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Compositional analysis of movement behaviors' association on high-sensitivity c-reactive protein: the Jackson heart study

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Abstract

Purpose: Movement behaviors (i.e. physical activity [PA], sedentary behavior [SB], and sleep) are intrinsically codependent, an issue resolved using compositional data analysis (CoDA). High-sensitivity C-reactive protein (hs-CRP) is a nonspecific inflammatory marker positively associated with cardiovascular diseases and affected by movement behaviors. Examine the relation between movement behaviors using CoDA and how time reallocation between two movement behaviors was associated with hs-CRP concentration.

Methods: The Jackson Heart Study was designed to investigate cardiovascular disease risk factors among African American participants in the Jackson, MS area. PA and sleep were self-reported with SB calculated as the remaining time in the day.

Results: The median untransformed hs-CRP concentration was 0.28 mg·dL $^{-1}$ (interquartile range; 0.11, 0.61). Reallocating 15 minutes of PA with SB, the hypothetical change in log hs-CRP concentration was 0.08 mg·dL $^{-1}$ (95% CIs; 0.04, 0.11) greater than the average log hs-CRP concentration. Substituting 15 minutes of SB or sleep with PA was associated with a hypothetical change in log hs-CRP concentration difference of −0.05 mg·dL $^{-1}$ (−0.08, −0.03) and −0.06 mg·dL $^{-1}$ (−0.08, −0.03), respectively. Reallocations between SB and sleep were not associated with the hypothetical difference in log hs-CRP concentration.

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Supplementary materials

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The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the U.S. Department of Health and Human Services. The results of the study are presented honestly, and without fabrication, falsification, or inappropriate data manipulation.

Conclusions: Modeling estimates suggest replacing 15 minutes of SB with PA is associated with lower inflammation.

Keywords

African Americans; Coda; Sedentary behaviour; Physical activity; Sleep; Cardiovascular disease

Introduction

High-sensitivity C-reactive protein (hs-CRP) is a nonspecific indicator of systemic inflammation and has been associated with multiple cardiometabolic maladies [1–3]. Cardiovascular mortality is greater among non-Hispanic Black individuals than White individuals and this trend is expected to persist [4]. Higher hs-CRP concentrations in Black compared with White adults may reflect a higher burden of cardiovascular disease (CVD) risk factors and explain the higher mortality rates from CVD among Black adults [5]. Physical activity (PA) is associated with lower levels of hs-CRP [6–8]. Independent associations of hs-CRP concentration with SB (positively) and sleep (inversely) have been observed [9–11]. Most individuals do not report meeting the PA Guidelines, with a lower prevalence among non-Hispanic Black individuals compared with White individuals (9% and 13%, respectively; [12]). High levels of SB (i.e. eight hours per day) often cooccur with not meeting the PA Guidelines [13]. However, movement behavior research has often neglected to examine all three behaviors in tandem.

Traditionally, examining the associations among movement behaviors has been conducted without consideration of time being finite during a day [14–17]. During a 24-hour day, each minute spent within a specific movement behavior is a minute an individual cannot spend in another. Therefore, an individual can only spend time during the day within one of the mutually exclusive movement behaviors. The use of compositional data analysis (CoDA) has been suggested when examining movement behaviors to more accurately examine real-world associations while reducing spurious correlations and collinearity [18]. Using CoDA with isotemporal substitution, researchers observed maintaining low levels of SB was still important to cardiometabolic risk reduction [18]. Exchanging time engaged in SB for light-intensity PA was associated with better cardiometabolic health, even while maintaining moderate-to-vigorous physical activities (MVPA; 18). Researchers have also observed reallocating time spent from MVPA to any other movement behavior to have a detrimental impact on cardiometabolic health [19]. CoDA and isotemporal substitution will allow the asymmetrical estimation of how reallocating time spent in one movement behavior for another influences hs-CRP concentration while accounting for the remaining movement behavior. We hypothesized an equal time amount substitution from PA to SB would be associated with higher hs-CRP concentration, while substitution from sleep or SB to PA would be associated with lower hs-CRP concentration.

Methodology

Participants

The Jackson Heart Study (JHS), a community-based observational longitudinal study, is designed to investigate CVD risk factors [20]. JHS participants were recruited from the tri-county area encompassing Hinds, Madison, and Rankin counties in Mississippi. At baseline, 20 0 0–20 04, 5306 participants aged 21–84 years old and self-reporting as African American or Black were recruited. During the third exam period, an eight-year follow-up between 2009 and 2013, there were 3819 individuals still participating in the JHS. The present study solely used exam three data due to data availability. The IRBs at the University of Mississippi Medical Center, Jackson State University, and Tougaloo College approved the JHS protocol.

High-sensitivity c-reactive protein

Blood samples of hs-CRP ($mg{\cdot}dL^{-1}$) were measured by the immunoturbidimetric CRP-latex assay method (Kamiya Biomedical Company, Seattle, WA). Measurements of hs-CRP were analyzed in duplicate and duplicates outside three standard deviations from one another were reanalyzed. At a hs-CRP concentration of 4.5 $mg{\cdot}dL^{-1}$ and 15.6 $mg{\cdot}dL^{-1}$, the interassay coefficients of variation on control samples were 4.5% and 4.4%, respectively [3]. For the primary analysis of the present study, we examined hs-CRP concentration as a continuous variable following the convention established in large prospective cohort studies including the JHS [21], the Coronary Artery Risk Development in Young Adults (CAR-DIA) Study [22–26], and the Multi-Ethnic Study of Atherosclerosis (MESA) Study [27, 28]. Additionally, there is evidence that hs-CRP concentration varies by race and sex and the established clinical cut points [29] may not be the ideal method for examining hs-CRP concentration [5, 27]. The range of values for hs-CRP concentration is similar across the JHS, CARDIA, and MESA studies. We acknowledge the usefulness of clinical cut-points for informing the course of treatment regarding risk mitigation; therefore, we conducted a secondary analysis of the odds of having a “high risk” hs-CRP concentration (> 3.0 $mg{\cdot}dL^{-1}$; 29).

Movement behaviors

The PA variable was derived from responses to the JHS Physical Activity Cohort (JPAC) survey, a yearly recall, which encompassed four domains – active living; occupational activities; home, family, yard, and garden; and sports and exercise [30]. The JPAC provides the ability to calculate continuous measures of PA from all four domains. From the description of the duration of the PA performed and the frequency of the PA as indicated by the participant, minutes per day of PA can be calculated from the self-reported duration and frequency of PA. Metabolic equivalent (MET) values were identified in the most recent Compendium of Physical Activities and used to properly classify activities as PA based on the description in the JPAC [31]. Any activity above 1.5 METs was considered PA and total time, across all four domains, was aggregated for a total daily PA time.

The JHS Sleep History Form assessed the amount of sleep. The question: *“How much sleep do you usually get at night (or your main sleep period) on weekdays or workdays?”*

measures how much sleep, measured in hours, an individual achieves on a typical night. Hours of sleep were converted into minutes of sleep.

SB involves activity in a sitting, reclining, or lying position of 1.5 METs or less [32]. SB was calculated using a three-component compositional model of a normal 24-hour day [18, 33]. Movement behaviors are mutually exclusive; thus, knowing time spent in two of the three movement behaviors allows the time spent in the final movement behavior to be derived. To calculate daily minutes of SB, PA and sleep were summated and then subtracted from 1,440 minutes.

Covariates

All covariates were self-reported. Sex was categorized as female and male. Smoking status was categorized as current smokers to former and never smokers. Education level was categorized as participants who reported less than high school education to those who graduated from high school, attended vocational or trade school, or who earned a college degree or higher.

Statistical analysis

Continuous variables are reported with means and standard deviations while discrete variables are reported with frequencies. Due to right skewness of hs-CRP (6.48) in the JHS cohort [21, 29, 34–36], hs-CRP was natural logarithmic transformed to normalize distribution (−1.00) for linear regressions. CoDA was used to describe the movement behavior variables, determine their codependence, and assess the association of movement behaviors on log hs-CRP concentration [37]. CoDA is suitable for data that make up portions of a finite whole (i.e. movement behaviors [18, 19, 38]. The proportion of movement behaviors was calculated by dividing by 1,440 minutes. Then the movement behavior proportions were transformed using isometric log-ratio (ilr) transformation. The use of ilr transformation is paramount to CoDA as it removes the codependence of movement behavior allowing for traditional statistical methods to be used.

Using isotemporal substitution linear regression models, we estimated how 15-minute substitutions between two movement behaviors, while maintaining the time in the third, were associated with a change in log hs-CRP concentrations. A reallocation of 15-minutes was chosen to increase the real-world viability as most individuals do not meet the 30 minutes of daily PA recommendations [13]. All six possible substitutions between two-movement behaviors are presented as they are all feasible in the real world and standard practice for CoDA isotemporal substitution of movement behaviors [18, 33, 37, 39–41]. The results from the isotemporal substitution models are interpreted as the expected change in the mean log hs-CRP concentration given the substitution between the movement behaviors [33, 41, 42]. Each isotemporal substitution model is independent as changes are made to the individual movement behavior data. An advantage of using CoDA isotemporal substitution models over traditional isotemporal substitution models is CoDA produces asymmetrical results when substituting time between two movement behaviors [39]. The secondary analysis examining the odds of “high risk” hs-CRP concentration used 15-minute isotemporal substitution binary logistic regression models.

All models controlled for age, sex, smoking status, and education. The assumptions for linear and logistic regression models were checked with no violations. Multicollinearity was checked using the variance inflation factor where values less than five are indicative of low multicollinearity. All variables in the models had a variance inflation factor under five. Significance was set *a priori* at $P < .05$ or when 95% confidence intervals (CIs) did not cross zero. All analyses were conducted using R (R Foundation for Statistical Computing, Vienna, Austria) using the "epicoda" package [37].

Results

The final sample included 2805 participants after removing 62 participants with missing hs-CRP data and another 46 with missing movement behavior data. Additionally, as CoDA cannot include zero values, 911 participants with any movement behavior value not greater than 15 minutes were excluded to allow for 15-minute isotemporal substitutions. Table 1. displays participant characteristics. The mean age of the study cohort was 60.7 ± 11.7 years and the majority of participants were female (62.0%). Most participants (70.8%) attended vocational school, trade school, or college and 10.1% were current smokers. The median hs-CRP concentration (non-transformed) among participants was 0.28 mg·dL $^{-1}$ (interquartile range [IQR]; 0.11, 0.61). Compositional and arithmetic means for movement behaviors are shown in Table 2. The majority of daily minutes was spent in SB (70.7%), followed by sleep (26.4%), and PA (2.8%). The variability of the data is located in the compositional variation matrix (Table 3). The values in the compositional variation matrix are log ratios of pair-wise variation of two movement behaviors. A zero value within the compositional variation matrix is indicative of the two movement behaviors being completely proportional and whereas higher values are indicative of the two movement behaviors having lower proportionality. The smallest variance was observed between PA and sleep (0.101). SB had a similar variance with both PA (0.374) and sleep (0.364).

The hypothetical differences in log hs-CRP concentration following a 15-minute isotemporal substitution between movement behaviors are found in Table 4. When reallocating 15 minutes of PA with SB the hypothetical change in log hs-CRP concentration was 0.08 mg·dL $^{-1}$ (95% CIs; 0.04, 0.11) greater than the log hs-CRP concentration of the average participant. When reallocating 15 minutes of PA with sleep, a similar log hs-CRP concentration change was observed (0.08 mg·dL $^{-1}$ [0.05, 0.12]). Substituting 15 minutes of SB with PA was associated with a hypothetical lowering of the log hs-CRP concentration of 0.05 mg·dL $^{-1}$ (−0.08, −0.03) and was similar to substituting 15 minutes of sleep of 0.06 mg·dL $^{-1}$ (−0.08, −0.03). Substituting 15 minutes of SB for sleep, or sleep for SB was associated with no hypothetical change in log hs-CRP concentration.

Sensitivity analysis was conducted among a subsample of participants ($n = 1224$) who achieved 6–9 hours of sleep, one hour below and above the recommended amount of sleep for older adults [43]. Results from the isotemporal substitution models were marginally attenuated but maintained the direction of the association. When reallocating 15 minutes of PA with sleep the hypothetical change in log hs-CRP concentration was 0.07 mg·dL $^{-1}$ (0.02, 0.13) higher. Similar results were found when reallocating 15 minutes of PA for SB (0.08 mg·dL $^{-1}$ [0.02, 0.13]). When reallocating 15 minutes of SB with PA the hypothetical

change in log hs-CRP concentration was −0.05 mg·dL $^{-1}$ (−0.09, −0.02) lower and was similar to the effect associated with reallocating sleep to PA (−0.05 mg·dL $^{-1}$ [−0.10, −0.01]). When reallocating 15 minutes in either direction between SB or sleep, there was no difference in the hypothetical change in log hs-CRP concentration. Due to the high number of participants not included in the initial analysis, who had a statistically higher hs-CRP concentration, for having less than 15 minutes in each movement behavior, we replicated the CoDA isotemporal substitutions using 5-minute reallocations among participants with at least 5 minutes in each movement behavior (n = 3401). Arithmetic mean PA was 40.58 (39.61, 41.55) minutes per day, still meeting the PA Guidelines. There was neither change in statistical significance nor direction of association from the 15-minutes reallocations. Additionally, we repeated the CoDA isotemporal substitutions using 15-minute reallocations among participants who met the PA Guidelines of at least 30 minutes of daily PA (n = 1871) and again, there was no change in statistical significance or direction of association from the primary analytic sample of participants with at least 15 minutes in each movement behavior.

Results from the secondary analysis examining change in odds of having “high risk” hs-CRP concentration are presented in Table S1. The results of the binary logistic isotemporal regression models corroborate the results of the primary analysis. Reallocating 15 minutes of PA for SB (odds ratio [95% CIs]; 1.19 [1.12, 1.27]) and sleep (1.20 [1.23, 1.29]) were both associated with increased odds of having “high risk” hs-CRP concentration. Again, substantiating the findings from using a continuous hs-CRP concentration measure, increasing 15 minutes of PA at the expense of SB (0.89 [0.85, 0.93]) and sleep (0.88 [0.84, 0.92]) was associated with lower odds of having “high risk” hs-CRP concentration. There were no associations with odds of having “high risk” hs-CRP concentration when reallocating time between SB and sleep in either direction.

Discussion

In this study of older African American adults living in the southern United States, we found that the daily proportion of movement behaviors were associated with inflammation. In the present sample, 66.7% of participants met the recommended amount of daily PA [13]. When examining putative changes in movement behaviors, a hypothetical increase of PA by 15 minutes at the expense of either SB or sleep was associated with lower inflammation levels. Conversely, a hypothetical increase of either SB or sleep by 15 minutes at the expense of PA had a stronger association with worsening inflammation.

Using a CoDA approach when examining the association between movement behaviors and CRP concentration, Chastin and colleagues observed sleep and MVPA to be associated with CRP concentration [18]. The proportion of sleep was positively and MVPA negatively associated with CRP concentration, with no association for SB or light PA [18]. As sleep is often unaccounted for when examining SB and PA, the present results may highlight the importance of CoDA as it allows examination of sleep with SB and PA. Examining sleep via non-CoDA techniques, sleeping less than five and more than nine hours per night were found to be significantly associated with increased hs-CRP concentrations [44].

The isotemporal substitution modeling showed a hypothetical change in hs-CRP concentration was associated with a 15-minute reallocation of some, but not all, movement behaviors. Reallocation of PA for an increase in either SB or sleep was associated with an increased hs-CRP concentration. Reallocating time by increasing PA and decreasing either SB or sleep was associated with a decreased hs-CRP concentration. While we observed a positive association of the hypothetical difference in hs-CRP when reducing PA for SB, Henson and colleagues found a reallocation of 60 minutes from sitting to standing or sitting to light stepping to not be associated with hs-CRP concentration [45]. Movement behavior data are compositional, mutually exclusive, and independently associated with inflammation [7–10]. As compositional data, the relative time spent engaged in each movement behavior is informative and not the total time engaged in each behavior [18, 40]. However, the present results are supported by other researchers' findings using isotemporal substitution modeling which saw reallocating time from SB to PA to reduce hs-CRP concentration [45–47]. Reallocating 30 minutes of SB for moderate-to-vigorous PA (MVPA) is associated with lower CRP concentration [47]. Additionally, Henson and colleagues found a 60-minute reallocation from sitting to MVPA stepping to be associated with lower hs-CRP concentration, but only among participants with sitting time over 9.3 hours per day [45]. The concentration of hs-CRP was lower when substituting 60 minutes of SB for light PA or MVPA, but not LPA for MVPA [46]. However, some studies did not include sleep in the analysis [45–47]. The reallocation of time was associated with a significant change in hs-CRP concentration in the present study demonstrating the novel information that can come from CoDA and isotemporal modeling. Researchers and practitioners can use CoDA isotemporal substitution to model the influence of time trade-offs before actually intervening. Thus, interventions can be better tailored to the specific movement behavior reallocations needed to optimize and individual's health.

Within the JHS several groups of researchers have examined hs-CRP concentration. The concentration of hs-CRP was found to be positively associated with peripheral artery disease and aortic valve calcification but not carotid intima-media thickness, all of which are progenitors of atherosclerosis [36]. When examining the role of PA on hs-CRP concentration among JHS participants, Kamimura and colleagues observed with increasing category of American Heart Association's Life's Simples 7's PA Index, PA is associated with lower hs-CRP concentration [48]. The present study furthers the research of Kamimura and colleagues by using contemporary analytical techniques for examining movement behaviors. The use of metrics for assessing CVD risk, such as the American Heart Association's Life's Simple 7, are useful practical tools for quickly identifying a general idea of cardiovascular health. For research purposes, categorizing PA is contradictory to the current understanding of PA, where each minute conveys health benefits [13]. CoDA is the emerging gold-standard treatment of movement behavior data, as it allows for examining all movement behaviors at once [18].

There are several limitations and strengths to the present study. Participants excluded due to having less than 15 minutes of a movement behavior did have a significantly greater hs-CRP concentration compared with included participants (0.69 and 0.53 mg·dL $^{-1}$, respectively; P =.0 0 01). Excluding these participants could lead to selection bias influencing the results. However, we did find reaffirming results when limiting to less than 5 minutes

of each movement behavior. The present study is cross-sectional, and causality cannot be established. The JHS is a single-site cohort of African American individuals in the southern United States limiting the generalizability to other populations. PA and sleep data were self-reported and may be incorrectly estimated by the participant, with PA often over-estimated; however, this is a universally acknowledged limitation of survey-based research [49]. Using the most conservative indicator of time from the JPAC, we attempted to not overestimate PA. Multiple studies have used the JPAC as ordinal data [50–53], and although the JPAC was not designed to collect 24-hour PA data, some studies have calculated MVPA minutes per week from the sports and exercise domain [50, 51], with some studying from multiple [48] including all domains [54]. A major strength of the current study was calculating a continuous PA from all four domains of the JPAC allowed for the estimation of SB. Deriving SB provided the ability to examine all movement behaviors using a more appropriate analytical technique via CoDA but is dependent upon accurate PA and sleep recall. We did not control for other known factors associated with hs-CRP concentration and on the causal path to cardiometabolic disease, as we wanted to examine the ability of CoDA to produce results in line with the known associations with hs-CRP (see van Apeldoorn, et al., 2022 for a directed acyclic graph for the potential confounders that could attenuate the relations between movement behaviors and hs-CRP; [55]).

Conclusions

There was an association between movement behaviors and hs-CRP concentration among African Americans participating in the JHS. Further, estimated using CoDA, a theoretical increase in PA relative to SB and sleep was associated with reductions in hs-CRP concentration. The current results add to the growing field of literature on time trade-offs in movement behaviors. Due to an existing CVD disparity with greater prevalence among African American individuals, research focusing specifically on an African American population is vital to beginning to achieve health equity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Participant characteristics

	***N* = 2805**
hs-CRP (mg·dL^{-1}) *	0.28 (0.11, 0.61)
Age (years)	60.7 ± 11.7
Sex (Female)	1739 (62.0%)
Current Smoker	281 (10.1%)
Education	
Less than High School	325 (11.6%)
High School Graduate/GED	493 (17.6%)
Attended Vocational School, Trade School, or College	1981 (70.8%)

Continuous variables reported as mean±standard deviation.

Categorical variables reported as n (%).

GED = general equivalency degree; hs-CRP = high-sensitivity C-reactive protein.

*hs-CRP reported untransformed median (interquartile range)

Table 2

Compositional and arithmetic means of movement behaviors

	Compositional mean	Arithmetic mean
Sedentary Behavior	1018.58 (70.73%)	1007.88 (1004.67, 1011.09)
Physical Activity	40.66 (2.82%)	47.12 (46.09, 48.14)
Sleep	380.76 (26.44%)	385.01 (381.97, 388.04)

All movement behaviors are minutes·day $^{-1}$.

Arithmetic mean (95% CIs).

Compositional mean (%).

Table 3

Compositional variation matrix of movement behaviors

	Sedentary behavior	Physical activity	Sleep
Sedentary Behavior	0.000		
Physical Activity	0.374	0.000	
Sleep	0.364	0.101	0.000

Table 4

Movement behavior isotemporal substitution hypothetical change in change in hs-CRP concentration

	Decreased by 15 min		
Increased by 15 min	**↓Sedentary behavior**	**↓Physical activity**	**↓Sleep**
↑Sedentary Behavior		0.08 (0.04, 0.11)	−0.00 (−0.01, 0.00)
↑Physical Activity	−0.05 (−0.08, −0.03)		−0.06 (−0.08, −0.03)
↑Sleep	0.00 (−0.00, 0.01)	0.08 (0.05, 0.12)	

Values are hypothetical change in hs-CRP concentration (95% CIs).

hs-CRP = high-sensitivity C-reactive protein ($mg \cdot dL^{-1}$).

hs-CRP concentration was natural logarithmic transformed.

Analysis adjusted for age, sex, smoking status, and education.