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Experimental simulation of the effects of increased geomagnetic activity upon nocturnal seizures in epileptic rats

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Abstract

This experiment was designed to simulate experimentally the specific parameters of geomagnetic activity that evoke epileptic seizures. The numbers of overt limbic seizures (rearing, paroxysmal forelimb clonus and falling) in a population of epileptic rats were recorded nightly for 65 successive days between 0200 and 0400 h during red light conditions. On some nights an experimental 7 Hz magnetic field whose magnitudes shifted in successive steps from zero to approximately 50 nT every 3 min was presented. The partial regression coefficients from the analysis indicated that either the presence of the 'synthetic' geomagnetic activity or increased magnitudes of the daily, natural geomagnetic activity (regional range approximately 10–70 nT) during the observational period significantly ($P < 0.05$) increased the proportion of nightly seizures. The effect sizes (6–8%) for both magnetic sources were comparable and additive. Concerted efforts to experimentally simulate the temporal profiles of geomagnetic activity may help reveal the neuromechanisms by which biobehavioral changes during geomagnetic perturbations occur within susceptible populations. © 1997 Elsevier Science Ireland Ltd.

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Several studies have suggested a statistically significant, positive association between increases in the numerical indices of geomagnetic activity and the numbers of overt seizures or suspected subclinical electrical seizures in populations of humans who display partial complex (temporal lobe) epilepsy [4,7,10,12,16,18,19] and in populations of rodents in which chronic limbic epilepsy has been induced experimentally [2,3,13]. The effect sizes of these associations (or the amount of shared variance between the geomagnetic activity and numbers of seizures) usually ranged between 10 and 25% which is equivalent to correlation coefficients between 0.33 and 0.50. Because the typical indices of geomagnetic activity reflect only the magnitude (in nanotesla, nT) of the displacement of the most disturbed component of the magnetogram from a station or aggregate of stations, the specific parameters of the temporal fluctuations in geomagnetic activity which evoke limbic epileptic seizures are not clear.

Although brief (1 h), single exposures to 60 Hz power frequency magnetic fields or to intermittent reversals of the polarity of steady-state magnetic fields [20,21] have evoked significant suppressions of the nocturnal levels of the intrinsic antiepileptic compound, melatonin [1,6,26] both the field strengths and wave structure of most previous experimental conditions have not simulated natural geomagnetic activity. In the pursuit of these optimal parameters, we [9,11,13,17,22] found that a ripple frequency, such as a 7 or 45 Hz square wave, whose amplitude increased incrementally and then decreased incrementally over successive, 4 min periods, evoked significant increases in the proportions of nocturnal seizures in chronic epileptic rats. The present study was designed to discern if an experimentally generated magnetic field could simulate vectorially (direction and magnitude) the correlations between the incidence of spontaneous seizures and natural geomagnetic activity.

The latter half of the year 1995 was considered optimal to test the hypothesis because very few days of geomagnetic activity with daily values exceeding 40 nT (or a daily 'A' value of 20 at the Fredericksburg station), which has been shown to increase seizure risk, was expected. The predominance of quiet days was considered conducive for discrimi-

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nating the effects from presenting the synthetic geomagnetic field from the effects due to natural geomagnetic variation. A total of 12 male Wistar rats, 180 days of age at the beginning of this study, were housed singly in plastic cages within a temperature controlled room [9]. Chronic limbic epilepsy had been induced about 3 months previously by a single systemic injection of lithium chloride (3 mEq/kg) and 4 h later by 30 mg/kg of pilocarpine [15]. Food and water were available ad libitum.

The 12 cages containing the rats were placed in an aluminum rack (four cages per row) that was wrapped around its 112 × 125 cm perimeter by 72 turns of 30 American wire gauge (AWG). The experimental field was generated by a custom designed generator that was set to increase the intensity of a 7 Hz sine wave of the magnetic field from 0 to the maximum value in 3, 30 s steps and to then to decrease the intensity from the maximum value to 0 in 3, 30 s steps (after a 30 s maximum plateau); the peak-to-peak duration was 3 min (5.5 mHz). Direct measurement by a Metex 3800 multimeter and magnetic sensor probe (Electric Field Measurements) indicated that the strength of the median, maximum value was 50 nT (0.5 milligauss) within the central cages and about 70–100 nT along the inner periphery of the coil. When the experimental fields were not operative the 60 Hz background was less than 10 nT (limits of meter).

The light/dark cycle was 12:12; light onset was 0700 h (local time). During the light cycle, the ambient lighting (5 × 40 W cool white fluorescent lamps) ranged between a maximum of 3000 lx in the upper cages to 100–1000 lx in the lower cages. During the entire ‘dark’ cycle the room was illuminated by a single overhead (1.25 m to the closest cage) red 40 W fluorescent light. A Gossen electronic luxmeter indicated maximum values between 15 (upper cages) and 7 lx (lower cages). Between 0200 and 0400 h local time, a programmable timer activated quietly a videocamera that recorded the activity of the rats in their cages. The rats were allowed to habituate to this condition for 1 month. The period of 9 September through 11 November was selected as our test period because it contained an uninterrupted sequence of data (n = 65 nights). During this period the synthetic field was activated, according to a random schedule, on three separate occasions for between 3 to 5 days between 0200 and 0400 h for a total of 12 nights. There was at least 10 days between presentation sequences.

The numbers of rats that displayed overt seizures per night during the 2 h period were determined visually from the videotapes at a later date. The overt paroxysmal motor patterns were very conspicuous (even in dull red light) and were characterized by a sequence of sniffing, headnoding, rearing, rapid forelimb clonus and falling (followed by tonic-clonic seizures in about 20% of the cases). The percentage of the population ($n/12 \times 100$) that displayed seizures during both hours, the 1st and the 2nd h were obtained. They also served as the dependent variables.

The primary analysis was multiple regression (time-series) and the cases were the days of our test period. There were two independent variables. The first variable was the absence or presence of the experimental ‘geomagnetic’ field while the second variable was the daily ‘A’ value (an index of the amplitude of geomagnetic activity) from Fredericksburg, Virginia. To insure temporal specificity, six lags for the daily ‘A’ values and six lags for the absence/presence of the experimental field were calculated. Because the first lag of the percentages of seizures was employed as the actual dependent variable, this allowed the option for natural or experimental activity of the day after the observation day to enter the equation. All analysis involved SPSS software on a VAX 4000 computer.

The mean and SD for the percentages of overt seizures within the population between 0200 and 0400 h were 11.3% (range 0–33%) and 8.5%, respectively. The results of the multiple regression analysis are shown in Table 1. Only two variables entered the equation ($F(2,58) = 5.77$, $P < 0.01$; MR = 0.41; r-squared = 14%) and both of these variables exhibited comparable β weights for accommodating the variance in the percentages of nightly seizures. The first variable was the presence of the experimental magnetic field on the same nights as the observations and the second variable was the geomagnetic activity on the same nights as the observations. Because the first lag of the dependent variable had been employed, the entry of the first lag of the independent variables indicated their temporal contiguity. The Durbin–Watson Index was within the acceptable range (1.91); the Spearman rho coefficient also indicated no statistically significant ($P > 0.05$) serial correlation between successive nights and either the percentages of seizures (rho = 0.03) or geomagnetic activity (rho = 0.04).

The partial regression coefficients indicated that the percentages of overt seizures significantly ($P < 0.05$) increased by about 6% if the experimental field was present and significantly ($P < 0.05$) increased by an additional 3% if the ‘A’ value increased by 10 units during the same 24 h interval. Because the range of ‘A’ values during the test period was between 2 and 33 (mean, SD = 12.1 and 7.9, respectively), a change in 20 units above the mean which is

Table 1

Statistics and variables associated with the multiple regression equation for the percentages of limbic epileptic rats that displayed overt seizures between 0200 and 0400 h as a function of the presence or absence of the experimental (coil) magnetic field (median peak 50 nT) and natural geomagnetic activity (range 4–60 nT)

Variable	B	SEB	β	t-value	P-value	Change in r-squared (%)
Coil field	5.9	2.4	0.30	2.51	<0.05	6
Geomagnetic (‘A’)	0.3	0.1	0.30	2.46	<0.05	8

MR = 0.41, $P < 0.01$; B, partial slope; SEB, standard error of B; β, standardized partial regression coefficient; P-value, probability level; change in r-squared refers to the separate contributions of each source (natural and experimental fields) to the seizures.

within the range of the 15–20 nT threshold for increased seizure activity [2,3,12], would be associated with an additional 6% of the population exhibiting overt seizures. The 'A' values for the Fredericksburg site was adjusted (× 2) to obtain values in nanotesla. Consequently this indicated that a change of approximately 50 nT in the daily, regional geomagnetic activity was associated with an increase in the percentages of overt seizures that was comparable to activation of our approximately 50 nT experimental field. (The correlation between the daily provisional average antipodal (aa) values [8] for the northern hemisphere and the Fredericksburg 'A' values for the duration of our study was 0.95. Substitution of 'A' values with provisional aa values did not alter the strength of the association between proportions of seizures, the presence of the experimental field and daily geomagnetic activity in the northern hemisphere, i.e. MR = 0.41).

Post hoc analysis was completed to verify if the contribution from the ambient geomagnetic activity was specific to the local time during which the seizures occurred. The 8, 3-h *K* values (a series of integers from 0 to 9 that reflect quasilog increases in intensity) per day from Fredericksburg were correlated with the percentages of seizures. The only statistically significant association occurred between the percentages of seizures and the 3-h *K* values for universal time 0300–0559 h ($r = 0.40$, $P < 0.01$) and 0600–0859 h (0.24, $P < 0.05$). All other coefficients for the remaining six intervals were less than 0.22. If the 4 h delay (since most of the interval involved Eastern daylight savings time) between universal time and local time is accommodated, then the proportions of seizures were maximally associated with the geomagnetic activity during the time of their occurrence. To insure the predominant contribution from this temporal interval, partial correlation analyses were completed for all 8, 3-h values. After first removing the shared variance between the 3-h values and the daily 'A' value, only the correlation between percentages of seizures and geomagnetic activity for the 0300–0559 h universal time (or 2300–0259 h local time), remained significant statistically (first order $r = 0.28$, $P < 0.01$).

The results of this experiment indicated that the contributions from geomagnetic activity and an experimental field that was intended to simulate this activity both produced vectorially similar, statistically significant ($P < 0.05$) changes in overt seizure activity by chronically epileptic rats. Because the algorithms of multiple regression do not allow the entry of redundant sources of variance, the contributions for the two field sources were considered independent but additive. The possibility that contributions from an experimental field would be summated with an incidental increase in geomagnetic activity at the same time could not be tested in this study. Inspection of the data indicated that geomagnetic (Fredericksburg 'A') values for the days in which the experimental fields were presented were less than 15 (30 nT).

However other experimental studies [9] have indicated that the statistically significant correlations between overt seizures in limbic epileptic rats and geomagnetic activity emerged when the daily global values exceed about 20–30 nT. Cumulative seizures (due to the experimental field or incidental values exceeding this threshold) were not observed and suggest that either an experimental field or the natural perturbations may be sufficient to produce the maximum effect. This phenomenon is consistent with the concept of depletion of a neurochemical which we suspect is or is related to melatonin. It displays a threshold for an all-or-none change in white light intensities of less than 1 nW/cm^2 [20]. Once depleted, a critical period of several days is required for baseline values to return [20].

We had been waiting for this very quiet period between solar cycle 22 and 23 to test this hypothesis. That the geomagnetic-seizure effect upon the display of overt seizures is transient, i.e. 1 or 2 days, and attenuates thereafter despite the continued presentation of either experimental fields [13] or the same or subsequent geomagnetic activity may have masked the existence of this association within vulnerable populations [5,7,14,23–25] during periods of past decades when enhanced geomagnetic activity was more frequent. The possibility still exists that the effects were amplified because of the presence of red light during the scotophase. It may be relevant that the effect of the experimental magnetic field upon seizure activity was more apparent during the 2nd h than during the 1st h and suggests a response latency of about 1 h.

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