SEASONAL DIFFERENCES IN CIRCADIAN RHYTHM OF RESISTANCE TO HYPOXIA AND SEIZURES

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The modern stage of development of medical and biological science has demonstrated the need for a study of diseases of the brain to the extent to which they depend on its functional state, which obeys a distinct circadian and seasonal dynamics. Analysis of epileptic activity in a 24-hourly cycle leads to the conclusion that the relationship between the epileptic focus and the changing functional state of the brain is one of the main causes responsible for the dynamics of the clinical manifestations of epilepsy [5, 7]. It has been observed that hypoxia has a significant effect on the onset and course of epilepsy [9, 10]. We know that resistance to hypoxia has a well marked circadian [3] and seasonal [6] dynamics, and that correlation exists between resistance to hypoxia and resistance to seizures [1, 4].

The aim of this investigation was to study to what degree the circadian rhythm of resistance to seizures and hypoxia depends on the season of the year.

EXPERIMENTAL METHOD

Experiments were carried out on 1280 noninbred male albino rats weighing 180-250 g. Resistance to hypoxia (RH) and resistance to seizures (RS) was investigated in rats every 3 h for 24 h in different seasons of the year. Two groups, with 10 rats in each group, were formed at each time period. Resistance to hypoxia was studied in the animals of one group, resistance to seizures in rats of the other group. RH was determined in a pressure chamber by measuring the duration of stay at a high altitude (11,000 m; rate of ascent 183 m/sec) until reversible respiratory arrest – i.e., the survival time (ST) at that "altitude." RS was determined as the latent period (LP) of development of seizures arising after intraperitoneal injection of a 0.1% solution of strychnine (2.5 mg/kg). The experiments were carried out over a period of 2 years (1988-1990); in the fall – in October, winter – January, spring – April, and summer – at the end of June. No experiments were carried out on days with bad weather conditions.

EXPERIMENTAL RESULTS

The results indicate that resistance to hypoxia, like resistance to seizures, has a circardian rhythm, but the character of these changes differs in different seasons of the year. To bring to light the most general tendencies in fluctuations of resistance to seizures and hypoxia, we summarized the results of investigations over a period of 2 years (Fig. 1).

Experiments carried out in the fall show that the greatest values of both RH and RS characterize the time of darkness: resistance to hypoxia at 7 p.m. (ST = 7.7 ± 1.0 min), resistance to seizures at 4 a.m. (LP = 14.9 ± 2.9 min). The lowest values of both parameters were observed in the morning and afternoon: RH was minimal at 10 a.m. (ST 3.9 ± 0.4 min), RS at 4 p.m. (LP = 6.9 ± 1.0 min). Significant differences ($p < 0.01$ and $p < 0.05$ respectively) were found between maxima and minima of resistance to hypoxia and to seizures.

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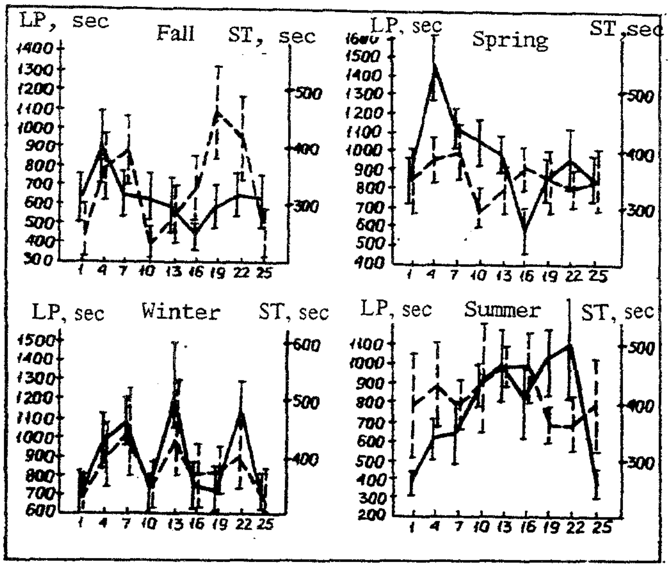

Fig. 1. Circadian rhythm of changes in resistance to hypoxia and seizures in different seasons of the year. Broken line – survival time, continuous – latent period of development of seizures.

In winter resistance to hypoxia and seizures changed along a parallel course during the 24-h period. The highest values of RH and RS occurred at 4-7 a.m., 1 p.m., and 10 p.m. Minimal values were observed at 1 a.m., 10 a.m., and 4-7 p.m. Thus two of the three periods of high hypoxia and high seizure resistance occurred during darkness (ST at 7 a.m. was 7.3 ± 1.2 min, LP was 18.4 ± 1.6 min; ST at 10 p.m. was 6.7 ± 0.9 min, LP 19.8 ± 1.8 min), and one during daylight (ST at 1 p.m. was 7.1 ± 1.0 min, LP 20.6 ± 3.1 min). No significant differences could be found between values of ST in winter, whereas values of LP changed significantly within the periods from 10 a.m. to 1 p.m., 1 to 7 p.m. ($p < 0.05$), and between 7 and 10 p.m. ($p < 0.01$).

As the results of the investigation in spring show, parameters of RH and RS were minimal in the morning and afternoon (ST at 10 a.m. was 4.9 ± 0.6 min, LP at 4 p.m. was 9.6 ± 1.9 min). The greatest resistance to hypoxia was observed after sunrise – at 7 a.m. (ST was 6.7 ± 0.8 min), whereas maximal LP for seizure development was found during darkness – at 4 a.m. (LP = 24.5 ± 2.9 min). No significant differences in ST were found at an "altitude" of 11,000 m at different times of the 24-h period during this season of the year. Significant differences were obtained between values of LP between 4 a.m. and 4 p.m. ($p < 0.01$).

Analysis of parameters of RH and RS recorded in the rats in summer shows that their minimal and maximal values occurred at different times of the 24-h period: hypoxic resistance rose to a maximum at 4 p.m. (ST = 7.8 ± 0.9 min), whereas the latent period of development of seizures reached a maximum at 10 p.m., namely 18.3 ± 4.5 min. The lowest value of ST was found at 7 p.m., during daylight (ST = 5.9 ± 0.5 min). LP of seizure development was minimal at 1 a.m. (6.0 ± 0.8 min). Significant differences with respect to ST were obtained between 1 p.m. and 7 p.m., and in the values of LP between 10 p.m. and 1 a.m. ($p < 0.05$).

In order to discover in which seasons of the year the animals were more resistant to hypoxia and seizures, we averaged the values of survival time and latent period of seizure development obtained in the course of 24 h in each season of the year (Table 1).

The results thus indicate that resistance of animals to seizures in the course of the 24-h period changes similarly in the fall and spring. Peak values of LP are found at 4 a.m. and minima at 4 p.m. The greatest similarity in changes in ST during the 24-h period also are observed in the fall and spring. They were recorded in the time interval from 1 a.m. to 4 p.m. In winter minimal correlation was found between the circadian rhythm of each of these resistances with the corresponding value in other seasons of the year, but in winter maximal synchronization of rhythms of RH and RS was noted. Synchronization of several rhythms is known to be accompanied by a change in their natural rhythm [8]. In the modern view synchronization takes place through the existence of special control

TABLE 1. Parameters of Resistance to Seizures and Hypoxia Season by Season

Season	Survival time, min	Latent period of development of epileptic fit, min	Latent period of depth, min
Fall	5,7±0,3	10,5±0,7	15,0±1,0
Winter	6,4±0,3	15,4±0,7	21,6±1,0
Spring	5,9±0,2	16,4±0,7	23,3±0,9
Summer	6,9±0,4	12,1±0,9	18,7±1,2

structures (pacemakers). One such pacemaker may be the suprachiasmatic nucleus, and the periodically changing impulses arising in it may be synchronizing factors [11].

Analysis of the facts described above thus suggests that in the winter season any pacemaker arising in the body functions most actively, leading to synchronization of rhythms of RS and RH. Elements of disturbance of synchronization in the intermediate seasons of the year may be introduced by unstable weather conditions and lability of the hormonal background.

The fact that resistance to seizures is greatest during darkness at all seasons of the year (at 10 p.m. and 4 a.m.) can be explained by high activity of cerebellar neurons-in rodents in the evening and night and a decrease of this activity during daylight hours [2].

Comparison of the values of RH and RS at different seasons of the year showed that in the fall seizure resistance and resistance to hypoxia are minimal. Maximal values of LP are observed in spring, the highest values of ST are found in summer. The study of cerebellar neuronal activity in different seasons of the year during exposure to hyperthermia [2] showed that in spring and summer the general level of circadian resistance to hyperthermia is higher than in the fall and winter. The temperature factor, acting primarily on the neuron membrane, changes in resistance, thereby creating a depolarization background for the nerve tissue. In the fall, exposure to temperature stimuli led to more serious changes in membrane conduction, evidence of its unstable state in this season of the year, which could be one explanation of the increased proneness of the brain to seizures in the fall.

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