressions. The first factor score reflected EAA markers developed to predict cross-sectional state (age, health state), and was labeled "State--Predictive"; the second factor reflected epigenetic markers developed to predict change (change in health status, death), and was labeled "Decline-Predictive".

To control for multiple testing, q-values was used in addition to p-values. The q-value provides a bound to the false discovery rate (FDR), the proportion of false positives among all positive (i.e., significant) test results. It can also be thought of as the greatest lower bound to the posterior probability of the null being true given the observed test statistic (Storey, 2002, 2003). The q-value R library (Storey, et al., 2023) was used to estimate q-values.

2. Results

Results for associations between epigenetic age acceleration factor scores and socioeconomic and stress predictors are given in Tables 2 and 3 (results for specific EAA markers are given in Tables 4 and 5 and S4-S6, and analyses adjusted only for basic methodological and demographic covariates are presented in Tables S7–S8). In general, relationships were stronger (in terms of R^2, for example) for the decline-predictive factor than the state-predictive factor. Associations were also generally in the directions consistent with theory (for example, socioeconomic resources were estimated to be negatively associated with aging, variance in income and stress estimated to be positively associated with aging).

For the decline-predictive factor, six predictors were significantly associated with decline-predictive aging markers: education ($\beta = -0.121$, $p < 0.001$), mean household income ($\beta = -0.103$, $p < 0.001$), net assets ($\beta = -0.104$, $p = 0.002$), general social stress ($\beta = 0.124$, $p < 0.001$), inequality stress ($\beta = 0.109$, $p < 0.001$), and financial stress ($\beta = 0.127$, $p < 0.001$). In addition, discrimination stress was related to aging more weakly ($\beta = 0.070$, $p = 0.043$). For the state-predictive factor, only psychosocial stress related to perceived inequality was significantly related to aging, albeit more weakly ($\beta = 0.065$, $p = 0.020$); the significance, moreover, decreased just above the 0.05 threshold when corrected for multiple testing ($q = 0.057$).

A polygenic index (PGI) for educational attainment was used to control for genetic contributions to the association between education and epigenetic aging. Although educational attainment PGI and actual attained education were significantly correlated ($r = 0.294$; $p < 0.0001$), controlling for educational attainment PGI did not significantly or meaningfully decrease the relationship between education and the decline-predictive epigenetic aging factor ($\beta = -0.117$, $p = 0.002$), suggesting that genetic factors, at least as indexed by common polymorphisms, do not account for the education-epigenetic aging relationship.

3. Discussion

We examined associations between epigenetic aging and socioeconomic and psychosocial stress variables over a period of 3 decades in a large ongoing study of midlife adults in the United States. Results are consistent with prior research in drawing attention to the importance of

Table 4
Effects on GrimAge epigenetic age acceleration.

	R^2	β	se(β)	LR	p
Education	0.017	−0.132	0.032	17.122	<0.001
Mean Household Income	0.007	−0.085	0.029	8.422	0.004
Variance Household Income	0.001	−0.025	0.035	0.512	0.474
Assets	0.016	−0.092	0.033	7.567	0.006
General Social Stress	0.013	0.114	0.035	10.876	<0.001
Discrimination	0.002	0.040	0.036	1.191	0.275
Home & Work	0.000	0.007	0.044	0.029	0.866
Inequality	0.009	0.094	0.036	6.849	0.009
Relationship	0.005	0.074	0.036	4.384	0.036
Financial	0.016	0.125	0.033	14.702	<0.001

Table 5
Effects on DunedinPACE epigenetic age acceleration.

	R^2	β	$se(\beta)$	LR	p
Education	0.011	−0.105	0.031	11.086	<0.001
Mean Household Income	0.013	−0.114	0.031	13.761	<0.001
Variance Household Income	0.001	0.027	0.041	0.442	0.506
Assets	0.010	−0.097	0.033	8.659	0.003
General Social Stress	0.014	0.118	0.031	14.439	<0.001
Discrimination	0.006	0.077	0.034	5.131	0.023
Home & Work	0.002	0.042	0.041	1.034	0.309
Inequality	0.011	0.105	0.029	12.581	<0.001
Relationship	0.001	0.026	0.033	0.628	0.428
Financial	0.014	0.118	0.030	15.349	<0.001

socioeconomic variables such as educational background, income, and assets in understanding aging processes (Simons et al., 2022), and extend this research literature to illustrate its importance as measured longitudinally over the course of adulthood. Our findings also point to the importance of psychosocial stress as a predictor of aging processes (i.e., above and beyond objective economic metrics), particularly stress related to finances, perceived inequality, and interpersonal experiences of discrimination.

Prior research on related phenomena is also consistent with these findings. For example, previous research in MIDUS suggested that net assets are an important predictor of mortality (Finegood et al., 2021); these findings confirm those and point to their effects as manifested in biological indices of aging. Also, many lines of research have documented the effects of discrimination and socioeconomic inequality on well-being, health, and other related variables (e.g., Simons et al., 2022). Our research underscores the importance of these variables as determinants of aging and health continuing into late adulthood.

Subjective and Objective Socioeconomic Variables. Our results are also informative regarding the relative contributions of objective and subjective components of socioeconomic functioning to epigenetic aging. Both types of variables were roughly comparable in their predictive information about epigenetic aging, with objective variables such as household income, education, and assets as well as subjective variables such as financial and inequality-related stress both having R^2 values in the range of 0.011–0.016. Further research is needed to better understand the mediators of these two classes of socioeconomic variables, in terms of how similar or different they are in their social and biological causal mediating pathways.

Delineation of Mediating Pathways and Aging Indicators. A number of features of our results also help clarify the etiologic processes underlying associations between socioeconomic and psychosocial variables and aging. For instance, the identified associations held even when controlling for variables such as weight, substance use, sleep, BMI, ethnicity, chronological age, and cognitive functioning. Moreover, the association between education and epigenetic aging also remained largely the same after controlling for polygenic predictors of education, suggesting that this relationship cannot be accounted largely by identified common genetic factors in this domain.

The null features of our results are also worth noting. For example, in contrast to some theories of health status and aging (Miller et al., 2020), we did not find that income variability over adulthood was significantly related to epigenetic aging markers above and beyond effects of average income. As such, much of the effect of income is likely mediated through the increased access to resources that income provides over the lifetime, or causal factors associated with that, rather than changes and unpredictability in income per se. Also, in contrast to a number of previous studies (e.g., Lawrence et al., 2020), we did not find any significant relationships between socioeconomic factors and epigenetic markers reflecting health or biological age (i.e., the state factor), but, instead, relationships were observed with epigenetic markers reflecting *changes* in health and mortality. The strongest relationships with health *state* markers were with perceived inequalities at work (e.g., feeling cheated about the chance to work at good jobs), at home (e.g., most people live in a better neighborhood), and with family (e.g., not feeling good about the opportunities provided to one's children). This finding underscores the importance of perceived social inequality in relation to well-being and health outcomes.

Limitations and Future Directions. Additional data involving family designs are needed to rigorously evaluate the effect of family of origin on adult aging. Various family-of-origin effects might mediate relationships between adult socioeconomic and psychosocial factors and EAA, such as childhood environmental effects or genetic effects (Kim, et al., 2023; Kong et al., 2023). Polygenic risk score analyses suggest that the associations of some variables with epigenetic age acceleration are unlikely to be due to previously identified relevant genetic factors, but other environmental factors associated with family of origin could be of importance. Furthermore, we could only examine polygenic contributors to educational attainment, as it was the only polygenic index available in MIDUS. Further research involving family studies and genetically informative designs are needed to evaluate these hypotheses, and to develop polygenic indices for other potentially genetically mediating contributors to other variables examined, such as general social stress and income.

Although MIDUS was designed to be reasonably representative of the United States, the results presented here should be replicated in other samples and possible heterogeneity in findings due to background and other variables should be examined. For instance, the mean household income of this sample is similar to that of the US during the time period examined, perhaps even somewhat lower (e.g., mean household income in the US in 2009 and 2019 was 78540 and 116700; U.S. Census Bureau, 2024). However, the sample is also relatively well-educated compared to the US at large (U.S. Census Bureau, 2024). Further study is needed to determine how the current results generalize to other samples and populations.

Finally, studies incorporating longitudinal assessment of EAA measures in tandem with psychosocial and socioeconomic variables (Poganik et al., 2023; Reynolds et al., 2020; Simons et al., 2022) will also help delineate causal pathways involved in aging. The present study clarified associations between average socioeconomic status and stress over time on the one hand, and epigenetic aging markers on the other; however, additional research with epigenetic markers observed at multiple timepoints is needed to better understand how longitudinal changes in psychosocial variables are related to epigenetic changes, and how those changes might be causally directed. These designs would also help delineate the way in which psychosocial factors act on aging processes — for example, whether they act cumulatively, or predictively as indicators of a stable process.

CRediT authorship contribution statement

Kristian E. Markon: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Frank Mann:** Writing – review & editing, Methodology, Formal analysis. **Colin Freilich:** Writing – review & editing, Data curation. **Steve Cole:** Writing – review & editing, Investigation, Funding acquisition, Data curation, Conceptualization. **Robert F. Krueger:** Writing – review & editing, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data used in this article is publicly available through ISPCR and

the MIDUS website.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2024.116990.

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