Influence of Depression on the Association between Colder Indoor Temperature and Higher Blood Pressure

Short title: Depression, Cold Exposure and Higher BP

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Abstract

***Objectives*: ** Cold exposure accounts for >7% of all-cause mortality worldwide, and cold-induced blood pressure (BP) elevation and consequent cardiovascular events are partially responsible. For prevention, it is important to identify risk factors for exaggerated temperature-sensitivity of BP, but this is not fully understood. This study investigated whether depressive symptoms affect the relationship between indoor temperature and BP.

***Methods*: ** We conducted a cross-sectional analysis of 1,076 community-based individuals who were ≥60 years of age. Depressive symptoms were assessed using the 15-item Geriatric Depression Scale at a cutoff point of 4/5. We performed ambulatory BP monitoring and indoor temperature measurement on two consecutive days during the cold season in Nara, Japan.

***Results*: ** When using daytime systolic BP (SBP) as a dependent variable, multilevel linear regression analyses showed that lower daytime indoor temperature was significantly associated with higher daytime SBP in the depressive group ($n = 216$, $\beta = -0.804$, $p < 0.001$), but not in the non-depressive group ($n = 860$, $\beta = -0.173$, $p = 0.120$); moreover, a significant interaction between depression and daytime indoor temperature was observed ($p = 0.014$). These relationships were independent of potential confounders including age, gender, body mass index, medications, and physical activity. Similar results were obtained for morning SBP, nocturnal SBP dipping, and morning BP surge.

***Conclusions*: ** The results suggest that depressive subjects are more likely to have cold-induced BP elevation than non-depressive subjects. Further longitudinal studies are warranted to determine whether people with depressive symptoms are at a high risk for cold-related cardiovascular events.

Keywords Ambulatory blood pressure monitoring, Cold exposure, Depression, Epidemiologic study, Hypertension, Indoor temperature, Older adults

Introduction

Depressive disorders, which are common mental illnesses among older adults, are characterized by cardiovascular mortality and comorbidities. The prevalence of clinically significant depressive symptoms in a community-based geriatric population ranges from approximately 8% to 16% [1], and late-life depression is a risk factor for suicide and non-suicide mortality [1,2]. A possible cause of non-suicide mortality in depression is cardiovascular disease [2], as indicated by meta-analyses and systematic reviews that have shown that depression independently increases the risk of cardiovascular diseases [3,4]; however, the mechanisms are not fully understood.

Colder, non-optimum temperature has been linked to >7% of the mortality incidence worldwide [5], and increase in cardiovascular events due to cold-induced blood pressure (BP) elevation has been suggested as a causative factor in certain cold-related mortalities. Cardiovascular events are known to be more frequent in winter months [6,7], and a meta-analysis reported that a 1°C decrease in indoor and outdoor temperature was associated with 0.38 mmHg (95% confidence interval [CI]: 0.18 to 0.58) and 0.26 mmHg (95% CI: 0.18 to 0.33) increase in systolic BP (SBP), respectively [8]. A recent cross-sectional study carefully adjusted for confounding factors, including physical activity and outdoor temperature, also showed that indoor temperature was independently associated with SBP (β: −0.48, 95% CI: −0.72 to −0.25) and diastolic BP (DBP) (β: −0.45, 95% CI: −0.63 to −0.27) [9]. Recent prospective studies suggest that higher morning BP is associated with a higher risk of winter-onset cardiovascular disease [10], and that a temperature-induced increase in BP potentially mediates the association between colder temperature and cardiovascular events [11]. As per our previous randomized control study [12], intensive room heating can lower BP in winter, but providing intervention for everyone is not practical; therefore, it is important to identify the high-risk population that needs to be prioritized for intervention.

Cold-induced BP elevation is hypothesized to be greater in patients with depression, because these patients have been found to have attenuated vasodilation [13,14]. Furthermore, depression has been reported to be associated with hyper-reactivity of the sympathetic nervous system in response to stress, including cold [15] and mental stress [16–18]. However, it is unknown whether depressive symptoms cause an effect modification of the association between temperature and BP. Therefore, the purpose of this study was to investigate whether depressive symptoms affect the relationships between indoor temperature and BP parameters in a large sample of community-based older adults.

Methods

Participants and Study Protocol

A total of 1,127 community-based older adults ≥60 years of age were recruited into the Housing Environments and Health Investigation among Japanese Older People in Nara, Kansai Region (HEIJO-KYO) Study, which is a prospective community-based cohort study for which a baseline survey was conducted between September 2010 and March 2014. Among the participants, 1,076 (95.5%) for whom all valid data for the depressive status, ambulatory BP monitoring (ABPM), and indoor temperature were available were included in the current analysis. The study protocol was previously described [19] and was approved by the Ethics Committee of Nara Medical University. All participants provided their written informed consent before participating.

Assessment of Depressive Symptoms

Depressive symptoms were assessed using the 15-item Geriatric Depression Scale (GDS-15). Participants with a GDS-15 score of 5 or higher were classified as "depressive" because the sensitivity and specificity of the GDS-15 at a cutoff point of 4/5 have been reported to be 92.7% and 65.2%, respectively, based on the diagnostic criteria of the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision*, for major depressive episode [20].

Ambulatory BP Monitoring

Ambulatory BP monitoring (ABPM) was performed during the cold season (September – March) for all subjects, using a validated ambulatory recorder (TM-2430; A&D Co. Ltd., Tokyo, Japan) positioned on the participant's non-dominant arm. SBP and DBP were measured at 30-min intervals for 48 hours, and all parameters were calculated as subsequently discussed for each 24-hour period. Pulse pressure (PP) was defined as the difference between SBP and DBP. Subjects with <10 daytime or <5 night-time SBP readings on both days were excluded from analyses based on the criteria of a previous study [21]. Daytime and night-time were defined from the participants' self-reported data of their bed-in and bed-out times, as recorded in a standardized sleep diary, and mean daytime and night-time SBP readings were calculated correspondingly. Nocturnal SBP dipping was defined as the percentage of decrease in night-time SBP relative to daytime SBP [22].

Morning SBP was calculated as the 2-hour average of SBP just after bed-out time. MBPS was calculated according to two commonly used classifications, namely, pre-waking MBPS (morning SBP minus pre-waking SBP [2-hour average of SBP just before waking up]) and sleep-trough MBPS (morning SBP minus the lowest SBP [1-hour average of three readings around the lowest nocturnal SBP reading]) [23].

Indoor and Outdoor Temperatures

The indoor temperatures of the participants' living rooms, on the same days as ABPM, were measured at 10-min intervals approximately 60 cm above floor level using Thermochron iButton (Maxim Integrated, Dallas, TX, USA). Outdoor temperatures obtained from the local meteorological office in Nara, Japan (latitude, 34° N) were measured every 10 minutes. We calculated the average indoor and outdoor temperatures during the daytime and in the morning for each day, within the definition of periods for daytime SBP and morning SBP.

Other Variables

Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Current smoking status, habitual alcohol consumption, use of antidepressant medication, use of antihypertensive medication, educational background, and household income were evaluated using a questionnaire survey. Daytime, night-time, and morning physical activities were calculated as the average of all valid physical activity counts per minute, which were evaluated using an actigraphy device (Actiwatch 2; Phillips Respironics Inc., Murrysville, PA, USA), during periods corresponding to the ABPM parameters.

Statistical Analysis

Variables with normal distribution are presented as the mean and standard deviation (SD), and the difference between the means of the depressive and non-depressive groups were compared using Welch's *t*-test. A comparison of the dichotomous variables was performed using the chi-squared test. After the daytime indoor temperatures were stratified into lower and higher temperatures based on the median, we drew smoothed spline curves to represent the temporal trend of the SBP around bed-out time for each depressive status group by fitting a generalized additive model with generalized cross-validation.

The relationships between indoor temperatures and ABPM parameters were depicted based on depressive status by using linear regression lines. To assess the interaction effect of the depressive status on the relation, we analyzed linear regression models with an interaction term (depressive status × indoor temperature) in addition to the depressive status and indoor temperature, which were used as independent variables, and the MBPS parameters, used as the dependent variable.

With the data stratified by depressive status, we conducted multilevel linear regression analyses to examine the association between indoor temperature and ABPM parameters, with the assumptions made about the random slope and intercept for each depressive status group. The multilevel models were as follows:

Level 1 (day level; variables that change from day to day):

$$\mathrm{ABPM}_{ij} = \beta_{0j} + \beta_{1j} \times \mathrm{Temp}_{ij} + r_{ij}$$

where ABPM_{ij} denotes an observed ABPM parameter (such as daytime SBP) for the individual j on day i; Temp_{ij} denotes the observed temperature (such as daytime indoor temperature) for individual j on day i; β_{0j} denotes a random intercept for individual j; β_{1j} denotes a random slope of Temp_{ij} for individual j; and r_{1j} denotes the residual for individual j on day i.

Level 2 (individual level; variables that are different from individual to individual, not changing from day to day):

$$\beta_{0j} = \gamma_{00} + \sum_{s=1}^{m} (\gamma_{0s} \times X_{sj}) + u_{0j}$$

$$\beta_{1j} = \gamma_{10} + u_{1j}$$

where X_{sj} denotes observed covariates (such as age and gender; only when multivariable models) for individual j; γ_{00}, and γ_{0s} denote the fixed effects of intercept and regression coefficients of covariate X_{sj}; u_{0j} denotes a random effect in the random intercept for individual j; γ_{10} denotes the fixed effect of the regression coefficient of Temp_{ij}; and u_{1j} denotes a random effect in the random slope of Temp_{ij} for individual j.

In addition, the interaction effects of the depressive status were analyzed in a whole sample that included both depressive and non-depressive subjects, using the same multilevel models that included the depressive status terms in level 2:

$$\beta_{0j} = \gamma_{00} + \gamma_{01} \times \text{Depressive}_j + \sum_{s=2}^{m} \left(\gamma_{0s} \times X_{sj}\right) + u_{0j}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11} \times \text{Depressive}_j + u_{1j}$$

where Depressive_j denotes an observed depressive status for individual j; γ_{01} denotes a regression coefficient of Depressive_j; and γ_{11} denotes a regression coefficient of an interaction term ($\text{Depressive}_j \times \text{Temp}_{ij}$).

In addition to multilevel analyses, we performed single-level linear regression analyses using the same models except using two-day average data. We also conducted multilevel linear regression analyses using outdoor instead of indoor temperatures.

All multivariable models above were consistently adjusted with potential confounders, including gender (male, female), age (continuous), and BMI (≥25, <25) in model 1; with the addition of current smoker (“yes,” “no”), ethanol intake (≥30, <30 g/day), antihypertensive use (“yes,” “no”), antidepressant use (“yes,” “no”), education history (≥13, <13 years), and household income (≥4, <4 million Japanese yen) in model 2; and the addition of daytime physical activity (continuous; when dependent variable is daytime SBP or nocturnal SBP dipping) or morning physical activity (continuous; when dependent variable is morning SBP or

MBPS) in model 3.

Multilevel analyses used two days of data, whereas all other analyses used the two-day average. Missing values were replaced with series averages when the variables were continuous or with the proportion among all participants when the variables were dichotomous. We considered $p < 0.05$ as statistically significant. All statistical analyses were performed using R Version 4.1.1 [24] and the following packages: "mgcv" [25], generalized additive models; "lme4" [26] and "lmerTest" [27], multilevel linear models; "ggplot2" [28], preparing figures; and "tidyverse" [29], applicable for underlying data manipulations and analyses.

Results

Of the 1,076 participants, 508 (47.2%) were male, 216 (20.1%) were depressive, 479 (44.5%) used antihypertensives, and 15 (1.4%) used antidepressants. Compared with the non-depressive group, the depressive group had fewer male participants (421 [49.0%] vs. 87 [40.3%], $p = 0.022$), more smokers (38 [4.4%] vs. 17 [7.9%], $p = 0.039$), more antihypertensive users (367 [42.7%] vs. 112 [51.9%], $p = 0.015$), and more antidepressant users (8 [0.9%] vs. 7 [3.2%], $p = 0.010$) (**Table 1**). Indoor temperature and physical activity were not significantly different between the depressive and non-depressive groups (**Table 1**).

The median of the daytime indoor temperature was 16.46°C, and participants were divided into lower and higher temperature groups based on the median temperature (**Figure 1A, C**); coincidentally, the number of depressive and non-depressive subjects were distributed equally (108 depressive subjects and 430 non-depressive subjects) in both groups. Depressive individuals demonstrated higher SBP than non-depressive individuals during the daytime in the lower temperature group (**Figure 1B**), but not in the higher temperature group (**Figure 1D**).

The depressive group showed a steeper decline in daytime (**Figure 2A**) and morning SBP (**Figure 2B**) than the non-depressive group, which was associated with a higher indoor temperature in simple linear regression models. Significant interaction effects of the depressive status in the relationships were identified (**Figure 2**).

In the multilevel linear regression models, the daytime and morning indoor temperatures were significantly associated with daytime and morning SBP, respectively, in the depressive group (daytime SBP: β = −0.725, 95% CI = −1.161 to −0.289, p = 0.001; morning SBP: β = −0.602, 95% CI = −1.113 to −0.091, p = 0.021), but not in the non-depressive group (daytime SBP: β = −0.102, 95% CI = −0.314 to 0.110, p = 0.345; morning SBP: β = −0.153, 95% CI = −0.388 to 0.081, p = 0.199) (**Table 2**). Significant interaction effects of the depressive status were detected in relation to daytime SBP (β [Indoor temperature × depressive status] = −0.551, p = 0.023), although slightly not significant in relation to morning SBP (β [Indoor temperature × depressive status] = −0.474, p = 0.086) (**Table 2**). These relationships and interactions were independent of potential confounders, including age, gender, BMI, alcohol intake, smoking habit, medications, education history, household income, and physical activity. Similar associations were also found in the BP parameters reflecting diurnal variation in BP; negative relations between daytime indoor temperature and nocturnal BP dipping (depressive: β = −0.500, 95% CI = −0.775 to 0.224, $p < 0.001$; non-depressive: β = −0.128, 95% CI = −0.274 to 0.019, p = 0.087; interaction: β [Indoor temperature × depressive status] = −0.358, p = 0.030); between morning indoor temperature and pre-waking MBPS (depressive: β = −0.650, 95% CI = −1.135 to −0.165, p = 0.009; non-depressive: β = −0.218, 95% CI = −0.429 to −0.007, p = 0.043; interaction: β [Indoor temperature × depressive status] = −0.469, p = 0.062); and between morning indoor temperature and sleep-trough MBPS (depressive: β = −0.562, 95% CI = −1.056 to −0.068, p = 0.026; non-depressive: β = −0.353, 95% CI = −0.564 to −0.141, p = 0.001; interaction: β [Indoor temperature × depressive status] = −0.250, p = 0.320) were steeper in the depressive group than in the non-depressive group, although interactions were not statistically significant for MBPS (**Table 3**).

Similar to the results of the multilevel analyses, linear regression analyses using two-day averages also showed that the associations between BP parameters and indoor temperatures were stronger in the depressive group than in the non-depressive group, and significant interaction effects of the depressive status on the relationships were observed (**Table S1, Table S2**).

When using the outdoor temperature instead of indoor temperature, we failed to detect significant associations between the outdoor temperature and BP parameters in both the depressive and non-depressive groups (**Table S3, Table S4**).

Analyses using daytime DBP and PP yielded results similar to that for daytime SBP, but with smaller effects (depressive: [daytime DBP: β = −0.389, 95% CI = −0.645 to −0.134, p = 0.003; daytime PP: β = −0.313, 95% CI = −0.661 to 0.036, p = 0.078]; non-depressive: [daytime DBP: β = −0.045, 95% CI = −0.170 to 0.081, p = 0.485; daytime PP: β = −0.012, 95% CI = −0.158 to 0.134, p = 0.870]; **Table S5**).

Discussion

This study first revealed that the association between indoor temperature and BP parameters differed depending on the depressive status; i.e., the slopes of the associations between lower indoor temperature and higher BP parameters were steeper in the depressive group than in the non-depressive group. Interestingly, associations between temperature and BP parameters were generally observed, but some associations were insignificant in non-depressive group, which comprised the majority and was considered to be a more general population. These results suggest that certain populations, which can be distinguished by depressive symptoms, have higher temperature-sensitivity correlated with BP fluctuations.

By examining three factors—depressive symptoms, indoor temperature, and BP—simultaneously in a large population, we found that depressive symptoms and temperature cannot be assessed independently in relation to BP. This was the strongest finding of this study. Although many previous studies have reported the relationship between lower temperature and higher BP [8], the variability of the reported effect size may have been caused by differences in the prevalence of depressive symptoms. Additionally, a meta-analysis found that depression increases the incidence of hypertension [30], although other studies have reported inconsistent results [31,32]. This may be attributed to the different temperatures of the research environment. Therefore, in future BP research, depression and temperature should be examined as simultaneously occurring influences on BP. Moreover, it was essential to measure the indoor temperature accurately to achieve these results. To assess the thermal environment, outdoor temperature is relatively easy to obtain but is an inaccurate indicator of temperature exposure for subjects who spend most of their time indoors [33]. In fact, in our current analyses, the associations between outdoor temperature and BP parameters were not significant. The availability of accurate indoor temperature data in a large-scale population is a major strength of our study, because few large-scale studies have analyzed the association between indoor temperature and BP, as it requires a great deal of research effort and the cooperation of participants.

The stronger association between temperature and BP in the depressive group may be because some of the biological mechanisms underlying cold-induced BP elevation are likely to occur in depressive subjects. Cold exposure is associated with increased sympathetic nervous activity [34], and, consequently, peripheral vasoconstriction [35] or impaired endothelium-dependent vasodilation [36], which probably results in BP elevation [8,37]. Depressive subjects have impaired vasodilation, which is caused by endothelial dysfunction and a reduction in nitric oxide bioavailability [13,14]; accordingly, they may be predisposed to BP elevation. Moreover, individuals with higher depressive symptoms have greater sympathetic nervous reactivity to stress, including the cold pressor test [15] and mental stresses [16–18], it is possible that depressive subjects are more susceptible to BP changes due to ambient temperature. Furthermore, hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis, which is one of the most consistent biological findings in depression [38,39], may also mediate alterations in the relationship between temperature and BP in depressive subjects. A large-scale meta-analysis indicated that individuals with depression tend to have increased cortisol levels and adrenocorticotropic hormone levels [40], and an experimental study showed that administration of hydrocortisone (cortisol) significantly increased BP [41]. In a study on rats, chronic intermittent cold exposure sensitizes HPA axis response to acute stress by enhancing noradrenergic function in the paraventricular nucleus [42]. Additionally, we examined DBP and PP as well as SBP and found that SBP was most strongly associated with indoor temperature in individuals with depression; however similar associations were observed for both DBP and PP. This indicates that since PP alone could not explain this phenomenon, multiple factors may be responsible for the current results. Further detailed experimental studies are warranted to determine the biological mechanisms underlying the current results.

Our results suggest that for cold-related cardiovascular events, depressive symptoms may help identify a high-risk population. The World Health Organization Housing and health guidelines recommends keeping the indoor temperature at least 18°C to protect residents from the harmful effects of cold [43]; however, many houses do not meet this criterion [44]. A previous study reported that age and female gender are interacting factors in the association between indoor temperature and morning SBP, and older adults and women appear to be more vulnerable to cold-induced BP elevation [45]. The current study showed that depression was an independent factor affecting the relationships between indoor temperature and BP, even after adjusted for age and gender. Depressive symptoms may be associated more with the vulnerability of cold-induced BP elevation than with known risk factors because to our knowledge, there was no known population in which the association between temperature and BP almost disappeared, as in the non-depressive subjects; therefore, to efficiently reduce cold-induced BP elevation and further consequent cold-related cardiovascular events, it may be effective to encourage depressive populations preferentially to live in a warmer housing environment.

In addition to mean BP (daytime and morning SBP), diurnal variation in BP (nocturnal SBP dipping and MBPS) also tended to be greater in the depressive group than in the non-depressive group. This is probably because during the night-time, subjects are in bed and less affected by the indoor temperature, but during the daytime they are directly exposed to the cold from indoor temperature, and therefore, subjects with depression, who have higher temperature-sensitivity of BP, will have larger diurnal variation in BP. Nocturnal SBP dipping and MBPS are parameters that are positively correlated [46], but they are inversely associated with cardiovascular outcomes; increased MBPS are associated with cardiovascular risks corresponding to more cardiovascular events in the morning [47,48], whereas the lower nocturnal BP dipping (so-called non-dipper pattern) is another well-known cardiovascular risk factor [49,50]. Our results suggest that ABPM in depressive subjects in a cold environment overestimates nocturnal BP dipping; therefore, we should pay attention to classifying and interpreting dipping patterns.

This study has some limitations. First, owing to its cross-sectional design, we could not confirm the causal relationship. Second, we only evaluated older adults from Japan and the participants were not randomly sampled, thereby limiting the generalizability of our findings to other cultural and age groups. However, the proportion of participants using antihypertensive medications (479/1076 [44.5%]) and with BMI ≥ 25 (274/1076 [25.5%]) in the current study were similar to those of older adults (age ≥ 60) in the 2010 National Health and Nutrition Survey of Japan (antihypertensives: 1035/2375 [43.6%]; BMI ≥ 25: 803/2880 [27.9%]) [51]. Third, we conducted all ABPMs during the cold season, so we cannot draw conclusions about other seasons or temperature environments. Fourth, because we did not assess the onset of depressive symptoms, we cannot determine whether depression in our subjects was chronic or transient and if either or both were associated with the results. Fifth, our study participants were assessed using the GDS-15 score rather than by a certified psychiatrist for their depressive symptoms, so the current results may not be applicable to patients with actual depressive symptoms, including major depressive disorder. Finally, we did not assess vasocontraction, vasodilation, autonomic nervous systems, HPA axis, or other neuroendocrinological regulation functions; hence, we cannot explain the influence of these mechanisms.

In conclusion, our results indicate that the relationships between indoor temperature and BP are different depending on the presence or absence of depressive symptoms, i.e., compared with non-depressive subjects, depressive subjects are significantly more likely to have stronger associations between lower indoor temperature and higher BP parameters, which may explain why patients with depression are at a high risk for cardiovascular diseases. Additionally, evaluating depressive symptoms may allow for efficient screening of individuals at high risk for cold-induced BP elevation and consequent cardiovascular events. Further longitudinal and experimental research is needed to clarify the causality and mechanisms behind them, and depression and temperature should be considered simultaneously in future BP research.

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Figure Legends

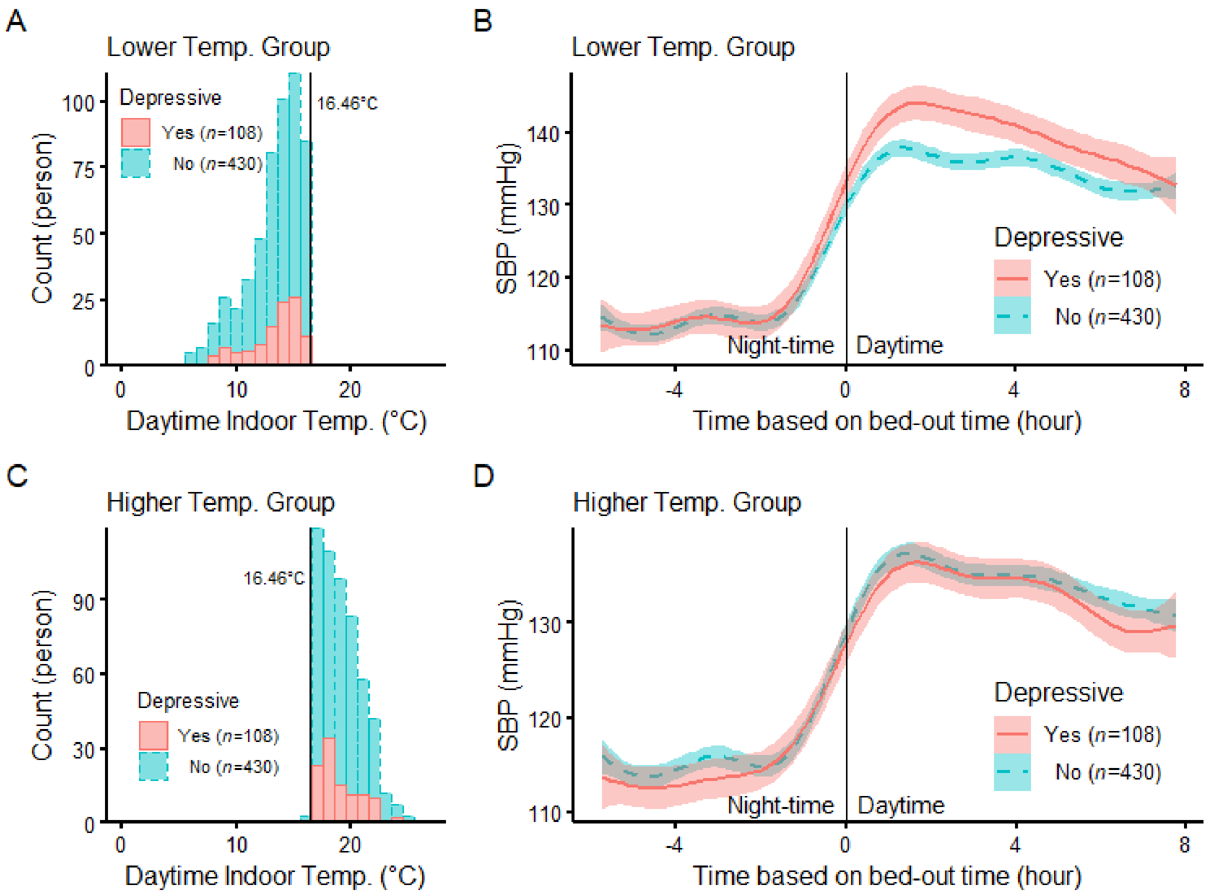

Figure 1. Participants were divided into lower (**A, B**) and higher (**C, D**) temperature groups based on the median of daytime indoor temperature (16.46°C). **A, C:** Histograms of daytime indoor temperature in each group. **B, D:** Temporal trends of systolic blood pressure (SBP) around bed-out time were drawn with a 95% confidence interval using general additive models. SBP tended to be low at night-time and high during daytime. Depressive subjects demonstrated relatively higher SBP during daytime in the lower temperature group (**B**), but not in the higher temperature group (**D**).

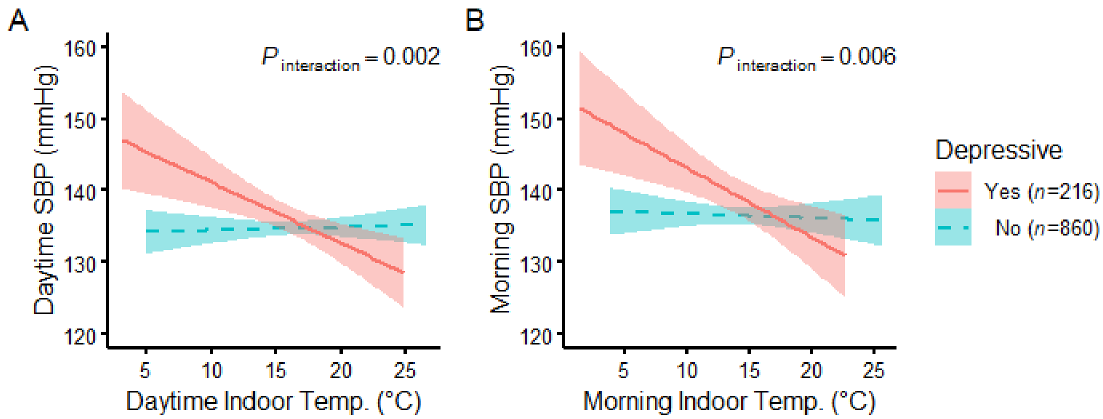

Figure 2. Relationships between the two-day average of indoor temperature and mean blood pressure (BP) were plotted by depressive status. Regression lines with 95% confidence intervals were drawn using linear models. *P* for interaction were calculated using linear models with an interaction term. Interactions between indoor temperature and depressive symptoms in relation to daytime systolic BP (SBP) (**A**) and morning SBP (**B**) were significant.

Table 1. Basic Characteristics of the Study Participants

	Depressive (GDS ≥ 5) *n* = 216	Non-depressive (GDS < 5) *n* = 860	p^*
Age, mean (SD)	72.5 (7.6)	71.7 (7.0)	0.175
Gender, male, *n* (%)	87 (40.3)	421 (49.0)	0.022
BMI ≥ 25 [kg/m^2], *n* (%)	55 (25.5)	219 (25.5)	0.999
Current Smoker, *n* (%)	17 (7.9)	38 (4.4)	0.039
Ethanol Intake ≥ 30 [g/day], *n* (%)	27 (12.5)	128 (14.9)	0.372
Higher Education History, *n* (%)	47 (21.8)	240 (27.9)	0.068
Higher Household Income, *n* (%)	73 (37.2)	362 (45.2)	0.043
Antihypertensive Medication, *n* (%)	112 (51.9)	367 (42.7)	0.015
Antidepressants Medication, *n* (%)	7 (3.2)	8 (0.9)	0.010
Indoor Temperature			
Daytime [°C], mean (SD)	16.03 (3.73)	16.20 (3.65)	0.553
Night-time [°C], mean (SD)	12.69 (4.23)	12.17 (4.27)	0.106
Morning [°C], mean (SD)	14.00 (4.13)	14.32 (4.04)	0.307
Physical Activity			
Daytime [counts/min], mean (SD)	221.6 (105.2)	221.1 (95.7)	0.954
Night-time [counts/min], mean (SD)	28.7 (53.4)	30.9 (115.6)	0.681
Morning [counts/min], mean (SD)	262.7 (152.7)	249.7 (141.9)	0.255
ABPM Parameter			
Daytime SBP [mmHg], mean (SD)	136.0 (14.3)	134.7 (13.9)	0.223
Night-time SBP [mmHg], mean (SD)	115.0 (15.7)	115.8 (16.1)	0.517
Morning SBP [mmHg], mean (SD)	139.3 (18.6)	136.5 (17.7)	0.046
Daytime DBP [mmHg], mean (SD)	79.7 (8.3)	79.5 (7.6)	0.648
Night-time DBP [mmHg], mean (SD)	66.2 (8.4)	67.0 (8.4)	0.190
Daytime PP [mmHg], mean (SD)	56.2 (9.8)	55.2 (10.0)	0.177
Night-time PP [mmHg], mean (SD)	48.9 (10.5)	48.8 (10.8)	0.936
Nocturnal Dipping [%], mean (SD)	15.2 (9.3)	13.9 (8.8)	0.068
Prewaking MBPS [mmHg], mean (SD)	21.7 (16.5)	18.6 (14.4)	0.012
Sleep-trough MBPS [mmHg], mean (SD)	38.6 (17.3)	33.7 (14.5)	<0.001

* *p* values were calculated using Welch's *t*-test (for continuous variables) or Chi-squared test (for dichotomous variables).

GDS, Geriatric Depression Scale; SD, standard deviation; BMI, body mass index; ABPM, ambulatory blood pressure monitoring; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MBPS, morning blood pressure surge

Table 2. Multilevel Linear Regression Analysis of the Association between Indoor Temperature and Mean SBP by Depressive Status

	Depressive (GDS ≥ 5)		Non-depressive (GDS < 5)		
	β (95% CI)	p	β (95% CI)	p	$p_{interaction}$
Daytime SBP (mmHg) ~ Daytime Indoor Temperature (°C)					
- Crude model	−0.804 (−1.239 to −0.368)	<0.001	−0.173 (−0.391 to 0.045)	0.120	0.014
- Adjusted model 1*	−0.851 (−1.282 to −0.420)	<0.001	−0.155 (−0.368 to 0.058)	0.154	0.011
- Adjusted model 2†	−0.819 (−1.252 to −0.386)	<0.001	−0.151 (−0.364 to 0.063)	0.166	0.013
- Adjusted model 3‡	−0.725 (−1.161 to −0.289)	0.001	−0.102 (−0.314 to 0.110)	0.345	0.023
Morning SBP (mmHg) ~ Morning Indoor Temperature (°C)					
- Crude model	−0.712 (−1.231 to −0.192)	0.007	−0.220 (−0.461 to 0.021)	0.073	0.099
- Adjusted model 1*	−0.728 (−1.240 to −0.215)	0.006	−0.180 (−0.415 to 0.056)	0.135	0.077
- Adjusted model 2†	−0.709 (−1.224 to −0.194)	0.007	−0.176 (−0.411 to 0.060)	0.144	0.072
- Adjusted model 3‡	−0.602 (−1.113 to −0.091)	0.021	−0.153 (−0.388 to 0.081)	0.199	0.086

* Model 1: adjusted for age, gender, and BMI.

† Model 2: adjusted for current smoker, ethanol intake, antidepressant use, antihypertensive use, educational status, and household income, in addition to model 1.

‡ Model 3: adjusted for daytime (for daytime SBP) or morning (for morning SBP) physical activity, in addition to model 2.

GDS, geriatric depression scale; β, regression coefficient; CI, confidence interval; SBP, systolic blood pressure; BMI, body mass index

Table 3. Multilevel Linear Regression Analysis of the Association between Indoor Temperature and Diurnal Variation in SBP by Depressive Status

	Depressive (GDS ≥ 5)		Non-depressive (GDS < 5)		
	β (95% CI)	*p*	*β* (95% CI)	*p*	$p_{interaction}$
Nocturnal SBP Dipping (%) ~ Daytime Indoor Temperature (°C)					
- Crude model	−0.568 (−0.858 to −0.279)	<0.001	−0.161 (−0.312 to −0.011)	0.036	0.019
- Adjusted model 1*	−0.566 (−0.850 to −0.282)	<0.001	−0.155 (−0.302 to −0.008)	0.039	0.015
- Adjusted model 2†	−0.566 (−0.862 to −0.271)	<0.001	−0.155 (−0.302 to −0.009)	0.038	0.014
- Adjusted model 3‡	−0.500 (−0.775 to −0.224)	<0.001	−0.128 (−0.274 to 0.019)	0.087	0.030
Prewaking MBPS (mmHg) ~ Morning Indoor Temperature (°C)					
- Crude model	−0.744 (−1.238 to −0.250)	0.003	−0.252 (−0.466 to −0.038)	0.021	0.055
- Adjusted model 1*	−0.747 (−1.234 to −0.259)	0.003	−0.248 (−0.461 to −0.035)	0.023	0.058
- Adjusted model 2†	−0.762 (−1.250 to −0.275)	0.002	−0.242 (−0.455 to −0.029)	0.026	0.044
- Adjusted model 3‡	−0.650 (−1.135 to −0.165)	0.009	−0.218 (−0.429 to −0.007)	0.043	0.062
Sleep-trough MBPS (mmHg) ~ Morning Indoor Temperature (°C)					
- Crude model	−0.671 (−1.174 to −0.167)	0.009	−0.412 (−0.628 to −0.195)	<0.001	0.305
- Adjusted model 1*	−0.634 (−1.136 to −0.132)	0.013	−0.381 (−0.594 to −0.168)	<0.001	0.333
- Adjusted model 2†	−0.683 (−1.187 to −0.180)	0.008	−0.373 (−0.586 to −0.160)	<0.001	0.256
- Adjusted model 3‡	−0.562 (−1.056 to −0.068)	0.026	−0.353 (−0.564 to −0.141)	0.001	0.320

* Model 1: adjusted for age, gender, and BMI.

† Model 2: adjusted for current smoker, ethanol intake, antidepressant use, antihypertensive use, educational status, and household income, in addition to model 1.

‡ Model 3: adjusted for daytime (for nocturnal SBP dipping) or morning (for MBPS) physical activity, in addition to model 2.

GDS, geriatric depression scale; β, regression coefficient; CI, confidence interval; SBP, systolic blood pressure; MBPS, morning blood pressure surge; BMI, body mass index

List of Supplemental Digital Content

DepTempBP_Supplement.docx

SUPPLEMENTAL MATERIAL

Influence of Depression on the Association between Colder Indoor Temperature and Higher Blood Pressure

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Table S3. Multilevel Linear Regression Analysis of the Association between the Outdoor Temperature and Mean SBP by Depressive Status

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Table S1. Association between the Two-day Average of Indoor Temperature and the Two-day Average of Mean SBP by Depressive Status

	Depressive (GDS ≥ 5, n = 216)		Non-depressive (GDS < 5, n = 860)		
	β (95% CI)	p	β (95% CI)	p	$p_{interaction}$
Daytime SBP (mmHg) ~ Daytime Indoor Temperature (°C)					
- Crude model	−0.852 (−1.355 to −0.349)	<0.001	0.045 (−0.211 to 0.300)	0.731	0.002
- Adjusted model 1*	−0.895 (−1.401 to −0.389)	<0.001	0.050 (−0.199 to 0.300)	0.692	0.002
- Adjusted model 2†	−0.860 (−1.378 to −0.342)	0.001	0.057 (−0.194 to 0.307)	0.656	0.002
- Adjusted model 3‡	−0.772 (−1.299 to −0.245)	0.004	0.079 (−0.170 to 0.328)	0.533	0.004
Morning SBP (mmHg) ~ Morning Indoor Temperature (°C)					
- Crude model	−0.963 (−1.557 to −0.368)	0.002	−0.058 (−0.351 to 0.236)	0.701	0.006
- Adjusted model 1*	−0.981 (−1.569 to −0.394)	0.001	−0.024 (−0.309 to 0.261)	0.870	0.005
- Adjusted model 2†	−0.963 (−1.563 to −0.363)	0.002	−0.021 (−0.308 to 0.265)	0.883	0.005
- Adjusted model 3‡	−0.899 (−1.498 to −0.299)	0.003	−0.000 (−0.285 to 0.285)	1.000	0.006

* Model 1: adjusted for age, gender, and BMI.

† Model 2: adjusted for current smoker, ethanol intake, antidepressant use, antihypertensive use, educational status, and household income, in addition to model 1.

‡ Model 3: adjusted for daytime (for daytime SBP) or morning (for morning SBP) physical activity, in addition to model 2.

GDS, geriatric depression scale; β, regression coefficient; CI, confidence interval; SBP, systolic blood pressure; BMI, body mass index

Table S2. Association between the Two-day Average of Indoor Temperature and the Two-day Average of Diurnal Variation in SBP by Depressive Status

	Depressive (GDS ≥ 5, *n* = 216)		Non-depressive (GDS < 5, *n* = 860)		
	β (95% CI)	*p*	*β* (95% CI)	*p*	$p_{interaction}$
Nocturnal SBP Dipping (%) ~ Daytime Indoor Temperature (°C)					
- Crude model	−0.661 (−0.985 to −0.336)	<0.001	−0.114 (−0.275 to 0.047)	0.164	0.003
- Adjusted model 1*	−0.650 (−0.971 to −0.330)	<0.001	−0.112 (−0.271 to 0.046)	0.166	0.002
- Adjusted model 2†	−0.666 (−0.993 to −0.340)	<0.001	−0.111 (−0.270 to 0.048)	0.171	0.001
- Adjusted model 3‡	−0.544 (−0.867 to −0.221)	0.001	−0.090 (−0.246 to 0.067)	0.261	0.004
Prewaking MBPS (mmHg) ~ Morning Indoor Temperature (°C)					
- Crude model	−0.893 (−1.419 to −0.367)	<0.001	−0.211 (−0.449 to 0.028)	0.084	0.013
- Adjusted model 1*	−0.897 (−1.421 to −0.373)	<0.001	−0.203 (−0.441 to 0.035)	0.094	0.014
- Adjusted model 2†	−0.938 (−1.470 to −0.407)	<0.001	−0.203 (−0.442 to 0.036)	0.096	0.009
- Adjusted model 3‡	−0.882 (−1.413 to −0.351)	0.001	−0.177 (−0.414 to 0.059)	0.142	0.011
Sleep-trough MBPS (mmHg) ~ Morning Indoor Temperature (°C)					
- Crude model	−0.842 (−1.396 to −0.289)	0.003	−0.318 (−0.557 to −0.079)	0.009	0.060
- Adjusted model 1*	−0.806 (−1.362 to −0.250)	0.005	−0.289 (−0.526 to −0.052)	0.017	0.073
- Adjusted model 2†	−0.878 (−1.444 to −0.312)	0.003	−0.289 (−0.527 to −0.052)	0.017	0.049
- Adjusted model 3‡	−0.779 (−1.336 to −0.222)	0.006	−0.268 (−0.505 to −0.032)	0.026	0.060

* Model 1: adjusted for age, gender, and BMI.

† Model 2: adjusted for current smoker, ethanol intake, antidepressant use, antihypertensive use, educational status, and household income, in addition to model 1.

‡ Model 3: adjusted for daytime (for nocturnal SBP dipping) or morning (for MBPS) physical activity, in addition to model 2.

GDS, geriatric depression scale; β, regression coefficient; CI, confidence interval; SBP, systolic blood pressure; MBPS, morning blood pressure surge; BMI, body mass index

Table S3. Multilevel Linear Regression Analysis of the Association between the Outdoor Temperature and Mean SBP by Depressive Status

	Depressive (GDS ≥ 5)		Non-depressive (GDS < 5)		
	β (95% CI)	*p*	*β* (95% CI)	*p*	$p_{interaction}$
Daytime SBP (mmHg) ~ Daytime Outdoor Temperature (°C)					
- Crude model	−0.211 (−0.533 to 0.112)	0.200	0.011 (−0.143 to 0.166)	0.886	0.240
- Adjusted model 1*	−0.208 (−0.529 to 0.112)	0.202	0.008 (−0.145 to 0.161)	0.916	0.249
- Adjusted model 2†	−0.190 (−0.514 to 0.133)	0.248	0.013 (−0.140 to 0.167)	0.865	0.283
- Adjusted model 3‡	−0.198 (−0.517 to 0.121)	0.222	0.024 (−0.128 to 0.176)	0.754	0.221
Morning SBP (mmHg) ~ Morning Outdoor Temperature (°C)					
- Crude model	−0.252 (−0.688 to 0.184)	0.256	0.074 (−0.130 to 0.278)	0.475	0.212
- Adjusted model 1*	−0.249 (−0.676 to 0.177)	0.251	0.069 (−0.132 to 0.270)	0.499	0.177
- Adjusted model 2†	−0.217 (−0.651 to 0.217)	0.323	0.081 (−0.120 to 0.282)	0.429	0.190
- Adjusted model 3‡	−0.170 (−0.598 to 0.258)	0.433	0.098 (−0.102 to 0.297)	0.338	0.174

* Model 1: adjusted for age, gender, and BMI.

† Model 2: adjusted for current smoker, ethanol intake, antidepressant use, antihypertensive use, educational status, and household income, in addition to model 1.

‡ Model 3: adjusted for daytime (for daytime SBP) or morning (for morning SBP) physical activity, in addition to model 2.

GDS, geriatric depression scale; β, regression coefficient; CI, confidence interval; SBP, systolic blood pressure; BMI, body mass index

Table S4. Multilevel Linear Regression Analysis of the Association between the Outdoor Temperature and Diurnal Variation in SBP by Depressive Status

	Depressive (GDS ≥ 5)		Non-depressive (GDS < 5)		
	β (95% CI)	*p*	*β* (95% CI)	*p*	$p_{interaction}$
Nocturnal SBP Dipping (%) ~ Daytime Outdoor Temperature (°C)					
- Crude model	−0.086 (−0.324 to 0.152)	0.474	−0.054 (−0.162 to 0.054)	0.327	0.882
- Adjusted model 1*	−0.096 (−0.333 to 0.141)	0.425	−0.047 (−0.155 to 0.060)	0.389	0.785
- Adjusted model 2†	−0.124 (−0.359 to 0.111)	0.297	−0.051 (−0.159 to 0.057)	0.354	0.666
- Adjusted model 3‡	−0.146 (−0.375 to 0.083)	0.209	−0.047 (−0.154 to 0.059)	0.380	0.563
Prewaking MBPS (mmHg) ~ Morning Outdoor Temperature (°C)					
- Crude model	−0.298 (−0.687 to 0.092)	0.134	−0.130 (−0.323 to 0.063)	0.186	0.516
- Adjusted model 1*	−0.251 (−0.675 to 0.174)	0.243	−0.117 (−0.309 to 0.074)	0.230	0.459
- Adjusted model 2†	−0.241 (−0.677 to 0.195)	0.273	−0.123 (−0.316 to 0.069)	0.209	0.418
- Adjusted model 3‡	−0.196 (−0.632 to 0.241)	0.375	−0.103 (−0.292 to 0.085)	0.283	0.395
Sleep-trough MBPS (mmHg) ~ Morning Outdoor Temperature (°C)					
- Crude model	−0.415 (−0.860 to 0.031)	0.068	−0.077 (−0.268 to 0.115)	0.432	0.118
- Adjusted model 1*	−0.425 (−0.864 to 0.014)	0.058	−0.056 (−0.246 to 0.133)	0.558	0.082
- Adjusted model 2†	−0.394 (−0.843 to 0.055)	0.085	−0.061 (−0.251 to 0.129)	0.530	0.082
- Adjusted model 3‡	−0.359 (−0.801 to 0.082)	0.110	−0.044 (−0.231 to 0.144)	0.645	0.072

* Model 1: adjusted for age, gender, and BMI.

† Model 2: adjusted for current smoker, ethanol intake, antidepressant use, antihypertensive use, educational status, and household income, in addition to model 1.

‡ Model 3: adjusted for daytime (for nocturnal SBP dipping) or morning (for MBPS) physical activity, in addition to model 2.

GDS, geriatric depression scale; β, regression coefficient; CI, confidence interval; SBP, systolic blood pressure; MBPS, morning blood pressure surge; BMI, body mass index

Table S5. Multilevel Linear Regression Analysis of the Association between the Indoor Temperature and Mean DBP and PP by Depressive Status

	Depressive (GDS ≥ 5)		Non-depressive (GDS < 5)		
	β (95% CI)	*p*	*β* (95% CI)	*p*	$p_{interaction}$
Daytime DBP (mmHg) ~ Daytime Indoor Temperature (°C)					
- Crude model	−0.369 (−0.628 to −0.109)	0.006	−0.058 (−0.185 to 0.069)	0.369	0.035
- Adjusted model 1*	−0.447 (−0.700 to −0.194)	<0.001	−0.073 (−0.200 to 0.053)	0.255	0.023
- Adjusted model 2†	−0.435 (−0.688 to −0.181)	<0.001	−0.073 (−0.199 to 0.054)	0.259	0.022
- Adjusted model 3‡	−0.389 (−0.645 to −0.134)	0.003	−0.045 (−0.170 to 0.081)	0.485	0.041
Daytime PP (mmHg) ~ Daytime Indoor Temperature (°C)					
- Crude model	−0.437 (−0.780 to −0.095)	0.013	−0.074 (−0.229 to 0.081)	0.350	0.067
- Adjusted model 1*	−0.396 (−0.732 to −0.059)	0.022	−0.036 (−0.184 to 0.112)	0.632	0.062
- Adjusted model 2†	−0.428 (−0.704 to −0.153)	0.002	−0.031 (−0.179 to 0.116)	0.676	0.075
- Adjusted model 3‡	−0.313 (−0.661 to 0.036)	0.078	−0.012 (−0.158 to 0.134)	0.870	0.094

* Model 1: adjusted for age, gender, and BMI.

† Model 2: adjusted for current smoker, ethanol intake, antidepressant use, antihypertensive use, educational status, and household income, in addition to model 1.

‡ Model 3: adjusted for daytime physical activity, in addition to model 2.

GDS, geriatric depression scale; β, regression coefficient; CI, confidence interval; DBP, diastolic blood pressure; PP, pulse pressure; MBPS, morning blood pressure surge; BMI, body mass index