THE INFLUENCE OF ACCLIMATIZATION TO HYPOXIA ON EXPERIMENTAL EPILEPTIFORM SEIZURES IN RATS

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In recent years, the problem of hypoxia and adaptation thereto has acquired greater interest both theoretically and practically, since it has been found that oxygen lack occurs in an extremely wide range of pathological conditions. Also, adaptation to hypoxia enables recovery from these conditions to take place.

It is known that hypoxia plays a part in the pathogenesis of experimentally induced convulsions. N. D. Ershov [2] and E. V. Maistrakh [4] showed that the increased sensitivity of an animal at high altitudes to epileptogenic substances was due primarily to a cerebral hypoxia. W. Penfield and T. Erikson [6] and B. Ya. Rabinovich [7] and others have described the role of cerebral hypoxia in the development of epileptiform attacks.

On this account we have thought it interesting to study the influence of adaptation and acclimatization to hypoxia on the nature and course of epileptiform seizures.

METHOD

The experiments were carried out on rats. As the epileptogenic substance we used a 1 : 1 mixture of 20% camphor oil and ether, injected intravenously.

The first set of experiments was carried out on 16 rats in a pressure chamber.

We first determined the dose required to induce a well developed epileptiform attack with clonic and tonic phases, from which the animal should recover to a normal condition. In our experiments this dose was found to be 0.01 ml of the solution per animal (the rats weighed 200 g). An epileptiform attack lasting 10 - 15 minutes developed 2 - 3 seconds after the intravenous injection.

This set of experiments was carried out as follows. For the first 10 days, every day for half an hour the rats were placed in the pressure chamber at a "height" of 8000 m. On the 11th day, they remained in the pressure chamber at a "height" of 6500 m for 54 hours. At the end of this time they were removed from the chamber, and received an epileptogenic dose of camphor oil solution.

The results of this set of experiments were as follows: of the 16 rats used, 2 died immediately, 1 developed a strong attack from which it died, and in the remaining 13 there were no convulsions, even when the dose was increased to 0.015 ml.

From the results obtained we have formed the opinion that adaptation to hypoxia enhances the resistance of the organism to the epileptogenic agent.

For confirmation we carried out a second set of experiments on 30 rats weighing from 170 to 180 g. As in the previous set of experiments, each rat received 0.01 - 0.015 ml of camphor oil solution, which after 2 - 3 seconds induced a convulsive attack lasting 6 - 10 minutes, but which was not fatal. In all the animals, a blood count was made and the color index determined. Under normal conditions, the number of erythrocytes varied from 7 to 10 million per mm^3, and the hemoglobin from 86 to 96% of the Sahli standard (Table 1). After this preliminary investigation, all the animals were transported to the foothills of Mount El'brus, and then immediately taken up to a height of 3400 m ("Piket 105"). On the 8th day at this height the blood of 15 of the rats was examined. The red cell count and the hemoglobin had increased above normal (see Table 1). Then the same animals received a

solution of camphor, in the following amounts: two rats – 0.025 ml each, two others – 0.035 ml, while all the remainder received 0.02 ml. No rat suffered any convulsions from the dose of 0.02 ml, and no respiratory change was observed. The injection of 0.025 ml of the solution caused a transient increase in respiration rate, and a few isolated convulsive movements. A dose of 0.035 ml caused a mild epileptiform attack which occurred after 10 seconds, and which lasted for a total of one minute. The results obtained are shown in Table 2.

The rats were than transported to Kiev. On the 7 - 8th day after descent from the mountains (after they had been in Kiev for 4 - 5 days), in all 28 rats (two had died en route) a blood analysis was made, and an injection of camphor solution given. The red cell count and color index were within the normal values (see Table 1). A dose of 0.02-0.025 ml of camphor solution caused no response. An injection of 0.03-0.035 ml caused some convulsive movements in three of the eleven rats. In response to the injection of 0.04-0.05 ml of solution, three rats suffered convulsive attacks which lasted for 4 - 5 minutes. These results are shown in Table 3.

Thus both sets of experiments confirm that the oxygen supply to the brain plays an essential part in the pathogenesis of convulsive attacks. Adaptation and acclimatization to hypoxia increase resistance to the epileptogenic agent.

It is interesting to determine the mechanism of adaptation to hypoxia in these cases.

TABLE 1. Changes in Erythrocyte Count and Hemoglobin Index in Rats after a Period Spent in the Mountains

Number of animal	Kiev (58 m above sea level)		El'brus (3400 m) above sea level)		Kiev (58 m above sea level)	
	Number of erythrocytes per mm^3 (in millions)	Hemoglobin (in percentage, Sahli)	Number of erythrocytes per mm^3 (in millions)	Hemoglobin (in percentage, Sahli)	Number of erythrocytes per mm^3 (in millions)	Hemoglobin (in percentage, Sahli)
1	7.7	86	8.7	95	7.3	87
2	7.8	87	8.9	96	8	86.4
3	6.9	80	8	88	7.1	78.2
4	8	90.6	10.4	112	9.3	91
5	9.3	92	9.4	103	8.9	91
6	7.9	90	8.6	103	7.8	90
7	7.6	90	9.3	100	7.36	90
8	9	88	11.2	94	9.72	86.8
9	8.7	81	9.9	87	8.81	82
10	7.1	90.1	8.9	107	7.62	90
11	8	93	9	100	8	90
12	10.4	90.7	11.3	104	10	78.2
13	7.9	89	9.6	107	7.5	81
14	9.3	86	10.2	98	9	88
15	10.3	86	11.2	97	10	89.1

TABLE 2. Response of Rats to Injection of Epileptogenic Doses of Camphor, given on the 8th Day of Their Stay in the Mountains (Height 3400 m)

No. of rat	Response to a dose of 0.02 ml	No. of rat	Response to a dose of 0.025 ml	No. of rat	Response to a dose of 0.035 ml
1	-	12	+	14	++
2	-	13	+	15	++
3	-				
4	-				
5	-				
6	-				
7	-				
8	-				
9	-				
10	-				
11	-				

Note: + indicates isolated convulsive movements; ++ a convulsive attack; - no response.

TABLE 3. Response of Rats to Injection of Epileptogenic Doses of Camphor Solution Given on 7th and 8th Days after Their Return from the Mountains

No. of rat	Response to a dose of 0.02 - 0.025 ml	No. of rat	Response to a dose of 0.03 - 0.035 ml	No. of rat	Response to a dose of 0.04 - 0.05 ml
1	-	15	+	26	++
2	-	16	-	27	++
3	-	17	-	28	++
4	-	18	+		
5	-	19	-		
6	-	20	+		
7	-	21	-		
8	-	22	-		
9	-	23	-		
10	-	24	-		
11	-	25	-		
12	-				
13	-				
14	-				

Note: The same as Table 2.

N. V. Lauer and E. I. Chaika [8], M. E. Marshak [5] and E. M. Kreps [3] have shown that oxygen lack leads to an increased blood supply to the brain through increase in the hemoglobin per unit volume, as well as through a dilatation of the vessels and the formation of new capillaries. V. I. Voitkevich [1] showed that the increased volume of the cerebral vascular plexus is maintained in most animals, particularly in rats, for a long time after the hypoxia has been eliminated. It may be supposed that similar changes took place in our rats, but, of course, this problem requires careful study.

SUMMARY

The effect of reduced pressure in a pressure chamber and of a genuine high altitude (on Mount El'brus) on the course of epileptiform convulsions in rats was studied. The attacks were induced by intravenous injection of 20% camphor oil in ether. Red cell counts were made and the percentage hemoglobin determined. After "high altitude" conditions in the pressure chamber or after a stay in the mountains, epileptogenic doses of camphor solution produced no reaction. A double dose of this solution was required to cause convulsions. Thus, adaptation to hypoxia increased the body's resistance to the epileptogenic agent.

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