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Sexual Minority Stress and Cellular Aging in Methamphetamine-Using Sexual Minority Men With Treated HIV

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ABSTRACT

Objective: Sexual minority men (e.g., gay, bisexual, and other men who have sex with men) experience stigma and sexual minority stress, which are theorized to drive negative health outcomes. Sexual minority men with treated HIV display persistent immune dysregulation, which could be amplified by sexual minority stress responses to potentiate cellular aging.

Methods: This cross-sectional study included 52 sexual minority men living with HIV who had undetectable viral load (<40 copies/mL) and biologically confirmed recent methamphetamine use. Participants completed measures assessing sexual minority stress and openness about sexual minority status (i.e., outness). DNA methylation–derived outcomes included the following: the extrinsic epigenetic age acceleration clock, telomere length, naive CD4+ T-helper cells, and naive CD8+ T-cytotoxic/suppressor cells.

Results: After adjusting for negative affect and recent stimulant use, higher sexual minority stress was associated with a faster extrinsic epigenetic age acceleration clock ($\beta = 0.29$, $p = .030$), shorter telomere length ($\beta = -0.43$, $p = .002$), and fewer naive CD4+ ($\beta = -0.57$, $p < .001$) and naive CD8+ T cells ($\beta = -0.57$, $p < .001$). Greater outness was associated with higher naive CD4+ ($\beta = 0.32$, $p = .030$) and naive CD8+ T cells ($\beta = 0.38$, $p = .008$) as well as lower plasma interleukin 6 ($\beta = -0.33$, $p = .027$).

Conclusions: Sexual minority stress processes are associated with markers of cellular aging and inflammation in methamphetamine-using sexual minority men living with HIV. Longitudinal research should elucidate biobehavioral mechanisms linking sexual minority stress processes with accelerated cellular aging in those with and without HIV.

Key words: aging, epigenetic clock, HIV, methamphetamine, sexual minority stress.

INTRODUCTION

People with human immunodeficiency virus (HIV) receiving effective antiretroviral therapy (ART) experience accelerated biological aging (1), which is likely due to interacting pathophysiologic alterations driven in part by translocation of microbial products from the intestinal lumen into the systemic circulation (2–4). The resulting persistent immune activation and inflammation could partially account for evidence that people with HIV display accelerated cellular aging equivalent to 5.2 years, which is particularly associated with exhaustion of CD8+ cytotoxic/suppressor T cells (5). Ultimately, cellular and biological alterations may account for the disproportionate burden of HIV-associated non-AIDS comorbidities including greater risk for cardiovascular disease (6–12), diabetes (13–15), osteoporosis (16), frailty (17), renal disease (18,19), and neurocognitive disorders (20,21).

People with HIV are also more likely to have a faster epigenetic clock (5,22,23). Epigenetic clocks are biological age estimators with validated composite measures reflecting epigenetic alterations in genome-wide DNA methylation patterns (23). Derived from DNA methylation arrays, the extrinsic epigenetic age acceleration (EEAA) clock indexes alterations in methylation of select DNA cytosine-phosphate-guanosine dinucleotides (23,24). Interestingly,

ANS = autonomic nervous system, **ART** = antiretroviral therapy, **ASI** = Addiction Severity Index, **CTRA** = conserved transcriptional response to adversity, **EEAA** = extrinsic epigenetic age acceleration, **HIV** = human immunodeficiency virus, **HPA axis** = hypothalamic-pituitary-adrenal axis, **IL-6** = interleukin-6, **mRNA** = messenger RNA, **sCD14** = soluble CD14, **sCD163** = soluble CD163, **TNF-α** = tumor necrosis factor - alpha

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the faster EEAA clock persists among people with treated HIV for up to 24 months (22). This is consistent with findings that people with HIV receiving ART display shorter leukocyte telomere length, another validated measure of cellular aging (24,25).

Commonly used among persons with HIV (26), stimulants such as methamphetamine have been consistently linked to faster clinical HIV progression, even after adjusting for viral load and ART adherence (27,28). The deleterious consequences of stimulant use for HIV pathogenesis are supported partially by mechanistic studies documenting its direct and indirect effects on immune function (29,30). Several recent cross-sectional studies in those with treated HIV highlight that stimulant use could potentiate immune activation, inflammation, HIV persistence, and immunosenescence (31–35). Methamphetamine-induced alterations in these pathophysiologic processes could accelerate cellular aging. This is partially supported by one recent cross-sectional study where methamphetamine dependence and HIV were independently associated with shorter leukocyte telomere length (36).

Before the modern ART era (i.e., before 2007), cohort studies identified trauma and depression as risk factors for clinical HIV progression (37–40). These effects are theorized to be mediated in part by concomitant dysregulation of the autonomic nervous system (ANS) and hypothalamic-pituitary-adrenal (HPA) axis (41,42). Greater ANS activation at rest predicted poorer CD4+ T-helper cell recovery and higher HIV viral load in the year after highly active ART initiation (43). Interestingly, elevations in urinary levels of norepinephrine predict decrements in CD4+ T-cell count and increases in viral load for 4 years among highly active ART-treated people with HIV (44). An important gap is that few similar studies have been conducted in the modern ART era (i.e., 2007 to present) where life expectancy of individuals living with HIV in high-income countries is approaching that of the general population (45). Further research is especially warranted in high-priority populations that experience profound HIV-related health disparities, including racial and ethnic minorities, sexual minority men, and people who use stimulants (46,47).

The minority stress model (48,49) proposes that sexual minority populations experience unique forms of social stigma such as prejudice, anticipating prejudice, internalized stigma about being a sexual minority (i.e., internalized heterosexism), and concealment of sexual identity that have consequences for mental and physical health. These sexual minority stress processes are over and above stressors experienced by the general population, which is why sexual minority stress is theorized as a primary driver of health disparities. Thus, sexual minority stress could not only directly influence physical health but also indirectly via psychological (e.g., negative affect) and behavioral (e.g., stimulant use) pathways (Figure 1). Prior research observed that elevated sexual minority stress was associated with perturbations in leukocyte messenger RNA (mRNA) gene expression patterns relevant to inflammation and immune dysregulation in methamphetamine-using sexual minority men with treated HIV (50). This is consistent with other cross-sectional studies indicating that experiences of social adversity such as discrimination and homophobic victimization alter the conserved transcriptional response to adversity (CTRA) mRNA gene expression profile (51,52). The CTRA is often characterized by upregulated expression of genes involved in inflammation as well as downregulated expression of genes involved with type I interferon and antibody synthesis (53). An important gap is that few studies have examined the associations of sexual minority stress processes with alterations in DNA methylation patterns that could be mechanistically linked with mRNA gene expression and yield validated estimates of cellular aging such as the EEAA clock.

This cross-sectional study leveraged measures of leukocyte DNA methylation and soluble plasma markers of immune dysregulation (i.e., immune activation and inflammation) from 52 sexual

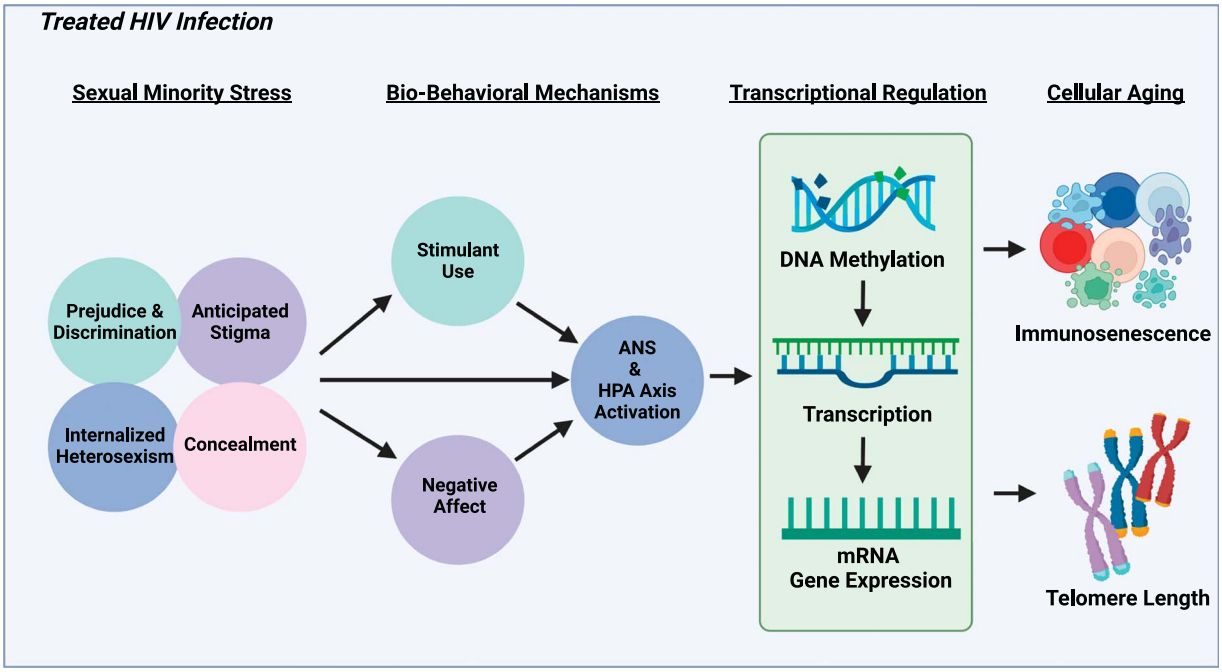

FIGURE 1. Conceptual model of the biobehavioral mechanism linking sexual minority stress processes with cellular aging in the context of treated HIV infection. ANS = autonomic nervous system; HIV = human immunodeficiency virus; HPA = hypothalamic-pituitary-adrenal; mRNA = messenger RNA.

minority men with treated HIV who use methamphetamine. As shown in Figure 1, the conceptual model illustrates the hypothesized pathways whereby sexual minority stress processes (i.e., anticipated stigma, prejudice and discrimination, internalized heterosexism, and concealment) may influence cellular senescence in the context of treated HIV infection. Prior research states that the experience of minority stress could potentiate activation of the ANS and HPA axis via increased negative affect and more frequent stimulant use (54–56). Alterations in the ANS and HPA axis could, in turn, influence transcriptional regulation in leukocytes such as alterations in DNA methylation patterns and downstream profiles of mRNA gene expression such as that observed in mechanisms related to the CTRA. Alterations in DNA methylation and mRNA gene expression could further alter processes relevant to cellular aging, including greater immunosenescence and shorter leukocyte telomere length. Drawing upon the proposed conceptual model, we hypothesized that sexual minority stress processes would be directly associated with DNA methylation–derived measures of cellular aging such as a faster EEAA clock, fewer naive CD4+ and CD8 + T cells, and shorter leukocyte telomere length. Similarly, we proposed that sexual minority stress processes would be directly associated with soluble measures of immune activation and inflammation. Because the correlates of outness (i.e., degree of openness about sexual minority status) have been previously shown to vary by race and ethnicity (57), we also explored whether the beneficial associations of outness with these outcomes were more pronounced among non-Hispanic White sexual minority men when compared with sexual minority men of color.

METHODS

Participants were 52 sexual minority men living with HIV who had undetectable viral load and biologically confirmed recent methamphetamine use based on urine or hair toxicology screening. Participants were recruited as part of a randomized controlled trial conducted from 2013 to 2017 in the San Francisco Bay Area. Additional details regarding the methods and outcomes of the randomized controlled trial are reported elsewhere (58,59). The institutional review board of the University of California at San Francisco approved all procedures, and reliance agreements were made with the University of Miami and Northwestern University. The present cross-sectional study focused on the baseline visit, which included self-report measures, a urine sample for onsite toxicology testing, and a peripheral venous blood sample to measure immune and HIV disease markers. From those who provided consent to bank biospecimens for future studies, we selected baseline leukocyte DNA samples for 52 participants who had an undetectable HIV viral load (i.e., <40 copies/mL) for measurement of genome-wide DNA methylation patterns and markers of immune activation.

Measures

Demographics and Health Status

Participants reported their age, race, ethnicity, education level, income, and time since HIV diagnosis in a demographic questionnaire. HIV viral load testing was performed to detect plasma HIV RNA using the Abbott Real Time HIV-1 assay (Abbott Molecular, Inc., Des Plaines, Illinois). The lower limit of detection was 40 copies/mL. CD4+ and CD8+ T-cell counts were measured with whole blood using flow cytometry by Quest Diagnostics.

Recent Stimulant Use

Urine samples were collected for onsite toxicology screenings for methamphetamine and cocaine using the iCup (Redwood Biotech, Inc., Santa Rosa, California). The iCup can detect any stimulant use (i.e., methamphetamine or cocaine) within the past 72 hours (coded as 1) versus no stimulant use (coded as 0).

Severity of Substance Use

The Addiction Severity Index (ASI) was administered to assess the severity of substance use (60). The ASI Drug Score includes the self-reported number of days using multiple illicit substances during the past 30 days, perceived impairment related to substance use, and perceived need for substance use disorder treatment.

Negative Affect

The modified Differential Emotions Scale was administered to assess positive and negative affect (61,62). Participants rated how frequently they felt a particular emotion in the past week from 0 (never) to 4 (most of the time). The eight negative affect items demonstrated adequate internal consistency in our sample (Cronbach $\alpha = .88$).

Sexual Minority Stress

The degree to which participants experienced sexual minority stress in theory-based domains—that is, concealment, isolation, internalized stigma, and social rejection—was measured using the five-item sexual minority stress subscale of the Cultural Assessment of Risk for Suicide scale (63). Sample items include, "The decision to hide or reveal my sexual orientation to others causes me significant distress," and "I was rejected by a family member or friend after telling him/her my sexual orientation." Likert-type response options ranged from 1 (strongly disagree) to 6 (strongly agree). Higher scores represent more sexual minority stress (Cronbach $\alpha = .70$).

Internalized Heterosexism

The revised Internalized Homophobia Scale (64), a measure that was previously validated among sexual minority people, was used to assess internalized stigma (Cronbach $\alpha = .85$). Sample items include, "I wish I weren't gay/bisexual" and "I have tried to stop being attracted to men in general." Participants rated five items from 1 (disagree strongly) to 5 (agree strongly) such that higher composite scores were indicative of greater internalized heterosexism.

Outness

The extent to which participants were out as sexual minority persons to other people was measured using the eight-item composite score of the Outness Inventory (65). Sample items included, "To which degree does your father know about your sexual orientation?" and "To which degree do your work peers know about your sexual orientation?" Likert-type response options ranged from 1 (person definitely does not know about your sexual orientation status) to 7 (person definitely knows about your sexual orientation status), with higher scores indicating more outness as a sexual minority person (Cronbach $\alpha = .91$).

DNA Methylation–Derived Estimates of Accelerated Cellular Aging

The EEAA measure and leukocyte telomere length were estimated with methylation of selected cytosine-phosphate-guanosine groups from genome-wide methylation of DNA extracted from leukocytes using the Infinium Methylation EPIC array (Illumina, San Diego, California). Samples were preprocessed using standard procedures as described previously (66) to yield validated estimates of the EEAA, leukocyte telomere length, and naive CD4+ and CD8+ T-cell levels (5,67–70).

Soluble Markers of Immune Activation and Inflammation

Plasma levels of soluble CD14 and soluble CD163 (sCD163) were determined using Human Quantikine Immunoassay (R&D Systems, Minneapolis, Minnesota) following the manufacturer's instructions. For soluble CD14 measurement, samples were diluted 400-fold, and results were expressed in nanograms per milliliter. For sCD163 measurement, samples were diluted 30-fold, and results were expressed in nanograms per milliliter. Plasma levels of tumor necrosis factor α and interleukin 6 (IL-6) were obtained via twofold undiluted plasma samples using the Human Quantikine Immunoassay (R&D Systems) following the manufacturer's instructions.

Statistical Analyses

We began by conducting zero-order correlations to examine bivariate associations among DNA methylation–derived estimates of accelerated cellular aging, sexual minority stress, and soluble markers of inflammation and immune activation. All measures were normally distributed except for sCD163 and tumor necrosis factor α, which were $\log_{10}$ transformed. Guided by zero-order correlations, we conducted 15 multiple linear regression analyses examining the associations of sexual minority stress processes with methylation-derived estimates of accelerated cellular aging and plasma IL-6 after adjusting for negative affect and recent stimulant use. A sensitivity analysis examined the robustness of these associations after replacing recent stimulant use with the ASI Drug Score. Each sexual minority stress measure was further tested in a separate linear regression because of collinearity among these conceptually related independent variables (71). Finally, we examined interaction effects to determine whether the beneficial associations of outness with these outcomes were moderated by race and ethnicity (i.e., more pronounced among non-Hispanic White men versus men of color).

RESULTS

Among the 52 participants, ages ranged from 24 to 59 years with a mean (standard deviation [SD]) of 43.3 (9.5) years. Half of the participants were White (52%), 25% were Hispanic/Latino, 12% were African American, 4% were Asian American, and 7% were other ethnic minorities or multiracial. Most participants completed at least some college (76%), and 67% had an income of less than US $16,000 per year. The median baseline CD4+ T-cell count was 670 (interquartile range = 468–9569) cells/mm^3. Participants had been living with HIV for an average (SD) of 14.1 (8.7) years. In addition, participants had been prescribed ART for a mean (SD) of 11.1 (7.1) years.

As shown in Table 1, we examined bivariate associations among sexual minority stress processes, DNA methylation–derived estimates relevant to cellular aging, and soluble markers of immune activation and dysregulation. Greater sexual minority stress scores were significantly associated with a faster EEAA clock ($r = 0.35$; $p = .011$), shorter leukocyte telomere length ($r = -0.049$; $p = .0003$), and fewer naive CD4+ ($r = -0.54$; $p < .0001$) and naive CD8+ ($r = -0.57$; $p < .0001$) T cells. Scatterplots of the associations of sexual minority stress with these outcomes are provided in Figure 2. Greater internalized heterosexism was significantly associated with shorter leukocyte telomere length ($r = -0.32$; $p = .020$) as well as fewer naive CD4+ ($r = -0.37$; $p = .008$) and naive CD8+ ($r = -0.34$; $p < .010$) T cells. Finally, higher outness scores were significantly associated with greater naive CD4+ ($r = 0.30$; $p = .030$) and naive CD8+ ($r = 0.40$; $p = .004$) T cells as well as lower plasma IL-6 ($r = -0.32$; $p = .020$). None of the soluble markers of immune activation or inflammation were significantly associated with DNA methylation–derived measures relevant to cellular aging.

Multiple linear regression analyses examined the direct associations of sexual minority stress with DNA methylation–derived measures of cellular aging and IL-6 (Table 2). After adjusting for negative affect and recent stimulant use, greater sexual minority stress was directly associated with a faster EEAA clock ($\beta = 0.29$; $p = .030$), shorter leukocyte telomere length ($\beta = -0.43$; $p = .002$), fewer naive CD4+ T cells ($\beta = -0.57$; $p < .001$), and fewer naive CD8+ T cells ($\beta = -0.57$; $p < .001$). These models accounted for 21.9% of the variance ($R^2 = 0.219$) in the EEAA clock, 30.4% of the variance ($R^2 = 0.304$) in leukocyte telomere length, 30.7% of the variance ($R^2 = 0.307$) in naive CD4+ T cells, and 33.0% of the variance ($R^2 = 0.330$) in naive CD8+ T cells. Higher internalized heterosexism was directly associated with lower counts of naive CD4+ ($\beta = -0.35$; $p = .012$) and CD8+ ($\beta = -0.31$; $p = .026$) T cells, with the models accounting for 14.6% ($R^2 = 0.146$) and 14.2% ($R^2 = 0.142$) of the variance in these outcomes. Finally, greater outness was directly associated with more naive CD4+ ($\beta = 0.32$;

TABLE 1. Associations Among DNA Methylation–Derived Markers of Cellular Aging, Soluble Markers of Immune Dysregulation, and Sexual Minority Stress ($N = 52$)

	1	2	3	4	5	6	7	8	9	10	11
1. EEAA clock	–										
2. Telomere length	−0.71***	—									
3. Naive CD4$^+$	−0.19	0.42**	—								
4. Naive CD8$^+$	−0.45***	0.60***	0.70***	—							
5. sCD14	0.25	−0.27	−0.09	−0.18	—						
6. sCD163 ($1og_{10}$)	−0.18	0.05	−0.14	−0.10	−0.06	—					
7. IL-6	−0.16	0.02	0.01	0.05	0.16	0.17	—				
8. TNF-α ($\log_{10}$)	−0.08	−0.02	−0.15	−0.08	0.17	−0.01	−0.27	—			
9. Sexual minority stress	0.35*	−0.49***	−0.54***	−0.57***	0.14	−0.05	0.16	0.15	—		
10. Internalized heterosexism	0.20	−0.32*	−0.37***	−0.34*	0.03	−0.24	0.17	0.17	0.39**	—	
11. Outness	−0.14	0.24	0.30*	0.40**	−0.11	−0.07	−0.32*	−0.07	−0.60**	−0.31*	—
Mean	0.96	6.89	618.32	211.71	1888.86	661.72	2.26	2.02	11.97	1.80	4.80
SD	12.58	0.34	85.03	37.32	496.23	379.32	1.88	0.09	5.71	0.93	1.75
Skewness	−0.87	0.22	0.34	0.17	0.49	4.91	2.03	−0.03	0.56	1.02	−0.73

EEAA = extrinsic epigenetic age acceleration; CD4+ = T-helper cells; CD8+ = T-cytotoxic/suppression cells; sCD14 = soluble CD14; sCD163 = soluble CD163; IL-6 = interleukin 6; TNF-α = tumor necrosis factor α; SD = standard deviation.

Analyses were zero-order Pearson correlations.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

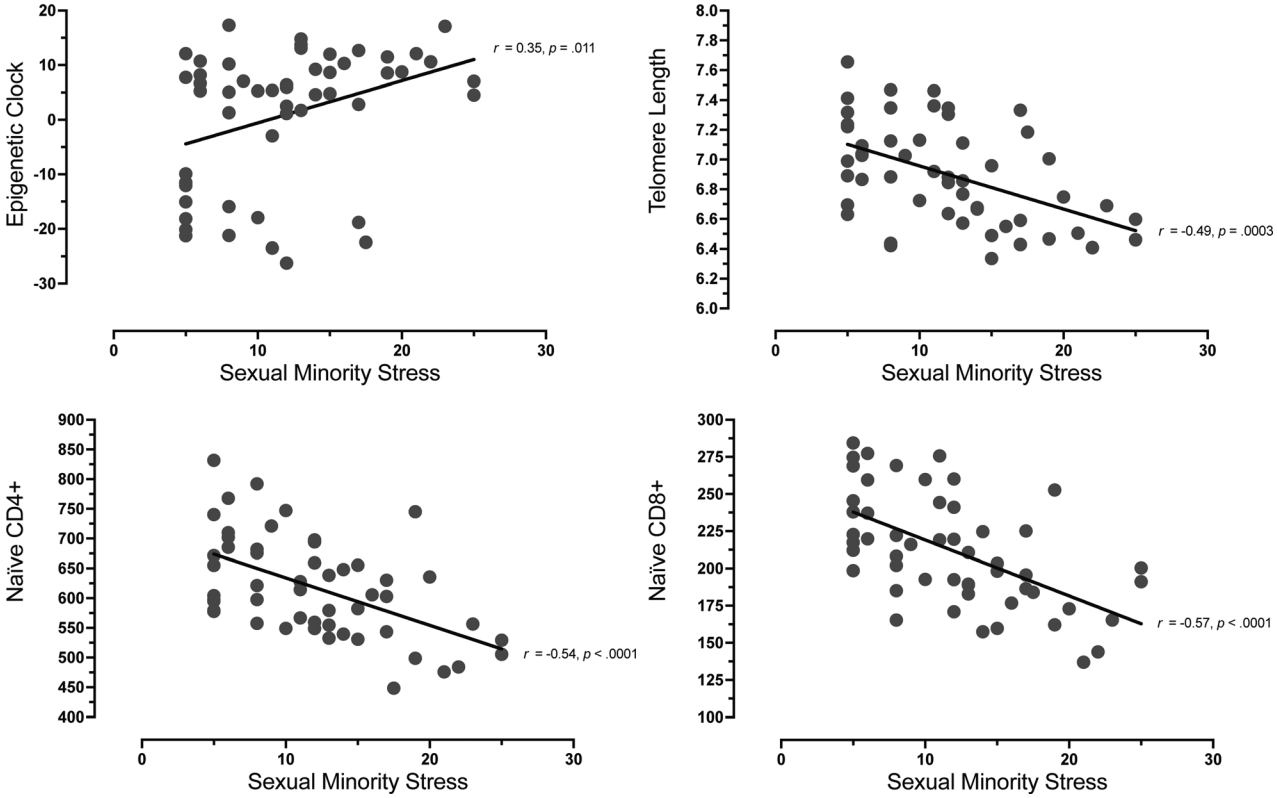

FIGURE 2. Scatterplots of the bivariate associations of greater sexual minority stress with DNA methylation–derived makers of cellular aging ($N = 52$). CD4+ = T-helper cells.

$p = .030$) naive CD8+ ($\beta = 0.38$; $p = .008$) T cells and lower plasma IL-6 ($\beta = -0.33$; $p = .027$), with models accounting for 11.1% ($R^2 = 0.111$), 17.8% ($R^2 = 0.178$), and 12.0% ($R^2 = 0.120$) of the variance in these outcomes. This pattern of findings was unchanged in models controlling for the ASI Drug Score instead of recent stimulant use. There was no evidence from moderation analyses that the beneficial associations of outness with these outcomes were more pronounced among non-Hispanic White men.

DISCUSSION

Findings from this cross-sectional study indicated that sexual minority stress is directly associated with DNA methylation–derived measures relevant to cellular aging after adjusting for prevailing negative affect and recent stimulant use. Most notably, the model examining a composite measure of sexual minority stress accounted for a medium-large proportion of the variance in the EEAA clock, which has been shown to be elevated in people with HIV up to 2 years after ART initiation (22). We also observed that sexual minority stress was directly associated with DNA methylation–derived estimates of shorter leukocyte telomere length as well as fewer naive CD4+ and CD8+ T cells. The fact that these associations remained even after adjusting for negative affect provides direct support for the minority stress model (48,49), which emphasizes the centrality of sexual minority stress processes in negative health outcomes and related disparities. Associations of sexual minority stress with measures of cellular aging also remained after adjusting for recent stimulant use and severity of substance use that have been previously linked to immune dysregulation in those with treated HIV

TABLE 2. Direct Associations of Sexual Minority Stress Processes With DNA Methylation–Derived Markers of Cellular Aging and Inflammation ($N = 52$)

	EEAA Clock	Telomere Length	Naive CD4+	Naive CD8+	IL-6
	β	β	β	β	β
Sexual minority stress	0.29*	−0.43**	−0.57***	−0.57***	0.19
Internalized heterosexism	0.14	−0.26	−0.35*	−0.31*	0.19
Outness	−0.14	0.23	0.32*	0.38**	−0.33*

EEAA = extrinsic epigenetic age acceleration; CD4+ = T-helper cells; CD8+ = T-cytotoxic/suppressor cells; IL-6 = interleukin 6.

Sexual minority stress processes were entered into separate linear regression models that included negative affect and recent stimulant use as covariates.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

(31–35). Based on the proposed conceptual model (Figure 1), these results will guide future longitudinal studies to examine the biobehavioral mechanisms for the indirect effects of sexual minority stress such as increased negative affect and stimulant use that alter ANS and HPA axis functioning to influence measures of cellular aging and immune dysregulation among people with and without HIV.

There was also some evidence that specific dimensions of sexual minority stress were directly associated with cellular aging and inflammation. Greater internalized heterosexism was associated with fewer naive CD4+ and CD8+ T cells after adjusting for negative affect and recent stimulant use. This is consistent with prior studies documenting the negative consequences of internalized heterosexism (72,73). Furthermore, greater outness was associated with more naive CD4+ and naive CD8+ T cells as well as lower plasma IL-6 levels. These findings are consistent with previously documented benefits of outness in sexual minority men with HIV before the modern ART era (74). Further research is needed to better characterize the potential benefits of outness in the context of important sources of social adversity affecting sexual minority men in different regions and among racially diverse populations (75,76). Although we did not observe that beneficial associations of outness were more pronounced among non-Hispanic White sexual minority men, the potential moderating effects of social adversity as well as race and ethnicity should be carefully examined in future longitudinal studies examining markers of cellular aging and inflammation. Taken together, findings highlight that there may be important health benefits of cognitive-behavioral treatments to provide coping skills for managing sexual minority stress, challenging cognitions linked to internalized heterosexism, and examining the potential benefits of disclosing one's sexual identity in contexts where there is likely to be a supportive outcome (77,78). Further clinical research is needed to determine whether and how interventions to modify sexual minority stress processes could alter epigenetic markers relevant to cellular aging and inflammation.

This study should be interpreted in the context of some limitations. First, the cross-sectional design and modest sample size limited our ability to determine if sexual minority stress predicted increases in cellular aging and inflammation over time. Longitudinal research is needed to replicate and extend these findings as well as examine multilevel determinants and biobehavioral mechanisms relevant to the effects of sexual minority stress. As shown in Figure 1, advancing our basic understanding of the mediating mechanisms (e.g., negative affect and stimulant use) for the associations of sexual minority stress processes would guide more comprehensive approaches to reduce cellular aging and inflammation in sexual minority men.

Randomized controlled trials should also test the efficacy of cognitive-behavioral interventions targeting sexual minority stress processes for improving epigenetic aging, which would provide more direct, causal evidence for the role of sexual minority stress processes on cellular aging and inflammation. Second, although prior studies have observed associations of shorter telomere length with inflammation (36), there were no significant associations of soluble markers of immune activation or inflammation with DNA methylation–derived measures of cellular aging. Future studies should include more comprehensive panels of soluble markers of immune activation and dysregulation to determine if measures of epigenetic aging can yield more precise estimates of risk for negative health outcomes. Third, the present study enrolled sexual minority men with treated HIV who use methamphetamine residing in San Francisco. The fact that sexual minority stress processes were associated with these outcomes in a progressive community underscores their potentially enduring consequences. Further research in more representative samples of sexual minority men with and without HIV is needed to examine the generalizability of these findings. Fourth, although we leveraged a composite measure of the EEAA clock to minimize the false discovery rate, future studies should plan for adequate statistical power with the appropriate statistical corrections for multiple tests as well as examining theory-based moderators (e.g., race and ethnicity) and mediators (e.g., negative affect).

Despite these limitations, this study is among the first to observe that sexual minority stress is associated with accelerated cellular aging in methamphetamine-using men with treated HIV. These results provide direct support for the scientific premise of longitudinal research to elucidate biobehavioral mechanisms whereby sexual minority stress processes accelerate biological aging in men with and without HIV. Furthermore, findings highlight the need for clinical research examining the efficacy of interventions targeting different aspects of sexual minority stress with respect to measures of accelerated cellular aging and immune dysregulation.

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