Clinical Epigenetics

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Sleep patterns and DNA methylation age acceleration in middle-aged and older Chinese adults

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Abstract

Background Sleep is a biological necessity and fundamental to health. However, the associations of sleep patterns (integrating sleep determinants) with DNA methylation age acceleration (DNAm AA) remain unknown. We aimed to investigate the associations of sleep patterns with DNAm AA.

Methods This cross-sectional and prospective cohort study used data from the Dongfeng-Tongji cohort collected from 2013 to December 31, 2018. Sleep patterns were reflected by sleep scores (range 0–4, with higher scores indicating healthier sleep patterns) characterized by bedtime, sleep duration, sleep quality, and midday napping. DNAm AA was estimated by PhenoAge acceleration (PhenoAgeAccel), GrimAge acceleration (GrimAgeAccel), DunedinPACE, and DNAm mortality risk score (DNAm MS). Linear regression models were used to estimate β and 95% confidence intervals (CIs) for the cross-sectional associations between sleep patterns and DNAm AA. Mediation models were applied to assess the mediating role of DNAm AA in the associations between sleep patterns and all-cause mortality in a prospective cohort.

Results Among 3566 participants (mean age 65.5 years), 426 participants died during a mean 5.4-year follow-up. A higher sleep score was associated with lower DNAm AA in a dose–response manner. Each 1-point increase in sleep score was associated with significantly lower PhenoAgeAccel (β = − 0.208; 95% CI − 0.369 to − 0.047), GrimAgeAccel (β = − 0.107; 95% CI − 0.207 to − 0.007), DunedinPACE (β = − 0.008; 95% CI − 0.012 to − 0.004), and DNAm MS (β = − 0.019; 95% CI − 0.030 to − 0.008). Chronological age modified the associations between higher sleep scores and lower PhenoAgeAccel (*p* for interaction = 0.031) and DunedinPACE (*p* for interaction = 0.027), with stronger associations observed in older adults. Moreover, a slower DunedinPACE mediated 6.2% (95% CI 0.8% to 11.5%) of the association between a higher sleep score and a lower all-cause mortality risk.

Conclusion In this cohort study, individuals with a higher sleep score had a slower DNAm AA, particularly in older adults. A slower DunedinPACE partially explained the association between higher sleep scores and lower all-cause mortality risk. These findings suggest that adopting healthy sleep patterns may promote healthy aging and further benefit premature mortality prevention, highlighting the value of sleep patterns as a potential tool for clinical management in aging.

Keywords Sleep pattern, DNA methylation age acceleration, Aging, Epigenetic clocks, All-cause mortality

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Introduction

Aging is currently a major global concern. China has one of the fastest-growing aging populations in the world. In 2023, 15.4% of the total population in China was aged 65 years or older [1]. This proportion is projected to rise to 26.1% by 2050 [2]. Thus, promoting healthy aging is urgent. As individuals of the same chronological age may have different biological ages [3], it is crucial to quantify individual biological aging and identify its modifiable risk factors.

Epigenetic clocks based on DNA methylation (DNAm) are among the most widely used metrics to characterize biological aging [4]. To date, several epigenetic clocks have been developed, each capturing different aspects of the biological aging process [5]. While first-generation epigenetic clocks (such as Horvath clock and Hannum clock), trained on chronological age, are more of an indicator of natural aging [6, 7], second-generation epigenetic clocks (such as PhenoAge, GrimAge, DunedinPACE, and DNAm mortality risk score [DNAm MS]), trained on morbidity biomarkers and mortality, exhibit improved predictive ability for health and life span and therefore tend to be more closely related to behaviors known to be associated with health outcomes [8–11].

Sleep is a biological necessity and fundamental to health and well-being. Growing evidence has linked suboptimal sleep habits, such as short sleep duration and poor sleep quality, with DNAm age acceleration (DNAm AA) [12–17]. However, these studies only focused on one or two aspects of sleep without considering its multifaceted nature [18, 19]. Our previous studies have proposed a healthy sleep pattern (integrating determinants of sleep, including timing, duration, and quality) and demonstrated its beneficial role in preventing cardiovascular disease, even in individuals with higher genetic risk [20, 21]. It remains unknown whether this healthy sleep pattern has the potential to slow down DNAm AA.

To address the evidence gap, we determined DNAm AA as PhenoAge acceleration (PhenoAgeAccel), GrimAge acceleration (GrimAgeAccel), DunedinPACE, and DNAm MS in middle-aged and older Chinese adults. We then evaluated the association of sleep patterns, as reflected by a sleep score integrating bedtime, sleep duration, sleep quality, and midday napping, with DNAm AA. In addition, we investigated whether DNAm AA could explain the association between sleep patterns and all-cause mortality.

Methods

Study population

The Dongfeng-Tongji (DFTJ) cohort is a prospective ongoing cohort study recruiting retired workers from the Dongfeng Motor Corporation (DMC) in Shiyan, China, since 2008 [22]. At the first follow-up survey in 2013, the DFTJ cohort enrolled 38,295 participants who completed standardized questionnaires and medical examinations and provided peripheral venous blood samples. After excluding those with coronary heart disease, stroke, cancer, or severely abnormal electrocardiogram at the study baseline (2013) and those with insufficient blood samples, 24,415 relatively healthy participants remained, of whom we selected 3888 whole blood samples collected at the study baseline for DNAm profiling to investigate epigenetic signature of incident chronic diseases and environmental factors. The 3888 samples consisted of incident cases of acute coronary syndrome, ischemic stroke, asymptomatic lacunar infarct, and lung cancer identified after the date of enrollment in 2013 until December 31, 2018, along with their corresponding randomly selected healthy controls. Among these 3888 samples, 3597 unique participants passed the quality control for DNAm data. We further excluded 31 participants with missing sleep information. The final samples included in this study were 3566 participants with DNAm data passing quality control and complete sleep information to cross-sectionally explore the associations between sleep patterns and DNAm AA and prospectively investigate the mediating role of DNAm AA in the associations between sleep patterns and all-cause mortality. This cohort study was approved by the Ethics and Human Subject Committees of Tongji Medical College, Huazhong University of Science and Technology, and Dongfeng General Hospital, DMC. All participants provided written informed consent.

Sleep patterns

We obtained sleep information using standardized questionnaires, details of which were in Supplementary Methods. To characterize sleep patterns, we established a sleep score integrating 4 low-risk sleep factors in our prior study [20]. Low-risk sleep factors included bedtime between 10:01 p.m. and 12:00 a.m., sleep duration of 7– < 8 h/night (i.e., sleep more than or equal to 7 h and less than eight hours per night), self-reported good or fair sleep quality, and midday napping ≤ 60 min, defined on the basis of previous knowledge [20, 23–27]. We categorized sleep factors into dichotomous variables, coding low-risk as 1 and high-risk as 0, and summed the sleep factors to calculate the sleep score (ranging from 0 to 4). A higher sleep score reflected a healthier sleep pattern.

DNA methylation age acceleration

We measured DNAm from whole-blood samples using the Infinium HumanMethylationEPIC v1.0 BeadChip (Illumina, USA). Detailed information on DNAm data processing, quality control, and normalization are

provided in Supplementary Methods. This study focused on four representative second-generation epigenetic clocks: PhenoAge [8], GrimAge [9], DunedinPACE [10], and DNAm MS [11]. We calculated PhenoAge and GrimAge using the online calculator (https://dnamage.genetics.ucla.edu/home), quantified PhenoAgeAccel and GrimAgeAccel as residuals derived from regressing PhenoAge and GrimAge on chronological age, respectively, and then used PhenoAgeAccel and GrimAgeAccel in the following analyses. We computed DunedinPACE using the code provided by Belsky et al. [10] and DNAm MS as the sum of regression coefficient-weighted methylation β-values of the selected cytosine-phosphate-guanine described by Zhang et al. [11]. As DunedinPACE and DNAm MS, by their design, could directly reflect the age acceleration or deceleration, we defined PhenoAgeAccel, GrimAgeAccel, DunedinPACE, and DNAm MS as DNAm AA in this study.

Mortality ascertainment

The vital status of participants in the DFTJ cohort could be tracked through the DMC's health care system and death certificates. Person-years were calculated from the date of recruitment in 2013 to the date of death or censoring (December 31, 2018), whichever came first.

Covariates

Covariates included in this study were chronological age, sex, educational level, drinking status, smoking status, and physical activity, as obtained through standardized questionnaires (details in Supplementary Methods). We also included body mass index (calculated as weight in kilograms divided by height in meters squared, with weight and standing height measured by trained physicians) as a covariate.

Statistical analysis

Baseline characteristics of participants were described as mean (SD) for continuous variables and numbers (percentages) for categorical variables. Linear regression models were applied to assess the cross-sectional associations of individual low-risk sleep factors and the sleep score with DNAm AA. The models were adjusted for chronological age, sex, educational level, drinking status, smoking status, physical activity, and body mass index. Tests for linear trends across increasing sleep scores were also conducted by treating the sleep score as a continuous variable.

Stratified analyses were conducted to investigate whether the associations between sleep score and DNAm AA differed by chronological age (<65; ≥ 65 years) and sex (male; female), with the multiplicative interaction terms between sleep score and the stratification variables included to explore the potential modification effect.

In addition, mediation analyses were constructed to explore the role of DNAm AA in the association between sleep score and the risk of all-cause mortality in a prospective cohort. Analyses were based on a linear model for the association of sleep score with DNAm AA and a Cox proportional hazard regression model for the association of sleep score with all-cause mortality, using an R package regmedint [28].

For comparison purposes, we assessed the associations of the sleep score with intrinsic epigenetic age acceleration (IEAA) and extrinsic epigenetic age acceleration (EEAA), the enhanced versions of two first-generation epigenetic clocks: HorvathAge and HannumAge, respectively [29]. IEAA, like first-generation clocks, mainly captures cell-intrinsic aging, and EEAA captures immune system aging, which is sensitive to environmental variation. We also conducted a sensitivity analysis by examining the association between sleep score and the DNAm AA after excluding participants who reported very poor sleep quality with frequent use of hypnotics. Adjustments for multiple comparisons were not performed in the analyses, as this study was theory-driven rather than purely data-driven, in which it was not necessary to control the type I error rate inflation due to multiplicity [30–34]. Moreover, the trade-off of controlling the type I error rate inflation is an increase in the likelihood of type II errors and a decrease in the statistical power, leading to the possibility of missing significant or interesting findings. Statistical significance was defined as 2-sided $p<0.05$. Data were analyzed using R software version 4.2.2 (R Core Team, Vienna, Austria).

Results

This study included 3566 participants (mean [SD] age, 65.5 [8.1] years; 1773 [49.7%] female), of which 426 (11.9%) died over a mean (SD) follow-up of 5.4 (0.8) years. Table 1 presents the participant characteristics according to the sleep score. Of 3566 participants, 455 (12.8%) had a sleep score of 0–1 and 450 (12.6%) had a sleep score of 4. Participants with higher sleep scores were more likely to be younger, female, and have a higher level of education and lower PhenoAge, GrimAge, DunedinPACE, and DNAm MS.

The associations of individual low-risk sleep factors with DNAm AA are shown in the Supplementary Table S1. Bedtime between 10:01 p.m. and 12:00 a.m. was associated with a lower PhenoAgeAccel, DunedinPACE, and DNAm MS, with a β (95% confidence interval [CI]) of − 0.362 (− 0.650, − 0.075), − 0.008 (− 0.015, − 0.001), and − 0.020 (− 0.039, − 0.001), respectively. Good/fair sleep quality was associated with a lower

Table 1 Characteristics of the study participants according to sleep score

Characteristics	Sleep score				*p* value[a]
	0–1 (n = 455)	2 (n = 1593)	3 (n = 1068)	4 (n = 450)	
Chronological age, mean (SD), y	67.7 (8.1)	66.2 (8.0)	64.1 (8.0)	63.9 (7.8)	< 0.001
Sex, n (%)					< 0.001
Male	257 (56.5)	829 (52.0)	505 (47.3)	202 (44.9)	
Female	198 (43.5)	764 (48.0)	563 (52.7)	248 (55.1)	
Education level, n (%)					< 0.001
Primary school or below	161 (35.4)	466 (29.3)	184 (17.2)	79 (17.6)	
Middle school	175 (38.5)	656 (41.2)	423 (39.6)	161 (35.8)	
High school or beyond	118 (25.9)	462 (29.0)	455 (42.6)	207 (46.0)	
Current smoking, n (%)	100 (22.0)	333 (20.9)	227 (21.3)	88 (19.6)	0.717
Current drinking, n (%)	133 (29.2)	419 (26.3)	302 (28.3)	116 (25.8)	0.430
Physical activity[b], n (%)	368 (80.9)	1298 (81.5)	861 (80.6)	381 (84.7)	0.401
Body mass index, mean (SD)[c]	24.6 (3.4)	24.3 (3.3)	24.1 (3.2)	24.4 (3.3)	0.129
DNAm measures of aging					
PhenoAge, mean (SD), y	58.0 (5.9)	56.7 (6.4)	55.3 (6.2)	55.0 (6.0)	< 0.001
PhenoAge acceleration, mean (SD)	0.5 (4.2)	0.1 (4.3)	− 0.2 (4.2)	− 0.4 (4.3)	0.012
GrimAge, mean (SD), y	74.6 (7.6)	73.3 (7.6)	71.3 (7.7)	70.9 (7.3)	< 0.001
GrimAge acceleration, mean (SD)	0.1 (3.9)	0.1 (3.9)	− 0.1 (3.7)	− 0.4 (3.7)	0.049
DunedinPACE, mean (SD)	1.3 (0.1)	1.2 (0.1)	1.2 (0.1)	1.2 (0.1)	< 0.001
DNAm mortality risk score, mean (SD)	− 0.2 (0.3)	− 0.2 (0.3)	− 0.3 (0.3)	− 0.3 (0.3)	< 0.001

DNAm, DNA methylation

[a] *p* values were estimated using ANOVA test for continuous variables and Chi-square tests for categorical variables

[b] Physical activity was defined as leisure-time physical activity ≥ 150 min/week

[c] Body mass index was calculated as weight in kilograms divided by height in meters squared

PhenoAgeAccel and DNAm MS, with a β (95% CI) of − 0.400 (− 0.797, − 0.002) and − 0.033 (− 0.059, − 0.006), respectively. Midday napping ≤ 60 min were associated with a lower DunedinPACE and DNAm MS, with a β (95% CI) of − 0.015 (− 0.025, − 0.006) and − 0.031 (− 0.057, − 0.006), respectively. Figure 1 demonstrates that a higher sleep score was associated with lower DNAm AA in a dose–response fashion ($p = 0.011$ for PhenoAgeAccel, $p = 0.036$ for GrimAgeAccel, $p < 0.001$ for DunedinPACE, and $p < 0.001$ for DNAm MS). Each 1-point increase in the sleep score was associated with lower DNAm AA, with a β (95% confidence interval [CI]) of − 0.208 (95% CI − 0.369 to − 0.047) for PhenoAgeAccel, − 0.107 (95% CI − 0.207 to − 0.007) for GrimAgeAccel, − 0.008 (95% CI − 0.012 to − 0.004) for DunedinPACE, and − 0.019 (95% CI − 0.030 to − 0.008) for DNAm MS (Supplementary Table S2). Compared with a sleep score of 0–1, a sleep score of 4 was associated with a β (95% CI) of − 0.687 (95% CI − 1.245 to − 0.129) for PhenoAgeAccel, − 0.243 (95% CI − 0.589 to 0.103) for GrimAgeAccel, − 0.024 (95% CI − 0.038 to − 0.010) for DunedinPACE, and − 0.049 (95% CI − 0.086 to − 0.012) for DNAm MS (Fig. 1; Supplementary Table S2).

Figure 2 illustrates the associations between sleep score and DNAm AA stratified by chronological age and sex. We observed significant interactions between sleep score and chronological age for PhenoAgeAccel (p for interaction = 0.031) and DunedinPACE (p for interaction = 0.027). The association of a higher sleep score with lower PhenoAgeAccel and DunedinPACE was stronger among participants aged ≥ 65 years, with a corresponding β (95% CI) of − 0.249 (95% CI − 0.474 to − 0.023) and − 0.011 (95% CI − 0.017 to − 0.005) for a 1-point increase in sleep score. We did not observe statistically significant effect modification by sex.

Based on the results above and the statistically significant associations of the sleep score, PhenoAgeAccel, GrimAgeAccel, DunedinPACE, and DNAm MS with all-cause mortality (Supplementary Table S3), we performed mediation analyses to assess whether these four DNAm AA mediated the association between sleep score and the risk of all-cause mortality. Results showed that DunedinPACE mediated 6.2% (95% CI 0.8% to 11.5%) of the association (indirect effect hazard ratio [HR], 0.985 [95% CI 0.974 to 0.995]) (Supplementary Figure S1). We also observed indirect associations via PhenoAgeAccel (HR 0.992; 95% CI 0. 0.984 to 0.999), GrimAgeAccel (HR

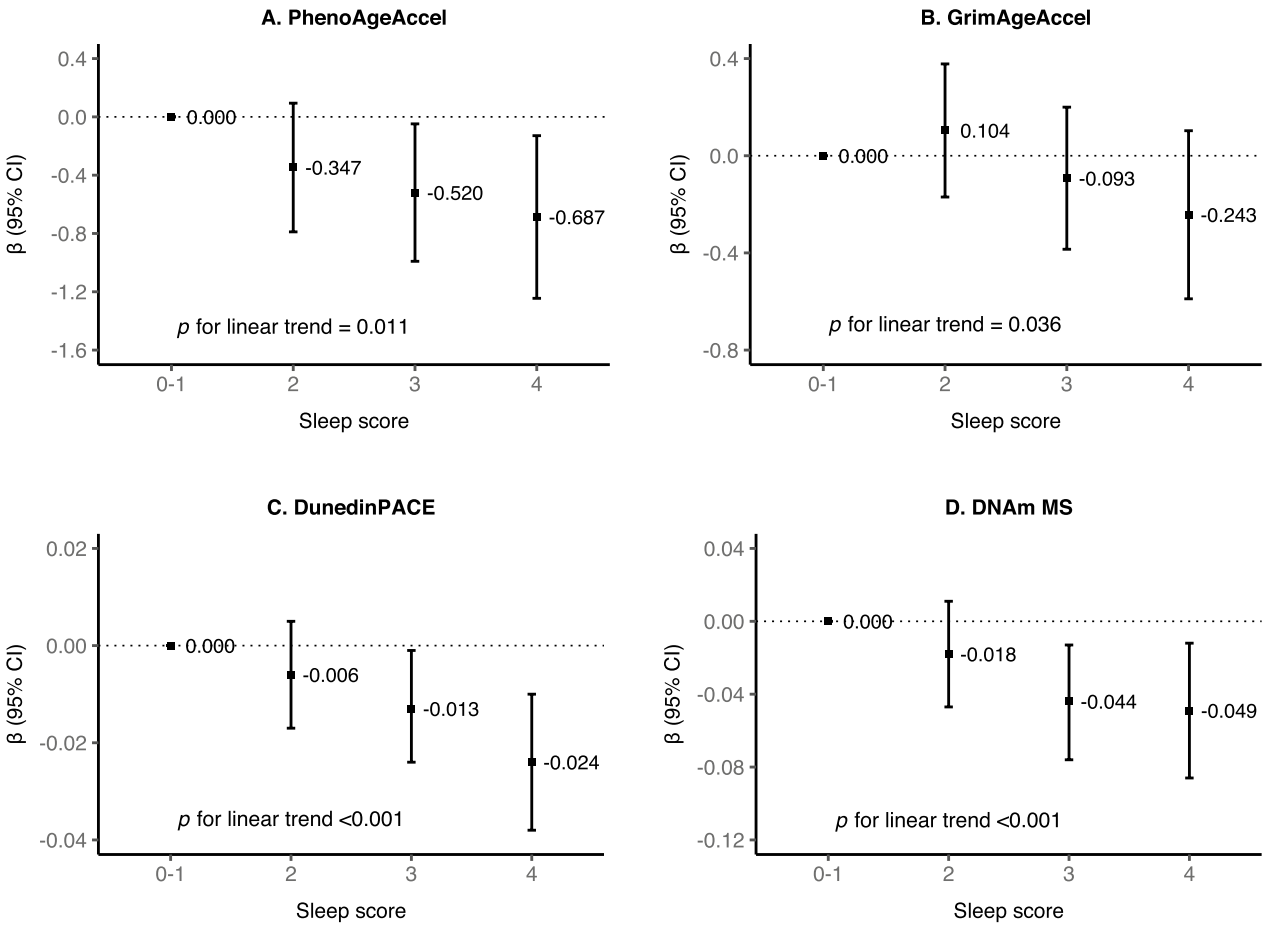

Fig. 1 Associations of sleep score with the DNA methylation age acceleration. The models were adjusted for chronological age, sex, education level, smoking status, drinking status, physical activity, and body mass index. CI indicates confidence interval; PhenoAgeAccel indicates PhenoAge acceleration; GrimAgeAccel indicates GrimAge acceleration; DNAm MS indicates DNA methylation mortality risk score

0.990; 95% CI 0.980 to 1.000), and DNAm MS (HR 0.991; 95% CI 0.983 to 0.999). However, the proportion of the association between sleep score and all-cause mortality mediated by PhenoAgeAccel, GrimAgeAccel, and DNAm MS was not statistically significant.

In comparative analyses, the results for EEAA were similar to those for the four primary DNAm AA, whereas the results for IEAA were not statistically significant (Supplementary Table S4). Sensitivity analysis excluding participants with very poor sleep quality with frequent use of hypnotics did not change our conclusions (Supplementary Table S5).

Discussion

In this cohort study, a higher sleep score (i.e., a healthier sleep pattern) was associated with lower PhenoAgeAccel, GrimAgeAccel, DunedinPACE, and DNAm MS in a dose–response manner. The associations of a higher sleep score with lower PhenoAgeAccel and DunedinPACE were more pronounced in older adults. In addition, a slower DunedinPACE partly explained the association between a higher sleep score and a lower risk of all-cause mortality.

Our study provides novel evidence of a dose–response association of a higher sleep score, which represents comprehensive healthy sleep patterns, with lower PhenoAgeAccel, GrimAgeAccel, DunedinPACE, and DNAm MS, suggesting that healthy sleep patterns are associated with slower biological aging. In support of our results, previous sleep-related studies reported that short sleep duration, poor sleep quality, and their combination were associated with DNAm AA [12–17]. As sleep patterns are easy to assess, they may have the potential to be a clinically useful tool in aging-related management. Meanwhile, these results should be interpreted with caution as this is an observational study.

Since PhenoAge, GrimAge, DunedinPACE, and DNAm MS are second-generation DNAm clocks, which could act as epigenetic surrogates for health-related behaviors, social factors, and their biological consequences [8–11],

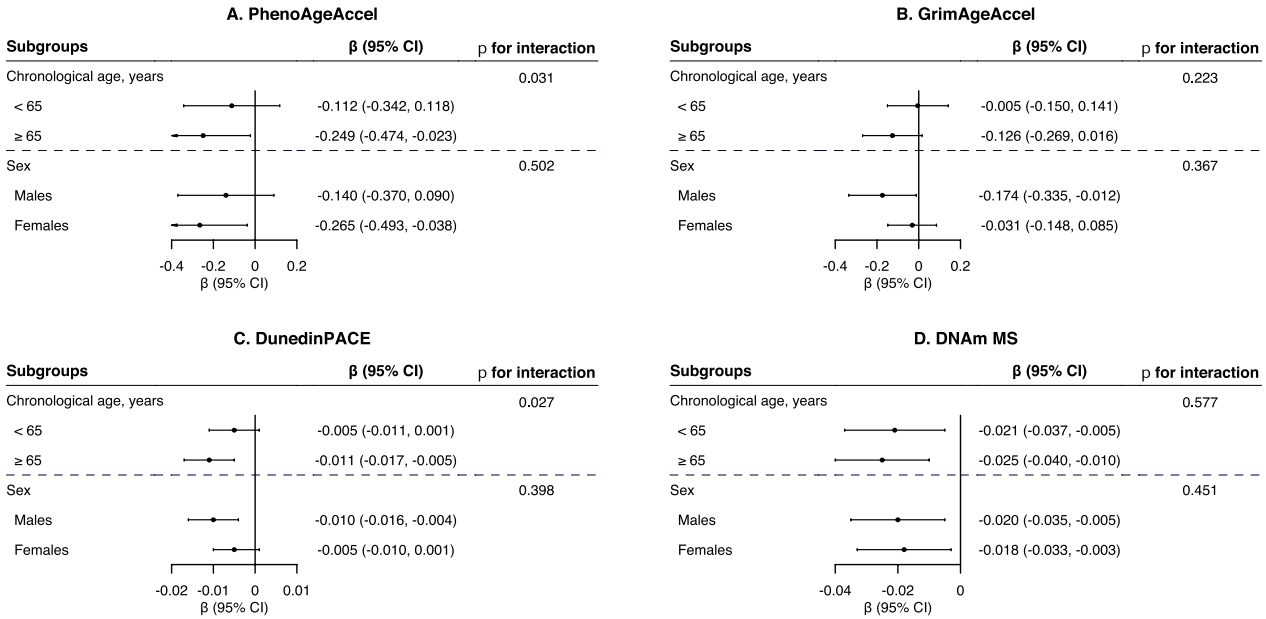

Fig. 2 Associations of sleep score with the DNA methylation age acceleration stratified by chronological age and sex. The models were adjusted for chronological age, sex, education level, smoking status, drinking status, physical activity, and body mass index. Each group adjusted for the other covariates except itself. Results are presented for each 1-point increase in sleep score. CI indicates confidence interval; PhenoAgeAccel indicates PhenoAge acceleration; GrimAgeAccel indicates GrimAge acceleration; DNAm MS indicates DNA methylation mortality risk score

the links between sleep pattern and DNAm AA may lie mainly in the behavior-, socially- and disease-related pathways. This speculation could be further supported by the results that a higher sleep score was associated with lower EEAA (sensitive to environmental variation) but not IEAA (capturing cell-intrinsic aging) [29]. These findings also suggest that second-generation epigenetic clocks offer superior sensitivity for detecting sleep-related aging effects than the first-generation. On the other hand, as many biomarkers selected for PhenoAge, GrimAge, and DunedinPACE are known to be markers of inflammation, and EEAA could reflect aspects of immunosenescence, our findings suggest that sleep patterns may impact the aging rate through regulation of inflammation and immune function rather than cell-intrinsic mechanisms. Furthermore, for two metrics with the same units, i.e., PhenoAge (capturing the functional state of many organ systems and tissues) and GrimAge (outstanding in predicting lifespan), the effect size of the association was bigger for PhenoAgeAccel than for GrimAgeAccel, suggesting sleep patterns may impact multi-system health more than lifespan.

We found interactions between sleep score and chronological age on PhenoAgeAccel and DunedinPACE. Results of stratified analyses showed that the associations of a higher sleep score with lower PhenoAgeAccel and DunedinPACE were more prominent in older adults. Interestingly, these two DNAm clocks, built on composite clinical measures, could serve as biomarkers of multi-system physiological dysregulation [8, 10]. Given that sleep health has long been considered a marker of physical health, especially in the elderly [35, 36], it is plausible that sleep habits may be differentially associated with the aging processes captured by PhenoAgeAccel and DunedinPACE in different age groups. Our findings are encouraging because they suggest the potential role of modifiable sleep habits in slowing the aging process. Still, these results should be interpreted with caution, given the possibility of chance findings and the observational nature of this study. Further clinical trials of sleep interventions are needed to substantiate our findings and assess whether our observed associations are causal.

Our study further demonstrates that a slower DunedinPACE partly explains the association between a higher sleep score and a lower risk of all-cause mortality. If causal, this finding may facilitate a better understanding of the sleep-mortality association and help identify relevant targets for potential interventions to prevent premature death [37]. Still, the mediating role of other biological and psychological factors in the sleep-mortality association needs to be explored, as the proportion mediated by DunedinPACE was relatively small (6.2%). It should be noted that we collected the sleep information and blood samples for DNA methylation cross-sectionally at baseline. Although it is reasonable to assume that the sleep pattern preceded the DNA methylation age

in temporal order since sleep habits of middle-aged and older retirees free from social constraints were relatively stable over some time and DNA methylation age, which typically correlates with chronological age, changed over time, data with clear temporal order would be better for mediation analyses. Therefore, future studies should measure DNAm AA at multiple time points to establish temporal precedence.

Our study has some limitations. First, this is an observational study, which precludes conclusions about causality. Second, as sleep factors were self-reported, misclassification might occur. However, self-reported sleep data were frequently used in large cohort studies [38–40]. Third, residual confounding from unmeasured factors, such as sleep apnea and depression, remained possible. Fourth, participants in our study were middle-aged and older Chinese adults, which may limit the generalizability of these findings. Fifth, a false-positive or false-negative conclusion remained possible since we did not perform adjustments for multiple comparisons.

Conclusions

A healthier sleep pattern was associated with slower DNAm AA, especially in older people. A slower DunedinPACE could partly explain the association between healthy sleep patterns and a lower risk of all-cause mortality. Our findings suggest that adopting healthy sleep patterns may promote healthy aging and further facilitate premature mortality prevention, highlighting the value of sleep patterns as a potential tool for clinical management in aging.

Abbreviations

DNAm	DNA methylation
DNAm MS	DNA methylation mortality risk score
DNAm AA	DNA methylation age acceleration
PhenoAgeAccel	PhenoAge acceleration
GrimAgeAccel	GrimAge acceleration
DFTJ	Dongfeng-Tongji
DMC	Dongfeng Motor Corporation
IEAA	Intrinsic epigenetic age acceleration
EEAA	Extrinsic epigenetic age acceleration
CI	Confidence interval
HR	Hazard ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13148-025-01898-w.

Supplementary Material 1.

Acknowledgements

We thank all staff and participants of the DFTJ cohort study as well as all participants for assisting in collecting the samples and data.

Author contributions

T.D.: conceptualization, data curation, formal Analysis, investigation, software, visualization, writing—original draft, writing – review & editing. K.L.: data curation, validation, writing—review & editing. L.Z., Q.W., J.L., Z.Z., F.C., W.Q., H.Y., C.W.: data curation, writing—review & editing. X.Z.: project administration, supervision, writing—review & editing. T.W.: conceptualization, project administration, resources, supervision, writing—review & editing. All authors read and approved the final manuscript.

Funding

The study was supported by grants 82021005, 82192903, and 81930092 from the National Natural Science Foundation of China. The funder had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Data availability

The data of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics and Human Subject Committees of Tongji Medical College, Huazhong University of Science and Technology, and Dongfeng General Hospital, DMC. All participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 18 July 2024 Accepted: 10 May 2025
Published online: 29 May 2025

References

1. Annual data of population. https://data.stats.gov.cn/easyquery.htm?cn=C01. Accessed 8 Apr.
2. World Population Prospects. 2022. https://population.un.org/wpp/. Accessed 8 Apr.
3. Hamczyk MR, Nevado RM, Barettino A, Fuster V, Andres V. Biological versus chronological aging: JACC focus seminar. J Am Coll Cardiol. 2020;75(8):919–30.
4. Horvath S, Raj K. DNA methylation-based biomarkers and the epigenetic clock theory of ageing. Nat Rev Genet. 2018;19(6):371–84.
5. Liu Z, Leung D, Thrush K, Zhao W, Ratliff S, Tanaka T, et al. Underlying features of epigenetic aging clocks in vivo and in vitro. Aging Cell. 2020;19(10): e13229.
6. Horvath S. DNA methylation age of human tissues and cell types. Genome Biol. 2013;14(10):R115.
7. Hannum G, Guinney J, Zhao L, Zhang L, Hughes G, Sadda S, et al. Genome-wide methylation profiles reveal quantitative views of human aging rates. Mol Cell. 2013;49(2):359–67.
8. Levine ME, Lu AT, Quach A, Chen BH, Assimes TL, Bandinelli S, et al. An epigenetic biomarker of aging for lifespan and healthspan. Aging (Albany N Y). 2018;10(4):573–91.

9. Lu AT, Quach A, Wilson JG, Reiner AP, Aviv A, Raj K, et al. DNA methylation GrimAge strongly predicts lifespan and healthspan. Aging (Albany N Y). 2019;11(2):303–27.
10. Belsky DW, Caspi A, Corcoran DL, Sugden K, Poulton R, Arseneault L, et al. DunedinPACE, a DNA methylation biomarker of the pace of aging. Elife. 2022;11:e73420.
11. Zhang Y, Wilson R, Heiss J, Breitling LP, Saum KU, Schottker B, et al. DNA methylation signatures in peripheral blood strongly predict all-cause mortality. Nat Commun. 2017;8:14617.
12. Carroll JE, Irwin MR, Levine M, Seeman TE, Absher D, Assimes T, et al. Epigenetic aging and immune senescence in women with insomnia symptoms: findings from the Women's Health Initiative Study. Biol Psychiatry. 2017;81(2):136–44.
13. Carroll JE, Ross KM, Horvath S, Okun M, Hobel C, Rentscher KE, et al. Postpartum sleep loss and accelerated epigenetic aging. Sleep Health. 2021;7(3):362–7.
14. Carskadon MA, Chappell KR, Barker DH, Hart AC, Dwyer K, Gredvig-Ardito C, et al. A pilot prospective study of sleep patterns and DNA methylation-characterized epigenetic aging in young adults. BMC Res Notes. 2019;12(1):583.
15. Kusters CDJ, Klopack ET, Crimmins EM, Seeman TE, Cole S, Carroll JE. Short sleep and insomnia are associated with accelerated epigenetic age. Psychosom Med. 2023;86:453–62.
16. Noroozi R, Rudnicka J, Pisarek A, Wysocka B, Masny A, Boron M, et al. Analysis of epigenetic clocks links yoga, sleep, education, reduced meat intake, coffee, and a SOCS2 gene variant to slower epigenetic aging. Geroscience. 2024;46(2):2583–604.
17. Lee HS, Kim B, Park T. The association between sleep quality and accelerated epigenetic aging with metabolic syndrome in Korean adults. Clin Epigenet. 2024;16(1):92.
18. Buysse DJ. Sleep health: can we define it? Does it matter? Sleep. 2014;37(1):9–17.
19. Erren TC, Gross JV. Re: "fragmentation and stability of circadian activity rhythms predict mortality: the Rotterdam study." Am J Epidemiol. 2015;182(2):185–6.
20. Diao T, Liu K, Wang Q, Lyu J, Zhou L, Yuan Y, et al. Bedtime, sleep pattern, and incident cardiovascular disease in middle-aged and older Chinese adults: the Dongfeng-Tongji cohort study. Sleep Med. 2023;110:82–8.
21. Diao T, Liu K, Lyu J, Zhou L, Yuan Y, Yang H, et al. Changes in sleep patterns, genetic susceptibility, and incident cardiovascular disease in China. JAMA Netw Open. 2024;7(4): e247974.
22. Wang F, Zhu J, Yao P, Li X, He M, Liu Y, et al. Cohort profile: the Dongfeng-Tongji cohort study of retired workers. Int J Epidemiol. 2013;42(3):731–40.
23. Diao T, Zhou L, Yang L, Yuan Y, Liu K, Peng R, et al. Bedtime, sleep duration, and sleep quality and all-cause mortality in middle-aged and older Chinese adults: the Dongfeng-Tongji cohort study. Sleep Health. 2023;9(5):751–7.
24. Sun J, Ma C, Zhao M, Magnussen CG, Xi B. Daytime napping and cardiovascular risk factors, cardiovascular disease, and mortality: a systematic review. Sleep Med Rev. 2022;65: 101682.
25. Yang L, Yang H, He M, Pan A, Li X, Min X, et al. Longer sleep duration and midday napping are associated with a higher risk of CHD incidence in middle-aged and older Chinese: the Dongfeng-Tongji cohort study. Sleep. 2016;39(3):645–52.
26. Zhou L, Yu K, Yang L, Wang H, Xiao Y, Qiu G, et al. Sleep duration, midday napping, and sleep quality and incident stroke: the Dongfeng-Tongji cohort. Neurology. 2020;94(4):e345–56.
27. Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's updated sleep duration recommendations: final report. Sleep Health. 2015;1(4):233–43.
28. Li Y, Yoshida K, Kaufman JS, Mathur MB. A brief primer on conducting regression-based causal mediation analysis. Psychol Trauma. 2023;15(6):930–8.
29. Chen BH, Marioni RE, Colicino E, Peters MJ, Ward-Caviness CK, Tsai PC, et al. DNA methylation-based measures of biological age: meta-analysis predicting time to death. Aging (Albany N Y). 2016;8(9):1844–65.
30. Rothman KJ. No adjustments are needed for multiple comparisons. Epidemiology. 1990;1(1):43–6.
31. Rothman KJ. Six persistent research misconceptions. J Gen Intern Med. 2014;29(7):1060–4.
32. Althouse AD. Adjust for multiple comparisons? It's not that simple. Ann Thorac Surg. 2016;101(5):1644–5.
33. Barnett MJ, Doroudgar S, Khosraviani V, Ip EJ. Multiple comparisons: to compare or not to compare, that is the question. Res Social Adm Pharm. 2022;18(2):2331–4.
34. Hooper R. To adjust, or not to adjust, for multiple comparisons. J Clin Epidemiol. 2025;180: 111688.
35. Driscoll HC, Serody L, Patrick S, Maurer J, Bensasi S, Houck PR, et al. Sleeping well, aging well: a descriptive and cross-sectional study of sleep in "successful agers" 75 and older. Am J Geriatr Psychiatry. 2008;16(1):74–82.
36. Reid KJ, Martinovich Z, Finkel S, Statsinger J, Golden R, Harter K, et al. Sleep: a marker of physical and mental health in the elderly. Am J Geriatr Psychiatry. 2006;14(10):860–6.
37. Hafeman DM, Schwartz S. Opening the black box: a motivation for the assessment of mediation. Int J Epidemiol. 2009;38(3):838–45.
38. Knutson KL, Wu D, Patel SR, Loredo JS, Redline S, Cai J, et al. Association between sleep timing, obesity, diabetes: the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Cohort Study. Sleep. 2017;40(4):zsx014.
39. Wang C, Bangdiwala SI, Rangarajan S, Lear SA, AlHabib KF, Mohan V, et al. Association of estimated sleep duration and naps with mortality and cardiovascular events: a study of 116 632 people from 21 countries. Eur Heart J. 2019;40(20):1620–9.
40. Yan B, Li R, Li J, Jin X, Gao F, Gao Y, et al. Sleep timing may predict congestive heart failure: a community-based cohort study. J Am Heart Assoc. 2021;10(6): e018385.

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