



Low ambient temperature as the only meteorological risk factor of seizure occurrence: A multivariate study

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ARTICLE INFO

Article history:

Received 2 March 2019

Revised 16 April 2019

Accepted 19 April 2019

Available online 13 September 2019

Keywords:

Seizure
Epilepsy
Meteorology
Temperature

ABSTRACT

Background: The onset of epileptic seizures is influenced by weather, which is multifactorial. It is unknown which specific weather factors affect the occurrence of seizures.

Objectives: We studied the correlation between the onset of epileptic seizures and multiple weather parameters based on a population-based registry profile.

Methods: We determined the number of patients who visited emergency services in Taiwan diagnosed as having epilepsy. Then we used a linear regression model to analyze the monthly average number of patients who received emergency treatment for epilepsy in relation to temperature, barometric pressure, accumulated precipitation, relative humidity, and hours of sunshine. The Poisson regression model was used to analyze multiple meteorological factors in relation to the number of daily emergency visits because of epilepsy. A receiver operating characteristic curve was used to determine the cutoff temperature for the occurrence of seizures.

Results: Temperature appeared to be the robust factor for the onset of epilepsy. For every 1 °C decrease in temperature, there was a relative risk increase of 1.016 in the number of emergency visits as a result of epilepsy. Temperature lower than 18 °C had the best predictive value for seizure. Barometric pressure, accumulated precipitation, relative humidity, and the number of hours of sunshine were not related to the occurrence of seizures.

Significance: Our results suggest that temperature is the only influential meteorological factor that affects seizure occurrence.

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1. Introduction

Epilepsy is a common neurologic disease. Patients with epilepsy have unexpected occurrence of seizures. As a result, these patients live in an unsafe environment and have poor quality of life [1]. The occurrence of seizures may be affected by the interaction of intrinsic factors, such as the etiology of epilepsy and physiologic status, as well as extrinsic factors, including medication and environmental factors. Weather strongly affects the function of the human body. Previous studies of weather and epilepsy focused on relationships among climate factors,

including atmospheric temperature [2–7], atmospheric pressure [5,6,8], precipitation [5,9], and exposure to sunlight [2,9,10].

The influence of these environmental factors on the frequency of onset of epilepsy is still controversial. For example, one study suggested that lower atmospheric pressure and higher humidity are associated with elevated risk of seizure [6], whereas previous studies found no association [5,11] or even contradictory results [2]. Weather factors are inter-related, and the occurrence of seizures in correlation with one weather factor may be misleading without consideration of multifactorial interactions between weather parameters. In this study, we investigated the correlation of multiple weather factors and the occurrence of seizures.

The presentation of seizures can vary, and some ictus may be undocumented if motor convulsions do not occur. To measure seizures effectively, we selected patients who presented to emergency services because of seizures as our target population because patients with

Abbreviations: DSN, daily seizure number; MAS, monthly average seizure occurrence.

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symptomatic seizures are often treated in the emergency department [12].

2. Methods

2.1. Collection of patients and weather information

2.1.1. Collection of patients

We obtained four-year data from the claim database of the Bureau of National Health Insurance (NHI) on patients equal or more than 20-year-old, who visited emergency services, and diagnosed as having epilepsy or seizure since Jan. 2000. This database included the medical services provided to approximately 95% of the entire population of Taiwan by a network of more than 16,100 contracted medical institutions. The data encompassed encrypted patient information that included sex, birth date, diagnosis of epilepsy according to the 9th revision of the *International Classification of Diseases* (ICD-9 code 345), and date of visit to emergency services. Additionally, the NHI also includes details of pharmaceutical prescription data. Individuals with the diagnosis code of epilepsy using at least one antiepileptic drug were included for analysis, as suggested by previous studies [13]. This study was approved by National Taiwan University Hospital (NTUH) Research Ethics Committee (REC).

2.1.2. Collection of weather information

Daily weather records were obtained from the Central Weather Bureau, Taiwan, which has 25 weather surveillance stations that were assigned equally to represent whole areas in Taiwan. Weather-related parameters were collected, including temperature, accumulated precipitation, atmospheric pressure, relative humidity, and number of hours of sunshine.

2.2. Statistical analysis

The daily seizure number (DSN) was defined by determining the total number of visits to emergency services in Taiwan in one day by patients diagnosed as having epilepsy. The monthly average seizure occurrence (MAS) was defined by a summation of DSN values in one month divided by the number of days in the month.

For trend analysis, linear regression was used for correlation of MAS to monthly average temperature, atmospheric pressure, daily accumulated precipitation, relative humidity, and daily number of hours of sunshine. Because weather can fluctuate within the month, the Poisson regression model was used to analyze the DSN according to daily weather parameters, and the likelihood ratio tests obtained with Poisson regression analysis were used to assess the statistical significance of the effect of weather parameters with a significance level of 5%.

To determine the optimal cutoff temperature for predicting the occurrence of seizure, we used the receiver operating characteristic (ROC) curve, and the area under curve (AUC) was calculated for comparison.

Table 1
Demographic profile of patients visiting emergency service because of seizure.

Age group	Female		Male		Total	
	n	%	n	%	n	%
20–29	1618	22.5	2817	19.6	4435	20.6
30–39	1228	17.1	2819	19.6	4047	18.8
40–49	1183	16.5	2942	20.5	4125	19.2
50–59	783	10.9	1876	13.1	2659	12.3
60–69	853	11.9	1631	11.4	2484	11.5
70–79	913	12.7	1615	11.2	2528	11.7
>79	604	8.4	664	4.6	1268	5.9
Total	7182		14,364		21,546	

Table 2
Distribution of atmospheric variables during the study period.

Day measurement	Mean	Standard deviation	Minimum	Maximum
Temperature (°C)	21.8	6.3	−6.8	33.1
Atmospheric pressure (hPa)	973.3	86.6	618.7	1030.6
Precipitation (mm)	6.3	22.9	0	774.5
Cumulative sun expose (h)	4.9	3.9	0	13.2
Humidity (%)	79.1	10.4	13	100

3. Results

3.1. Descriptive analysis

The total number of patients who visited emergency services because of seizure in the study period was 21,546 (Table 1). Of these, 14,364 (66.7%) were male adults, and 7182 (33.3%) were female adults. Younger patients had more visits than older patients. The daily average number was 14.75 cases per day. Table 2 shows the distribution of meteorological parameters. Mean temperature, precipitation, and humidity were 21.8 °C, 6.3 mm per day, and 79.1%, respectively. Because of its location, the northern part of Taiwan has a subtropical monsoon climate, and the southern part has a tropical monsoon climate.

3.2. Linear regression analyses

Figs. 1–3 show the trend of MAS along with monthly average temperature, atmospheric pressure, and precipitation. The trend of MAS repeated each year, suggesting the effect of seasonal variations. Fig. 1 shows an opposite trend of MAS associated with temperature. The

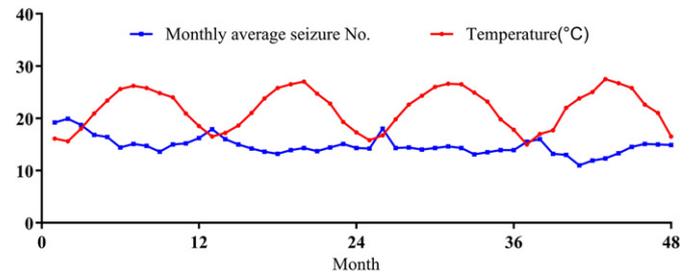


Fig. 1. Trend of temperature and monthly average seizure occurrence (MAS).

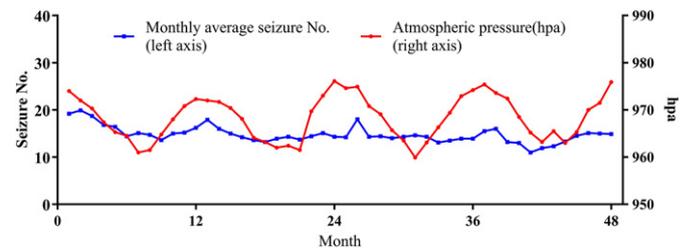


Fig. 2. Trend of pressure and monthly average seizure occurrence (MAS).

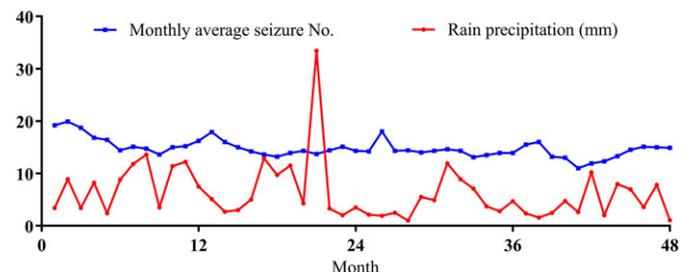


Fig. 3. Trend of precipitation and monthly average seizure occurrence (MAS).

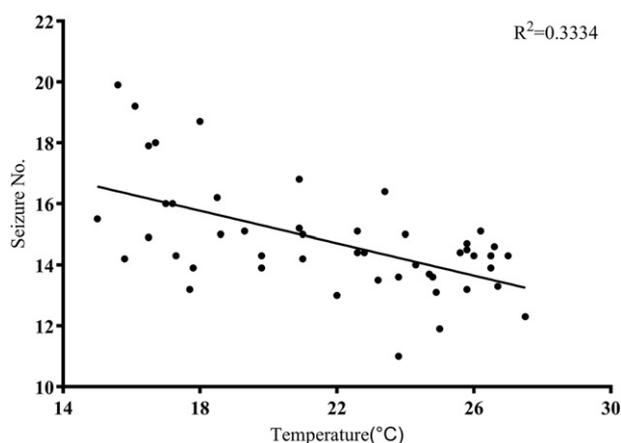


Fig. 4. Scatter plot of monthly average seizure occurrence (MAS) against temperature.

peak of MAS either coincided with or preceded the coldest month. On the contrary, MAS was similar in warmer months, forming a basin shape rather than a valley. Linear regression analysis of the overall results between MAS and temperature showed significant correlation (Fig. 4; $r^2 = 0.33$, $p < 0.0001$). For atmospheric pressure (Fig. 2), the peak of MAS usually occurred one or two months after the peak of atmospheric pressure. The coefficient of determination was also significant but less than that for temperature (Fig. 5; $r^2 = 0.18$, $p = 0.0026$). Correlation of MAS with precipitation (Fig. 3), relative humidity, and the number of hours of sunshine (not shown) was much lower. In summary, temperature and atmospheric pressure had much clearer correlation with MAS.

3.3. Poisson regression analyses

In univariate analysis of DSN to daily weather parameters by Poisson regression (Table 3), a temperature decrease of 1 °C showed significant correlation with DSN with a relative risk of 1.01. Increased atmospheric pressure by 1 hPa also showed significant correlation with DSN with a relative risk of 1.007, whereas increased precipitation by 1 mm had a relative risk of 0.998. In multivariate analysis, only temperature showed an association with DSN, with a 1 °C decrease correlating with a relative risk of 1.016.

3.4. Cutoff temperature for epilepsy prediction

Because MAS showed a peak only around the coldest months, we hypothesize that there may be a cutoff temperature that dramatically

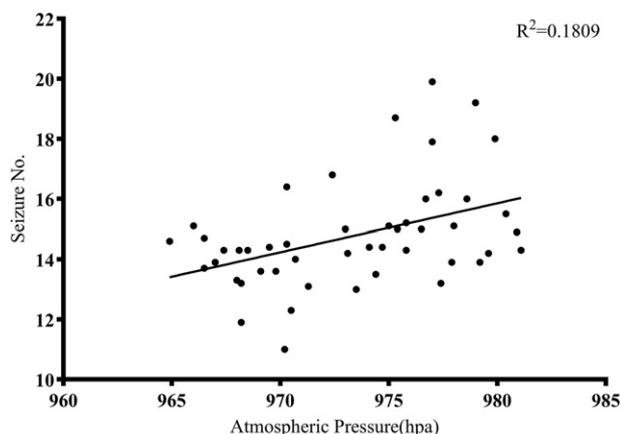


Fig. 5. Scatter plot of monthly average seizure occurrence (MAS) against atmospheric pressure.

Table 3

Relative risk (RR) of seizure occurrence for ambient temperature, atmospheric pressure, rain precipitation, sun expose, and humidity.

Poisson regression	Metrological factors	RR	(95% CI)	p-Value
Univariate	Temperature (decreasing 1 °C)	1.010	1.007–1.014	<0.0001
	Atmospheric pressure (increasing 1 hPa)	1.007	1.005–1.010	<0.0001
	Precipitation (increasing 1 mm)	0.998	0.997–0.999	0.0141
	Sun expose (h)	1.004	0.996–1.005	0.8523
	Humidity (%)	0.998	0.996–1.000	0.1229
	Temperature (decreasing 1 °C)	1.016	1.008–1.024	<0.0001
Multivariate	Atmospheric pressure (increasing 1 hPa)	0.997	0.992–1.003	0.3660
	Precipitation (increasing 1 mm)	0.999	0.998–1.000	0.0578
	Sun expose (h)	1.007	0.999–1.014	0.0961
	Humidity (%)	0.999	0.996–1.002	0.4834

increases the risk of seizure. We then analyzed temperature as two levels, for atmospheric temperature greater or less than a specific value. The AUCs were 60.8%, 61.8%, 60.5%, 58.9%, and 58.2% for 17 °C, 18 °C, 19 °C, 20 °C, and 21 °C, respectively. We then performed likelihood ratio tests with Poisson regression analysis using binary variant <18 °C versus ≥ 18 °C to DSN. The correlation was significant ($p < 0.0001$), and the relative risk was 1.12 when the temperature was less than 18 °C.

4. Discussion

4.1. Meteorological factors and seizure

This study addressed the relationship between the occurrence of seizures and meteorological variables. We observed a correlation between MAS and both temperature and atmospheric pressure. However, weather can vary significantly, even within one month, and the monthly average data did not precisely reflect the actual correlation between weather factors and the occurrence of seizures. Poisson regression of daily weather parameters to DSN much more accurately showed the influence of meteorological factors. Multivariate analysis showed that temperature was a robust factor. Barometric pressure, precipitation, humidity, and the number of hours of sunshine per day were not determinant factors for seizure after adjustment.

The interaction between weather factors is complex. Cold temperatures can create areas of high barometric pressure because cold air has greater density than warm air and can increase air pressure. Humidity and precipitation usually follow seasonal patterns determined by geographic factors. For example, in Central Europe, humidity is often higher in winter, whereas, in Taiwan, precipitation is usually lower in summer. These factors may reflect the underlying season and temperature in the area. At high latitudes, where there are dramatically fewer hours of sunshine in winter, the daily duration of sunshine has negative correlation with seizure occurrence [9,10]. However, we do not know whether the duration of sunshine affected the occurrence of seizures or whether the relevant factor was low temperature in winter. In our study, temperature was the only factor associated with seizures after statistical adjustment.

4.2. Temperature

Our finding of the potential effect of low temperatures on the occurrence of seizures is supported by numerous studies in several countries [3–7]. Rakers et al. [6] found that a temperature of more than 20 °C dramatically decreased the odds ratio of seizure occurrence. Our study identified 18 °C as a better cutoff point to determine seizure risk. These studies show that there may be a temperature threshold that significantly increases seizure risk. In an animal model of sudden unexpected death in epilepsy (SUDEP), rats exposed to cold temperatures

(14 ± 1 °C) had a significantly higher heart rate than that under normal temperature (22 ± 1 °C) [14]. Because cold weather is also a well-known risk factor for cardiovascular disease [15], cold-associated changes in autonomic function could influence seizure occurrence [16], especially when the room temperature is less than 18 °C.

4.3. Limitations

This study was limited because it used indirect measurements of seizure occurrence based on the number of visits to emergency services, which may underestimate the true incidence of seizures. Although the inclusion criteria included diagnosis of epilepsy and use of antiepileptic drug, patients diagnosed as having neuralgia or psychiatric disorders may still receive these kinds of medication. However, the general trend of epileptic occurrence was unlikely to be influenced by the minority of nonepileptic events, and our study could reflect clinically critical epilepsy that deserves attention. In addition, although this is a database study, the weather factor is objective and unlikely to be biased by retrospective review.

5. Conclusion

In this study, environmental temperature was the only determinant factor for seizure occurrence. The findings can be used to enhance strategies for adjustment of antiepileptic medication. Future studies are needed to identify autonomic effects in association with temperature change and seizure occurrence.

Conflict of interest

The authors have no relevant conflicts of interest to declare.

Funding

This work received no specific funding.

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