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Article

Sunshine Duration and Dementia: Mediating Role of Vitamin D, Calcium, and Accelerated Brain Aging

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Abstract: The current evidence regarding the relationship between sunlight exposure and dementia is limited and inconclusive, with potential modifiers and underlying mechanisms remaining largely unexplored. A total of 499,627 participants from the UK Biobank were included in the study. Sunshine duration and other meteorological exposures for each participant were estimated using the bilinear interpolation approach and time-weighted method. The association between sunshine duration and incident dementia was assessed using the time-dependent Cox proportional hazard model and generalized propensity score model. Multiplicative and additive interaction models were employed to identify the potential modifying effects of sociodemographic, lifestyle, environmental, and genetic factors. Brain age was predicted using machine learning methods based on neuroimaging phenotypes. The individual and joint parallel mediating effects of serum vitamin D, calcium, and brain age acceleration were further assessed using causal mediation analysis. With an average follow-up of 12.3 years, 7636 incident dementia cases were identified. Shorter sunshine duration was found to be associated with increased incidence of dementia with a hazard ratio of 1.05 (95% CI: 1.03, 1.07) for a 10-h decrease in average monthly sunshine duration. The adverse impact of reduced sunshine duration was modified by age, smoking status, household income, and time spent outdoors. The decrease in sunshine duration was also positively associated with brain age acceleration. The mediating effects of serum vitamin D, calcium, and brain age acceleration were estimated to be 16.20% (95% CI: 8.45%, 24.00%), 6.77% (95% CI: 4.01%, 9.78%), and 7.95% (95% CI: 6.48%, 9.00%), respectively, with a combined mediating proportion of 35.2%. Reduced sunshine duration associates positively with incident dementia and the brain aging process. Serum vitamin D, calcium, and brain age acceleration appear to serve as the underlying mechanism mediating the adverse impacts of reduced sunshine duration on dementia. The elderly, smokers, individuals with lower household income, and those with less time spent outdoors should be particularly vigilant.

Keywords: sunshine duration; dementia; mechanisms; causal inference; brain aging

1. Introduction

Dementia, a neurodegenerative syndrome, presents a significant burden on global public health. Currently, over 55 million individuals worldwide are suffering from dementia, with nearly 10 million new cases diagnosed annually [1]. Projections estimate that the number of people with dementia will rise to 152.8 million by 2050 [2]. Although the etiology of dementia remains unclear, environmental factors are increasingly considered to play an important role.

Sunlight is a critical environmental factor for vitamin D synthesis, calcium absorption, and the regulation of circadian rhythms, all of which are closely associated with dementia. However, current epidemiological evidence regarding the association between natural sunlight exposure and cognitive function or dementia remains inconclusive. For example, a study conducted in Finland reported that increased sunlight exposure was associated with improved cognitive function [3]. Conversely, Ma et al. identified a J-shaped relationship between time spent in outdoor light and dementia risk [4]. Moreover, in the UK, there is no dietary reference value for vitamin D for adults, as it is assumed that adequate levels are obtained through sunlight exposure alone [5–7]. However, the relevance of this assumption for dementia prevention has not been verified. Additionally, the potential modifiers and underlying mechanisms of sunlight exposure in relation to dementia remain largely unexplored.

Brain aging, characterized by a progressive decline in brain function, has been suggested to be influenced by sunlight exposure. Circadian rhythm disturbances, oxidative stress, and retinal damage may contribute to the effects of light on brain aging [8]. Aging itself is a significant pathogenic factor for dementia [9,10]. Given the role of brain aging in the relationship between sunlight exposure and dementia, accelerated brain aging may act as a mediating factor linking insufficient sunlight exposure to an increased risk of dementia.

Therefore, we conducted this study to evaluate the causal associations between sunshine duration and the risk of incident dementia, along with potential modifying factors. Furthermore, the mediating roles of serum vitamin D, calcium, and brain aging were examined.

2. Methods

2.1. Study Design and Participants

UK Biobank is a national cohort that recruited 502,940 individuals aged 40–69 years in England, Scotland, and Wales between 2006 and 2010 [11]. Participants' demographic, socioeconomic, health, and lifestyle information was collected through questionnaires and physical measurements at baseline and followed longitudinally thereafter. Detailed information of the study is available online http://www.ukbiobank.ac.uk/resources/ (accessed on 1 March 2024); http://biobank.ctsu.ox.ac.uk/crystal/docs.cgi) (accessed on 1 March 2024). Ethics approval was obtained from the North West Multicenter Research Ethics Committee, and all recruited participants provided informed consent (REC reference: 16/NW/0274).

In this analysis, we excluded 228 participants with dementia at baseline. We further excluded 2556 participants with missing data on sunshine duration. The missing data on covariates were imputed by multiple imputations with chained equations. The remaining 499,621 participants were included (Figure S1). Additionally, we excluded participants with missing data on variables for the mediators. Table S1 presents the sample size utilized in each analysis.

2.2. Environmental Exposure

The monthly sunshine duration and ambient temperature were collected from the HadUK-Grid dataset, which provides high-resolution meteorological data for the UK from 1862 to 2022 [12]. Sunshine duration was defined as the time period during which solar radiation exceeds 120 W/m^2, as measured by a Kipp and Zonen sunshine duration sensor [13]. Based on station observations, monthly meteorological variables were modelled on a 1 km × 1 km grid using the inverse distance-weighted interpolation method [14]. We employed the bilinear interpolation method to assess the monthly meteorological exposure of each participant with the grid data and geocoded home addresses.

Furthermore, as some participants may have changed residence during the follow-up period, we implemented a time-weighted method to calculate a more accurate exposure. First, we collected information on the participants' home addresses and the duration of their stay at each address. The time spent at each address was then calculated on a monthly basis. Finally, the duration of residence served as a weighting factor in computing the average exposure for study subjects in each month. A comprehensive description of the exposure assessment strategy can be found in a prior publication [15].

Air pollution data were obtained from the UK's Department for Environment, Food and Rural Affairs (DEFRA), which provides an annual mean concentration of air pollutants at a high resolution. These air pollution

data were generated on 1 km × 1 km grid using an air dispersion model that incorporates diverse sources from the National Atmospheric Emissions Inventory, a combination of air-pollutant and greenhouse-gas dataset. Subsequently, the data were calibrated using automatic air quality monitoring data from DEFRA's rural and urban network [16]. Grid data for fine particulate matter ($PM_{2.5}$), inhalable particulate matter (PM_{10}), nitrogen dioxide (NO_2), and nitrogen dioxides (NO_x) were extracted for the period 2003–2022. We also employed the bilinear interpolation approach and a time-weighted method to calculate the concentration of air pollution for each participant.

2.3. Genotyping and Imputation

The procedures for genotyping, imputation, and quality control in the UK Biobank have been detailed in earlier studies [17]. In summary, genotyping was conducted using Affymetrix UK BiLEVE Axiom and Affymetrix UK Biobank Axiom arrays, and the imputation was performed with the IMPUTE4 software. Comprehensive quality control measures were implemented at both the sample and marker levels to ensure high-quality genetic data. Individuals were excluded based on criteria such as discrepancies between self-reported and genetic sex, high rates of missing data, mixed ancestry, and genetic relatedness [18].

2.4. Serum Vitamin D and Calcium

Serum vitamin D and calcium levels were obtained from biochemical marker measurements collected at baseline in the UK Biobank study [19]. Biological samples were analyzed according to ISO 17025:2005 standards to ensure precise quantification. Rigorous quality control measures were implemented to maintain accuracy and consistency. The serum vitamin D and calcium data were normalized before the analysis.

2.5. MRI Data Acquisition and Pre-Processing

We utilized brain age, as determined by multiple neuroimaging modalities to construct markers of brain aging. Details regarding the acquisition and processing of brain MRI data from the UK Biobank are available on the UK Biobank website [20]. Several image-processing pipeline including FMRIB Software Library and FreeSurfer were employed to generate imaging-derived phenotypes [21]. A total of 1079 neuroimaging phenotypes were derived from five different modalities: T1-weighted imaging, T2-FLAIR, SWI, diffusion MRI, task-based fMRI, and resting-state fMRI.

2.6. Follow-Up and Ascertainment of Outcomes

All participants were followed until the first occurrence of dementia, loss to follow-up, death, or end of the follow-up date, whichever came first. The outcomes of this study were identified through linkage to the UK National Health Service. Incident dementia cases, including all-cause dementia, vascular dementia, and Alzheimer's dementia, were identified using algorithms developed by the UK Biobank Outcome Adjudication Group [22]. This algorithm, based on self-reported data, hospital admission records, and death registries, has been reported to reliably identify outcomes [23]. Dementia cases were recorded using the International Classification of Diseases (ICD) coding system, with detailed codes provided in Table S2.

2.7. Covariates

We considered potential confounders based on previous literature and further selected the variables that need to be controlled through directed acyclic graph (DAG) [24] (Figure S2). The covariates included as potential confounders in our analysis were age, sex (male/female), household income (unknown, ≥52,000£, 31,000–51,999£, 18,000–30,999£, or <18,000£), physical activity (unknow, high, moderate, or low), Townsend deprivation index (high, moderate, or low), time spent outdoors (high, moderate, or low), residential area (urban or rural), percentage of greenspace at 300 m buffers (%; high, moderate, or low), ambient temperature (low/moderate/high), air pollution (low/moderate/high), and disease history (cardiovascular disease, hypertension, diabetes, stroke, self-reported long-term illness disability or frailty, self-reported fair or poor health status). Further details on these variables were provided in Table S3.

2.8. Statistical Analyses

2.8.1. Association between Sunshine Duration and Incident Dementia

We conducted a time-dependent Cox proportional hazard model combined with a generalized propensity score (GPS) model to explore the causal relationship between sunshine duration and the incidence of dementia.

GPS represents a balancing score derived from the conditional probability density of exposure to continuous factors given the confounders. Employing GPS with a weighting method facilitates effective confounding balance by creating a pseudo-population that simulates a randomized controlled trial [25]. In consideration of machine-learning algorithms, recognized for their ability to enhance GPS estimation and prediction, we used an Extreme Gradient Boosting (XGboost) model [26]. Stabilized Inverse Probability Weights (IPWs) were computed with a specific formula, described in previous work [27]. Detailed information on GPS and IPW is shown in Supplementary Methods. To further enhance the stability of IPWs, we truncated the lowest and highest 1% of weights. The Absolute Correlation value (AC) served as an index for assessing covariate balance post-weighting, with a value below 0.1 considered indicative of good covariate balance [25].

The time-dependent Cox proportional hazard model was employed to investigate the associations between the sunshine duration and incident dementia. Sunshine duration was modelled as a time-varying exposure. Ambient temperature, air pollution, and age were treated as time-varying covariates. We assumed that sunshine duration and ambient temperature varied from season to season, and air pollution and age varied annually. Four models were constructed. Model 1 adjusted for age and sex. Model 2 additionally included adjustments for household income, physical activity, and Townsend deprivation index. Model 3 further incorporated adjustments for time spent outdoors, residential area, percentage of greenspace (%) at 300 m buffers, ambient temperature, and air pollution. Model 4 was developed using the causal inference method, serving as our primary model.

We calculated the risk ratio of dementia for every 10-h decline in sunshine duration. Furthermore, sunshine duration was divided into three quantiles as a categorical variable, and the hazard ratios for the groups with two shorter sunshine duration were calculated using the group with the longest sunshine duration as the reference.

2.8.2. Construction of Polygenic Risk Score

26 single nucleotide polymorphisms (SNPs) associated with dementia reported in previous study genome-wide association studies were included in this study to calculate polygenic risk score (PRS) (Table S4). A weighted approach was employed to compute the PRS. Each SNP was assigned a value of 0, 1, or 2, reflecting the count of risk alleles present. This value was then multiplied by a corresponding weighted risk estimate (β coefficient) for Alzheimer's Disease or cognitive disorder, derived from earlier genome-wide association studies [28]. The PRSs were categorized based on their quintile distribution into three groups: low (first quintile), intermediate (second to fourth quintiles), and high (fifth quintile).

2.8.3. Stratified Analysis

We used multiplicative and additive interaction models to assess potential modifiers including sociodemographic, lifestyle, environmental, and genetic factors. To evaluate the multiplicative interactions, the product term of sunshine duration and stratification factors was included in the model, and the *p* value of the product term was reported as the *p* for interaction. The relative excess risk due to interaction (RERI) was used to evaluate the additive interactions.

2.8.4. Construction of Brain Aging Markers

We first divided the data into a healthy and a non-healthy subset. Individuals with an ICD-10 diagnosis, self-reported long-term illness, disability or frailty, self-reported fair or poor health status, or a history of diabetes or stroke were classified as non-healthy [29]. The healthy subset was then randomly divided into training and test sets in a ratio of 8:2. All phenotypes were normalized. Least absolute shrinkage and selection operator (LASSO) regression, optimized with tenfold cross-validation, was applied to predict brain age based on the neuroimaging data [30]. The age bias was corrected using the regression slope and intercept between chronological age and predicted brain age [29].

2.8.5. Mediation Analysis

Causal mediation analyses were undertaken to investigate whether the serum vitamin D, calcium, and brain aging mediate the association between sunshine duration and dementia. As the mediators were not measured

seasonally, we utilized the average monthly sunshine duration over the 3 years preceding recruitment as the exposure. We estimated both the natural indirect effect (NIE) and the natural direct effect (NDE), where NIE indicates the causal effect and the indirect path from exposure through the mediator to outcome, and NDE indicates the causal effect and the direct path from exposure to outcome [31]. The proportion of the association mediated through the potential mediators was calculated by $log(NIE)/\big(log(NIE) + log(NDE)\big)$, with 95% confidence intervals estimated through Quasi-Bayesian methods [32]. We further performed a parallel mediation analysis to evaluate the joint mediation effect of the three potential mediators.

2.9. Sensitivity Analyses

We assessed the robustness of the results through the following sensitivity analyses: (1) calculating the E-value, an index commonly utilized to quantify the magnitude of unmeasured confounding [33]; (2) excluding participants with missing data on covariates and re-analysis; (3) excluding participants with dementia events or death within 1 year of follow-up; (4) using educational level as a surrogate for household income to control for the influence of social-economic background; (5) using the average monthly sunshine duration over the 4 and 5 years preceding recruitment date as the exposure to conduct mediation analysis.

3. Results

3.1. Descriptive Results

A total of 499,627 participants were included in the present analysis, with 7636 cases of dementia occurring over a median follow-up of 12.3 years. As shown in Table 1, the mean (SD) age of all participants was 56.53 (8.10) years and 54.4% were females. The mean exposure level to monthly sunshine duration was 127.99 ± 8.66 h. In comparison to participants without dementia, those with dementia tended to be male (52.6% vs 45.5%), older (64.24 years vs 56.41 years) and with less sunshine duration (127.16 h vs 128.00 h).

Table 1. Characteristics of study participants.

Characteristics	All Participants	None-Cases	Incident Dementia	*p*
Number of participants	499,627	491,991	7636	
Sex [n (%)]				<0.001
Female	271,823 (54.4)	268,204 (54.5)	3619 (47.4)	
Male	227,804 (45.6)	223,787 (45.5)	4017 (52.6)	
Age [year (mean ± SD)]	56.53 (8.10)	56.41 (8.08)	64.24 (4.80)	<0.001
Ethnicity [n (%)]				<0.001
Non-white	27,304 (5.5)	26,990 (5.5)	314 (4.1)	
White	472,323 (94.5)	465,001 (94.5)	7322 (95.9)	
Household income [n (%)]				<0.001
Less than 18,000 £	121,283 (24.3)	117,770 (23.9)	3513 (46.0)	
18,000 to 30,999 £	128,987 (25.8)	126,685 (25.7)	2302 (30.1)	
Greater than 31,000 £	249,357 (49.9)	247,536 (50.3)	1821 (23.8)	
Residential area [n (%)]				<0.001
Urban	426,228 (85.3)	419,549 (85.3)	6679 (87.5)	
Rural	73,399 (14.7)	72,442 (14.7)	957 (12.5)	
Physical activity [n (%)]				0.006
Low	95,332 (19.1)	93,786 (19.1)	1546 (20.2)	
Moderate	203,660 (40.8)	200,520 (40.8)	3140 (41.1)	
High	200,635 (40.2)	197,685 (40.2)	2950 (38.6)	
BMI [n (%)]				<0.001
Underweight	162,480 (32.5)	160,238 (32.6)	2242 (29.4)	
Normal	2630 (0.5)	2574 (0.5)	56 (0.7)	
Overweight	212,234 (42.5)	209,002 (42.5)	3232 (42.3)	
Obese	122,283 (24.5)	120,177 (24.4)	2106 (27.6)	
Smoking status [n (%)]				<0.001
Never	273,491 (54.7)	269,941 (54.9)	3550 (46.5)	
Former	173,077 (34.6)	169,811 (34.5)	3266 (42.8)	
Current	53,059 (10.6)	52,239 (10.6)	820 (10.7)	
Alcohol intake [n (%)]				<0.001
Never	40,597 (8.1)	39,522 (8.0)	1075 (14.1)	
Occasional	113,642 (22.7)	111,780 (22.7)	1862 (24.4)	
Moderate	244,004 (48.8)	240,866 (49.0)	3138 (41.1)	

Heavy	101,384 (20.3)	99,823 (20.3)	1561 (20.4)	
Educational level [n (%)]				<0.001
College education	163,468 (32.7)	161,846 (32.9)	1622 (21.2)	
Any school degree	189,587 (37.9)	187,355 (38.1)	2232 (29.2)	
Vocational qualification	33,441 (6.7)	32,855 (6.7)	586 (7.7)	
Other	113,131 (22.6)	109,935 (22.3)	3196 (41.9)	
Time spent outdoors [n (%)]				<0.001
Low	222,602 (44.6)	220,155 (44.7)	2447 (32.0)	
Moderate	113,868 (22.8)	112,056 (22.8)	1812 (23.7)	
High	163,157 (32.7)	159,780 (32.5)	3377 (44.2)	
Townsend deprivation index [n (%)]				<0.001
Low	164,936 (33.0)	162,624 (33.1)	2312 (30.3)	
Moderate	164,822 (33.0)	162,437 (33.0)	2385 (31.2)	
High	169,869 (34.0)	166,930 (33.9)	2939 (38.5)	
Greenspace [n (%)]				<0.001
Low	164,882 (33.0)	162,373 (33.0)	2509 (32.9)	
Moderate	164,874 (33.0)	162,157 (33.0)	2717 (35.6)	
High	169,871 (34.0)	167,461 (34.0)	2410 (31.6)	
Ambient temperature [n (%)]				<0.001
Low	164,877 (33.0)	162,314 (33.0)	2563 (33.6)	
Moderate	164,877 (33.0)	162,252 (33.0)	2625 (34.4)	
High	169,873 (34.0)	167,425 (34.0)	2448 (32.1)	
$PM_{2.5}$ [n (%)]				0.361
Low	164,877 (33.0)	162,304 (33.0)	2573 (33.7)	
Moderate	164,872 (33.0)	162,399 (33.0)	2473 (32.4)	
High	169,878 (34.0)	167,288 (34.0)	2590 (33.9)	
Disease history				
No	246,456 (49.3)	244,438 (49.7)	2018 (26.4)	<0.001
Yes	253,171 (50.7)	247,553 (50.3)	5618 (73.6)	
Sunshine duration [hour (mean ± SD)]	127.99 (8.66)	128.00 (8.66)	127.16 (8.77)	<0.001

3.2. Survival Analyses on the Association between Sunshine Duration and Dementia

The AC of covariates for both unweighted and weighted populations were presented in Table S5, illustrating a notable improvement in covariate balance after GPS weighting. The exposure-response curve indicated that the risk of incident dementia significantly decreased with increased sunshine duration (Figure 1). A significant adverse effect was observed when the average seasonal sunshine duration was less than 128 h. We further divided the sunshine duration into three quantiles, with the longest group as tertile1, the middle as tertile2, and the shortest as tertile3. As shown in Table 2, the participants with sunshine duration in the 2nd and 3rd tertiles had higher risk of incident dementia in all four models. Hazard Ratios (HRs) per 10-h decrease in monthly sunshine duration were 1.05 (95% CI: 1.03, 1.07), 1.12 (95% CI: 1.07, 1.18), and 1.05 (95% CI: 1.02, 1.09) for all-cause dementia, vascular dementia, and Alzheimer dementia in the unweighted-fully adjusted model (Model 3). Similar results were observed in the weighted model (Model 4), with HRs of 1.05 (95% CI: 1.03, 1.07), 1.17 (95% CI: 1.11, 1.24), and 1.11 (95% CI: 1.01, 1.23) for all-cause dementia, vascular dementia, and Alzheimer dementia, respectively.

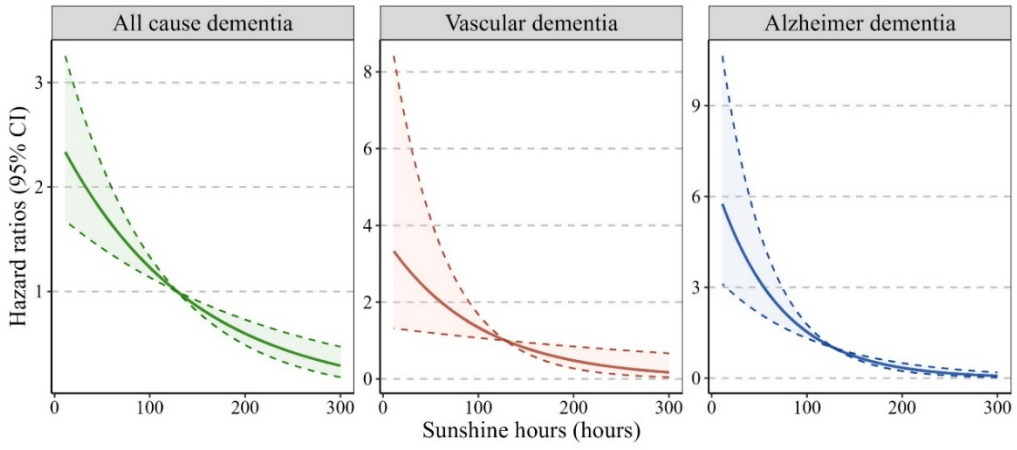

Figure 1. Exposure-response curve between sunshine duration and incident dementia.

Table 2. The association between sunshine duration and dementia.

Model	All Case Dementia		Vascular Dementia		Alzheimer Dementia	
	HR (95% CI)	***p***	**HR (95% CI)**	***p***	**HR (95% CI)**	***p***
			Model 1			
Tertile 1	Ref		Ref		Ref	
Tertile 2	1.29 (1.10, 1.51)	0.002	1.43 (1.20, 1.71)	<0.001	1.29 (1.14, 1.47)	<0.001
Tertile 3	1.31 (1.17, 1.45)	<0.001	1.68 (1.26, 2.25)	<0.001	1.40 (1.07, 1.82)	0.0147
P for trend		<0.001		<0.001		<0.001
Per 10 h decrease in the quarterly average monthly sunshine duration	1.05 (1.03, 1.08)	<0.001	1.13 (1.08, 1.19)	<0.001	1.05 (1.02, 1.09)	0.0029
			Model 2			
Tertile 1	Ref		Ref		Ref	
Tertile 2	1.20 (1.11, 1.31)	<0.001	1.39 (1.17, 1.66)	<0.001	1.29 (1.13, 1.46)	0.0001
Tertile 3	1.26 (1.08, 1.48)	0.004	1.59 (1.19, 2.13)	0.001	1.38 (1.06, 1.81)	0.0175
P for trend		<0.001		<0.001		<0.001
Per 10-h decrease in the quarterly average monthly sunshine duration	1.04 (1.02, 1.06)	<0.001	1.12 (1.06, 1.17)	<0.001	1.05 (1.02, 1.09)	0.0038
			Model 3			
Tertile 1	Ref		Ref		Ref	
Tertile 2	1.17 (1.08, 1.27)	<0.001	1.34 (1.12, 1.60)	0.001	1.26 (1.11, 1.43)	<0.001
Tertile 3	1.23 (1.07, 1.42)	0.003	1.69 (1.25, 2.27)	<0.001	1.39 (1.06, 1.83)	0.0185
P for trend		<0.001		<0.001		<0.001
Per 10-h decrease in the quarterly average monthly sunshine duration	1.05 (1.03, 1.07)	<0.001	1.12 (1.07, 1.18)	<0.001	1.05 (1.02, 1.09)	0.0025
			Model 4			
Tertile 1	Ref		Ref		Ref	
Tertile 2	1.17 (1.07, 1.26)	<0.001	1.27 (1.06, 1.51)	0.008	1.85 (1.32, 2.59)	<0.001
Tertile 3	1.24 (1.07, 1.43)	0.003	1.41 (1.05, 1.88)	0.022	2.72 (1.58, 4.69)	<0.001
P for trend		<0.001		<0.001		<0.001
Per 10-h decrease in the quarterly average monthly sunshine duration	1.05 (1.03, 1.07)	<0.001	1.17 (1.11, 1.24)	<0.001	1.11 (1.01, 1.23)	0.010

3.3. Stratified Analyses

Although there were no additive interactions (P for interaction >0.05, Table S6), there were some significant multiplicative interactions (Figure 2). Compared to the participants younger than 65 years old (HR: 1.04, 95% CI: 1.02, 1.06), the elderly were more vulnerable to reduced sunshine duration (HR: 1.06, 95% CI: 1.02, 1.09). We found the risk of incident dementia was higher among participants with lower household incomes (HR for 18,000 to 30,999 £: 1.03, 95% CI: 1.01, 1.06; HR for less than 18,000 £: 1.07, 95% CI: 1.05, 1.11) and shorter time spent outdoors (HR: 1.05, 95% CI: 1.03, 1.07), compared to those with higher incomes (HR: 1.02, 95% CI: 0.99, 1.04) and longer time spent outdoors (HR: 1.04, 95% CI: 1.02, 1.06). Furthermore, smokers (HR for former smokers: 1.04, 95% CI: 1.02, 1.07; HR for current smokers: 1.06, 95% CI: 1.04, 1.08) were more susceptible to reduced sunshine duration than non-smokers (HR: 1.02, 95% CI: 1.02, 1.06).

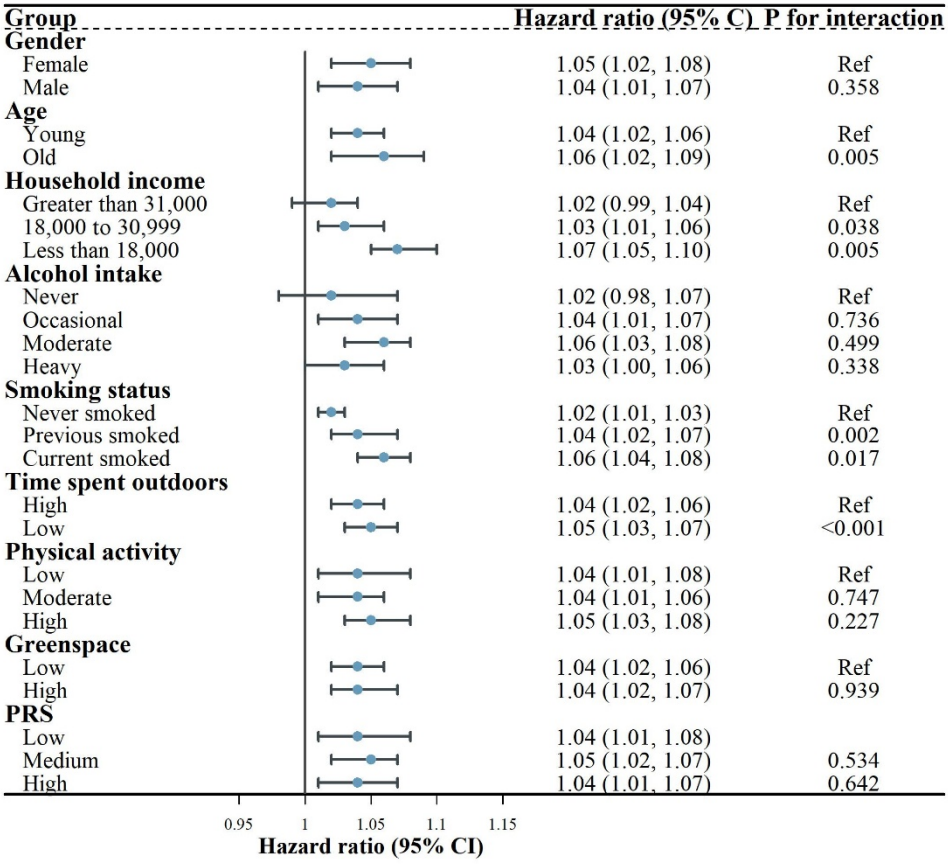

Figure 2. Results of stratified analyses.

3.4. Associations between Sunshine Duration and Aging Markers

A decrease in sunshine duration was negatively correlated with serum vitamin D and calcium. As shown in Table 3, a reduction of one hour in sunshine duration was associated with a decrease of 0.03 unit decrease in vitamin D (95% CI: 0.03, 0.04) and a 0.07 unit decrease in calcium (95% CI: 0.07, 0.08) in Model 4. However, decrease in sunshine duration was positively associated with brain age acceleration (β: 0.02, 95% CI: 0.01, 0.03).

Table 3. The association between sunshine duration and the three mediators.

Model	Vitamin D		Calcium		Brain Age Acceleration	
	β (95% CI)	*p*	β (95% CI)	*p*	β (95% CI)	*p*
Model 1	−0.08 (−0.09, −0.08)	<0.001	−0.05 (−0.06, −0.05)	<0.001	0.01 (0.01, 0.02)	<0.001
Model 2	−0.07 (−0.07, −0.07)	<0.001	−0.05 (−0.05, −0.05)	<0.001	0.01 (0.01, 0.02)	<0.001
Model 3	−0.03 (−0.04, −0.03)	<0.001	−0.07 (−0.08, −0.07)	<0.001	0.02 (0.01, 0.03)	<0.001
Model 4	−0.03 (−0.04, −0.03)	<0.001	−0.07 (−0.08, −0.07)	<0.001	0.02 (0.01, 0.03)	<0.001

3.5. Associations between Aging Markers and Incident Dementia

Both vitamin D and calcium were inversely associated with the risk of incident dementia (Table 4). In Model 4, each one-unit increase in vitamin D and calcium was associated with hazard ratios for incident dementia of 0.87 (95% CI: 0.85, 0.90) and 0.96 (95% CI: 0.94, 0.98). Conversely, brain age acceleration was positively associated with the risk of incident dementia, with a hazard ratio of 1.04 (95% CI: 1.03, 1.06).

Table 4. The association between the three mediators and incident dementia.

Model	Vitamin D		Calcium		Brain Age Acceleration	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Model 1	0.85 (0.83, 0.87)	<0.001	0.97 (0.95, 0.99)	0.035	1.04 (1.02, 1.06)	<0.001
Model 2	0.86 (0.84, 0.89)	<0.001	0.97 (0.95, 0.99)	0.030	1.04 (1.02, 1.06)	<0.001
Model 3	0.87 (0.85, 0.90)	<0.001	0.97 (0.95, 0.99)	0.023	1.04 (1.02, 1.06)	<0.001
Model 4	0.87 (0.85, 0.90)	<0.001	0.96 (0.94, 0.98)	0.001	1.04 (1.03, 1.06)	<0.001

3.6. Mediation Analyses

Serum vitamin D, calcium and brain age acceleration significantly mediated the associations between sunshine duration and the risk of incident dementia. As illustrated in Figure 3, the mediating proportions for vitamin D, calcium, and brain age acceleration were 16.20% (95% CI: 8.45%, 24.00%), 6.77% (95% CI: 4.01%, 9.78%), and 7.95% (95% CI: 6.48%, 9.00%), respectively. The combined mediating effect of these three factors accounted for 35.2% of the total effect of sunshine duration on the risk of incident dementia.

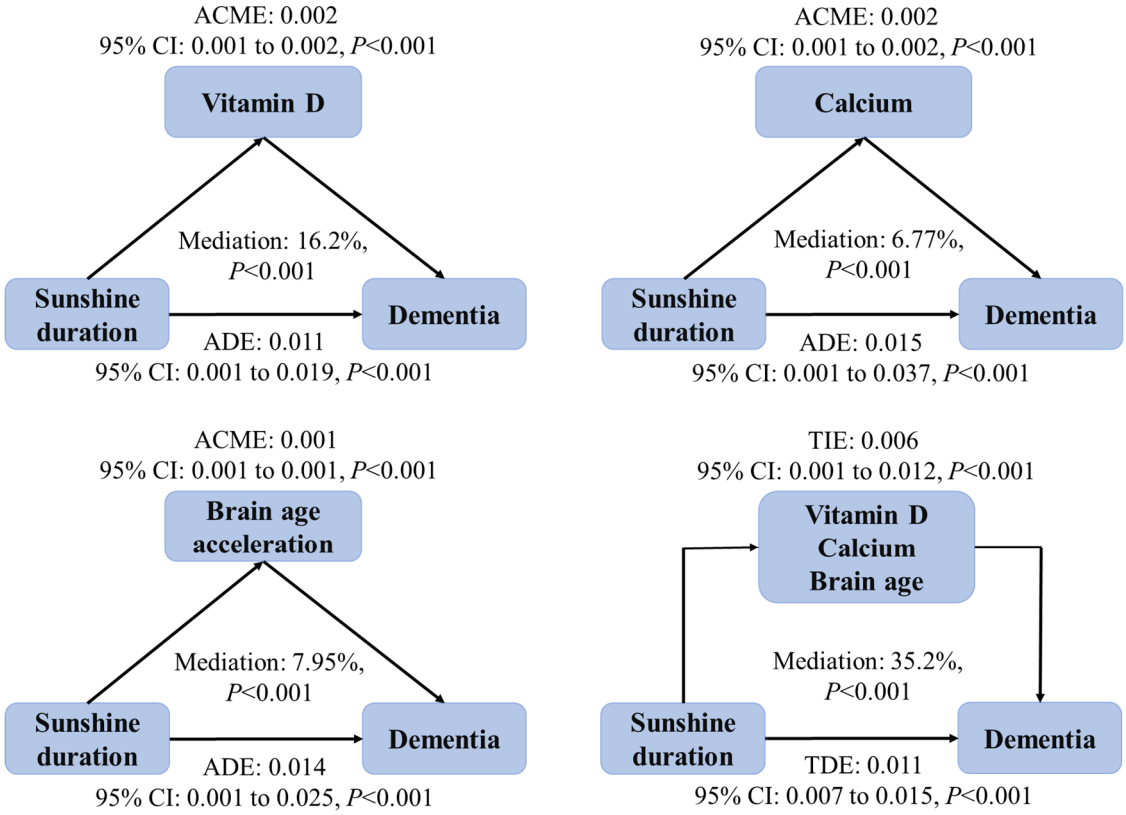

Figure 3. The association between sunshine duration and incident dementia was mediated by vitamin D, calcium, and brain age acceleration.

3.7. Sensitivity Analyses

The E-value was summarized in Table S7, showing that our results were overall robust to unmeasured confounding bias. The results remained stable when we imputed missing data on covariates with multiple imputations with chained equations, excluded participants with dementia events or death within 1 year of follow-up, and used educational level as a surrogate for household income, using the average monthly sunshine duration over the 4 or 5 years preceding recruitment date as the exposure to conduct mediation analysis (Tables S7 and S8).

4. Discussion

There are three main findings of this study. First, reduced sunshine duration was significantly associated with an increased risk of incident dementia, with more pronounced effects observed in elderly, smokers, individuals with less time spent outdoors and less household income. Second, reduced sunshine duration was positively associated with brain aging markers. Third, vitamin D, calcium, and brain aging served as the mediators in the pathway linking sunshine duration to the risk of incident dementia.

The existing evidence regarding the impact of sunshine duration on dementia is currently limited and ambiguous. Ma et al. observed a J-shaped relationship between time spent in outdoor light and dementia risk, suggesting harmful effects from both extremely high and low sunlight exposure [4]. However, there are also some studies that support our findings. For example, a study in Finland found that greater sunlight exposure was associated with better cognitive function [3]. Similarly, a study in Greater Manchester, United Kingdom, reported that simulated summer sunlight exposures could raise vitamin D levels in UK adults [34]. The inconsistencies in results may stem from variations in study design, methodologies, and study populations.

Unlike prior studies, our research utilized a national, longitudinal cohort and employed a model with a causal framework, potentially providing stronger evidence for causal inference. We identified that an average of 128 h of sunshine per month within a season was a critical threshold. Sunshine duration below this level was associated with an increased risk of incident dementia. Notably, the mean monthly sunshine duration differed only slightly between participants with and without dementia at baseline (127.16 vs. 128 h). This minimal difference reflects a descriptive comparison rather than the exposure contrast used in the risk models. The association analyses were based on tertiles of sunshine duration, capturing variability across the exposure distribution. Compared with the lowest tertile, participants in the second and third tertiles were associated with a 17% and 24% higher risk of dementia, respectively, suggesting a dose-response pattern. In large population-based cohorts, environmental exposures often exhibit relatively narrow differences in mean levels; however, meaningful risk gradients may still emerge when individuals are compared across exposure categories. Therefore, the small baseline mean difference should not be interpreted as inconsistent with the observed exposure-response relationship.

The harmful impacts for reduced sunshine duration were more pronounced among the elderly, smokers, individuals with lower household income, and those with less time spent outdoors. The increased vulnerability among the elderly may be attributed to pre-existing medical conditions and prolonged exposure to insufficient sunlight [35]. Participants who spent less time outdoors had fewer opportunities for light exposure, thereby increasing the likelihood of sunlight deficiency [4]. The higher susceptibility among individuals with low household incomes may be due to disparities related to social disadvantages, such as limited access to healthcare and education [36]. Additionally, previous studies have found a positive association between tobacco smoke exposure and vitamin D deficiency, which may exacerbate cognitive impairment resulting from inadequate sunlight exposure [37]. Notably, the hazard ratios across alcohol consumption categories increased progressively from never to occasional and moderate drinkers; however, in the heavy drinking group, the association appeared attenuated and the 95% confidence interval approached the null. This unexpected pattern may be partly explained by the relatively smaller sample size in the heavy drinking category, which could reduce statistical precision and lead to unstable estimates. In addition, heavy alcohol consumption is often associated with complex health profiles and competing risks, which may attenuate the observed association. Therefore, this finding should be interpreted cautiously and may reflect random variation rather than a true protective effect.

Several mechanisms may underlie the relationship between sunlight and dementia. Sunlight is involved in vitamin D synthesis, and vitamin D can cross the blood-brain barrier, with its receptors widely distributed in neurons and glial cells [38]. Vitamin D improves brain health through its neuroprotective, anti-inflammatory, and antioxidant effects on neurons [39]. Specifically, vitamin D may prevent neuronal death by reducing age-related hyperphosphorylation of tau protein, forming amyloid-β oligomers, and increasing amyloid clearance [40]. Previous studies have consistently found that vitamin D is beneficial for the neuronal growth of rat hippocampal cells [41,42].

Sunlight plays a crucial role in calcium absorption. Ultraviolet B (UVB) rays in sunlight stimulate the conversion of 7-dehydrocholesterol in the skin to vitamin D, which enhances calcium absorption in the intestines, calcium deposition in osteoblasts, and calcium reabsorption in the kidneys. Calcium regulates key neuronal processes, such as apoptosis, synaptic connectivity, and neurotransmitter transmission [43,44]. Calcium homeostasis is closely linked to the neurobiology of dementia, including mechanisms like apoptosis, hyperphosphorylation of tau protein, and amyloid β deposition [45]. Previous studies have shown that calcium can mitigate dementia-related pathological changes by protecting neurons, improving synaptic defects, and reducing

amyloid and tau aggregation [46]. Additionally, a mendelian randomization study found that increased serum calcium levels were associated with a reduced risk of Alzheimer's disease [47].

Additionally, sunlight may influence brain aging by regulating circadian rhythms. Some studies have reported that circadian rhythm regulation is associated with melatonin production, which plays a role in the decline of brain functions [42]. The systemic effects of circadian rhythms on body homeostasis, sleep regulation, and behavior are well established, and these factors are directly linked to brain aging [48]. Sunlight has also been suggested to exert systemic anti-inflammatory effects, and inflammation has been implicated in the aging process [49]. Among the various factors contributing to dementia, aging is the most significant. Advancing age is characterized by a reduction in brain volume, accompanied by neuroinflammation and disruptions in calcium homeostasis [48,50]. Aging is also associated with changes in synaptic physiology within the hippocampus and prefrontal cortex, leading to alterations in dendritic branching and spine density in neurons [9]. These changes are linked to cognitive decline and the onset of dementia.

Our study has several strengths. First, we firstly investigated the effects of sunshine duration on incident dementia and aging markers in the UK Biobank. The UK Biobank, being a national cohort study with a large sample size, significantly enhanced statistical power. Second, we employed the model with a causal framework to provide evidence for causal inference. Lastly, our stratified and mediation analysis provide evidence of potential modifiers and mechanisms.

There are also some limitations to the present study. First, the data on serum vitamin D and calcium were mainly assessed at baseline, constraining our ability to establish the chronological relationship between exposure and the mediators. Second, although meteorological variables, air pollution, and outcomes were time-varying, information on other covariates throughout the follow-up period was not available. Finally, one of the assumptions underlying causal models is the absence of unmeasured confounding. Despite our comprehensive consideration of potential covariates in the analysis, we cannot ensure the absence of residual confounders.

5. Conclusions

In conclusion, reduced sunshine duration is associated with a higher risk of incident dementia and accelerated brain aging. The elderly, smokers, individuals with lower household income, and those with less time spent outdoors should be particularly vigilant. Vitamin D deficiency, calcium deficiency, and accelerated brain aging appear to serve as the underlying mechanism for the adverse effects of sunshine duration on dementia.

Supplementary Materials

The supplementary materials, including additional figures and tables, can be downloaded at: https://media.sciltp.com/articles/others/260311034083860/ECDD-26010201-SM.pdf (accessed on 21 March 2026). Table S1 Sample sizes used in different analyses. Table S2 International Classification of Disease codes used to ascertain dementia and its subtypes. Table S3 UDI and notes of variables in the UK Biobank repository. Table S4 Characteristics of genetic variants associated with dementia in the UK biobank. Table S5 Absolute correlation of covariates for unweighted and weighted populations. Table S6 The results of additive interactions. Table S7 The results of sensitivity analyses. Table S8 The results of sensitivity analyses for the mediation analysis. Figure S1 The flowchart of participants selection in the study. Figure S2 The directed acyclic graph for covariate selection. References [50–54] are cited in the supplementary materials.

Author Contributions

J.F.: conceptualization, methodology, software, writing—reviewing and editing; F.T.: formal analysis, writing—original draft preparation; L.C.: visualization; Z.L.: visualization; Z.Y.: software, validation; X.C.: writing—reviewing and editing; S.R.: writing—reviewing and editing; C.W.: writing—reviewing and editing; X.G.: writing—reviewing and editing; H.L.: writing—reviewing and editing, supervision. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

Ethical approval for UK Biobank was granted by the North West Multi-Centre Research Ethics Committee (REC reference: 16/NW/0274). Access to the UK Biobank data was granted under Application Number [69550].

Informed Consent Statement

Written informed consent has been obtained from the patients of UK Biobank.

Data Availability Statement

Restrictions apply to the availability of these data. Data were obtained from UK Biobank (https://www.ukbiobank.ac.uk/) and are available from the authors with the permission of UK Biobank.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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