

Associations between use of chemical hair products and epigenetic age

Findings from the Sister Study

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Background: Hair products may be a source of harmful chemicals and have been linked to age-related health outcomes. We investigated whether the use of hair products is related to epigenetic age in a sample of Black (both Hispanic and non-Hispanic) and non-Hispanic White women.

Methods: In a subset of 4358 participants aged 35–74 years from the Sister Study, we estimated cross-sectional associations between self-reported use of four chemical hair products (permanent dye, semipermanent dye, straighteners/relaxers, and hair permanents/body waves) in the year before enrollment (2003–2009) and three DNA methylation-based measures of epigenetic age (DunedinPACE, GrimAge age acceleration [GrimAgeAccel], and PhenoAge age acceleration [PhenoAgeAccel]) using survey-weighted multivariable linear regressions. Associations were estimated both overall and by self-identified race and ethnicity, adjusting for chronological age, socioeconomic and lifestyle factors, body mass index, menopausal status, and DNA methylation platform.

Results: Associations between the use of hair products and the three epigenetic age measures were largely null. Use of hair permanents/body waves was modestly associated with higher DunedinPACE among all participants ($\beta_{\text{ever-never}} = 0.010$; 95% confidence interval [CI] = 0.001, 0.019) and with lower PhenoAgeAccel among Black women ($\beta_{\text{ever-never}} = -1.53$; 95% CI = -2.84, -0.21).

Conclusion: In this US-based study, we found little evidence of associations between chemical hair product use and epigenetic age in Black and non-Hispanic White women. Observed associations were modest and largely not supported by dose–response relationships or were inconsistent across epigenetic age measures. Previously observed associations between chemical hair product use and aging-related health outcomes may not be explained by the biological aging pathways captured by DunedinPACE, GrimAgeAccel, or PhenoAgeAccel. Alternative biological pathways are worth investigating in racially diverse samples.

Key words: Hair products; Hair preparations; DNA methylation; Epigenetic age; Biological age

Introduction

Some hair products, such as permanent hair dyes and chemical straighteners or relaxers, may contain harmful chemicals.^{1,2} The

use of these products, along with exposure to the chemicals commonly found in them, has been associated with various health outcomes,^{3–10} including a higher incidence of hormone-driven cancers in women.^{11–13} The biological pathways linking chemical hair product use to age-related health outcomes are not fully understood. DNA methylation-based measures of epigenetic age, such as DunedinPACE,¹⁴ GrimAge,¹⁵ and PhenoAge,¹⁶ have emerged as intermediate biomarkers of age-related health outcomes and may provide insights into the biologic changes linking chemical hair products and health.^{17,18} For example, environmental exposures related to aging-related health outcomes, including alcohol consumption,¹⁹ air pollution,^{20,21} and chemical exposures,²² have been shown to be associated with accelerated epigenetic age. Despite this, no studies have explored the relationship between the use of chemical hair products and epigenetic age.

Use of chemical hair products over the life course varies across different racial and ethnic groups, both in frequency of use and in the types of products and ingredients, which are tailored to meet different needs.²³ Notably, Black women often

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What this study adds:

In this first study to consider if the use of chemical hair products is related to DNA methylation-based measures of epigenetic age, we found little evidence of an association. However, considering that the use of chemical hair products has been linked to cancer incidence and other adverse health outcomes, it is worthwhile to investigate alternative biological pathways that may not be reflected in epigenetic age. This is particularly important in racially and ethnically diverse populations, given that the frequency, patterns, and types of product used over the life course vary across groups.

have higher exposure to harmful chemicals and endocrine-disrupting compounds (EDCs) in personal care products,^{24,25} leading to the hypothesis that this body burden of EDCs may be a contributor to health disparities in age-related outcomes.²⁶ This differential exposure burden underscores the importance of understanding the health impact of chemical hair product use with consideration of race and ethnicity.^{27,28} In this study, we assess associations between chemical hair product use and DNA methylation-based measures of epigenetic age among Black and non-Hispanic White (NHW) women.

Materials and methods

Study population and exposure assessment

The Sister Study enrolled 50,884 women, aged 35–74 years, with at least one sister who had breast cancer but no prior breast cancer themselves during 2003–2009.²⁹ In this analysis, we focused on a subset of Black (including Hispanic and non-Hispanic) and NHW women selected for a nested case-cohort study of breast cancer incidence who had existing DNA methylation data ($n = 4,482$).²⁰

At enrollment, details on covariates such as demographic and lifestyle factors were gathered via a computer-assisted phone interview. Information on the use of hair products in the past year (permanent dye, semipermanent dye, straighteners/relaxers, and hair permanents/body waves) was collected via a self-administered questionnaire.³⁰ Participants reported their frequency of hair product use with the response options including “did not use,” “1–2 times per year,” “every 3–4 months,” “every 5–8 weeks,” “once per month,” and “more than once per month.” Based on the distributions, we collapsed frequency variables to be ≤ 2 and > 2 times in the past year for hair permanents, and ≤ 4 and > 4 times in the past year for the other hair products among participants who reported ever use. Additionally, weight and height were measured during a home visit by trained examiners at enrollment. Participants with missing data on all products ($n = 79$) or any of the selected covariates ($n = 45$) were excluded, resulting in a sample of 667 Black and 3671 NHW women (Data Release 10.1, USA, follow-up information updated through October 2020). Written informed consent was obtained from all participants, and this study is overseen by the Institutional Review Board of the National Institutes of Health.

DNA methylation

DNA methylation was measured by Illumina Infinium HumanMethylation450 ($n = 2,752$) or MethylationEPIC v1 BeadChips (San Diego, CA) ($n = 2,076$) and preprocessed using previously described techniques in blood samples collected at baseline.³¹ For participants measured on both platforms ($n = 423$), we used values from MethylationEPIC v1 BeadChip. DunedinPACE is a measure of aging pace or rate.³² GrimAge age acceleration (GrimAgeAccel) and PhenoAge age acceleration (PhenoAgeAccel) are measures of “age acceleration,” calculated as the residuals from regressing GrimAge and PhenoAge on chronological age.^{18,20}

Statistical analyses

We used multivariable linear regressions to estimate cross-sectional associations between hair product use and epigenetic age measures. Models were adjusted for chronological age (continuous), attained education (high school or less, some college, college or above), household annual income ($< \$50,000$, $\$50,000$ – $100,000$, $\geq \$100,000$), menopausal status (premenopausal, postmenopausal), body mass index category (underweight and recommended, overweight, obesity), physical activity (metabolic equivalent task hours per week), smoking status (never, past, current), alcohol consumption (never or past, current < 1 drink per

day, current ≥ 1 drink per day), and DNA methylation platform (HumanMethylation450 BeadChip, MethylationEPIC BeadChip). To account for the case-cohort design used to sample women for DNA methylation measurements, all analyses integrated inverse probability of selection weights to ensure the generalizability of results to the entire sample of Black and non-Hispanic White women enrolled in the Sister Study.³³ In analyses of each epigenetic age measure, we excluded the measures that were outside four standard deviations of the mean ($n = 6$, DunedinPACE; $n = 12$, GrimAgeAccel; and $n = 3$, PhenoAgeAccel). We tested for monotonic relationships using Wald tests on ordinal categories for frequency of product use. Race and ethnicity-specific associations were estimated by including multiplicative interaction terms and we tested for heterogeneity using Wald tests. In sensitivity analyses, we additionally adjusted for self-reported hair characteristics, including grayness (yes, no) and thinness (yes, no), recognizing their potential influence on behaviors associated with the use of chemical hair products. All analyses were conducted in R version 4.2.3 (Vienna, Austria).

Results

Study participants had a median chronological age of 55.7 years; more than half attained a college degree or above. Black women had higher weighted median DunedinPACE (Black, 1.10; NHW, 1.05) and GrimAgeAccel (Black, 0.11; NHW, -0.75), but lower PhenoAgeAccel (PhenoAgeAccel: Black, -0.43 ; NHW, -0.37), compared with NHW women. Black women more frequently used semipermanent dye, straighteners/relaxers, and hair permanents/body waves than NHW women, whereas NHW women used permanent dye more frequently (Table 1).

We observed largely null associations between hair product use and DNA methylation-based epigenetic age. When associations were observed, results were inconsistent across epigenetic age measures and between racial groups. For example, in comparison to women who never used hair permanents/body waves, women who ever used these products showed a positive association with DunedinPACE, overall ($\beta_{\text{ever-never}} = 0.010$; 95% confidence interval [CI] = 0.001, 0.019) (Figure 1; Table S1; <http://links.lww.com/EE/A276>), with a slightly stronger association in NHW women ($\beta_{\text{ever-never}} = 0.012$; 95% CI = 0.001, 0.022) and an imprecise and near-null estimated association in Black women ($\beta_{\text{ever-never}} = 0.002$; 95% CI = -0.015 , 0.020; $P_{\text{het}} = 0.37$). In contrast, use of hair permanents/body waves showed an inverse association with PhenoAgeAccel in Black women ($\beta_{\text{ever-never}} = -1.53$; 95% CI = -2.84 , -0.21) with a more pronounced association when comparing frequent use to never use ($\beta_{\text{frequent-never}} = -1.62$, 95% CI = -3.00 , -0.2336 ; $P_{\text{trend}} = 0.02$) (Figure 2). However, no associations were observed between hair permanents/body waves and PhenoAgeAccel in NHW women ($\beta = 0.24$, 95% CI = -0.55 , 1.03; $P_{\text{het}} = 0.02$).

Ever use of semipermanent dye was inversely associated with GrimAgeAccel in Black women ($\beta = -0.70$; 95% CI = -1.30 , -0.09) but not in NHW women ($\beta = 0.07$, 95% CI = -0.25 , 0.40; $P_{\text{het}} = 0.03$) (Figure 1). Some nonnull associations were observed when comparing less frequent to never use, such as straighteners/relaxer use with DunedinPACE and PhenoAgeAccel in NHW women, and semipermanent dye with GrimAgeAccel in Black women (Figure 2). However, these associations did not hold for more frequent product use, and the tests for trend did not yield significant results. Estimates remained unchanged in sensitivity analyses additionally adjusting for either hair grayness or thinning (Table S1; <http://links.lww.com/EE/A276>).

Discussion

In a sample of US Black and NHW women in the Sister Study, we observed little evidence of associations between the use of chemical hair products and DNA methylation-based epigenetic

Table 1.
Characteristics of the participants in the Sister Study by race/ethnicity, enrolled 2003–2009 (N = 4,358)

	All (N = 4,358)	Black ^a (n = 667)	Non-Hispanic White (n = 3,691)
Chronological age (years); median (IQR) ^b	55.7 (13.2)	53.5 (11.6)	56.0 (13.4)
Educational attainment; n (%) ^c			
High school or less	632 (15%)	72 (11%)	560 (16%)
Some college	1,436 (34%)	229 (34%)	1,207 (34%)
College or above	2,290 (51%)	366 (55%)	1,924 (51%)
Household annual income; n (%) ^c			
<50,000	1,102 (25%)	221 (33%)	881 (24%)
50,000–<100,000	1,781 (40%)	292 (43%)	1,489 (39%)
≥100,000	1,475 (36%)	154 (24%)	1,321 (37%)
Body mass index; n (%) ^c			
Underweight (<18.5 kg/m ²)	35 (0.8%)	0 (0%)	35 (1%)
Recommended (18.5–25 kg/m ²)	1,528 (38%)	120 (18%)	1,408 (39%)
Overweight (25–30 kg/m ²)	1,416 (33%)	203 (31%)	1,213 (33%)
Obesity (≥30 kg/m ²)	1,379 (29%)	344 (50%)	1,035 (27%)
Menopausal status; n (%) ^c			
Premenopausal	1,341 (33%)	253 (41%)	1,088 (32%)
Postmenopausal	3,017 (67%)	414 (59%)	2,603 (68%)
Physical activity (metabolic equivalent hours/week); median (IQR) ^c	44.8 (41.5)	38.9 (32.1)	45.6 (41.8)
Smoking status; n (%) ^c			
Never	2,373 (55%)	428 (64%)	1,945 (53%)
Past	1,639 (37%)	180 (27%)	1,459 (38%)
Current	346 (9%)	59 (9%)	287 (9%)
Alcohol consumption; n (%) ^c			
Never or past	808 (18%)	213 (30%)	595 (17%)
Current <1 drink per day	2,958 (69%)	422 (65%)	2,536 (69%)
Current ≥1 drinks per day	592 (13%)	32 (5%)	560 (14%)
DunedinPACE; median (IQR) ^b	1.06 (0.11)	1.10 (0.12)	1.05 (0.11)
GrimAgeAccel; median (IQR) ^b	−0.65 (4.0)	0.11 (4.6)	−0.75 (3.9)
PhenoAgeAccel; median (IQR) ^b	−0.37 (7.9)	−0.43 (9.1)	−0.37 (7.8)
Use of permanent dye; n (%) ^c			
Never	2,039 (46%)	373 (58%)	1,666 (45%)
≤4 times in the past year	974 (22%)	183 (27%)	791 (22%)
>4 times in the past year	1,332 (32%)	107 (15%)	1,225 (33%)
Use of semipermanent dye; n (%) ^c			
Never	3,522 (82%)	428 (64%)	3,094 (84%)
≤4 times in the past year	491 (11%)	150 (23%)	341 (9%)
>4 times in the past year	321 (7%)	86 (13%)	235 (7%)
Use of straighteners/relaxers; n (%) ^c			
Never	3,754 (91%)	169 (27%)	3,585 (97%)
≤4 times in the past year	238 (4%)	180 (27%)	58 (2%)
>4 times in the past year	354 (5%)	312 (47%)	42 (1%)
Use of hair permanents/body waves; n (%) ^c			
Never	3,715 (87%)	494 (75%)	3,221 (88%)
≤2 times in the past year	275 (6%)	27 (4%)	248 (7%)
>2 times in the past year	357 (7%)	139 (21%)	218 (5%)

Missing: DunedinPACE (Black, n = 2), use of permanent dye (Black, n = 4; non-Hispanic White, n = 9), use of semipermanent dye (Black, n = 3; non-Hispanic White, n = 22), use of straighteners/relaxers (Black, n = 6; non-Hispanic White, n = 7), and use of hair permanents/body waves (Black, n = 7; non-Hispanic White, n = 5).

^aIncluding 19 Hispanic and 648 non-Hispanic Black/African Americans; combined in this study due to small sample numbers.

^bWeighted median and IQR to reflect the distribution in the entire Sister Study cohort.

^cSample numbers are actual numbers of participants included in the analyses. Percentages are weighted to reflect the distribution in the entire Sister Study cohort.

GrimAgeAccel indicates GrimAge age acceleration; IQR, interquartile range; PhenoAgeAccel, PhenoAge age acceleration.

age. While there are some signals suggesting that the use of hair permanents/body waves is associated with a modest increase in DunedinPACE, this finding was only observed in NHW women, with no corresponding evidence of increases in the other two measurements of epigenetic age. Other scattered statistically significant associations that we observed are mostly not supported by a dose–response relationship. Additionally, we did not observe a stronger adverse effect on the epigenetic aging measures for chemical hair product use in Black women than NHW women.

Strengths of this study include detailed information on hair product use (i.e., different types and frequencies), recently developed epigenetic age measures, and a large sample size. Notably, the inclusion of Black participants, who have been historically underrepresented in epigenetics research, is particularly significant because Black women use most hair products more

frequently than NHW women, with formulations potentially containing more harmful chemicals.^{24,25} Limitations include a lack of information on product brands and chemical ingredients and reliance on product use in the past year without capturing the exposures during the hypothesized sensitive windows such as prenatal and pubertal period.^{34,35} Moreover, the included epigenetic age measures were developed in predominantly White and European ancestry cohorts although there were validation efforts across racial groups.^{15,16,32}

To our knowledge, this is the first study investigating the associations between the use of chemical hair product use and epigenetic age. Although the use of chemical hair products, particularly permanent dye and straighteners/relaxers, has been linked to the incidence of cancers and other adverse health outcomes,^{5–13} our findings suggest that these relationships may not be primarily attributed to biological aging pathways captured by

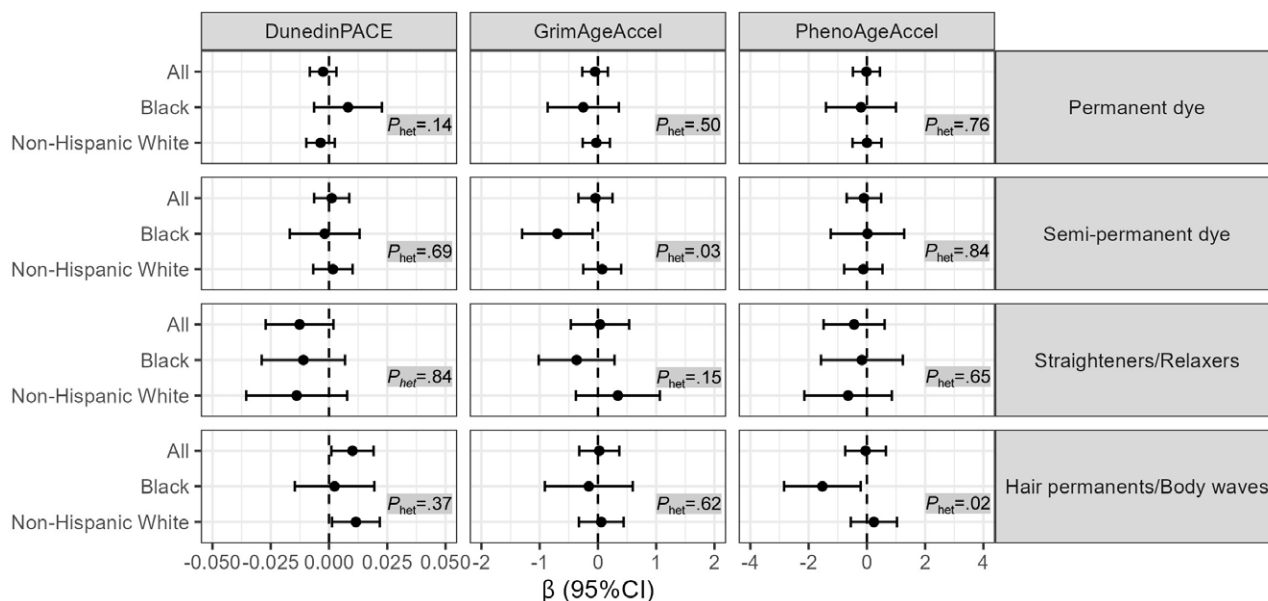


Figure 1. Effect estimates and 95% confidence intervals (CIs) for the differences in DNA methylation-based epigenetic age measures associated with ever versus never chemical hair products use in the past year (N = 4,358). P_{het} : P value for heterogeneity using Wald tests on the race-by-hair product interaction terms. β : effect estimates from the results of survey-weighted multivariable linear regressions. All survey-weighted models were adjusted for chronological age, educational attainment, household annual income, body mass index category, menopausal status, physical activity, smoking status, alcohol consumption, and DNA methylation platforms.

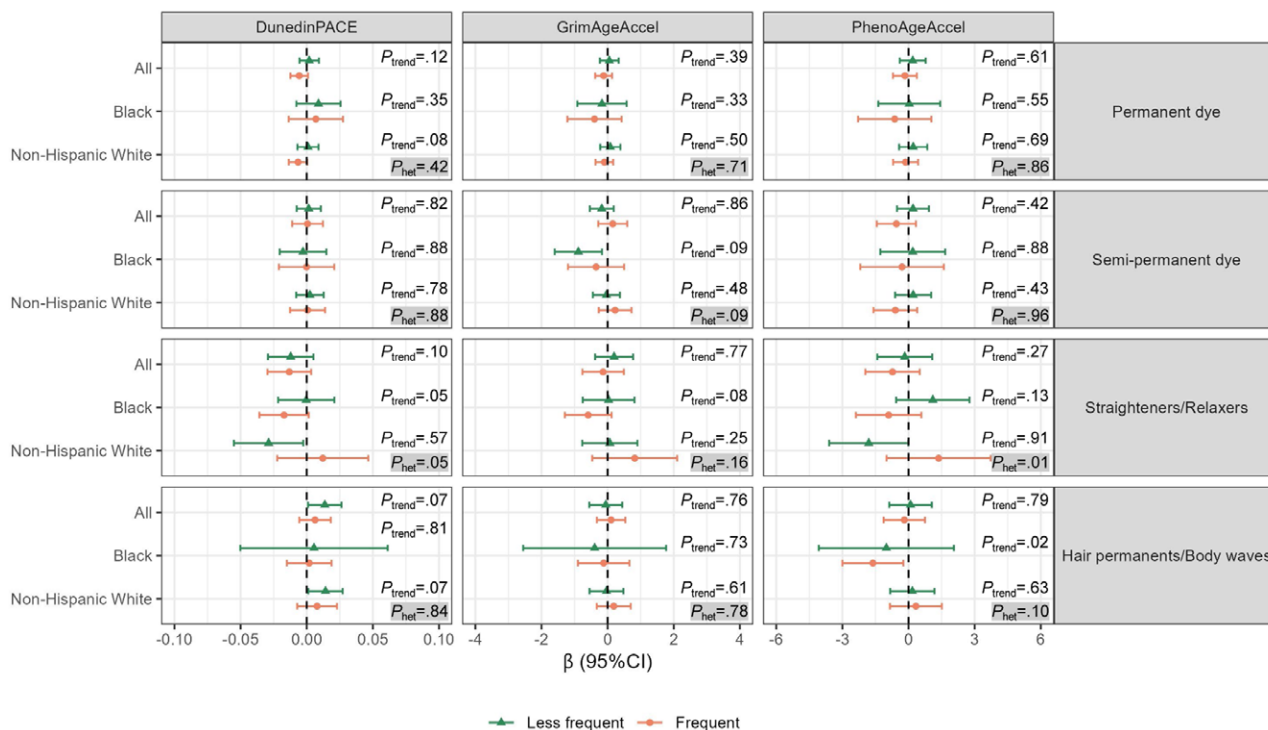


Figure 2. Effect estimates and 95% confidence intervals (CIs) for the differences in DNA methylation-based epigenetic age measures associated with frequent and less frequent versus never chemical hair product use in the past year (N = 4,358). P_{trend} : P value for trend using Wald test on ordinal categories of frequency of hair product use. P_{het} : P value for heterogeneity using Wald tests on the race-by-hair product interaction terms. β : effect estimates from the results of survey-weighted multivariable linear regressions. Less frequent use was defined as using the product 4 times or less for permanent dye, semipermanent dye, and straighteners/relaxers and 2 times or less for hair permanents/body waves; frequent use was defined as using the product more than 4 times for permanent dye, semipermanent dye, and straighteners/relaxers and more than 2 times for hair permanents/body waves. All survey-weighted models were adjusted for chronological age, educational attainment, household annual income, body mass index category, menopausal status, physical activity, smoking status, alcohol consumption, and DNA methylation platforms.

DunedinPACE, GrimAgeAccel, or PhenoAgeAccel. Alternative biological pathways may be worth investigating,³⁶ particularly in racially diverse populations, to better understand the impact of chemical hair products.

Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

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