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Ambient relative humidity-dependent obstructive sleep apnea severity in cold season: A case-control study

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Abbreviations: AASM, American Academy of Sleep Medicine; ANOVA, analysis of variance; AHI, apnea-hypopnea index; BMI, body-mass index; CWB, Central Weather Bureau; CPAP, continuous positive airway pressure; dfs, degrees of freedom; EPA, Environmental Protection Administration; IQR, interquartile range; IDW, inverse distance weighting; NO_2, nitrogen dioxide; OSA, Obstructive sleep apnea; OR, odds ratio; ODI, oxygen desaturation index; O_3, ozone; PM_{10}, particulate matter of <10 μm in aerodynamic diameter; $PM_{2.5}$, particulate matter of <2.5 μm in aerodynamic diameter; PSG, polysomnography; RBF, radial basis function; REM, rapid eye moment; RH, relative humidity; TST, total sleep time; TRPV1, transient receptor potential vanilloid type 1.

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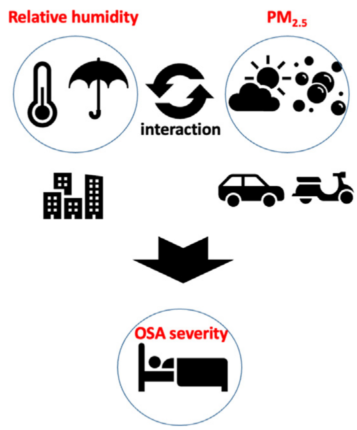
HIGHLIGHTS

- Associations of environmental factors with OSA severity were examined.
- Ambient RH-dependent AHI was observed in OSA patients.
- Decreased levels of $PM_{2.5}$ and RH were associated with lower AHI values in OSA patients.
- Patients staying in low-level $PM_{2.5}$ and RH outdoor environments may reverse OSA severity.
- Exposure of extreme weather could increase the risk of OSA severity.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: The objective of this study was to examine associations of daily averages and daily variations in ambient relative humidity (RH), temperature, and $PM_{2.5}$ on the obstructive sleep apnea (OSA) severity.
Methods: A case-control study was conducted to retrospectively recruit 8628 subjects in a sleep center between January 2015 and December 2021, including 1307 control (apnea-hypopnea index (AHI) < 5 events/h), 3661 mild-to-moderate OSA (AHI of 5–30 events/h), and 3597 severe OSA subjects (AHI > 30 events/h). A logistic regression was used to examine the odds ratio (OR) of outcome variables (daily mean or difference in RH, temperature, and $PM_{2.5}$ for 1, 7, and 30 days) with OSA severity (by the groups). Two-factor logistic regression models were conducted to examine the OR of RH with the daily mean or difference in temperature or $PM_{2.5}$ with OSA severity. An exposure-response relationship analysis was conducted to examine the outcome variables with OSA severity in all, cold and warm seasons.
Results: We observed associations of mean $PM_{2.5}$ and RH with respective increases of 0.04–0.08 and 0.01–0.03 events/h for the AHI in OSA patients. An increase in the daily difference of 1 % RH increased the AHI by 0.02–0.03 events/h in OSA patients. A daily $PM_{2.5}$ decrease of 1 μg/m^3 reduced the AHI by 0.03 events/h, whereas a daily decrease in the RH of 1 % reduced the AHI by 0.03–0.04 events/h. The two-factor model confirmed the most robust associations of ambient RH with AHI in OSA patients. The exposure-response relationship in temperature and RH showed obviously seasonal patterns with OSA severity.
Conclusion: Short-term ambient variations in RH and $PM_{2.5}$ were associated with changes in the AHI in OSA patients, especially RH in cold season. Reducing exposure to high ambient RH and $PM_{2.5}$ levels may have protective effects on the AHI in OSA patients.

1. Introduction

Environmental factors have been documented to be potential risks of lung function decline (Tasmin et al., 2022) and increasing respiratory morbidity and mortality (Gerardi and Kellerman, 2014). Obstructive sleep apnea (OSA) is recognized as a seasonal disease, which often occurs in winter due to seasonal changes (Cassol et al., 2012). Also, continuous positive airway pressure (CPAP) adherence in OSA patients is associated with seasonal changes (Fujino et al., 2021). Our previous work further showed that outdoor relative humidity (RH) and temperature were associated with changes in the apnea-hypopnea index (AHI) in positional OSA patients (Liu et al., 2022). The epidemiological evidence points to meteorological factors as possible risk factors for regulating OSA severity.

Air pollution, another important environmental factor, has been linked to OSA (Tung et al., 2021). A study of 4312 subjects showed significant AHI and oxygen desaturation index (ODI) responses to 1-year mean particulate matter of <2.5 μm in aerodynamic diameter ($PM_{2.5}$) and ozone (O_3) in spring and winter (Shen et al., 2018). OSA patients with a low arousal threshold were more susceptible to long-term nitrogen dioxide (NO_2) due to a reduced sleep efficiency (Qiu et al., 2022). Another study further showed that short- and long-term exposures to NO_2 were associated with increases in the AHI and ODI in OSA patients with an AHI of <15 events/h through mediating the rapid eye moment (REM) sleep stage (He et al., 2022). The results implied that air pollution is another environmental factor associated with OSA severity.

A systemic review reported that air pollution is associated with OSA; however, how the duration of air pollution exposure in OSA patients varies across different seasons, temperatures, RH levels, and countries remains unclear (Clark et al., 2020). Furthermore, a study in 500 patients with OSA observed that the REM-related AHI was positively correlated with the RH (Yıldız Gülhan et al., 2020). Those authors also indicated that exposure to particulate matter of <10 μm in aerodynamic diameter (PM_{10}) increased the risk of OSA during winter. The effects of seasonal variations in environmental factors on environmental-associated OSA led to the hypothesis that meteorology-air pollution interactions affect the severity of OSA in a seasonal fashion. However, the effects of daily variations in environmental factors such as RH, temperature, and air pollution on OSA severity remain unclear. The objective of this study was to examine associations of the daily average of and variations in ambient RH, temperature, and $PM_{2.5}$ levels on the OSA severity.

2. Materials and methods

2.1. Ethical considerations

This study was carried out in accordance with a protocol approved by the Taipei Medical University-Joint Institution Review Board (Taipei, Taiwan) (TMU-JIRB no. N201910048).

2.2. Study population

A case-control study was conducted in a sleep center of a hospital (New Taipei City, Taiwan) from January 2015 to December 2021. The inclusion criteria consisted of subjects 20–80 years old who had completed 1-night polysomnography (PSG). Subjects currently using CPAP, who had undergone uvulopalatopharyngoplasty, a tonsillectomy, or adenoidectomy, were pregnant, had a fever, regularly consumed alcohol, or had pulmonary disease with oxygen therapy, kidney disease on hemodialysis, or an unstable disease were excluded from this study. Data of age, gender, the body-mass index (BMI, kg/m^2), neck circumference (cm), and waist circumference (cm) were collected.

2.3. Sleep parameters

One-night sleep parameters were recorded using a digital PSG system (Embla N7000, Medcare, Reykjavik, Iceland) followed by an analysis with Somnologica (Medcare) and a reevaluation by a sleep technician according to American Academy of Sleep Medicine (AASM) criteria (Ruehland et al., 2009). The definition of hypopnea was nasal airflow decreasing 30 % ~ 89 % for at least 10 s with arousal or at least 3 % oxygen desaturation. The definition of apnea was oral airflow reduced by >90 % for at least 10 s with or without arousal or desaturation. The AHI was the number of hypopneas plus apnea events divided by the total sleep time (TST; events/h). AHI of <5 events/h was defined as the control group. AHI of 5–30 events/h was defined as the mild-to-moderate OSA group, whereas AHI of >30 events/h was defined as the severe OSA group.

2.4. Ambient RH, temperature, and $PM_{2.5}$

Meteorological and $PM_{2.5}$ data from 2015 to 2021 were collected and analyzed. The daily-scale RH and temperature meteorological data were collected from stations of the Central Weather Bureau (CWB) in Taiwan. Hourly-scale $PM_{2.5}$ pollutant concentration data were collected from stations of the Environmental Protection Administration (EPA) in Taiwan. Hourly-scale $PM_{2.5}$ data underwent preliminary data rearrangement and data cleaning, and the hourly $PM_{2.5}$ concentration was converted into average data on a daily scale. Then, through the radial basis function (RBF) interpolation method, the temperature and humidity data of the CWB and $PM_{2.5}$ data of the EPA were spatially estimated according to coordinate points of each case. Finally, the RH, temperature, and $PM_{2.5}$ concentration of each case were respectively estimated to derive daily average values and daily differences in different time periods.

2.4.1. RBF spatial interpolation

The RBF method was used to spatially estimate meteorological and $PM_{2.5}$ data of each case location, which is one of the advanced methods used for spatial interpolation of multidimensional data, and compared to inverse distance weighting (IDW), the RBF creates smoother and less oscillatory interpolations (Kamińska and Grzywna, 2014). The RBF has been used for many applications in computer graphics, such as surface reconstruction (Cohen-Or et al., 2015), animation blending (Anjyo et al., 2014), and face simulation (Wan et al., 2011). The RBF is an advanced method in approximation theory for constructing accurate interpolations of unstructured data in high-dimensional spaces. It is also a meshless method, where data points do not need to lie on a structured grid, nor do they need to form a grid.

The RBF uses a kernel function, and each kernel function point generates a concentric surface with central symmetry and high inner and low outer values. Each surface is multiplied by weights and superimposed to meet values of all function points. The equations are expressed as:

$$f(x) = \Sigma_{i=1}^{n} w_i \Phi(\|x - x_i\|) \text{ and} \tag{1}$$

$$f(x_i) = f_i, \text{ for } 1 \le i \le n. \tag{2}$$

In these equations, $f(x)$ is the data point value, n is the number of data, w_i is the weight, Φ is the kernel function, x are expected location points to be estimated, and x_i are location points of data. The kernel function only depends on the distance between x, and the superposition of each kernel function is equal to the value of all function points, which is written as the following formula in matrix notation:

$$\begin{bmatrix} \Phi_{1,1} & \cdots & \Phi_{1,n} \\ \vdots & \ddots & \vdots \\ \Phi_{n,1} & \cdots & \Phi_{n,n} \end{bmatrix} \begin{bmatrix} w_1 \\ \vdots \\ w_n \end{bmatrix} = \begin{bmatrix} f_1 \\ \vdots \\ f_n \end{bmatrix}. \tag{3}$$

The weights of the functions ($w_1 \ldots w_n$) and the interpolation equation are obtained by the matrix equation system. The RBF has many kinds of kernel functions that can be used. Common kernel functions are Gaussian, multiquadrics, linear, cubic, thinplate, etc. The formula of each kernel function is as follows:

$$\Phi_{\text{Gaussian}} = \exp\left(-r^2/\left(2\sigma^2\right)\right); \tag{4}$$

$$\Phi_{\text{Multiquadrics}} = \sqrt{1 + \frac{r^2}{\sigma^2}}; \tag{5}$$

$$\Phi_{\text{Linear}} = r; \tag{6}$$

$$\Phi_{\text{Cubic}} = r^3; \text{ and} \tag{7}$$

$$\Phi_{\text{Thinplate}} = r^2 \ \ln(r+1). \tag{8}$$

In these equations, r is the distance between x. In this study, we tried different kernel functions, and finally used the linear function to achieve the best spatial estimation effect in the study area.

2.4.2. Calculation of average and difference values of RH, temperature, and $PM_{2.5}$ in each time period

Traditionally, when investigating the relationship between variables, we usually use the raw data of the variables, or calculate the average value to represent the value over a period of time. However, due to different influence mechanisms, raw data or average values may not be enough to understand the correlation, so some variable feature calculations need to be done.

As a common and basic variable feature extraction method, we compare with each other by calculating the "difference value" and "mean value" of each ambient variable, in order to investigate the effect of exposure to the target of the "change" of ambient variables during a period of time. "Mean value" could analyze the overall values, and "difference value" could analyze the magnitude of the change between different periods.

Average and difference values of RH, temperature, and $PM_{2.5}$ were calculated for different time periods. The time periods were 1, 7, and 30 days. The average value from *t-1* day (*t* is the time period: 1, 7, or 30 days) before the case to the day of the case was calculated for each case. For example, the 7-day time period average value was calculated from 6 days before the case to the day of the case. The formula is expressed as:

$$\bar{x} = \frac{\sum_{i=(1-t)}^{0} x_i}{t}; \tag{9}$$

where, $\bar{x}$ is the average value of the time period, x_i is the environmental factor (RH, temperature, or $PM_{2.5}$) of *-i* days before the case time (x_0 is the case day), and t is the different time period (1, 7, or 30 days).

The difference value was calculated by subtracting the average value, the t-day (t is 1, 7, or 30) time period average value of the case minus the previous t-day (t is 1, 7, or 30) time period average value for each case. The formula is expressed as:

$$\Delta\overline{x} = \frac{\sum_{i=(1-t)}^{0} x_i}{t} - \frac{\sum_{i=(1-2t)}^{-t} x_i}{t}; \tag{10}$$

where $\Delta\overline{x}$ is the difference in that time period. $\Delta\overline{x}>0$ means that the average value of the time period in which the case occurred was higher than the average value of the previous time period, and the environmental factor (RH, temperature, and $PM_{2.5}$) had an upward trend. Otherwise, $\Delta\overline{x} < 0$ indicates that the environmental and meteorological factors had a downward trend.

2.5. Statistical analyses

All data of ambient RH, temperature, $PM_{2.5}$, and the AHI were treated as continuous variables. A winsorization approach was used to minimize the influence of outliers and better achieve a normal distribution of residuals for the variables (Tsai et al., 2012). A normality test was conducted to examine if the data were normally distributed. A Chi-squared test was used for comparison between nominal variables. A one-way analysis of variance (ANOVA) with Tukey's post-hoc test was used to compare multiple values. Pearson's correlation coefficients were used to evaluate relationships among the daily mean or difference of RH, temperature, and $PM_{2.5}$ for 1, 7, and 30 days. A logistic regression was used to examine the odds ratio (OR) of outcome variables (mean or difference of RH, temperature, and $PM_{2.5}$ for 1, 7, and 30 days) between the case (mild-to-moderate OSA and severe OSA) and control groups. Two-factor logistic regression models were conducted to examine the ORs of the daily mean or difference in RH and temperature or $PM_{2.5}$ for 1-, 7-, and 30-day averages with the AHI between the case and control groups. Covariates adjusted in the models included age, sex, and the BMI. To control potential confounders, several covariates were included in the main model for adjustment. We included smoothing spline with four degrees of freedom (dfs) for environmental factors to control the nonlinear effects of them. Personal characteristics (continuous variables: age and BMI; categorical variables: sex) were adjusted to account for between-subject variability. We defined outcome variable with three ordered levels of OSA severity (control, mild-to-moderate OSA and severe-OSA) and applied the generalized additive mixed model with ordered categorical family to estimate OR of OSA severity associated with personal environmental factors and to examined the exposure-response relationship curves in all seasons, cold season (November–April) and warm season (May–October). The regression analyses were conducted using SPSS vers. 26 (SPSS, Chicago, IL, USA). The exposure-response relationship analysis was conducted using R software with MGCV package (version 4.2.2). Statistical significance was accepted at $p < 0.05$.

3. Results

3.1. Characteristics of study subjects

There were 8628 subjects recruited in this study, including 1307 control, 3661 mild-to-moderate OSA, and 3597 severe OSA subjects; their baseline demographic characteristics are summarized in Table 1. Subjects in the severe OSA group had the highest ages (50.2 years), percentage of males (82.0 %), BMI values (29.4 kg/m^2), neck circumference (40.4 cm), and waist circumference (98.8 cm) compared to subjects in the control and mild-to-moderate groups. Mean AHI values in the control, mild-to-moderate, and severe OSA groups were 2.0, 16.1, and 56.7 events/h,

Table 1
Basic characteristics in the study subjects (mean ± SD).

	Total	Control	Mild-to-Moderate OSA	Severe OSA	*p*-Value
N	8628	1370	3661	3597	
Age, years	48.9 ± 13.6	43.8 ± 13.9	49.4 ± 13.6	50.2 ± 13.1	<0.05
Male (%)	5903 (68.4)	546 (39.9)	2409 (65.8)	2948 (82.0)	<0.05
Height, cm	166.4 ± 8.7	163.1 ± 8.6	166.0 ± 9.0	168.0 ± 8.0	<0.05
Body-mass index, kg/m^2	27.0 ± 5.0	23.2 ± 3.4	26.0 ± 4.2	29.4 ± 5.1	<0.05
Neck circumference, cm	38.2 ± 6.3	34.6 ± 5.4	37.3 ± 5.7	40.4 ± 6.3	<0.05
Waist circumference, cm	91.8 ± 16.1	79.8 ± 10.4	89.5 ± 17.7	98.8 ± 12.3	<0.05
Waist-height ratio	0.55 ± 0.09	0.49 ± 0.06	0.54 ± 0.11	0.59 ± 0.07	<0.05
Apnea index, events/h	9.8 ± 17.1	0.2 ± 0.5	2.7 ± 3.9	20.6 ± 22.1	<0.05
Hypopnea index, events/h	21.0 ± 19.3	1.8 ± 1.4	13.4 ± 6.6	36.1 ± 20.6	<0.05
AHI, events/h	30.8 ± 26.6	2.0 ± 1.5	16.1 ± 7.0	56.7 ± 21.1	<0.05
Environmental exposure					
RH, % (min–max)					
1-Day average	73.8 (46.4–99.4)	73.4 (48.1–98.4)	73.8 (47.2–99.4)	74.0 (46.4–98.1)	0.128
7-Day average	74.0 (56.0–95.7)	73.8 (56.1–93.4)	74.0 (56.6–95.7)	74.0 (56.0–92.7)	0.325
1-Month average	73.9 (63.9–94.8)	73.7 (64.8–88.9)	74.0 (64.1–94.8)	74.0 (63.9–89.5)	0.097
1-Day difference	−0.1 (−29.5–32.2)	−0.2 (−26.5–32.2)	−0.2 (−29.4–32.0)	0.1 (−29.5–32.2)	0.242
7-Day difference	0.1 (−21.1–21.2)	0.1 (−20.3–20.5)	0.0 (−21.1–20.5)	0.1 (−19.5–21.2)	0.858
1-Month difference	0.0 (−14.3–14.9)	0.1 (−13.9–14.2)	0.0 (−14.0–14.7)	−0.1 (−14.3–14.9)	0.347
Temperature, °C (min–max)					
1-Day average	24.1 (5.6–32.9)	24.1 (7.9–32.7)	24.3 (7.9–32.9)	23.9 (5.6–32.8)	<0.05
7-Day average	24.0 (9.8–32.4)	24.2 (10.8–31.9)	24.2 (10.1–32.3)	23.8 (9.8–32.4)	<0.05
1-Month average	24.1 (12.9–32.2)	24.1 (14.7–31.2)	24.3 (12.9–31.2)	23.9 (13.6–32.2)	<0.05
1-Day difference	0.0 (−8.8–6.9)	0.1 (−8.8–6.7)	0.1 (−8.8–6.9)	0.0 (−8.8–5.4)	0.311
7-Day difference	0.0 (−9.4–8.7)	0.0 (−6.5–8.5)	0.0 (−9.3–8.7)	0.0 (−9.4–8.2)	0.432
1-Month difference	0.0 (−7.0–6.5)	0.1 (−7.0–6.5)	−0.1 (−6.7–6.5)	−0.1 (−7.0–6.5)	0.244
$PM_{2.5}$, μg/m^3 (min–max)					
1-Day average	15.2 (1.3–68.3)	15.7 (1.8–67.3)	14.8 (1.3–68.3)	15.3 (1.6–67.6)	<0.05
7-Day average	15.2 (2.7–44.6)	15.8 (3.9–39.0)	14.8 (2.7–44.6)	15.4 (3.7–42.8)	<0.05
1-Month average	15.3 (4.7–43.4)	15.9 (6.8–31.3)	14.9 (4.7–33.3)	15.4 (5.7–43.4)	<0.05
1-Day difference	0.0 (−38.2–36.2)	0.2 (−35.1–33.8)	0.1 (−36.0–35.4)	−0.2 (−38.2–36.2)	0.071
7-Day difference	−0.1 (−22.7–23.2)	−0.2 (−2.5–22.6)	−0.2 (−22.7–22.6)	0.0 (−22.5–23.2)	0.293
1-Month difference	−0.2 (−12.1–16.5)	−0.3 (−11.1–11.9)	−0.2 (−-11.9–16.5)	−0.2 (−12.1–14.7)	0.861

AHI, apnea/hypopnea index; RH, relative humidity; $PM_{2.5}$, particulate matter of <2.5 μm in aerodynamic diameter.

respectively. Distributions of the daily mean or difference in ambient RH, temperature, and $PM_{2.5}$ for 1, 7, and 30 days among study subjects during the study periods are shown in Fig. 1. The 1-, 7- and 30-day RH, temperature and $PM_{2.5}$ averages (minimum ~ maximum) were 73.8 % ~ 74.0 % (46.4 % ~ 99.4 %), 24.0–24.1 (5.6–32.9) °C, and 15.18–15.28 (1.32–68.30) μg/m^3, respectively. Regarding the daily difference, the 1-, 7-, and 30-day RH, temperature, and $PM_{2.5}$ differences were −0.08 % ~ 0.06 % (−29.5 % ~ 32.2 %), −0.03–0.03 (−9.4–8.7) °C, and −0.19 ~ −0.04 (−38.17–36.17) μg/m^3, respectively. Correlations among daily means or differences in ambient RH, temperature, and $PM_{2.5}$ for 1, 7, and 30 days among study subjects are shown in Table 2. We observed that daily means and differences of both ambient RH and temperature had negative correlations with $PM_{2.5}$ for 1, 7, and 30 days.

3.2. Associations of ambient RH, temperature, and $PM_{2.5}$ with OSA severity

Associations of ambient RH, temperature, and $PM_{2.5}$ with the AHI in OSA patients are shown in Fig. 2. We observed that a 1-μg/m^3 increase in the mean $PM_{2.5}$ increased the OR by 1.04–1.08-fold (0.04–0.08 events/h) of the AHI of mild-to-moderate OSA subjects and the OR by 1.05–1.08-fold (0.05–0.08 events/h) of the AHI of severe OSA subjects with 1, 7, and 30 days of exposure ($p < 0.05$). A 1 % increase in the mean RH increased the OR by 1.01–1.03-fold (0.01–0.03 events/h) of the AHI of mild-to-moderate OSA subjects for 7 and 30 days and the OR by 1.01–1.03-fold (0.01–0.03 events/h) of the AHI of severe OSA subjects for 1, 7, and 30 days ($p < 0.05$). There were no significant associations of mean temperature, or differences in the RH, temperature, and $PM_{2.5}$ with the AHI.

3.3. Effects of changes in ambient RH, temperature, and $PM_{2.5}$ on OSA severity

Daily difference changes of 1-, 7-, and 30-day ambient RH, temperature, and $PM_{2.5}$ values were associated with the AHI in OSA patients (Fig. 3). We observed that an increase in the 1-day RH difference of 1 % was associated with a 1.03-fold increase in the OR (0.03 events/h) of the AHI in mild-to-moderate OSA subjects and with a 1.02-fold increase in the OR (0.02 events/h) of the AHI in severe OSA subjects ($p < 0.05$). Notably, a decrease of 1 μg/m^3 in the 1-day $PM_{2.5}$ was associated with a 0.97-fold OR decrease (−0.03 events/h) in the AHI of mild-to-moderate OSA subjects ($p < 0.05$), but that was not observed in severe OSA subjects. A decrease of 1 % in the 30-day RH was associated with a 0.96-fold OR decrease (−0.04 events/h) in the AHI of mild-to-moderate OSA subjects, and a decrease of 1 % in the 7-day RH was associated with a 0.97-fold OR decrease (−0.03 events/h) in the AHI of severe OSA subjects ($p < 0.05$).

3.4. Associations of ambient RH with temperature or $PM_{2.5}$ in OSA severity

Associations of ambient RH with temperature or $PM_{2.5}$ in OSA severity using a two-pollutant model analysis were determined (Fig. 4). A 1 % increase in the 1-month mean RH with $PM_{2.5}$ increased the OR (0.02 events/h) of the AHI by 1.02-fold in mild-to-moderate OSA subjects ($p < 0.05$). A 1 % increase in the mean RH with temperature increased the OR (0.00–0.04 events/h) of the AHI by 1.00–1.04-fold in mild-to-moderate OSA subjects and increased the OR (0.01–0.04 events/h) of the AHI by 1.01–1.04-fold in severe OSA subjects for 1, 7, and 30 days ($p < 0.05$). Next, we observed that a 1-day RH increase of 1 % with $PM_{2.5}$ or temperature was associated with 1.02-fold (0.02 events/h) and 1.02-fold increases in the OR (0.02 events/h) of the AHI in mild-to-moderate and severe OSA subjects ($p < 0.05$), respectively. Also, a decrease of 1 % in the 7-day RH difference with $PM_{2.5}$ was associated with 0.97-fold (−0.03 events/h) and 0.97-fold OR decreases (−0.03 events/h) in the AHI in mild-to-moderate and severe OSA subjects ($p < 0.05$), respectively. We observed that decreases of 1 % in the 7- and 30-day RH with temperature were associated with 0.95-fold (−0.05 events/h) and 0.92-fold decreases in the OR (−0.08 events/h) of the AHI in mild-to-moderate OSA subjects ($p < 0.05$), respectively. A decrease of 1 % in the 7-day RH with temperature was associated with a 0.96-fold decrease in the OR (−0.04 events/h) of the AHI in severe OSA subjects ($p < 0.05$).

3.5. Exposure-response relationship of ambient RH, temperature, and $PM_{2.5}$ with OSA severity

The exposure-response relationship of ambient RH, temperature, and $PM_{2.5}$ with OSA severity in all seasons is shown in Fig. 5. We observed that $PM_{2.5}$ in mean (1 day, 7 day and 1 month) and difference (7-day and 1 month) and temperature in difference (1 day) presented a significant exposure-response relationship. However, the changing degree of effects in mean and difference $PM_{2.5}$ were relatively small. The exposure-response relationship of ambient RH, temperature, and $PM_{2.5}$ with OSA severity in cold and warm seasons is shown in Figs. 6 and 7. We observed that $PM_{2.5}$, temperature and RH in 1-day, 7-day and 1-month mean and difference presented a significant exposure-response relationship. The exposure-response relationship in temperature and RH showed obviously seasonal patterns with OSA severity, which indicate that warm season had the same exposure-response curve with the whole year exposure-response curve. However, there were no differences in seasonal patterns of $PM_{2.5}$ on OSA severity in warm and cold seasons.

4. Discussion

The significance and novelty of this study are that we examined associations of environmental factors with OSA severity using a case-control study. We observed the ambient RH-dependent OSA severity. Furthermore, decreased levels of $PM_{2.5}$ and RH were associated with reducing OSA severity. A significant seasonal effect in RH was associated with OSA severity. Our results suggest that patients staying in low-level $PM_{2.5}$ and RH outdoor environments may reverse OSA severity as assessed by the AHI.

We observed that the mean $PM_{2.5}$ mass concentration decreased with an increase in the mean RH or temperature in the study area. Consistently, previous reports showed that mean levels of $PM_{2.5}$ were reduced by high RH and temperature in China (Chen et al., 2018; Lou et al., 2017). We further showed that the daily difference in $PM_{2.5}$ decreased with an increase in the RH or temperature. Meteorological conditions were reported to be the main determinants for air pollution production in the ambient environment. For example, the gas-phase oxidation of nitrogen oxides occurs by the addition of OH formed through O_3 photolysis in daytime due to a high water vapor content, O_3, and stronger solar radiation. High RH occurs when the temperature drops, enhancing the gas-particle partitioning of HNO_3 and the occurrence of the N_2O_5 heterogeneous hydrolysis reaction at night (Ding et al., 2021). Production of SO_2^{4-} is relatively higher at lower temperatures and higher RHs (T < 0 °C, RH > 80 %). The results suggested that extreme weather may play an important role in the production of $PM_{2.5}$, resulting in adverse human health effects.

Environmental factors have been associated with OSA severity (Tung et al., 2021). To study the short-term effects of environmental factors on the AHI in mild-to-moderate and severe OSA, the 1-, 7-, and 30-day daily means of ambient RH, temperature, and $PM_{2.5}$ were estimated for each subject on the recruitment day. We observed that short-term ambient exposure to mean $PM_{2.5}$ increased the risk of OSA severity. Air pollution is considered to be a risk factor for OSA (Billings et al., 2019). One study showed that an increase in the interquartile range (IQR) of the annual mean $PM_{2.5}$ resulted in a 4.7 % increase in the AHI in Taiwan (Shen et al., 2018). Furthermore, 1- and 2-year mean exposure to traffic-related air pollution was found to be associated with the risk of mild OSA in patients (He et al., 2022). Our previous work identified that 1-year mean ambient RH was associated with the AHI in positional OSA patients, which was mediated by the sleep cycle (Liu et al., 2022). In this study, we further found that short-term ambient exposure to mean RH increased the risk of OSA severity. Consistently, a retrospectively study observed that the AHI was inversely correlated with the ambient RH (Cassol et al., 2012). The evidence suggests that environmental factors, especially $PM_{2.5}$ and RH, may temporarily modify the OSA severity.

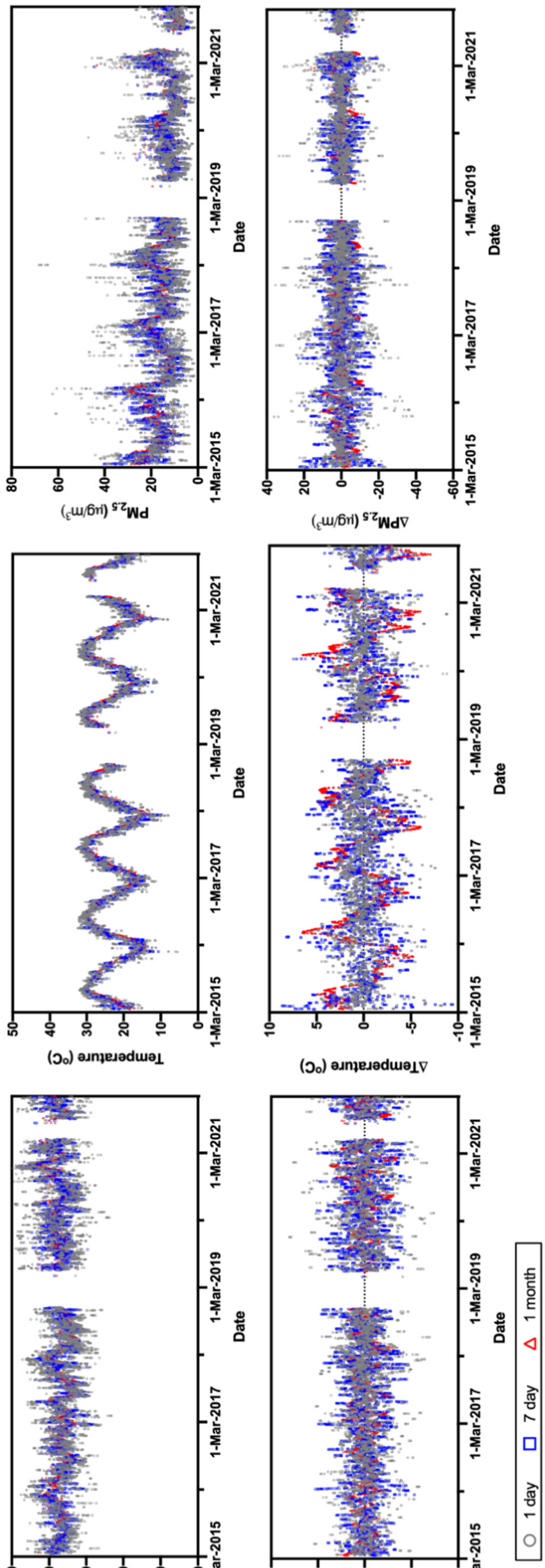

Fig. 1. Distribution of the daily mean and difference (Δ) in ambient relative humidity (RH), temperature, and particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) for 1-, 7-, and 30-day averages for study subjects.

Table 2
Correlation between ambient relative humidity (RH), temperatures and $PM_{2.5}$ in daily mean and difference for 1-day, 7-day, and 1-month averages for study subjects ($N = 8628$).

	1-day $PM_{2.5}$	7-day $PM_{2.5}$	1-month $PM_{2.5}$	1-day RH	7-day RH	1-month RH	1-day Temperature	7-day Temperature	1-month Temperature
1-day $PM_{2.5}$		-0.105**	-0.059**	-0.362**	0.029**	0.015	-0.065**	0.029**	0.027*
7-day $PM_{2.5}$	0.632**		0.022*	-0.038**	-0.227**	-0.028*	0.032**	-0.313**	0.030**
1-month $PM_{2.5}$	0.499**	0.761**		-0.008	-0.064**	-0.0362**	0.009	0.013	-0.216**
1-day RH	-0.151**	-0.073**	-0.010		-0.151**	0.014	0.079**	-0.077**	-0.019
7-day RH	-0.114**	-0.188**	-0.060**	0.581**		0.214**	-0.048**	0.310**	-0.054**
1-month RH	-0.005	-0.019	-0.058**	0.400**	0.664**		-0.010	-0.066**	-0.158**
1-day Temperature	-0.106**	-0.216**	-0.233**	-0.338**	-0.437**	-0.510**		-0.110**	-0.030**
7-day Temperature	-0.207**	-0.251**	-0.277**	-0.249**	-0.410**	-0.542**	0.920**		-0.007
1-month Temperature	-0.294**	-0.407**	-0.421**	-0.221**	-0.329**	-0.534**	0.865**	0.940**	

Orange: daily mean.
Blue: daily difference.
$^{*}p < 0.05$; $^{**}p < 0.01$.

Although daily mean levels of environment factors have been linked to OSA severity, the effects of extreme weather and daily variations in these environmental factors on OSA remain unclear. To clarify the association, the daily difference for 1-, 7-, and 30-day ambient RH, temperature, and $PM_{2.5}$ values were obtained for each subject in this work. These data enabled us to further investigate daily variations by increases or decreases in the ambient RH, temperature, and $PM_{2.5}$. First, we observed no associations of daily differences in environmental factors with OSA severity. However, we found a higher increasing difference in the RH increased the risk of OSA severity. In contrast, a higher decreasing difference in $PM_{2.5}$ or RH decreased the risk of OSA severity. A previous study observed that there was no significant difference between high and low ambient RH over 2 nights on OSA severity after adjusting for the body position and sleep stage (Jokic et al., 1999). Those results suggested that extreme weather as signified by high daily variations in $PM_{2.5}$ and RH may play important roles in regulating OSA severity. Our results further suggested that significant reductions in daily $PM_{2.5}$ and RH could have short-term effects on reducing the OSA severity.

A previous study found an association between AHI and PM_{10} during winter (Yıldız Gülhan et al., 2020). Notably, we found that the daily mean and difference in ambient RH were key factors in the association with the OSA severity, confirmed by two-pollutant model analyses with $PM_{2.5}$ and

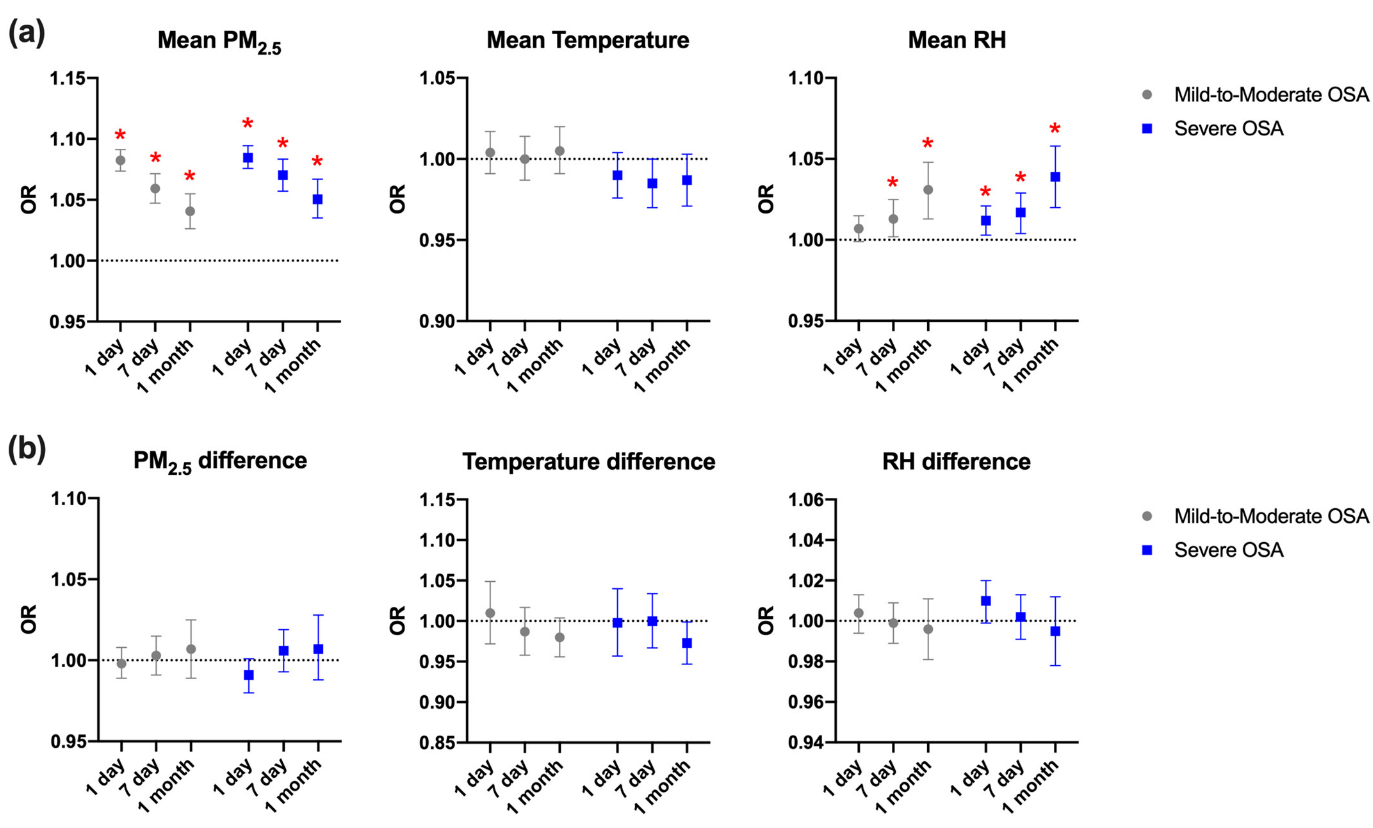

Fig. 2. Associations of the daily mean and difference in ambient relative humidity (RH), temperature, and particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) for 1-, 7-, and 30-day averages (mild-to-moderate and severe OSA to control as reference group). Data are presented as the odds ratio (OR) and 95 % confident interval (CI). Covariates adjusted for in the models were age, sex, and the body-mass index (BMI). Red indicates statistical significance at $p < 0.05$.

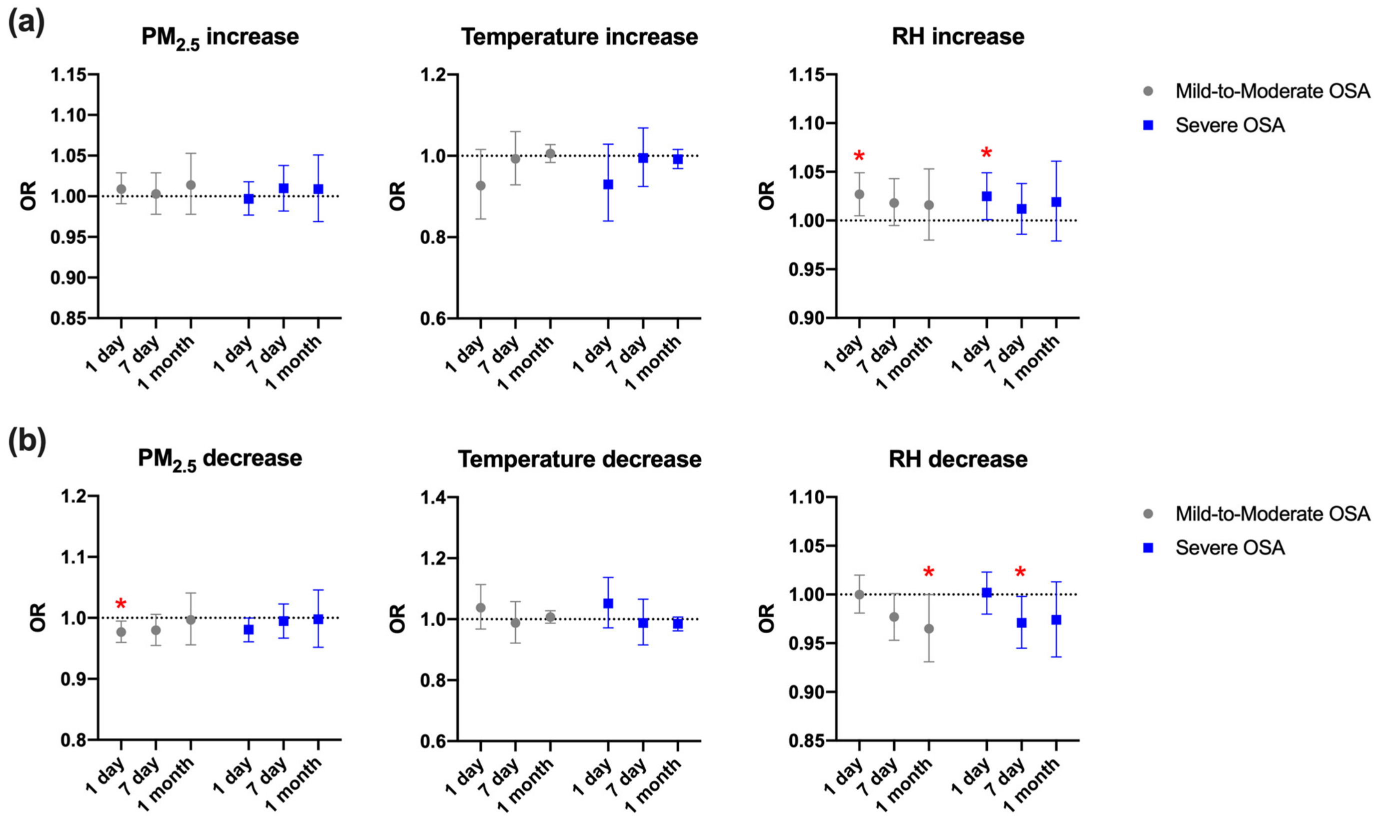

Fig. 3. Associations of daily differences by increases and decreases in the ambient relative humidity (RH), temperature, and particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) in for 1-, 7-, and 30-day averages with the OSA severity (mild-to-moderate and severe OSA to control as reference group). Data are presented as the odds ratio (OR) and 95 % confident interval (CI). Covariates adjusted for in the models were age, sex and the body-mass index (BMI). Red indicates statistical significance at $p < 0.05$.

temperature. We further observed that the exposure-response relationship in temperature and RH showed obviously seasonal patterns with OSA severity. The results suggest that OSA patients may suffer more in from RH in the cold season. A previous report indicated that OSA often occurred in winter with more sleep-disordered breathing events than other seasons (Cassol et al., 2012). Addition to this, $PM_{2.5}$ was associated with OSA severity in an exposure-response relationship. However, the relationship is not present in a seasonal pattern in the study subjects. Together, these results imply that OSA severity is more sensitive to seasonal-changed RH than the other environmental factors. It has higher risk occurred in the cold season by exposure to higher RH.

We suspect that cholinergic neurons may exhibit an important biological response to RH in terms of OSA severity. Hyperventilation of humid hot air induces coughing and bronchoconstriction in asthma patients, which is mediated through the cholinergic reflex pathway (Hayes et al., 2012). A study on guinea pigs showed that humidified hot air induced transient airway constriction, which was mediated through the cholinergic reflex (Lin et al., 2009). Airway constriction occurs by activation of the transient receptor potential vanilloid type 1 (TRPV1)-expressing airway afferent nervous system. Another study showed that exposure to high environmental RH (90 %) and carbon nanoparticles aggravated airway hyperreactivity, remodeling, and inflammation in mice with ovalbumin-induced asthma (Deng et al., 2022). Those authors further showed that co-exposure to carbon nanoparticles under high environmental RH caused adjuvant effects on the development of asthma, which could have occurred through activation of an oxidative stress pathway and TRPV1 pathway, thus facilitating type I hypersensitivity. Together, alterations in the daily mean and difference in ambient RH may mediate OSA severity through the TRPV1 pathway. However, further biological evidence regarding RH-dependent TRPV1 expression in OSA needs to be explored.

There are some limitations to the current study. Data on comorbidities for OSA were not included in this study. Other co-factors (i.e., alcohol consumption, smoking, noise exposure, and physical activities) and other air pollutants should be considered. Indoor environmental factors should be included in future work.

5. Conclusions

We observed that short-term alterations in ambient RH and $PM_{2.5}$ were associated with the AHI in OSA patients, especially RH during cold seasons. It is important to understand that reducing exposure to high ambient RH and $PM_{2.5}$ may have protective effects against the AHI in OSA patients. Exposure to extreme weather could increase the risks of OSA severity.

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CRediT authorship contribution statement

YCL and HCC: Conceptualization, Methodology, Software. **KJB, WTL, YLL and HCC:** Data curation, Writing- Original draft preparation. **DW, CYT, and KL**: Visualization, Investigation. **TYC, LTC, and KJC**: Supervision. **CYL:** Software, Validation. **KFC and KFH:** Writing- Reviewing and Editing.

Data availability

Data will be made available on request.

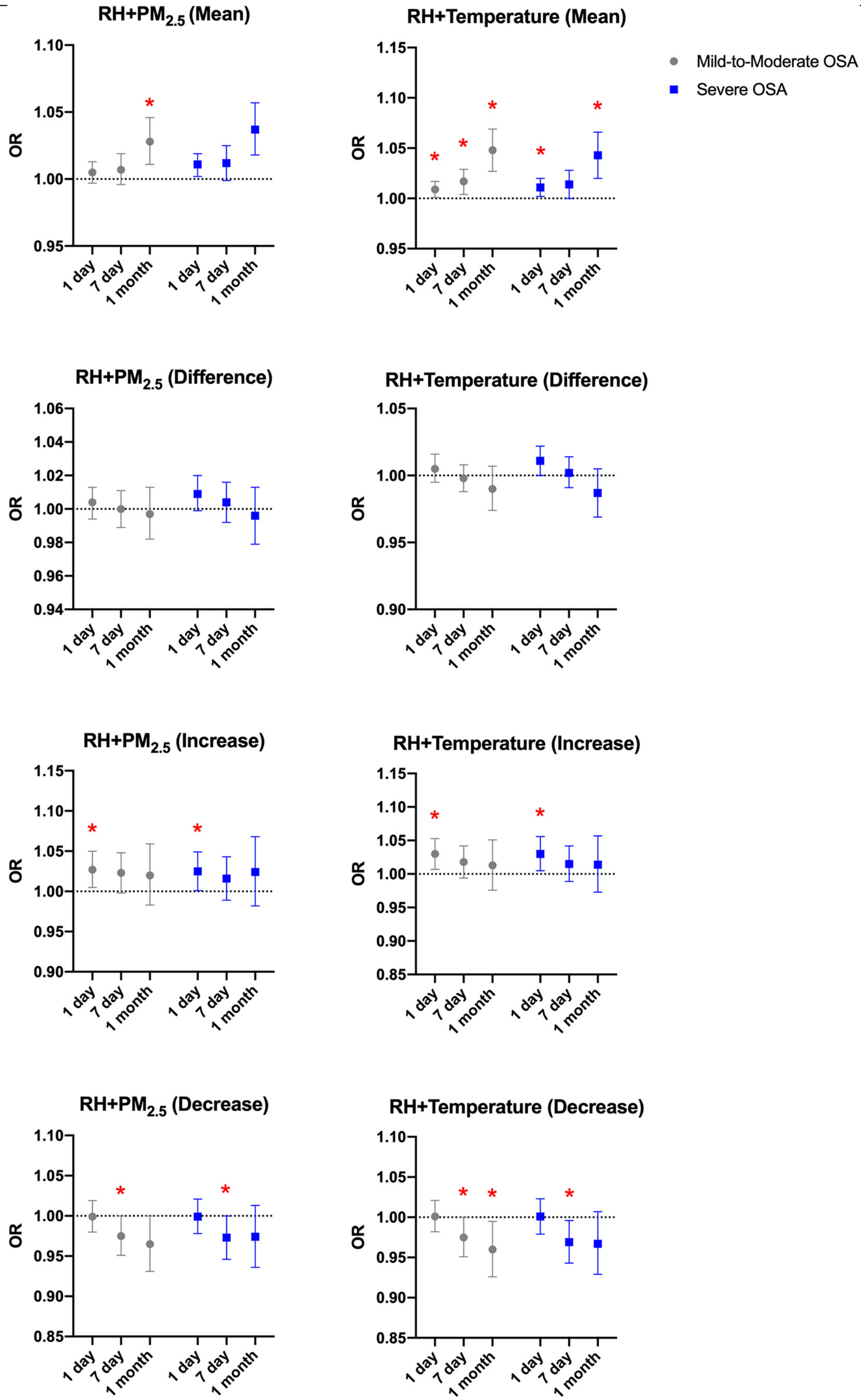

Fig. 4. Two-factor models of associations of the daily mean, difference, and difference by increases and decreases in the ambient relative humidity (RH) and temperature or particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) for 1-, 7-, and 30-day averages with the OSA severity (mild-to-moderate and severe OSA to control as reference group). Data are presented as the odds ratio (OR) and 95 % confident interval (CI). Covariates adjusted for in the models were age, sex and the body-mass index (BMI). Red indicates statistical significance at $p < 0.05$.

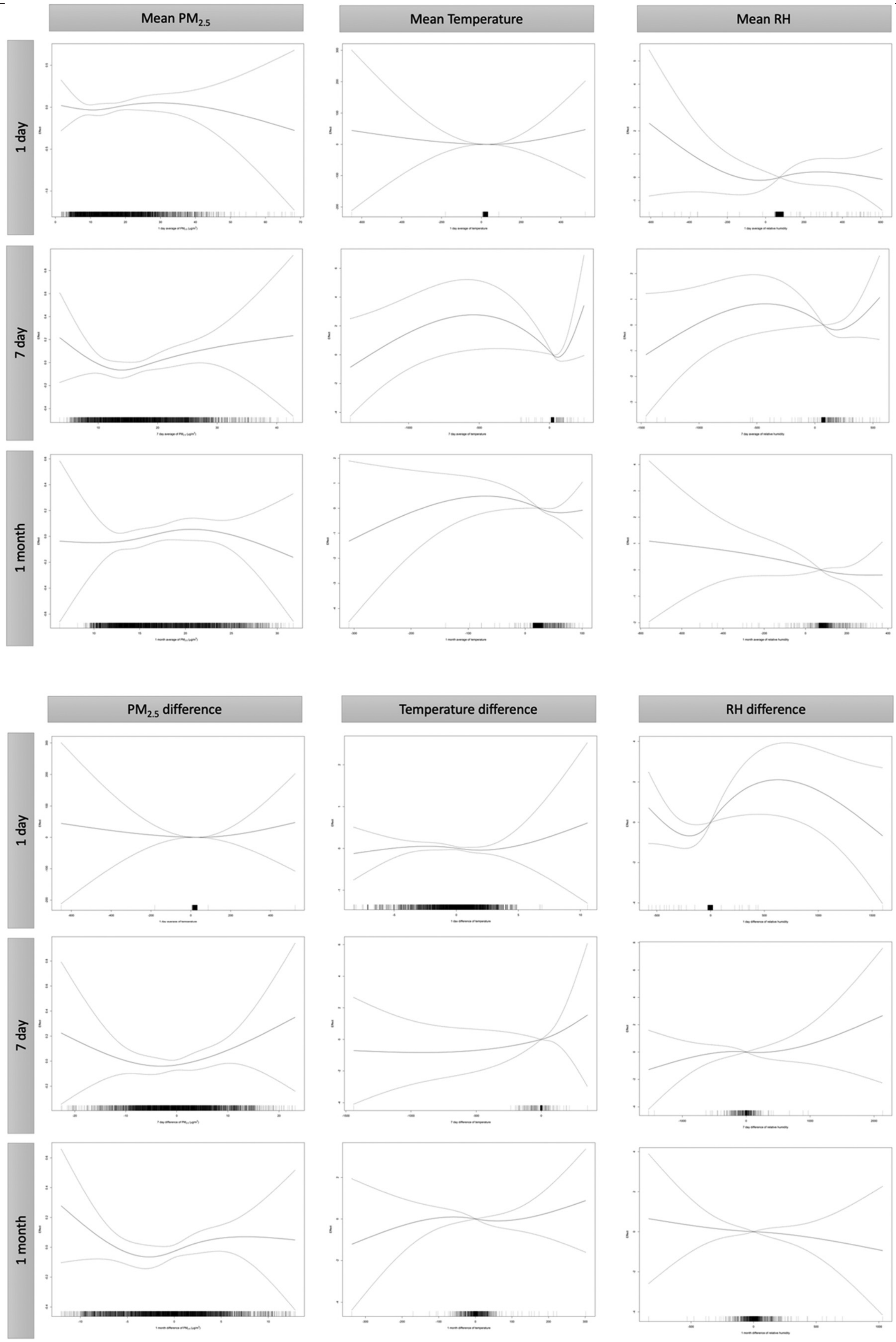

Fig. 5. Exposure-response relationship curves for the association of the daily mean and difference in the ambient relative humidity (RH) and temperature or particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) for 1-, 7-, and 30-day averages with the OSA severity. Data are presented as the effects and 95 % confident interval (CI). Covariates adjusted for in the models were age, sex and the body-mass index (BMI).

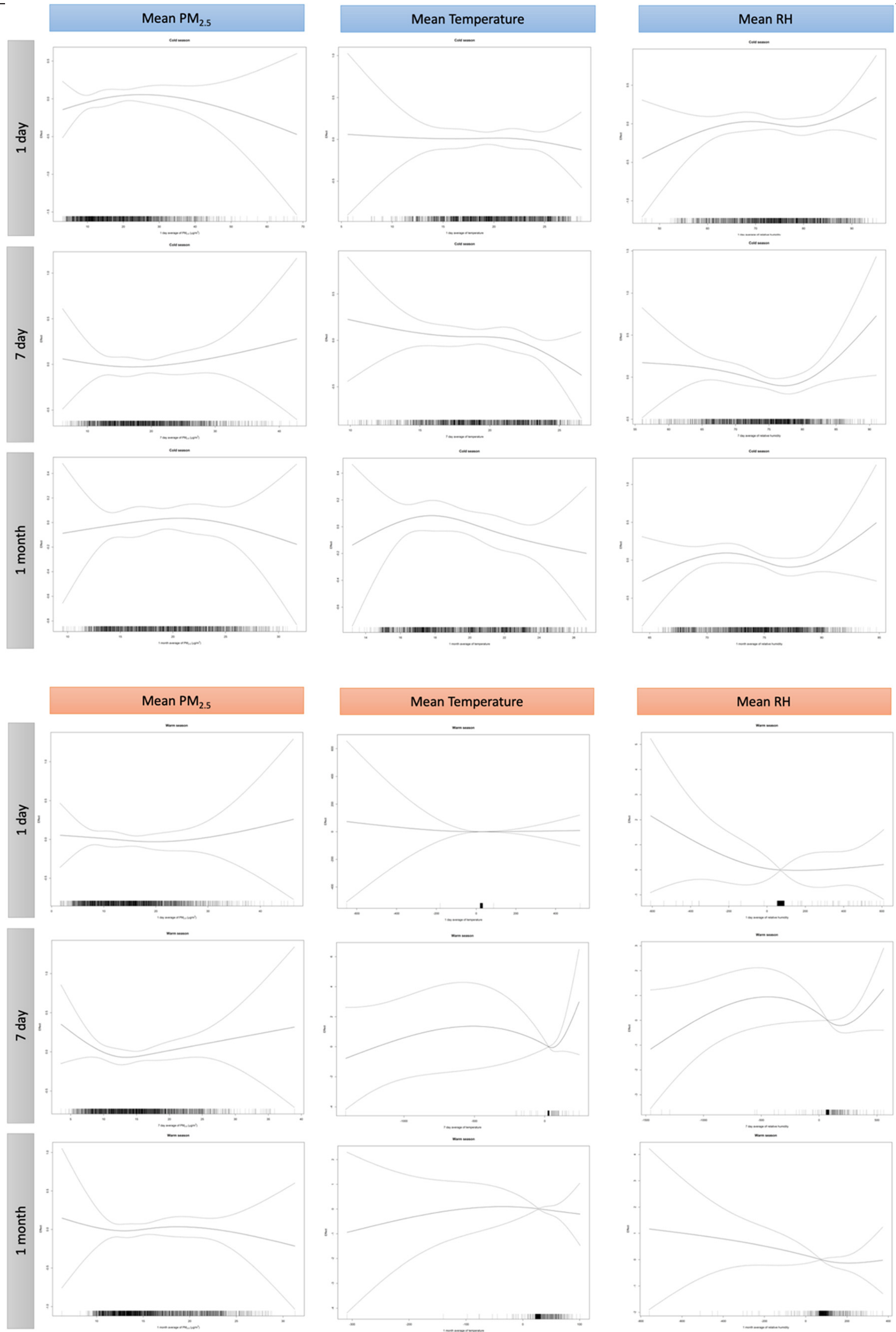

Fig. 6. Exposure-response relationship curves for the association of the daily mean in the ambient relative humidity (RH) and temperature or particulate matter with an aerodynamic diameter of <2.5 μm ($PM_{2.5}$) for 1-, 7-, and 30-day averages with the apnea-hypopnea index (AHI) of cold and warm seasons in patients with mild-to-moderate and severe OSA. Data are presented as the effects and 95 % confident interval (CI). Covariates adjusted for in the models were age, sex and the body-mass index (BMI).

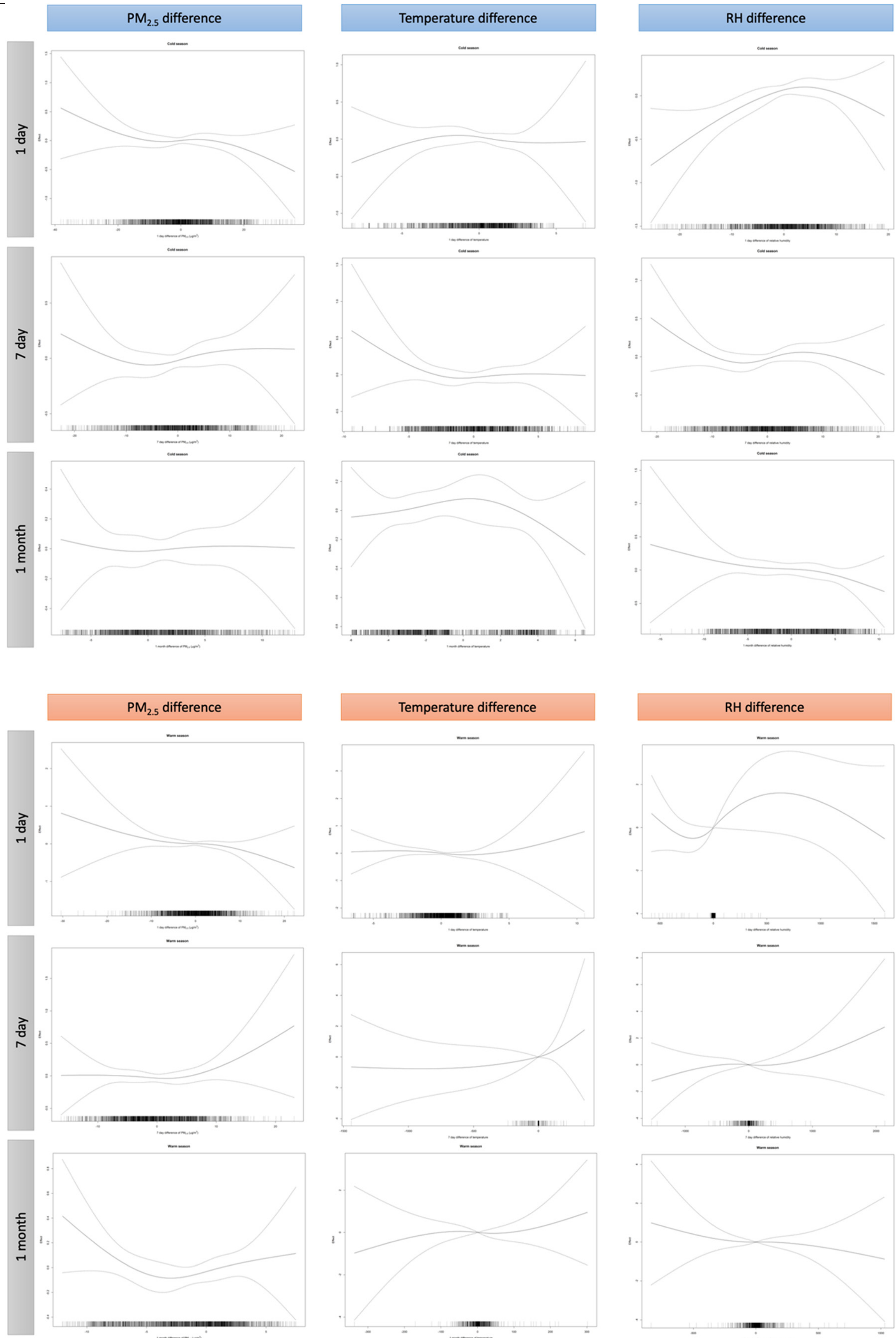

Fig. 7. Exposure-response relationship curves for the association of the daily difference in the ambient relative humidity (RH) and temperature or particulate matter with an aerodynamic diameter of <2.5 μm (PM$_{2.5}$) for 1-, 7-, and 30-day averages of cold and warm seasons with the apnea-hypopnea index (AHI) in patients with mild-to-moderate and severe OSA. Data are presented as the effects and 95 % confident interval (CI). Covariates adjusted for in the models were age, sex and the body-mass index (BMI).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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