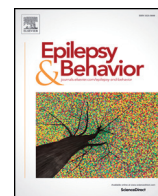


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Influence of weather on seizure frequency – Clinical experience in the emergency room of a tertiary hospital

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ABSTRACT

Introduction: Some patients with epilepsy identify weather as a typical seizure trigger. However, it is yet to be confirmed. Thus, we aimed to evaluate possible relationships between daily meteorological conditions and the daily incidence of seizures.

Methods: This was a retrospective single center study that included adult patients who were admitted to the emergency room of a tertiary hospital in Lisbon, with a seizure, between January and December 2015. The influence of temperature, atmospheric pressure, relative humidity, wind, precipitation, sunlight duration, and the seasons on seizure frequency was evaluated.

Results: Three hundred seven seizure episodes were included (from 286 patients) in a total of 365 days, 117 (38.1%) first unprovoked seizures and 190 (61.9%) with previous seizure episodes. There were 82 days with higher incidence of seizures (≥ 2) and 171 days without seizures. We found a statistical significant relation between lower ambient temperatures, higher atmospheric pressure, and higher maximum humidity with days with two or more seizures. We also found a statistically significant higher incidence of seizures in the winter days (p-value: 0.001) and in days with lower daylight duration (10.8 vs. 12.7 h; p-value: 0.0001). With the exception of humidity, these findings remained true when analyzing the subgroup of patients with previous seizures, but there was no significant difference in the subgroup of first unprovoked seizures.

Conclusions: Our results support the possible influence of the weather on seizure frequency in the overall admissions of the emergency department of a tertiary hospital. In particular, these findings suggest that winter conditions, such as, lower ambient temperatures, higher atmospheric pressure, higher humidity, and reduced sunlight exposure, may have impact in the occurrence of higher incidence of seizures in patients with epilepsy.

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1. Introduction

The unpredictability of seizures is a concern of relevant impact in people with epilepsy. Many surveys indicate that a substantial proportion of these patients identify environmental, physical, or emotional factors that are associated with an increase in seizure frequency [1–7]. Stress is the most frequent trigger reported by patients with epilepsy, followed by sleep deprivation and tiredness. For a better seizure control, in addition to anticonvulsant therapy, avoiding seizure triggers may be important for many patients. The recognition and understanding of these triggers is therefore of significant importance.

In spite of some patients report of the weather, or weather changes, as one of their possible seizure triggers [1, 7], the evidence supporting a significant influence of specific meteorological parameters in seizure

frequency is scarce and inconsistent [8–16]. Thus, it is still unclear what the influence of weather is on the general risk of seizures. The aim of our study was to assess if daily weather conditions and variations were associated with an increase in seizure frequency.

2. Material and methods

2.1. Type of study

This was a retrospective single-center study, based on the review of medical records of all patients observed in the emergency room assessed by a neurologist, in a tertiary hospital in Lisbon, from January to December 2015. The incidence of seizure was recorded every day.

2.2. Population inclusion and exclusion criteria

Patients were included in the study if they fulfilled the following criteria: 1) age older than 18 years, 2) admitted to the emergency

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room with an episode clinically compatible with a seizure, including patients with a first unprovoked seizure. Acute symptomatic seizures and seizures in noncompliant patients with epilepsy or patients with changes in antiepileptic medication in the last 3 months were excluded. In patients with more than one seizure in a 24-hour period, only one seizure was considered.

This study was approved by all relevant ethics committees.

2.3. Data collected

2.3.1. Patients

Demographic and clinical characteristics were collected for all patients, including age, gender, seizure type (generalized tonic-clonic, focal with impairment of consciousness, or focal without impairment of consciousness), and seizure time.

2.3.2. Meteorological data

For each day, the following data were collected from the Portuguese Institute for Sea and Atmosphere, I. P. (IPMA, IP): minimum, maximum, and mean values of daily ambient temperature ($^{\circ}\text{C}$); mean value of daily atmospheric pressure (hPa); minimum, maximum, and mean values of daily relative humidity (%); mean and maximum values of daily wind (km/h); and total daily precipitation (mm).

Additionally, for each day, the total hours of daylight duration was collected as well.

2.4. Statistical analysis

A day with a higher incidence of seizures was defined as a day with more seizures than the daily average for the whole study period. We decided to use this definition to allow the inclusion of days with a higher than average frequency of seizures and exclusion of days with the mean number of seizures. By doing so, we wanted to compare days with extreme values – no seizures versus higher number of seizures – and see if the meteorological parameters were significantly different in the latter days.

Considering the whole year, we sorted out four groups: days without seizures, days with at least one seizure, days with higher seizure incidence, and a final group that includes the days before those with a higher seizure incidence.

We searched for an association between weather changes and seizures by a) comparing meteorological parameters between days with at least one seizure and days without seizures, b) comparing meteorological parameters between days with higher seizure incidence and days without seizures, c) comparing meteorological parameters between days with higher seizure incidence and the preceding days, and d) comparing the absolute 24-hour variation value of all the meteorological data between days with higher seizure incidence and days without seizures.

Finally, we compare the seizure frequency between the four seasons of the year (winter, spring, summer, and autumn).

We performed the same analysis for the two subgroups: patients with first unprovoked seizure and patients with previous seizures.

2.5. Statistical tests

The program SPSS 20.0 was used to conduct all statistical tests. Statistical significance of relationships was assessed with p -value < 0.05 .

Mann–Whitney tests were applied to compare medians between days with higher seizure incidence and days without seizures.

Wilcoxon signed rank tests were used to compare medians between days with higher seizure incidence and the previous days.

Kruskal–Wallis H test was first performed to assess seizure frequency main effect within the four seasons of the year. Then paired Mann–Whitney tests were used to compare the seasons.

3. Results

In the 365-day period analyzed, from a total of 3544 urgency episodes, 532 were seizures, of which 225 were excluded, since they occurred in patients with unstable antiepileptic therapy (noncompliant patients or those with changes in antiepileptic medication in the last 3 months) ($n = 155$) or were acute symptomatic seizures ($n = 70$). A total of 307 seizures were included, the majority (87.9%) tonic-clonic generalized seizures and 81.4% diurnal seizures (Table 1).

These occurred in a total of 286 patients, 165 males (57.5%). Mean age was 54.1 ± 20.6 years. The mean number of seizures per patient and seizures per day were 1.07 ± 1 (maximum 3) and 0.84 ± 1 (maximum 5), respectively.

The group of days with no seizures comprises nearly half of the year ($n = 171$, 46.8%), and the group with at least one seizure (≥ 1 seizures) included the other 194 (53.2%) days. On the other hand, 82 (22.5%) days had two or more seizures (≥ 2 seizures), so they represented the group with higher seizure incidence. The maximum number of seizures per day was 5 ($n = 3$, 0.82%).

In Table 2 are the results of the comparison of the meteorological data between days without seizures and days with the following: A) at least one seizure and B) higher incidence of seizures. Of relevance, there was a statistically significant lower temperature (maximum, minimum, and average) only in the days with higher seizure frequency (18.6 vs. 22.4 $^{\circ}\text{C}$, p -value: 0.004; 11.3 vs. 14.2 $^{\circ}\text{C}$, p -value: 0.001; and 15 vs. 17.5 $^{\circ}\text{C}$, p -value: 0.002) (Fig. 1.a). In addition, we found a statistically significant higher atmospheric pressure (1022.6 vs. 1018.6 hPa; p -value: 0.003) (Fig. 1.b) and higher maximum humidity (97 vs. 94%; p -value: 0.043) (Fig. 1.c) only in days with two or more seizures. However, when comparing days without seizures with days with at least one seizure there were not a statistically significant difference between them.

The number of hours of daylight duration was significantly lower on days with at least one seizure (11.8 vs. 12.7 h; p -value: 0.019) and in days with two or more seizures (10.8 vs. 12.7 h; p -value: 0.0001).

No difference was found in any meteorological data between the days with higher incidence of seizures and the days before these.

As shown in Fig. 2, the seizure distribution by season revealed a peak in winter (34.5%) and a nadir in spring (19.2%). Thereafter, seizure counts progressively increased: 21.8% in summer and 24.4% in autumn.

The Kruskal–Wallis H test revealed a statistically significant difference in seizure frequency between the different seasons, with a main effect of $\chi^2(2) = 14.655$, p -value: 0.002 (with a mean rank seizure frequency of 214.76 for winter, 161.15 for spring, 174.27 for summer, and 183.15 for autumn) (Fig. 2). Posthoc comparison of winter seizure frequency with those of the other seasons revealed significant difference for spring ($p = 0.0003$), summer ($p = 0.004$), and autumn ($p = 0.038$). The difference between the percentage averages in winter and spring was 28.4%.

In the subgroup of first unprovoked seizures, with 117 episodes, the analysis revealed no statistically significant difference between days without seizures and days with higher seizure incidence (Table 3). However, in the other subgroup, with 190 seizures in patients with previous seizures, the same statistical significant difference described above for the all group was identified, with the exception for humidity (p -value: 0.098) (Table 4).

Table 1
Seizures characteristics, $n = 307$.

	n (%)
First seizure	117 (38.1)
Nocturne seizure	57 (18.6)
Seizure type	
Generalized tonic-clonic	270 (87.9)
Focal with impairment of consciousness	18 (5.9)
Focal without impairment of consciousness	19 (6.2)

Table 2

Comparison of the meteorological data between days without seizures and: A) days with at least one seizure; B) days with higher incidence of seizures.

	Days without seizures (n = 171)	A		B	
		Days with ≥ 1 seizure (n = 194)	p-Value*	Days with ≥ 2 seizures (n = 82)	p-Value*
<i>Ambient temperature, °C</i>					
Minimum	14.2 (10.8–16.9)	13.0 (10.0–16.4)	0.067	11.3 (8.6–15.8)	0.001
Maximum	22.4 (18.5–27.3)	20.6 (16.5–26.4)	0.055	18.6 (15.7–24.5)	0.002
Average	17.5 (14.3–20.9)	16.4 (13.0–20.4)	0.076	15 (11.5–18.9)	0.002
<i>Relative humidity, %</i>					
Minimum	49 (39–60)	49 (38–63.5)	0.510	52.5 (41–63.5)	0.198
	49.8 ± 17.8	51.5 ± 19.8		52.9 ± 18.9	
Maximum	100 (92–100)	100 (91.8–100)	0.709	100 (97.5–100)	0.043
	94.2 ± 10.5	94.2 ± 10.8		96.7 ± 6.8	
Average	76 (66–85)	77 (65–88.3)	0.527	80 (70–90)	0.152
	75 ± 15.4	76 ± 16.1		78.1 ± 14.4	
<i>Atmospheric pressure, hPa</i>					
Average	1018.6 (1016.2–1023.1)	1019.1 (1016.1–1026.2)	0.286	1022.6 (1017–1029)	0.003
<i>Wind, km/h</i>					
Maximum	10.6 (8.1–12.7)	10.8 (8.6–13.5)	0.481	10.1 (8–13.4)	0.724
Average	3.3 (2.6–4.1)	3.4 (2.7–4.3)	0.333	3.5 (3.5–4.3)	0.754
<i>Precipitation, mm</i>					
Total	1.4 ± 4.9	1.4 ± 4.5	0.378	0.9 ± 2.4	0.886

Values presented correspond to medians (interquartile range), except for relative humidity which is presented with both median and mean ± standard deviation values and precipitation, which is presented with the mean ± standard deviation values.

* p-Value of Mann–Whitney tests performed.

4. Discussion

The present study revealed a significant relationship between the occurrence of days with a higher incidence of seizures in the overall admissions of an emergency department and some weather factors, namely temperature, atmospheric pressure, and humidity. Of note, these findings did not hold true for days with at least one seizure, reinforcing the idea that weather conditions can influence a higher seizure frequency.

When performing the same analysis for the two subgroups of seizures separately, the same results remained true only for days with seizures in patients with previous episodes. This difference is indicative that patients with epilepsy have a higher susceptibility to weather conditions and supports its possible influence in reducing their epileptic threshold. Patients with a first unprovoked seizure represent a more heterogeneous group and only some of them really have epilepsy.

4.1. Ambient temperature

Concerning the effects of temperature, our findings suggest a relationship between low temperatures and seizures. Indeed, the influence of low temperatures and winter days with the increase of seizure risk has been already suggested in previous studies [10, 13]. Motta et al. analyzed electroencephalograph (EEG) recordings in different seasons and showed that the smallest proportion of normal EEG recordings was noted in winter, and epileptiform discharges were noted more frequently in winter [13]. Similarly, Danesi et al. recorded EEG in various seasons among patients susceptible to photic stimulation and found that epileptiform discharges were most prevalent in winter. This author proposed that these unclear results might be related with the lower air temperature and insolation in winter [10]. Recently, in line with our findings, Rakers et al. found that high ambient temperatures of >20 °C decreased seizure risk by 46% in the overall study population (OR: 0.54, 95% CI: 0.32–0.90) [16]. Likewise, Ruegg et al. also described the same protective effect of high temperature in the incidence of status epilepticus [14].

The reproducibility of all these findings toward the same direction may suggest a significant impact of low temperature and/or winter days in the pathophysiology of seizures initiation.

4.2. Atmospheric pressure

We found a possible effect from higher atmospheric pressure on seizure frequency. However, these results are in disagreement with others previously reported [11, 16]. Doherty et al. found no evidence of a relation between atmospheric pressure changes and seizure occurrence in an epilepsy monitoring unit [11]. On the other hand, Rakers et al. found that for every 10.7-hPa lower atmospheric pressure, seizure risk increased in the entire study population by 14% (OR: 1.14, 95% CI: 1.01–1.28) [16]. In spite of the exact mechanisms for this being still unclear, a study in rats has shown that lowering the atmospheric pressure in an air pressure chamber increased neuronal activity [17].

4.3. Relative air humidity

Finally, we also found a significant relation between higher humidity levels and seizures. This findings were similar to those previously described by Rakers et al., who reported that a high relative air humidity of >80% increased seizure risk in the entire study population by up to 48% (OR: 1.48, 95% CI: 1.11–1.96) 3 days after exposure [16]. In contrast to our results, Ruegg et al. described that a high relative air humidity is a protective factor for epileptic seizures; however, this study was conducted on patients with status epilepticus admitted to the intensive care unit [14].

4.4. Winter

Grouping all the above-mentioned results, we can say that lower temperatures, higher atmospheric pressure, and higher humidity have in common most frequently occurring in winter days. In fact, we found a statistically significant increased seizure frequency in winter compared with all the other seasons (Fig. 2), revealing a seasonal distribution of seizures. Besides, the average difference between winter and

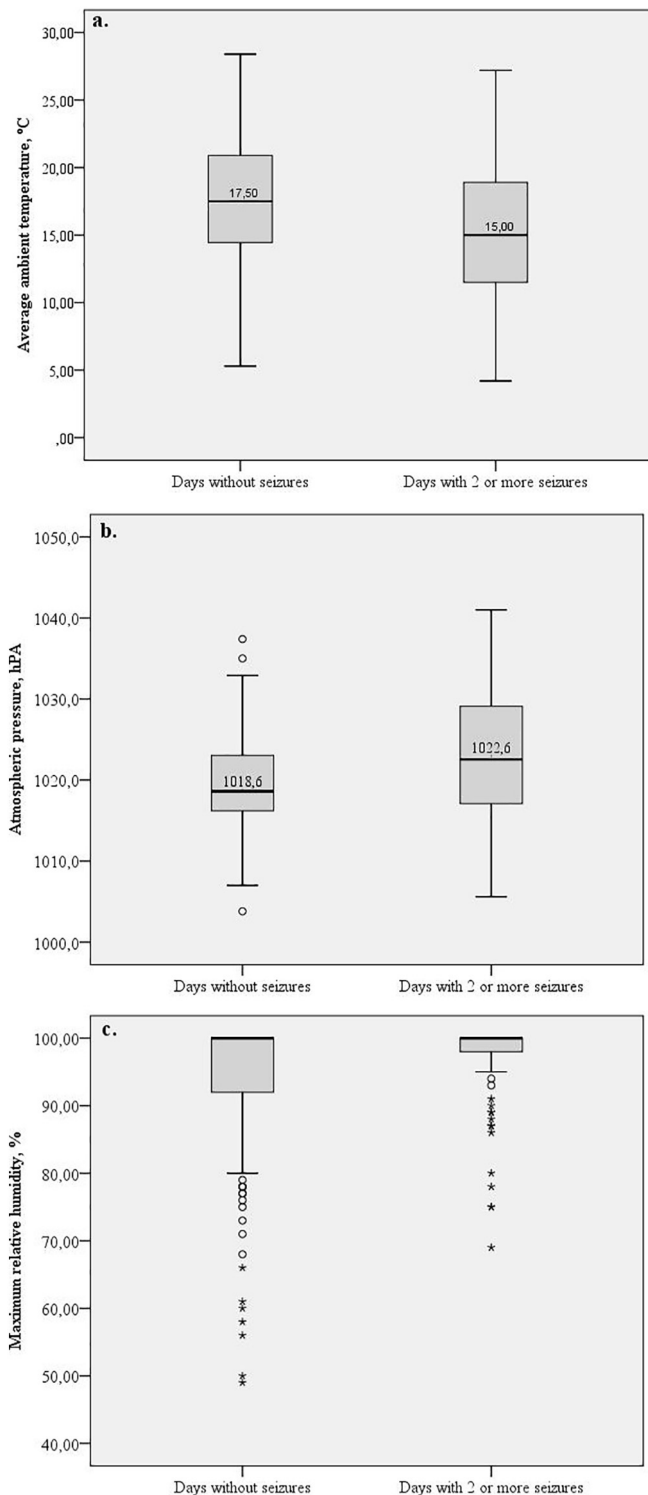


Fig. 1. Boxplot of the three meteorological parameters with statistical significance in seizures incidence: a. ambient temperature, b. atmospheric pressure, and c. maximum relative humidity. Comparison between days without seizures and the days with higher incidence of seizures.

spring, accounting for 28%, is substantial. These results are in line with those of Clemens et al. who found a similar difference of 31.1% between January and August [18].

We can speculate that other nonmeteorological factors related to winter days might exist, which could also increase the risk of seizure occurrence in our study population. One possible factor could be the lower duration of sun exposure during winter days, as already proposed by

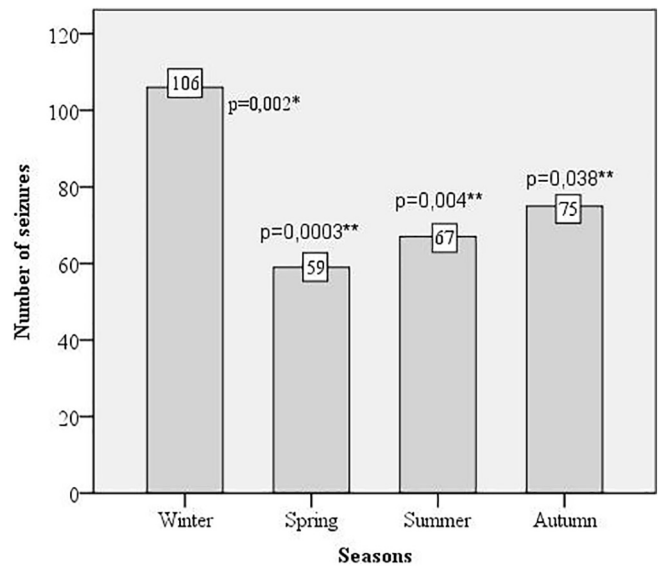


Fig. 2. Distribution of seizures for each season in the year. *p-Value of Kruskal–Wallis *H* Test for comparison between the four seasons. **p-Value of Mann–Whitney posthoc comparison of winter with those of the other seasons.

Danesi et al. Our analysis revealed a lower daylight duration in days with higher incidence of seizures (10.8 vs. 12.7 h; p-value: 0.0001). These findings are in agreement with what was suggested by Danesi et al. – brain excitability is possibly related with the number of hours exposed to sunlight [10]. Baxendale also found that epileptic seizures were less likely to occur in bright sunny days, than in dull days [19]. One possible explanation could be the seasonal fluctuations of melatonin secretion, with higher levels in winter [20, 21]. However, in spite of some of the reports found that melatonin can raise the risk of seizures, the effect of this hormone on seizure frequency is still controversial [22]. Another potential reason could be the lower vitamin D levels, which fall significantly during winter, as already suggested in other

Table 3

Comparison of the meteorological data including only the subgroup of first unprovoked seizures, between days without seizures and days with higher incidence of seizures.

	Days without seizures (n = 266)	Days with first unprovoked seizures (n = 99)	p-Value*
<i>Ambient temperature, °C</i>			
Minimum	13.7 (10.4–16.9)	13 (10.1–16.2)	0.268
Maximum	21.9 (17.5–27.2)	20.6 (17–26.3)	0.349
Average	17.2 (13.5–20.9)	16.4 (13.4–19.6)	0.270
<i>Relative humidity, %</i>			
Minimum	49 (37.8–61)	49 (39–62)	0.954
	50.8 ± 19.6	50.3 ± 17	
Maximum	100 (92–100)	100 (94–100)	0.630
	94 ± 10.9	94.9 ± 9.6	
Average	76 (65–88)	77 (67–88)	0.836
	75.4 ± 16.1	75.9 ± 14.9	
<i>Atmospheric pressure, hPa</i>			
Average	1018.7 (1016.2–1024.1)	1019.2 (1016.1–1026.1)	0.400
<i>Wind, km/h</i>			
Maximum	10.7 (8.2–13.5)	10.3 (8.8–13)	0.693
Average	3.4 (2.7–4.2)	3.2 (2.6–4.2)	0.456
<i>Precipitation, mm</i>			
Total	1.4 ± 4.8	1.2 ± 4.4	0.916

Values presented correspond to medians (interquartile range), except for relative humidity, which is presented with both median and mean ± standard deviation values and precipitation, which is presented with the mean ± standard deviation values.

* p-Value of Mann–Whitney tests performed.

Table 4

Comparison of the meteorological data including only the subgroup of seizures with previous episodes, between days without seizures and days with higher incidence of seizures.

	Days without seizures (n = 226)	Days with seizures with previous episodes (n = 139)	p-Value*
<i>Ambient temperature, °C</i>			
Minimum	14.1 (10.9–16.9)	12 (9.2–16.5)	0.011
Maximum	22.3 (18.6–27.4)	19.6 (15.9–26.1)	0.006
Average	17.6 (14.3–20.9)	15.2 (12.1–20.2)	0.011
<i>Relative humidity, %</i>			
Minimum	48 (36–60)	50 (40–66)	0.164
	49.5 ± 17.7	52.7 ± 20.5	
Maximum	100 (92–100)	100 (93–100)	0.098
	93.9 ± 10.6	94.7 ± 10.6	
Average	76 (65–86)	79 (67–89)	0.163
	74.7 ± 15.5	76.9 ± 16	
<i>Atmospheric pressure, hPa</i>			
Average	1018.4 (1015.9–1023.2)	1019.6 (1016.6–1027.3)	0.021
<i>Wind, km/h</i>			
Maximum	10.7 (8.6–13)	10.4 (8.2–13.7)	0.770
Average	3.3 (2.6–4.2)	3.5 (2.7–4.4)	0.124
<i>Precipitation, mm</i>			
Total	1.4 ± 5	1.3 ± 4.1	0.520

Values presented correspond to medians (interquartile range), except for relative humidity, which is presented with both median and mean ± standard deviation values and precipitation, which is presented with the mean ± standard deviation values.

* p-Value of Mann–Whitney tests performed.

studies [18]. Indeed, a few studies have demonstrated a possible anti-convulsant effect of vitamin D [23, 24], so the seasonal variation in seizures could be viewed as an indirect effect of low levels of vitamin D, which could be involved in the pathophysiology of seizure initiation.

Whether these meteorological and nonmeteorological factors related to winter work independently or synergically is unclear. Based on our findings, we believe that the multitude of variables associated with winter had contributed together to the increase of seizure incidence in our study population.

4.5. Study strengths and limitations

One of the strengths that our study has is the inclusion of a broad population comprising outpatients with or without previously diagnosed epilepsy. It also involved the analysis of an entire year period, which allowed the inclusion of all the seasons of the year and weather variability.

One of the limitations of our work is its retrospective nature, basing the diagnosis of a seizure only in clinical data described in each day. Another limitation is that the seizure frequency was based only in the admissions to the emergency department. Therefore, the present study cannot make conclusions about the global seizure frequency. However, we can make some conclusions about the seizure frequency in the global emergency admissions of the hospital in one entire year.

5. Conclusions

In this study, the incidence of seizure admissions in an emergency room was higher in relation with the following: a) lower temperatures, higher atmospheric pressure, and higher humidity; b) days with lower sunlight duration; and c) winter days.

We suggest that winter associated factors (both meteorological and nonmeteorological) contribute to a higher seizure incidence. For instance, reduced light exposure could influence seizure seasonality by inducing hormonal fluctuations, like melatonin or vitamin D.

Our findings are important as they support the subjective idea of some patients that seizure risk increases with certain weather

conditions. However, besides the apparent consensual and unexplained effect of low ambient temperature on seizures, all the other meteorological parameters appears to be more controversial. These contradictory results remain to be clarified. Few reports still exist in the literature to elucidate the impact of weather on epilepsy. Furthermore, very different study populations and clinical scenarios in all those existing studies make it even more difficult for its interpretation and comparison.

Investigating potential relationships between environmental factors and the occurrence of seizures is important, as it may contribute to a better understanding of mechanisms underlying the generation of seizures and could potentially suggest behavioral management strategies for reducing seizure occurrence. Moreover, the seasonal distribution of seizures should be considered in assessing the efficacy of antiepileptic drugs.

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Conflicts of interest

None.

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