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Featured Article

Socioeconomic Status, Knee Pain, and Epigenetic Aging in Community-Dwelling Middle-to-Older Age Adults

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Abstract: **Chronic musculoskeletal pain is often associated with lower socioeconomic status (SES). SES correlates with psychological and environmental conditions that could contribute to the disproportionate burden of chronic stress. Chronic stress can induce changes in global DNA methylation and gene expression, which increases risk of chronic pain. We aimed to explore the association of epigenetic aging and SES in middle-to-older age individuals with varying degrees of knee pain. Participants completed self-reported pain, a blood draw, and answered demographic questions pertaining to SES. We used an epigenetic clock previously associated with knee pain (DNAmGrimAge) and the subsequent difference of predicted epigenetic age (DNAmGrimAge-Diff). Overall, the mean DNAmGrimAge was 60.3 (±7.6), and the average DNAmGrimAge-diff was 2.4 years (±5.6 years). Those experiencing high-impact pain earned less income and had lower education levels compared to both low-impact and no pain groups. Differences in DNAmGrimAge-diff across pain groups were found, whereby individuals with high-impact pain had accelerated epigenetic aging (~5 years) compared to low-impact pain and no pain control groups (both ~1 year). Our main finding was that epigenetic aging mediated the associations of income and education with pain impact, as such the relationship between SES and pain outcomes may occur through potential interactions with the epigenome reflective of accelerated cellular aging.**

Perspective: ***Socioeconomic status (SES) has previously been implicated in the pain experience. The present manuscript aims to present a potential social–biological link between SES and pain via accelerated epigenetic aging.***

Key Words: *Chronic pain, socioeconomic status, epigenetic aging, DNAmGrimAge, aging*

Chronic pain affects millions of Americans with occurrence rates estimating 11 to 40%, with higher prevalence associated with advancing age.[1,2] Despite significant improvements in healthcare access and chronic pain management, those with lower socioeconomic status (SES) tend to experience higher impact pain than those with higher SES,[1,3] even within nations whereby healthcare is available at little cost.[4] Furthermore, among those with chronic pain and lower SES, living with a chronic pain condition was disproportionately burdensome compared to individuals who had a higher SES.[5,6]

There is a pronounced socioeconomic (SES) gradient in pain among middle-aged and older adults.[7,8] Low-SES settings present a complex array of health disparities due to recognized patterns of lower levels of education and health literacy, reduced access to quality healthcare, and the myriad effects of stress associated with low income.[9] To better understand the relationship between SES and chronic pain, it is important examine factors that may

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influence this association including education, income, and employment status. In the past 5 years, age-adjusted prevalence's of chronic pain have been shown to be higher among women, adults who had worked previously but were not currently employed, adults living in/near poverty, and those living in rural settings. Furthermore, the age-adjusted prevalence's of chronic pain were significantly lower among individuals with a minimum education level of a bachelor's degree compared to all other education levels.[1]

SES is highly correlated with a plethora of psychological and environmental conditions.[10,11] Accelerated epigenetic aging, which has been previously shown to change across the lifespan upon exposure to biopsychosocial factors, is suggested to be the overarching link of SES with health outcomes.[12] SES has been previously associated with changes in global DNA methylation and gene expression.[13] Epigenetic clocks have been used to predict an individual's epigenetic age against chronological age (time spent on earth) to indicate accelerated or decelerated aging processes.[14] Epigenetic clocks have been associated with sociocultural aspects[12,15,16] and with exposure to stressors in ones environment.[17] One clock in particular, DNAmGrimAge, uses chronological age, sex, and DNAm-based surrogate biomarkers for several plasma proteins and smoking pack-years to predict biological aging.[18] DNAmGrimAge has demonstrated stronger relationships with a variety of health-related metrics compared to other epigenetic clocks[19] including chronic pain.[20,21] The relationship between SES and epigenetics still largely remains a mystery.

Recent literature has begun to explore the topic of epigenetics and chronic pain, SES and chronic pain, and epigenetics and SES; however, a gap in the literature exists on the intersection of SES, chronic pain, and epigenetic aging. Therefore, this study sought to explore the relationships among self-reported pain impact, epigenetic aging, and SES in individuals with chronic knee pain. This study was conducted to test the hypothesis that epigenetic aging will mediate the association of SES with pain impact, including education, income, and employment status as measures of SES. The goal of this study was to highlight the critical role that epigenetic aging plays as a potentially important mechanism bridging SES and chronic pain.

Methods

Participants

Participants were recruited as part of a larger cohort investigation primarily examining racial and ethnic differences in persons with knee osteoarthritis and healthy controls pain recruited from the surrounding communities of the University of Florida (Gainesville, FL) and the University of Alabama at Birmingham (Birmingham, AL). Participants were adults between the ages of 45 to 85 with and without symptomatic knee osteoarthritis pain that were recruited via newspaper, online advertisements, radio, and flyers. Individuals who self-identified as non-Hispanic and "African American/Black" or non-Hispanic and "White/Caucasian/European," English speaking, and for those experiencing pain, knee osteoarthritis pain either persistent or recurring for more than 6 months were eligible for inclusion. Exclusion criteria included 1) significant surgery to the index (ie, most painful) knee (eg, total knee replacement surgery); 2) cardiovascular disease or history of acute myocardial infarction; 3) uncontrolled hypertension (blood pressure > 150/95 mmHg); 4) systemic rheumatic diseases (eg, rheumatoid arthritis, systemic lupus erythematosus, and fibromyalgia); 5) neuropathy; 6) chronic opioid use; 7) serious psychiatric illness; 8) neurological disease (eg, Parkinson's, multiple sclerosis, stroke with loss of sensory or motor function, or uncontrolled seizures); 9) pregnant; 10) significantly greater pain in a body site other than the knee. Exclusion criteria were confirmed by medical review. All participants provided written informed consent prior to study commencement. The study was approved by the institutional review board at both institutions and were conducted in accordance with the Declaration of Helsinki.

Procedures

Demographic information including age, ethnicity/race, and sex were self-reported during initial phone screening. Eligible individuals were scheduled for an initial visit, at which informed consent and SES information were obtained, followed by health and pain history review and a physical exam. Approximately 1 week later, participants attended a second session, where clinical pain measures and blood samples were collected. For transparency, we have previously used these data that have been previously used in other works examining associations between epigenetics and other pain-related variables.[21-25] While some previous analyses of epigenetic findings have been reported, those analyses involved other phenotypic variables that do not overlap with the focus of the present study.

Graded Chronic Pain Scale

The Graded Chronic Pain Scale (GCPS) is a self-reported questionnaire that measures pain intensity and pain-related disability. The 7-item questionnaire asking participants to report their current, average, and worst pain over the last 6 months (ie, 0 = "no pain" to 10 = "pain as bad as it can be"), and how much pain has interfered with daily activities, recreation/social/family activities, and ability to work (ie, 0 = "no interference" to 10 = "unable to carry out activities"). Scores are calculated as the mean intensity ratings for the current, worst, and average pain multiplied by 10; and the pain-related disability score, which is calculated as the mean rating for difficult performing daily, social- and work-related activities multiplied by 10, with each score ranging from 0 to 100. Higher scores indicate greater pain and pain-related disability.[15] The GCPS also allows classification where grade 0 is no pain, grade I is low disability–low intensity, grade II is low disability–high intensity, grade III is high disability–moderately limiting, and grade IV is high disability–severely limiting.[26] Consistent with the Task Force for the Classification of Chronic Pain consensus for the 11th version of the International Classification of Diseases,[27] we grouped participants into 3

groups: 1) no chronic pain controls (ie, GCPS grade 0), 2) low-impact pain (ie, GCPS grades 1–2), and 3) high-impact pain (ie, GCPS grade 3–4).

Blood Collection and Processing

Blood samples were collected from the forearm or hand vein at the onset of the session using a 10 mL K^2 EDTA (Ethylenediaminetetraacetic acid) tube that were subsequently used for DNA methylation analyses.

DNA Extraction and Methylation Analysis

The EDTA tube was centrifuged at 3000 rpm for 10 minutes and the buffy coat was carefully extracted and transferred to a cryovial for –80° storage. To isolate genomic DNA, the frozen buffy coat samples were thawed at 37 °C to dissolve homogeneously. Approximately 200 μL (or 150–200 μL) of sample was lysed in red blood cell lysis buffer and centrifuged at 6000 rpm for 5 minutes at room temperature. The supernatant was discarded and sodium EDTA solution was added to the pellet and vortex gently to remove red blood cell clumps. Homogenate was incubated at 50 to 55 °C with Proteinase K and SDS (Sodium dodecyl sulfate) solution. Following incubation, equal volume of phenol was added, mixed, and centrifuged at 10,000 rpm for 10 minutes. Supernatant was transferred in a fresh tube and equal volume of phenol–chloroform–isoamyl alcohol was added, mixed, and centrifuged at the same rpm. Again, supernatant was transferred in a fresh tube and equal volume of chloroform–isoamyl alcohol was added followed by centrifugation at same rpm conditions. Supernatant was transferred in a fresh tube and one-tenth volume of 3 M sodium acetate along with 2 volumes of absolute alcohol was added. The precipitated DNA was washed with 70% ethanol by centrifugation at 10,000 rpm for 5 minutes. The pellet was air dried and dissolved in Tris-EDTA buffer. The dissolved DNA was qubit quantified and visualized on agarose gel for quality assessment. Sodium bisulfite conversion and EPIC methylation array was performed by Moffitt Cancer Center, Molecular Genomics Core (Tampa, FL) using the Infinium Human Methylation EPIC Bead Chip kit covering over 850,000 CpG sites, with each CpG assay replicated.

DNA Methylation Age Calculation

Prior to the calculation of DNAGrimAge via an online calculator (https://dnamage.genetics.ucla.edu/home), the raw data generated by Illumina EPIC array (.idat files) underwent quality control and normalization. The normalized beta values were obtained using ChAMP (Chip Analysis Methylation Pipeline for Illumina HumanMethylation EPIC) protocol.[28] These normalized beta values were subset to sites required for the calculation of DNA Methylation Age and uploaded with a sample annotation file as per the protocol document that accompanies the online calculator. The DNAmGrimAge uses 1,030 CpG sites for the calculation and has shown predictability of mortality in previous work.[19] The age-adjusted DNAmGrimAge-diff variable was calculated as the DNAmGrimAge minus chronological age.

Socioeconomic Status Variables

SES variables were self-reported by participants and independently analyzed in the 3 separate components: income, education, and employment status. Income was reported as follows: $0 to $9,999; $10,000 to $19,999; $20,000 to $29,999; $30,000 to $39,999; $40,000 to $49,999; $50,000 to $59,999; $60,000 to $79,999; $80,000 to $99,999; $100,000 to $149,999; $150,000 or higher. Education was reported as an ordinal variable (some school but did not complete high school; high school degree; 2-year college degree; 4-year college degree; master's degree; doctoral degree or equivalent). Employment was reported as a categorical variable (working now; only temporarily laid off, on sick leave, or maternity leave; looking for work, unemployed; retired; disabled, permanently or temporarily; student; other). Variables were numerically dummy coded (income 1–10; education 1–6; employment 1–7) for analyses.

Statistical Analyses

All analyses were completed using SPSS v27.0 (IBM Corp, Armonk, NY). Prior to running analyses, the data were cleaned so that only those with data for all variables of interest were included in the analyses. Chi-square analyses were used to test pain group differences in categorical variables (ie, employment status, education, sex, race, and study site), while analysis of variance tests were employed to test differences across pain groups in ordinal and continuous variables (ie, income, chronological age, DNAmAge, DNAmGrimAge-diff). Bonferroni post hoc analyses were then conducted to further probe the differences between groups. Next, ordinal logistic regression mediation analyses were performed to determine whether DNAmGrimAge-diff mediated the relationship between pain and disability, with income and education status as the independent variables (X), DNAmGrimAge-diff as the mediator (M), and pain impact group (no pain vs low-impact pain vs high-impact pain) as the dependent/outcome variables (Y). Age, race, sex, pain duration, and study site were included as covariates in all analyses due to their known association with the variables of interest (ie, SES variables, DNAmGrimAge-diff, pain impact). Indirect effects for the models were calculated by multiplying the pathways constituting the effect. Proportion of mediation (P_M) was calculated by dividing the indirect effect by the direct effect (ie, P_M = ab/c). To overcome unmet assumptions found in mediation analysis, bootstrapping procedures were employed with 5,000 samples and reported as estimates and standard errors or as 95% bootstrapped confidence intervals. Statistical significance was set at a probability less than .05.

Results

Sample Characteristics

Of the 245 individuals who participated in the study, only 174 individuals had complete pain, epigenetic, SES,

and all covariate data comprising the present study sample. Participants in the entire sample were mostly female (62.7%) and had a mean age of 57.9 years (±8.0 years). Overall, the mean DNAmGrimAge was 60.3 (±7.6), and the average DNAmGrimAge-diff was 2.4 years (±5.6 years). There was a difference in race distribution across pain impact groups ($F(2,173) = 4.186$, $P = .017$). Though non-Hispanic Black individuals only made up 44.6% of the total sample, they made up the majority (60.4%) of individuals classified as having high-impact pain; higher than those with low-impact pain ($P = .024$). There were no differences in race distribution between low-impact pain and no pain groups. There were no differences in pain duration, sex, and study site categories across pain groups ($P > .05$). Pain medication use, particularly over the counter medication ($P = .006$), prescription medication ($P = .016$), and no use of medication ($P = .020$) significantly differed across groups. Sample demographic characteristics across the 3 pain impact groups are presented in Table 1. Scatter plots of chronological age, DNAmGrimAge, and DNAmGrimAge-diff as well as the estimated marginal means have been previously published.[20]

Accelerated Epigenetic Aging Associations With Pain Impact Groups

DNAmGrimAge-diff differed across pain impact groups ($F(2,172) = 11.77$, $P < .001$), whereby the high-impact pain group had accelerated epigenetic aging (DNAmGrimAge-diff) compared to both low-impact pain ($P < .001$) and no pain ($P < .001$) groups. There was no difference in DNAmGrimAge-diff between low-impact and no pain groups.

SES Variables Across Pain Impact Groups

Income (Fig 1). Income differed by pain impact ($F(2,171) = 4.955$, $P = .008$), and post hoc tests revealed that income was significantly lower for high-impact pain compared to low-impact pain ($P = .038$) and no pain ($P = .015$) groups. There was no difference found in income between low-impact and no pain groups.

Education level (Fig 2). Education was significantly different by pain impact ($X^2(2,171) = 3.687$, $P = .033$) in the overall model, with the proportion of lower education categories in the high-impact pain group compared to no pain group and low-impact pain group. There was no significant difference in income between low-impact and no pain groups.

Employment status. There were no significant differences in employment status across pain impact groups ($X^2(2,171) = .068$, $P = .934$).

Epigenetic Aging Mediates the Association Between Socioeconomic Variables and Pain Impact

Income. With pain impact as the dependent variable, a complete mediation of income by DNAmGrimAge-diff was observed. Even after controlling for pain duration, pain medication, age, race, sex, and study site, there was an indirect effect of income level on pain impact through DNAmGrimAge-diff ab = –.0113; CI [–.0260, –.009] (Fig 3). The mediator DNAmGrimAge-diff accounted for a large portion of the total effect, $P_M = 47.6\%$.

Education level. With pain impact as the dependent variable, a complete mediation of education level by DNAmGrimAge-diff was observed. Even after controlling for pain duration, pain medication, age, race, sex, and study site there was an indirect effect of education level on pain impact through DNAmGrimAge-diff ab = –.0244; CI [–.0493, –.0038] (Fig 4). The mediator DNAmGrimAge-diff accounted for a large portion of the total effect, $P_M = 48.3\%$.

Discussion

SES has previously been reported as a contributor to negative pain outcomes in the literature.[29] Here, we present evidence that supports the social–biological link in the relationship between SES, epigenetic aging, and pain outcomes. In the present study, we found that those experiencing high-impact pain earned less income and had lower education levels compared to both low-impact and no pain control groups. Differences in accelerated epigenetic aging (DNAmGrimAge-diff) across pain groups were also found, whereby individuals with high-impact pain had greater DNAmGrimAge-diff (~5 years) compared to low-impact pain and no pain groups (both ~1 year). Our main finding was that DNAmGrimAge-diff mediated the associations of income and education with pain impact, as such the relationship between SES and pain outcomes may occur through potential interactions with the epigenome and accelerated cellular aging.

The pain experience is a unique biopsychosocial phenomenon. Studies have shown biological variables, such as age, sex[30] and race;[31,32] psychological variables (ie, depression and anxiety[33]); and social variables (ie, SES,[5] social support[34]) all contribute to overall pain outcomes. Many of these social variables associated with pain outcomes are also linked with a variety of other health outcomes, emphasizing the broad influence that social determinants of health have on an individual's well-being.[35] Inequalities in chronic pain severity previously were thought to be more related to race and ethnic difference.[36] Since then, there has been a growing body of evidence that socioeconomic differences seem to be more causative than race and ethnic differences.[37] In a study investigating SES on rates of complex regional pain syndrome, 20.9% of those in the lowest SES quartile reported having severe complex regional pain syndrome compared to those in the highest quartile (14.3%).[5] Other studies including, but not limited to, those examining chronic low back pain[38] and functional abdominal pain[39] showed that low neighborhood SES was associated with negative pain outcomes in populations of various demographics. SES is thought to contribute to the pain experience via multiple contributors (ie, access to goods and services that may aid with pain self-management, occupational risks,

Table 1. Demographic Characteristics of Present Study Sample by Pain Impact Group

	Mean (SD) or No. (%)			*P**
	No pain	*Low-impact pain*	*High-impact pain*	
N	26 (14.4)	95 (54.6)	53 (30.5)	
Chronological age (y)	59.5 (±9.3)	58.63 (±7.9)	56.4 (±7.11)	.159
DNAmGrimAge (y)	59.7 (±7.1)	60.0 (±7.5)	61.6 (±8.2)	.414
DNAmGrimAge-diff (y)	0.09 (±3.3)	1.3 (±5.4)	5.1 (±5.7)	**< .001***
Sex				
Male	8 (30.8)	33 (34.7)	23 (43.4)	.460
Female	18 (69.2)	62 (65.3)	30 (56.6)	
Race				
Non-Hispanic Black	9 (34.6)	36 (37.9)	32 (60.4)	**.017***
Non-Hispanic White	17 (65.4)	59 (62.1)	21 (39.6)	
Study site				
University of Florida	17 (65.4)	62 (65.3)	30 (56.6)	.557
University of Alabama at Birmingham	9 (34.6)	33 (34.7)	23 (43.4)	
Income				
$0–9,999	2 (7.7)	14 (14.7)	18 (34.0)	**.008***
$10,000–19,999	2 (7.7)	9 (9.5)	8 (15.1)	
$20,000–29,999	2 (7.7)	13 (13.7)	7 (13.2)	
$30,000–39,999	5 (19.2)	5 (5.3)	1 (1.9)	
$40,000–49,999	1 (3.8)	9 (9.5)	3 (5.7)	
$50,000–59,999	5 (19.2)	12 (12.6)	3 (5.7)	
$60,000–79,999	4 (15.4)	12 (12.6)	3 (5.7)	
$80,000–99,999	2 (7.7)	3 (3.2)	6 (11.3)	
$100,000–149,000	2 (7.7)	9 (9.5)	2 (3.8)	
$150,000+	1 (3.8)	7 (7.4)	1 (1.9)	
Education				
Did not complete high school	0 (0.0)	4 (4.2)	6 (11.3)	**.031***
High school degree/equivalent	8 (30.8)	34 (35.8)	19 (35.8)	
Associates degree	5 (19.2)	12 (12.6)	13 (24.5)	
Bachelor's degree	6 (23.1)	24 (25.3)	9 (17.0)	
Master's degree	5 (19.2)	14 (14.7)	6 (11.3)	
Doctoral degree	2 (7.7)	7 (7.4)	0 (0.0)	
Employment status				
Currently working	16 (61.5)	52 (54.7)	18 (34.0)	.934
Temporarily laid off, on sick or maternity leave	0 (0.0)	1 (1.1)	3 (5.7)	
Unemployed, looking for work	2 (7.7)	7 (7.4)	12 (22.6)	
Retired	6 (23.1)	26 (27.4)	9 (17.6)	
Disabled, permanently or temporarily	1 (3.8)	6 (6.3)	9 (17.6)	
Student	0 (0.0)	0 (0.0)	0 (0.0)	
Other	0 (0.0)	0 (0.0)	0 (0.0)	
Pain duration				
Less than 6 mo	-	7 (7.4)	5 (9.4)	.076
6 mo to 1 y	-	7 (7.4)	2 (3.8)	
1–3 y	-	22 (23.2)	13 (24.5)	
3–5 y	-	13 (13.7)	8 (15.1)	
Greater than 5 y	-	29 (30.5)	25 (47.2)	
Pain medication				
None	23 (88.4)	32 (33.7)	16 (30.2)	**.020***
Over the counter	3 (11.6)	31 (32.6)	25 (47.1)	**.006***
Non-opioid prescription	0	30 (31.5)	10 (18.9)	**.016***
Opioids	0	2 (2.1)	2 (3.7)	.623

*$p < 0.05$.

impacts on nutritional quality, as well as access to appropriate heathcare and treatment options).[18,40,41] While we acknowledge the impact that SES has on pain through health care access, we also emphasize a potential influence of social factors on one's biology through the interplay of epigenetics.

Epigenetics refers to changes in gene expression without changes in the DNA sequence, and abundant evidence demonstrates that environmental exposures can produce epigenetic changes.[42] Unlike genetic changes, epigenetic changes are reversible, yet epigenetic modifications can be passed to future generations much like permanent genetic changes and can be influenced at any point of an individual's lifetime.[43] Interestingly, SES has been associated with changes in these underlying molecular signatures, with low SES

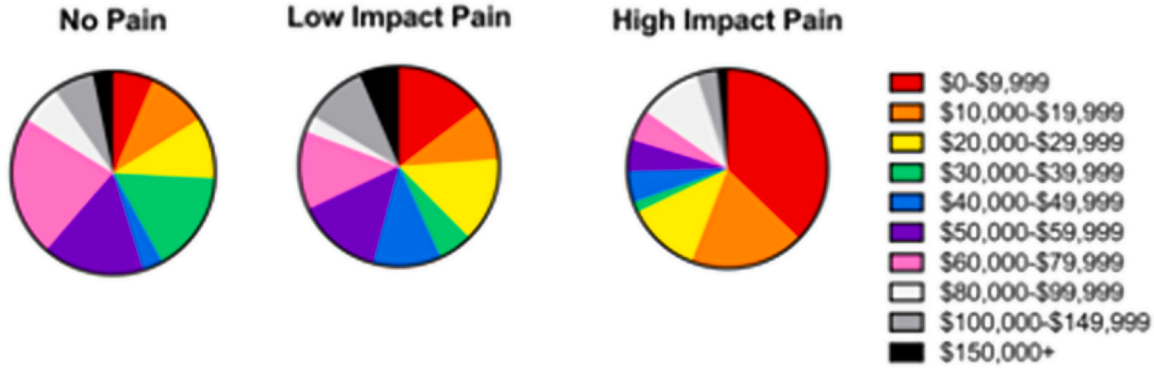

Figure 1. Self-reported income data across pain impact groups.

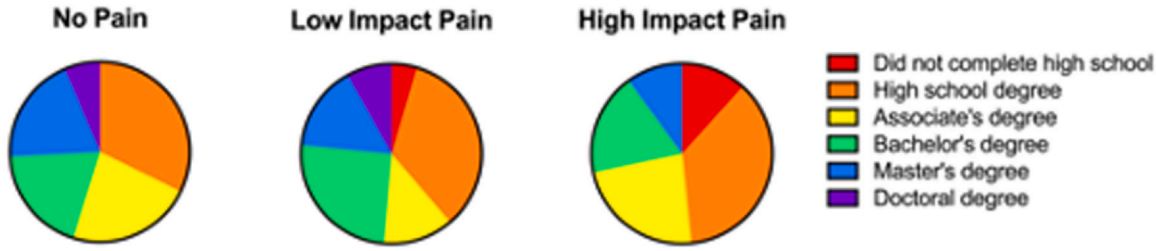

Figure 2. Self-reported education data across pain impact groups.

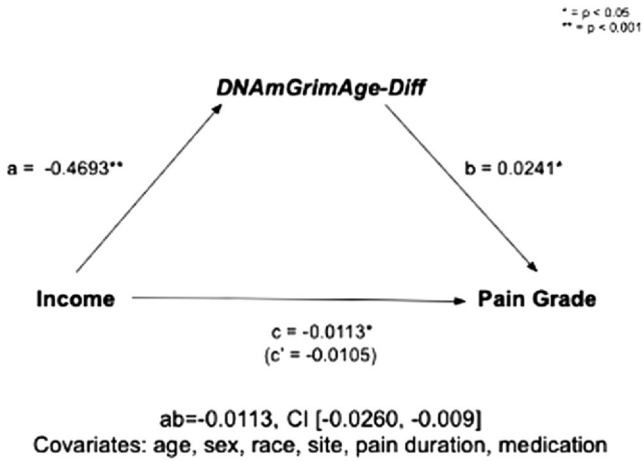

Figure 3. Mediation analysis schematic with income and the independent variable (X), DNAmGrimAge-diff as the mediator (M), and pain impact as the outcome variable (Y). a = a path, effect of X on M; b = b path, effect of M on Y; c = indirect effect of X on Y; c′ = direct effect of X on Y.

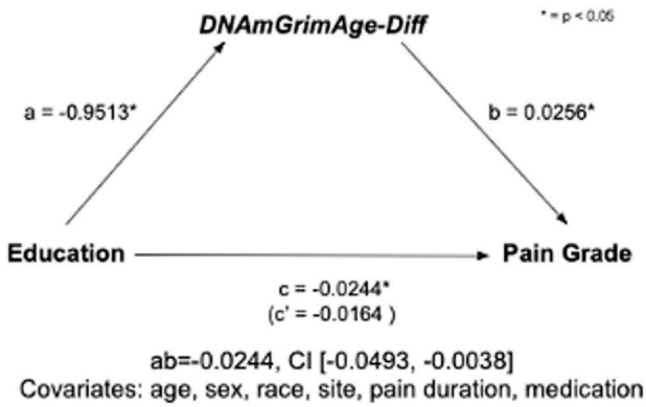

Figure 4. Mediation analysis schematic with education as the independent variable (X), DNAmGrimAge-diff as the mediator (M), and pain impact as the outcome variable (Y). a = a path, effect of X on M; b = b path, effect of M on Y; c = indirect effect of X on Y; c′ = direct effect of X on Y.

linked to DNA methylation differences in epigenome-wide association studies. Specifically, epigenetic changes in the genes for the serotonin-transporter (SLC6A4; 5-HTTLPR), melatonin receptor 1A (MTT1A), brain-derived neurotrophic factor, tyrosine hydroxylase, and various DNA methyltransferases have been noted in samples with differential SES.[44,45] Here, we show that the SES variables of income and education are associated with the epigenetic clock, DNAmGrimAge. DNAGrimAge is made up of several DNA surrogates, and the difference between it and chronological age (accelerated epigenetic aging; DNAmGrimAge-diff) has been associated with many health outcomes, including chronic pain.[19,46] In our sample, the accelerated epigenetic aging variable DNAmGrimAge-diff mediated the relationship between SES variables income and education with pain outcomes, suggesting a potential epigenome–environment link that could influence one's pain phenotype. Of the variables that comprise SES, income and education seem to have the greatest impact compared to employment status on a variety of health outcomes, including chronic pain, due to the fact that they have a greater influence on the ability to seek out and afford quality healthcare, and treatment modalities. Additionally, increased income and education are associated with one's ability to live in advantaged

environments, decreasing exposure to psychological and social threats and potential environmental toxins associated with low-SES environments.[47,48] Income and education have also been associated with differences in exercise habits, nutrition status, stress, and sleep, as those working multiple low-income jobs often do not have time to prioritize these important lifestyle factors.[49-51] These factors (exercise, nutrient status, sleep, and psychological stress) are also independently associated with epigenetic modifications, both genome-wide and with epigenetic clock calculations.[24,46,52-54] This not only compounds the importance of SES on the pain experience but also warrants further investigation to understand the complex underlying mechanisms surrounding SES, epigenetics, and pain.

Limitations

Future studies should aim to include more individuals from more diverse racial groups and using other additional variables to better refine and conceptualize SES as well as examine any potential mediating effects with the variables of interest of this paper. In addition, other variables not measured in our study may be important to consider in future work (ie, health literacy, exercise, diet, psychological stress). Additionally, because DNAmGrimAge has the ability to predict mortality,[19] it is possible that the relationship between pain, SES, and DNAmGrimAge may be contributing to a shortened lifespan. As such, longitudinal research in this area is warranted. Further, we also acknowledge the limitations of cross-sectional studies, and future longitudinal research is needed to understand temporally ordered relationships in larger more diverse samples with respect to all the variables of interest.

Conclusions

While novel, this study highlights the role that SES may play on the epigenomic environment in relation to chronic knee pain. Findings add to the body of literature that suggest that pain is not just a simple biological experience, but can be influenced by our social environment through a social–biological link (ie, epigenetics). It is becoming increasingly clear that achieving healthy populations will require greater attention to social determinants of health. Continued research is needed to inform strategies to promote social health, equity, thereby improving quality of life for individuals with pain.

Disclosures

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The authors have no conflicts of interest to declare.

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