Low apparent temperature increases the number of epilepsy-related clinic visits in a humid subtropical region: a time-series study

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Abstract

Background. At present, the effect of apparent temperature (AT) on epilepsy has not been confirmed. Therefore, we conducted this study in Hefei, China, a city in a humid subtropical region, to investigate the effects of AT on the daily number of epilepsy-related clinic visits. Methods. A time-series analysis of the number of daily epilepsy clinic visits during 2015–2020 was performed using a quasi-Poisson regression model combined with a distributed lag nonlinear model (DLNM). Time trends, days of the week, relative humidity, and PM2.5 concentration were adjusted for in the model. Subgroup analyses were performed by sex and age. Results. A total of 28,020 epilepsy-related clinic visits were reported by the hospital during the study period. Low AT showed significant negative and delayed effects on the number of epilepsy clinic visits, but no such effects were observed with high AT. The median apparent temperature (17 °C) was used as the reference, and the single-day lag effect of low AT (5th percentile, −1.5 °C) on the number of epilepsy clinic visits peaked on lag day 1, with a relative risk (RR) of 1.055 (95% CI: 1.015–1.097). The cumulative effect of low AT was most obvious on lag days 0–12, with a maximum RR of 1.451 (95% CI: 1.180–1.783). Males and young adults (0–14 years and 15–29 years) were more likely to be affected by low AT. Conclusions. We found that low AT led to an increase in the number of epilepsy-related clinic visits. This result provides an important scientific basis for the allocation of outpatient medical resources and the development of interventions.

1. Introduction

Epilepsy is a common chronic neurological disorder that causes brain dysfunction. It is characterized by sudden abnormal firing of neurons in the brain [1]. This disease is a critical public health and socioeconomic problem worldwide, affecting approximately 70 million people and all age groups. It often requires long-term management and treatment, imposing a substantial economic burden on society [2, 3]. The epileptic brain has increased susceptibility to seizures, and repeated epileptic seizures affect people’s physical, psychological, and spiritual states and reduce their quality of life [4, 5]. Most people with epilepsy usually have no obvious
symptoms, but seizures are usually high-risk, even life-threatening [6], and their unpredictability leads to the need for someone to care for the patient, which creates an additional burden [7].

The effects of ambient temperature on chronic illnesses have received considerable critical attention in recent years. It has been widely documented that exposure to low and high ambient temperatures result in increased morbidity and mortality [8–10]. However, most of these studies have focused on circulatory diseases, respiratory diseases or endocrine diseases, and most of them include inpatient cases, while outpatient cases have rarely attracted the attention of researchers. Some scholars believe that outpatient cases reflect initial responses to the effects of climate factors on human health, which is more realistic [11, 12]. Currently, there is little evidence on the correlation of epilepsy with ambient temperature, and existing results are controversial. A study from Taiwan, China, showed that low ambient temperature was the only meteorological factor contributing to the increased risk of epileptic seizures [13]. However, according to a hospital-based case–crossover study in 604 patients with epilepsy in central Germany, high air pressure and low relative humidity also had negative effects on seizure risk, whereas high ambient temperature appeared to be protective against epileptic seizures [14]. Another retrospective study on weather and acute epileptic seizures in Korean children showed that low mean temperature increased the number of emergency visits among children with epileptic seizures, while high mean temperature decreased the number of emergency visits among children with epileptic seizures [15]. These differences may be due to the different climatic regions and different study populations. Therefore, further studies in additional geographic areas are needed to confirm the relationship between epilepsy and temperature. Several studies have shown that because humans are exposed to multiple meteorological factors, the actual ambient temperature may not accurately reflect thermal sensation in humans when sensing changes in the ambient temperature [16]. Apparent temperature (AT), which comprehensively takes into account ambient temperature, relative humidity, wind velocity, and other meteorological factors, has been proven to be more objective than the environmental temperature alone in reflecting the human body’s sense of heat [17].

To our knowledge, the effect of AT on the number of epilepsy clinic visits has not been investigated. This study aimed to investigate the effects of AT on the number of daily epilepsy clinic visits in Hefei, China, between 2015 and 2020 using a time-series approach. Additionally, we performed age and sex subgroup analyses to identify vulnerable populations.

2. Materials and methods

2.1. Study area

Hefei was chosen as our research site. Hefei is located in the middle and lower Yangtze River region of China (31°52′N, 117°17′E) and serves as the centre of political and economic culture in Anhui Province. The city has a humid subtropical climate with pronounced monsoons and distinct seasons. It covers an area of 11445 square kilometres, with steady population growth. In 2020 (the year of the seventh national census of Hefei), the permanent resident population was 9.37 million.

2.2. Data collection

We collected data on daily epilepsy clinic visits, including the date of presentation and patient age, sex, and address among outpatients of three hospital districts of a large tertiary hospital. These three outpatient districts are widely distributed in different regions of Hefei. This hospital is the medical institution with the largest number of annual outpatient visits in Anhui Province. Epilepsy cases were identified by the International Classification of Diseases, 10th Edition (ICD-10 codes: G40–G41, R56) and screened through the outpatient electronic medical record system. Patients with an residence address outside Hefei were excluded. The time period was from January 1, 2015, to December 31, 2020. A review board from the First Affiliated Hospital of Anhui Medical University ethics committee reviewed and approved this study (PJ2022-03-38).

Daily meteorological data, including ambient temperature (°C), wind velocity (m s⁻¹), relative humidity (%), atmospheric pressure (hPa), 24-hour rainfall (mm) and sunshine duration (h), were obtained from the China National Meteorological Information Center (http://data.cma.cn). For the same time period, daily air pollutant data were obtained from 10 fixed air quality monitors in Hefei; air quality data included concentration data on particles with an aerodynamic equivalent diameter less than or equal to 2.5 μm and 10 μm (PM2.5, PM10), carbon monoxide (CO) and ozone (O3).

2.3. Calculation of AT

According to the above meteorological data, which include ambient temperature, wind velocity and relative humidity, AT was calculated. The specific formulas used are as follows [18, 19]:

\[
AT = T_{\text{mean}} + 0.33 \times a - 0.70 \times WV - 4.00
\]  

(1)
\[ a = \frac{\text{RH}}{100} \times 6.105 \times \exp \left[ 17.27 \times \frac{T_{\text{mean}}}{(237.7 + T_{\text{mean}})} \right] \]  

where \( T_a \) represents the ambient mean temperature (°C); \( a \) is vapour pressure (hPa), calculated using equation (2); \( \text{WV} \) is wind velocity (m s\(^{-1}\)), and RH is relative humidity (%).

### 2.4. Statistical analysis

Descriptive analyses were performed for daily number of seizure-related visits, meteorological variables, and air pollutant data. Previous studies have shown that environmental variables often have a nonlinear lag effect on human health [20–22]. Time-series analysis and the distributed lag nonlinear model (DLNM) have been widely used to assess associations between health outcomes and environmental variables and can describe lag dependencies and complex nonlinearity by combining traditional exposure-response associations with additional lag-response associations [23, 24]. This result is consistent with a quasi-Poisson distribution in which the number of outpatient visits is large. Therefore, an estimation of the nonlinear and lag impacts of AT on the daily number of epilepsy-related clinic visits was conducted using the quasi-Poisson regression model coupled with the DLNM. First, variables associated with the daily number of epilepsy-related clinic visits, including mean temperature, relative humidity, PM2.5, PM10, CO and apparent temperature, were identified using Spearman correlation analysis. A Spearman correlation coefficient \(<0.5\) was used as the criterion to select covariates to avoid multicollinearity [25]. Spearman correlation coefficients and scatter figures between air pollutants and meteorological conditions are shown in supplementary figure S1 (available online at stacks.iop.org/ERC/4/095011/mmedia) in the attachment. The final variables included were apparent temperature, relative humidity and PM2.5 concentration. The maximum number of lag days was determined to be 12 days by the Akaike information criterion, and the optimal degrees of freedom for covariates, season, and secular trends were selected. The specific model is as follows:

\[ Y_t \sim \text{quasi-Poisson}(\mu_t) \]

\[ \log(\mu_t) = \alpha + \text{ns}(\text{RH}_{t, 3}) + \text{ns}(\text{PM2.5}_{t, 3}) + a\text{Time}_t + \beta_1\text{Dow}_t + \gamma_1\text{Holiday}_t + \delta_1 A T_{t,l} \]

where \( Y_t \) represents the expected daily count of epilepsy-related clinic visits on observation day \( t \); \( \log() \) is a link function; \( \alpha \) indicates the intercept of the model; \( \text{ns}() \) represents the natural spline function; \( l \) is the lag days; \( A T_{t,h}, \text{RH}_{t,3} \) and \( \text{PM2.5}_{t,3} \) are cross-basis matrices of AT, relative humidity and PM2.5, respectively; \( \beta, \gamma \) and \( \delta \) are the coefficients for \( \text{Dow}, \text{Holiday} \), and \( A T_{t,l} \) matrices, respectively; \( \text{ns}(\text{RH}_{t,3}) \) and \( \text{ns}(\text{PM2.5}_{t,3}) \) represent natural spline functions with 3 degrees of freedom to control the influence of relative humidity and PM2.5, respectively; and \( \text{ns}(\text{Time}_t, 7) \) represents 7 degrees of freedom to adjust for seasonal and long-term trends. The choice of degrees of freedom here is based on previous literature [26]. Dow, and Holiday, were applied to control for day of the week and holidays, respectively.

Referring to previous literature, we chose the median apparent temperature (17°C) as the reference value [15]. Apparent temperature in the fifth percentile was defined as low apparent temperature. To detect disadvantaged populations, we performed subgroup analyses by age and sex. This study performed statistical analyses with the aid of the ‘DLNM’ and ‘Splines’ packages in R software (version 4.1.2). The effects of apparent temperature are described as the relative risk (RR) of an epilepsy-related clinic visit and its 95% confidence interval (CI). Two-sided p values \(<0.05\) were considered statistically significant.

To confirm that the model was robust, we performed the following sensitivity analysis. We varied the degrees of freedom of relative humidity (3–5 df), PM2.5 (3–5 df) and time (6–8 df). In addition, we used different maximum lag days (7 and 12). For the specific sensitivity analysis, refer to supplementary figures S2–5.

### 3. Results

#### 3.1. Descriptive statistics

A total of 28,020 epileptic patients visited the clinic due to seizures during the study period, of which 58.2% were men. Among the different age groups, the 15- to 29-year-old group (35.4%) was larger than the 0- to 14-year-old group (18.8%), 30- to 44-year-old group (28.4%), 45- to 59-year-old group (23.2%) and ≥60-year-old group (7.0%). There was little difference between the mean AT (16.9°C) and the mean ambient temperature (16.8°C). Specific data on daily epilepsy-related clinic visits, meteorological data and air pollutant data during the study period are shown in table 1.

#### 3.2. Overall effects of AT on epilepsy-related clinic visits

Figure 1 shows the overall exposure-response relationship of apparent temperature with epilepsy-related clinic visits, with the median apparent temperature (17°C) as a reference. A lower AT had a significant negative and delayed effect on the number of epilepsy-related clinic visits, while a higher AT had no obvious effect on the
number of epilepsy-related clinic visits. Figure 2 and 3 show the exposure-response relationships in each subgroup, with 17°C as the reference. A higher AT seemed to have no significant effect on the number of epilepsy-related clinic visits in the different subgroups. Regarding sex, the effect of a lower AT on the number of epilepsy-related visits was more obvious in males, and the number of epilepsy-related visits increased with decreasing apparent temperature. Among the various age groups, the most affected age group was the 15- to 29-year-old group. The 0- to 14-year-old group was significantly affected only when the AT was very low, while no significant effects of AT were observed in the other groups.

Table 1. Statistics and summary of epilepsy clinic visits, meteorological data and air pollutants in Hefei, China, 2015–2020.

| Group               | Sum  | Mean ± SD | Min | P5   | P25  | P50  | P75  | P95  | Max  |
|---------------------|------|-----------|-----|------|------|------|------|------|------|
| Total               | 28020| 12.8 ± 10.2| 0   | 1    | 5    | 10   | 19   | 33   | 57   |
| Sex                 |      |           |     |      |      |      |      |      |      |
| Female              | 11719| 5.4 ± 4.8 | 0   | 0    | 2    | 4    | 8    | 15   | 27   |
| Male                | 16301| 7.4 ± 6.1 | 0   | 0    | 3    | 6    | 11   | 19   | 40   |
| Age                 |      |           |     |      |      |      |      |      |      |
| 0–14 years          | 5266 | 2.4 ± 2.8 | 0   | 0    | 0    | 1    | 4    | 8    | 19   |
| 15–29 years         | 9917 | 4.5 ± 4.2 | 0   | 0    | 1    | 3    | 7    | 13   | 26   |
| 30–44 years         | 6534 | 3.0 ± 2.7 | 0   | 0    | 1    | 2    | 4    | 8    | 17   |
| 45–59 years         | 4322 | 2.0 ± 2.0 | 0   | 0    | 0    | 1    | 3    | 6    | 13   |
| ≥60 years           | 1981 | 0.9 ± 1.2 | 0   | 0    | 0    | 1    | 1    | 3    | 11   |
| Apparent temperature | /    | 16.9 ± 12.2| −12.2| −1.5 | 5.9  | 16.9 | 27.4 | 35.8 | 45.1 |
| Ambient temperature | /    | 16.8 ± 9.2 | −5.9 | 2.1  | 8.6  | 17.4 | 24.5 | 30.4 | 35.6 |
| Relative humidity   | /    | 77.0 ± 12.3| 33.0 | 55.0 | 69.0 | 78.0 | 86.0 | 96.0 | 100.0|
| Atmospheric pressure| /    | 1012.2 ± 9.7| 987.5| 997.6| 1003.7| 1012.3| 1019.7| 1028.1| 1041.4|
| Wind velocity (m/s)| /    | 2.0 ± 0.8 | 0.3 | 0.9  | 1.4  | 1.9  | 2.4  | 3.6  | 6.2  |
| 24 h rainfall (mm)  | /    | 3.4 ± 11.0| 0   | 0    | 0    | 0.9  | 19.4 | 197.0|
| Sunshine duration (h)| /    | 4.8 ± 4.2 | 0   | 0    | 0    | 4.8  | 8.6  | 11.3 | 12.9 |
| PM2.5 (mg m⁻³)      | /    | 51.2 ± 33.1| 5.0 | 15.0 | 28.0 | 43.0 | 65.0 | 115.4 | 243.0|
| PM10 (mg m⁻³)       | /    | 79.8 ± 41.7| 11.0| 26.0 | 50.0 | 73.0 | 102.0| 153.0| 361.0|
| CO (μg m⁻³)         | /    | 0.9 ± 0.3 | 0.3 | 0.5  | 0.6  | 0.8  | 1.0  | 1.5  | 2.8  |
| O₃ (mg m⁻³)         | /    | 108.1 ± 48.6| 6.0 | 38.6 | 71.0 | 103.0| 140.0| 194.4| 309.0|

Note: P5, P25, P50, P75, P95: the 5th percentile, the 25th percentile, the 50th percentile, the 75th percentile, the 95th percentile.
3.3. Delayed effects of low AT on epilepsy clinic visits

The single-day lag effects of low AT (5th percentile, $-1.5^\circ C$) on the numbers of epilepsy-related clinic visits in the total population and in the different subgroups are shown in figure 4 and table 2. For the overall study population, the single-day lag effect lasted approximately 6 days, and the largest effect occurred on lag day 1 (RR: 1.055, 95% CI: 1.015–1.097). Low AT had different effects on the different sexes. In males, the effect was largest (RR: 1.060, 95% CI: 1.014–1.107) on lag day 1 and declined over successive days, lasting for approximately 7 days; in females, the effect was weaker (RR: 1.045, 95% CI: 1.008–1.084) than that in males and appeared on lag day 2, lasting only 2 days. There were also different lag effects among the different age groups. The 0- to 14-year-old group and 15- to 29-year-old group had maximum risks on the current day, with maximum RR values of 1.113 (95% CI: 1.005–1.234) and 1.104 (95% CI: 1.023–1.191), respectively, while the 45- to 59-year-old group had maximum risk (RR: 1.056, 95% CI: 1.001–1.115) on lag day 5, which was the most obvious in the 15- to 29-year-old group. No lag effect was observed in the 30- to 44-year-old group or the $\geq$60-year-old group.

The cumulative lag effects of low AT (5th percentile, $-1.5^\circ C$) on the numbers of epilepsy-related clinic visits in the total population and in the different subgroups are shown in figure 5 and table 3. The cumulative effects were significantly higher than the single-day lag effects, which seemed to increase initially and then gradually decline with increasing lag time. In the total population, the cumulative lag effect occurred from the first day after exposure, with the RR varying from 1.117 (95% CI: 1.014–1.229) on lag day 0–1 to 1.427 (95% CI: 1.120–1.818) on lag days 0–12, with the maximum RR (RR: 1.451, 95% CI: 1.180–1.783) on lag days 0–10. In males, the highest RR was observed on lag days 0–11 (RR: 1.544, 95% CI: 1.207–1.975). The maximum RR value was lower in women than in men and occurred on lag days 0–6 (RR: 1.336, 95% CI: 1.041–1.716). For analyses stratified by age, similar to single-day lag effects, cumulative effects were more pronounced in young
adults (0- to 14-year-old group and 15- to 29-year-old group). The maximum RRs in the 0- to 14-year-old group (RR: 1.498, 95% CI: 1.082–2.074) and the 15- to 29-year-old group (RR: 1.579, 95% CI: 1.218–2.047) were observed on lags days 0–8 and 0–9, respectively.

4. Discussion

Previous studies on the effect of temperature on epileptic seizures have mainly been performed in developed countries or regions, such as Germany, South Korea, Poland, and Taiwan, China [13–15, 27, 28], while few have been performed in developing regions. Most of these studies showed that lower ambient temperature was a risk factor for epileptic seizures. For example, Kai-Chieh et al conducted a study in epilepsy patients in Taiwan and found through Poisson regression analysis that each 1 °C reduction in temperature increased the relative risk of an epileptic seizure by 1.6% [13]. Kuo-Liang et al calculated the average values of 7-day lag data for 18 environmental factors (meteorological factors and air pollutants) and found that the number of patients with epilepsy was significantly inversely related to ambient temperature [27]. Whether high ambient temperature is a protective factor against epileptic seizures is still debated. Some researchers suggest that high temperature is a protective factor against epileptic seizures. In a city in central Germany, Rakers et al found that ambient temperatures above 20 °C significantly reduced the number of epileptic seizures [14]. Our findings were consistent with most of those in the literature and suggested that only low AT was associated with an increased risk of epileptic seizures. Differences in findings may be related to differences in climates and levels of economic development among different regions. Unlike previous studies, we used AT to better represent perceived temperature and reflect heat and cold effects more realistically and objectively than simple ambient temperature.

We also found nonlinear and hysteretic effects of AT on epileptic seizures. Numerous prior studies investigating the lag characteristics of relationships between temperature and health factors have shown long lag periods between cold exposure and adverse health effects [29–31]. Our lag analysis indicated that the effect of low AT on the number of epileptic seizures appeared and was highest on the second day, and the effects lasted for approximately 6 days. These results indicate that immediate and prolonged preventative interventions are required to prevent epileptic seizures following exposure to cold weather. Few previous studies have assessed the delayed effect of temperature on epileptic seizures and quantified it.

After a stratified analysis of the number of epilepsy clinic visits by sex and age, we identified some susceptible populations. Males and younger age groups (0–14 and 15–29 years old) had a higher risk of epileptic seizures and longer duration after exposure to low AT. Previous scholars have ignored this. The findings in sensitive populations may be attributable to differences in outdoor exposure durations. Men in China are more prone to socialize and work outdoors than women and therefore are typically more exposed to cold temperatures [18]. Some studies have suggested that the stronger effects of temperature in children may be related to the fact that they participate in more outdoor activities than adults [32].

Figure 4. The single day lag effects low AT (5th, −1.5 °C) on the number of epilepsy visitors in different subgroups with reference of 17 °C.
Table 2. The single day lag effects of low AT (5th percentile, −1.5 °C) on epilepsy clinic visits, refer to 17 °C.

| Single-day(lag(s)) | Total    | male    | female | 0–14 years | 15–29 years | 30–44 years | 45–59 years | ≥60 years |
|---------------------|----------|---------|--------|------------|-------------|-------------|-------------|-----------|
| Lag0                | 1.058    | 1.063   | 1.051  | 1.113      | 1.104       | 1.047       | 1.006       | 0.866     |
|                     | (0.999 ~ 1.121) | (0.996 ~ 1.135) | (0.972 ~ 1.136) | (1.005 ~ 1.234) | (1.023 ~ 1.191) | (0.957 ~ 1.145) | (0.901 ~ 1.124) | (0.732 ~ 1.025) |
| Lag1                | 1.055    | 1.060   | 1.048  | 1.091      | 1.088       | 1.044       | 1.023       | 0.920     |
|                     | (1.015 ~ 1.097) | (1.014 ~ 1.107) | (1.008 ~ 1.105) | (1.018 ~ 1.169) | (1.034 ~ 1.146) | (0.983 ~ 1.108) | (0.950 ~ 1.102) | (0.821 ~ 1.029) |
| Lag2                | 1.052    | 1.056   | 1.045  | 1.070      | 1.074       | 1.040       | 1.038       | 0.970     |
|                     | (1.024 ~ 1.081) | (1.024 ~ 1.088) | (1.008 ~ 1.084) | (1.020 ~ 1.122) | (1.036 ~ 1.113) | (0.998 ~ 1.085) | (0.986 ~ 1.093) | (0.897 ~ 1.048) |
| Lag3                | 1.048    | 1.052   | 1.041  | 1.052      | 1.060       | 1.037       | 1.049       | 1.010     |
|                     | (1.022 ~ 1.074) | (1.023 ~ 1.081) | (1.007 ~ 1.076) | (1.007 ~ 1.099) | (1.026 ~ 1.096) | (0.998 ~ 1.078) | (1.000 ~ 1.099) | (0.941 ~ 1.084) |
| Lag4                | 1.043    | 1.047   | 1.036  | 1.038      | 1.048       | 1.033       | 1.054       | 1.038     |
|                     | (1.015 ~ 1.071) | (1.016 ~ 1.079) | (0.999 ~ 1.074) | (1.002 ~ 1.086) | (0.999 ~ 1.077) | (1.002 ~ 1.110) | (0.961 ~ 1.122) |
| Lag5                | 1.037    | 1.042   | 1.030  | 1.026      | 1.038       | 1.029       | 1.056       | 1.035     |
|                     | (1.008 ~ 1.067) | (1.009 ~ 1.075) | (0.991 ~ 1.070) | (1.000 ~ 1.077) | (0.984 ~ 1.075) | (1.001 ~ 1.115) | (0.972 ~ 1.145) |
| Lag6                | 1.031    | 1.036   | 1.023  | 1.017      | 1.028       | 1.024       | 1.054       | 1.062     |
|                     | (1.003 ~ 1.060) | (1.004 ~ 1.069) | (0.985 ~ 1.062) | (0.986 ~ 1.068) | (0.981 ~ 1.069) | (0.981 ~ 1.069) | (0.980 ~ 1.151) |
| Lag7                | 1.025    | 1.030   | 1.015  | 1.009      | 1.019       | 1.019       | 1.049       | 1.059     |
|                     | (0.999 ~ 1.051) | (1.001 ~ 1.060) | (0.981 ~ 1.050) | (0.984 ~ 1.054) | (0.980 ~ 1.061) | (0.999 ~ 1.101) | (0.984 ~ 1.140) |
| Lag8                | 1.018    | 1.024   | 1.007  | 1.003      | 1.011       | 1.015       | 1.041       | 1.049     |
|                     | (0.994 ~ 1.042) | (0.998 ~ 1.051) | (0.976 ~ 1.039) | (0.962 ~ 1.046) | (0.980 ~ 1.042) | (0.979 ~ 1.051) | (0.997 ~ 1.088) | (0.981 ~ 1.122) |
| Lag9                | 1.011    | 1.018   | 0.999  | 0.998      | 1.003       | 1.009       | 1.032       | 1.034     |
|                     | (0.987 ~ 1.035) | (0.991 ~ 1.045) | (0.967 ~ 1.032) | (0.965 ~ 1.042) | (0.972 ~ 1.035) | (0.973 ~ 1.047) | (0.986 ~ 1.079) | (0.965 ~ 1.107) |
| Lag10               | 1.003    | 1.011   | 0.990  | 0.994      | 0.996       | 1.004       | 1.020       | 1.014     |
|                     | (0.974 ~ 1.033) | (0.979 ~ 1.045) | (0.952 ~ 1.030) | (0.944 ~ 1.048) | (0.958 ~ 1.035) | (0.960 ~ 1.051) | (0.966 ~ 1.078) | (0.931 ~ 1.103) |
| Lag11               | 0.966    | 1.005   | 0.981  | 0.991      | 0.989       | 0.999       | 1.008       | 0.991     |
|                     | (0.958 ~ 1.035) | (0.962 ~ 1.049) | (0.932 ~ 1.034) | (0.926 ~ 1.062) | (0.940 ~ 1.040) | (0.941 ~ 1.061) | (0.938 ~ 1.085) | (0.886 ~ 1.109) |
| Lag12               | 0.988    | 0.998   | 0.973  | 0.988      | 0.982       | 0.994       | 0.996       | 0.968     |
|                     | (0.940 ~ 1.039) | (0.944 ~ 1.056) | (0.909 ~ 1.040) | (0.904 ~ 1.080) | (0.919 ~ 1.048) | (0.919 ~ 1.075) | (0.906 ~ 1.095) | (0.836 ~ 1.120) |

* Relative risk values are statistically significant.
The mechanism by which hypothermia affects epileptic seizures is still unclear. Several hypotheses have been proposed to explain this. First, high body temperature is mainly caused by infection. When the ambient temperature is low, people are more prone to infections and colds [33]. Increased core brain temperature can lead to increased excitability of brain neurons and epileptic seizures [34]. Second, cold-related changes in autonomic nervous function may influence the onset of epileptic seizures [35]. Third, hypothermia directly affects a person’s physiological state, but it may also indirectly cause socioeconomic status changes due to increased social stress, fatigue, and sleep deprivation, which are common triggers of epilepsy [36]. Fourth, low temperatures increase air pressure because cold air is denser than warm air. Small changes in the partial pressure of oxygen caused by atmospheric pressure may lead to relative hyperventilation, which increases neuronal excitability, triggering an epileptic seizure [37].

5. Conclusions

In this work, we used a DLNM to examine the association between AT and the number of epileptic seizure-related outpatient visits. We found that low AT increased the risk of an epileptic seizure. The single-day lag effect of AT on epileptic seizures appeared and was highest on the second day, and the effect lasted for approximately 6 days. The cumulative-day lag effect was most evident on lag days 0–10. In addition, differences were also observed between subgroups after stratifying the numbers of epilepsy clinic visits by sex and age. Low AT was more likely to affect males and younger patients (0–14 years and 15–29 years).

There are several broad implications of this work. Our study offers a more representative picture of the association between temperature and epileptic seizures in a humid subtropical region. This study provides substantial evidence of modifiable environmental risk factors for epileptic seizures that would benefit epileptic seizure prevention. Under conditions of low AT, intervention measures, such as increasing heating in public areas and reminding people with epilepsy, especially vulnerable people, to take protective measures in advance, should be implemented. At the same time, outpatient and emergency medical systems should optimize the allocation of medical resources and increase the number of outpatient appointments in corresponding departments.

This study has some limitations. First, this was an ecological study of climate factors, which inevitably may have led to ecological fallacies. It is necessary to conduct comparative studies in other regions and populations. Second, we could not entirely exclude confounders (e.g., behavioural and social risk factors such as social stress, economic level, and medication adherence). Third, meteorological data monitored at fixed sites were used to reflect individuals’ actual environmental exposure levels; this may have led to measurement errors. This effect is limited due to the absence of central heating in winter in Hefei. Fourth, this study lacked information about the severity and type of epilepsy. We were unable to assess the effect of AT on seizure severity. Future research should further explore these aspects.
| Multi-day(day(s)) | Total    | male    | female   | 0–14 years | 15–29 years | 30–44 years | 45–59 years | ≥60 years |
|------------------|----------|---------|----------|------------|-------------|-------------|-------------|-----------|
| Lag0-0           | 1.058    | 1.063   | 1.051    | 1.113      | 1.104       | 1.047       | 1.006       | 0.866     |
|                  | (0.999 ~ 1.121) | (0.996 ~ 1.135) | (0.972 ~ 1.136) | (1.005 ~ 1.234) | (1.023 ~ 1.191) | (0.957 ~ 1.145) | (0.901 ~ 1.124) | (0.732 ~ 1.025) |
| Lag0-1           | 1.117    | 1.127   | 1.102    | 1.214      | 1.201       | 1.092       | 1.030       | 0.796     |
|                  | (1.014 ~ 1.229) | (1.012 ~ 1.235) | (0.968 ~ 1.233) | (1.024 ~ 1.440) | (1.058 ~ 1.363) | (0.941 ~ 1.268) | (0.858 ~ 1.236) | (0.602 ~ 1.053) |
| Lag0-2           | 1.174    | 1.190   | 1.151    | 1.299      | 1.289       | 1.136       | 1.069       | 0.772     |
|                  | (1.043 ~ 1.322) | (1.041 ~ 1.360) | (0.981 ~ 1.350) | (1.053 ~ 1.603) | (1.102 ~ 1.508) | (0.946 ~ 1.365) | (0.853 ~ 1.340) | (0.547 ~ 1.090) |
| Lag0-3           | 1.230    | 1.251   | 1.198    | 1.367      | 1.367       | 1.178       | 1.121       | 0.780     |
|                  | (1.078 ~ 1.404) | (1.079 ~ 1.451) | (1.003 ~ 1.431) | (1.082 ~ 1.727) | (1.148 ~ 1.628) | (0.961 ~ 1.445) | (0.872 ~ 1.440) | (0.533 ~ 1.142) |
| Lag0-4           | 1.283    | 1.310   | 1.241    | 1.419      | 1.433       | 1.217       | 1.182       | 0.810     |
|                  | (1.114 ~ 1.478) | (1.118 ~ 1.535) | (1.025 ~ 1.502) | (1.105 ~ 1.823) | (1.188 ~ 1.729) | (0.978 ~ 1.515) | (0.903 ~ 1.547) | (0.538 ~ 1.217) |
| Lag0-5           | 1.331    | 1.365   | 1.278    | 1.456      | 1.487       | 1.252       | 1.248       | 0.854     |
|                  | (1.144 ~ 1.549) | (1.152 ~ 1.617) | (1.042 ~ 1.567) | (1.115 ~ 1.902) | (1.217 ~ 1.818) | (0.991 ~ 1.582) | (0.936 ~ 1.664) | (0.553 ~ 1.320) |
| Lag0-6           | 1.373    | 1.414   | 1.307    | 1.480      | 1.528       | 1.283       | 1.316       | 0.907     |
|                  | (1.167 ~ 1.614) | (1.179 ~ 1.696) | (1.050 ~ 1.627) | (1.113 ~ 1.970) | (1.232 ~ 1.896) | (0.998 ~ 1.648) | (0.967 ~ 1.791) | (0.569 ~ 1.446) |
| Lag0-7           | 1.406    | 1.457   | 1.327    | 1.494      | 1.557       | 1.308       | 1.380       | 0.961     |
|                  | (1.182 ~ 1.674) | (1.199 ~ 1.770) | (1.049 ~ 1.678) | (1.100 ~ 2.028) | (1.236 ~ 1.962) | (0.999 ~ 1.711) | (0.992 ~ 1.921) | (0.583 ~ 1.585) |
| Lag0-8           | 1.431    | 1.492   | 1.336    | 1.498      | 1.574       | 1.327       | 1.437       | 1.008     |
|                  | (1.189 ~ 1.723) | (1.212 ~ 1.836) | (1.041 ~ 1.716) | (1.082 ~ 2.074) | (1.231 ~ 2.012) | (0.996 ~ 1.767) | (1.010 ~ 2.044) | (0.591 ~ 1.721) |
| Lag0-9           | 1.446    | 1.519   | 1.335    | 1.496      | 1.579       | 1.339       | 1.483       | 1.042     |
|                  | (1.189 ~ 1.759) | (1.220 ~ 1.890) | (1.025 ~ 1.738) | (1.061 ~ 2.109) | (1.218 ~ 2.047) | (0.990 ~ 1.812) | (1.022 ~ 2.151) | (0.591 ~ 1.838) |
| Lag0-10          | 1.451    | 1.536   | 1.322    | 1.488      | 1.572       | 1.345       | 1.513       | 1.056     |
|                  | (1.180 ~ 1.783) | (1.219 ~ 1.935) | (1.000 ~ 1.746) | (1.036 ~ 2.136) | (1.195 ~ 2.067) | (0.978 ~ 1.849) | (1.022 ~ 2.240) | (0.579 ~ 1.927) |
| Lag0-11          | 1.444    | 1.544   | 1.297    | 1.475      | 1.554       | 1.343       | 1.526       | 1.047     |
|                  | (1.159 ~ 1.800) | (1.207 ~ 1.975) | (0.963 ~ 1.746) | (1.002 ~ 2.170) | (1.160 ~ 2.081) | (0.957 ~ 1.886) | (1.004 ~ 2.318) | (0.549 ~ 1.996) |
| Lag0-12          | 1.427    | 1.541   | 1.261    | 1.457      | 1.526       | 1.335       | 1.520       | 1.013     |
|                  | (1.120 ~ 1.818) | (1.176 ~ 2.020) | (0.910 ~ 1.749) | (0.953 ~ 2.230) | (1.108 ~ 2.102) | (0.919 ~ 1.938) | (0.960 ~ 2.406) | (0.497 ~ 2.060) |

* Relative risk values are statistically significant.
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Data availability statement

The data that support the findings of this study are available upon reasonable request from the authors.

Author’s contribution

Haoxiang Sun: Methodology, Software, Data curation, Writing - original draft, Writing - review & editing. Xiaoyu Zhang: Resources, Software, Writing - review & editing. Linlin Wang: Conceptualization, Software, Formal Analysis. Min Tao: Resources. Xiaosong Wang: Data curation, Funding acquisition. Kun Li: Data curation, Supervision. Shuang Zhao: Data curation, Project administration. Yue Hu: Data curation, Supervision. Huaqing Hu: Writing - review & editing, Supervision, Funding acquisition.

Declaration of interests

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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