Effect of Hippocampal Ablation on the Audiogenic Seizure in Rats※

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In recent years there has appeared increasing number of reports with the notion that pathological changes of the hippocampus are often encountered in the autopsy findings of epileptics[2,3]. In the course of search for the function of the hippocampus, the author studied the audiogenic seizure in rats to see whether the hippocampus has anything to do with convulsive manifestations.

Material and Method

The subjects were albino rats of both sexes, whose body weight ranged from 220 to 260 gm. Throughout the experimental period, they were fed on a balanced stock diet of constant quality with sufficient amount of minerals and vitamins. Each rat was put in a small screened cage, the size of 26×22×16.5 cm, which was hung on a funnel-shaped tambour covered with a strong rubber membrane and fixed on the ceiling of a 32×26×34 cm. wooden box. Through rubber tubing the tambour was connected to another smaller tambour, which recorded on a kymograph the movement of the rat in the screened cage (Fig. 1). Two bells were fixed on the ceiling of the wooden box. One or both of them were rung for two minutes through a timer circuit and the moments of onset and cessation of the sound were marked on the kymograph. Watching the activity of the animal through the glass window constituting the front of the wooden box, the experimenter recorded the onset and cessation of the convulsion on the kymograph through a key and a signal magnet (Fig. 2), and measured the duration of coma with a stop watch.

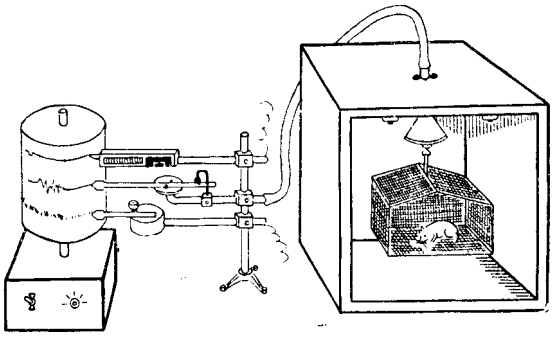

Fig. 1. Setup for the observation and recording of the audiogenic seizure.

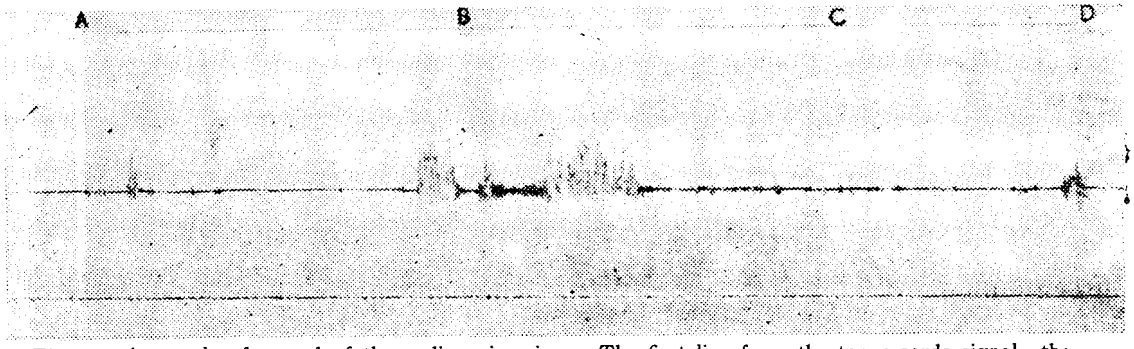

Fig. 2. A sample of record of the audiogenic seizure. The first line from the top records signal, the second line activity of the rat, and the third line time in seconds. Onset of sound at A, convulsion begins at B, coma begins at C, and sound off at D.

Each animal was exposed twice to a "weak" sound (105~107 decibels) produced by one bell and twice to a "strong" sound(110~114 decibels) produced by

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both bells. At least 48 hours were elapsed between successive trials. Then the animals were divided into two groups and subjected to hippocampal or neocortical ablation after equating them according to their performance, body weight, and sex.

The operative procedures were as follows. After removing most of the parietal bone on both sides excepting the part along the sagittal sinus, an oval-shaped portion of neocortex on the dorsal surface of the brain overlying the hippocampus was sucked out, and then an attempt was made to remove as much as possible of the hippocampus by suction. Special care was taken to remove the dorsal portion of the hippocampus and to interrupt the fimbria and hippocampal commissure without damaging the overlying mid-line cortical tissues. This preparation served as the hippocampus-ablated rat. A second group of rats was prepared in which only the portion of neocortex over the hippocampus was ablated. This was the neocortex-ablated rat.

Originally 44 animals were subjected to this study but deaths after operation left only 32 animals with which to complete the study. Postoperative trials were carried out under identical situation as in the preoperative period, beginning the first postoperative trial more than three weeks after the brain ablation.

Examination of the brain of the hippocampus-ablated animals after completion of the experiment showed that practically all of the dorsal portion of the hippocampus between the mid-line cortical tissue and the thalamus extending from the level of the anterior commissure to the level of the posterior commissure had been successfully removed, while the posteroventral portion of the same structure caudal to the posterior commissure remained largely intact.

Results

The results are summarized in Tables 1, 2, and 3. The frequency of the audiogenic seizure was increased after brain ablation both in hippocampus-ablated rats and neocortex-ablated animals. Under weak sound, however, the increased susceptibility to seizure activity was more marked in hippocampus-ablated rats. Neocortex-ablated rats, on the other hand, became as much susceptible as the hippocampus-ablated ones only under strong sound(Table 1).

Table 1. Frequency of convulsion and running attack before and after brain ablations

Brain ablation	Observation	Weak sound (105~107 db) Before	Weak sound (105~107 db) After	Strong sound (110~114 db) Before	Strong sound (110~114 db) After
Hippocampus-ablated	Convulsion	5	14	7	14
	Running attack	8	22	10	22
Neocortex-ablated	Convulsion	4	5	5	14
	Running attack	6	8	8	20

Each numeral indicates the total number observed in 32 trials with 16 rats.

Table 2. Change in frequency of convulsion and running attack following brain ablations

Brain ablation	Observation	Weak sound (105~107 db) Increased	Weak sound (105~107 db) Decreased	Strong sound (110~114 db) Increased	Strong sound (110~114 db) Decreased
Hippocampus-ablated	Convulsion	7	0	4	1
	Running attack	9	0	7	1
Neocortex-ablated	Convulsion	1	1	7	1
	Running attack	3	2	9	1

Each numeral represents number of animals.

Table 3. Latency and duration of running attack and convulsion, and duration of coma before and after brain ablation

Brain ablation	Weak sound (105~107 db) Before	Weak sound (105~107 db) After	Srong sound (110~114 db) Before	Srong sound (110~114 db) After
	Latency of running attack			
Hippocampus-ablated	32.6(8)	24.1(22)	23.4(10)	13.6(22)
Neocortex-ablated	46.1(6)	38.0(8)	39.0(8)	33.5(20)
	Duration of running attack			
Hippocampus-ablated	14.5(8)	24.4(22)	10.0(10)	24.9(22)
Neocortex-ablated	7.0(6)	33.8(8)	10.3(8)	13.9(20)
	Latency of convulsion			
Hippocampus-ablated	21.0(5)	40.3(14)	19.5(7)	34.0(14)
Neocortex-ablated	52.3(4)	54.0(5)	50.8(5)	46.7(14)
	Duration of convulsion			
Hippocampus-ablated	42.2(5)	52.5(14)	50.0(7)	53.6(14)
Neocortex-ablated	23.0(4)	32.5(5)	26.5(5)	36.2(14)
	Duration of coma			
Hippocampus-ablated	2m18s(5)	15m57s(14)	10s(7)	22m16s(14)
Neocortex-ablated	1m18s(4)	32s(5)	21s(5)	3m10s(14)

Each numeral represents median value in seconds, except in the case of duration of coma, where m stands for minutes, and s for seconds. The numeral in the parentheses indicates the number of observations.

There were a few exceptional cases where the frequency of seizure activity decreased postoperatively(Table 2). Besides, in each group of hippocampus-ablated and neocortex-ablated animals, there were four animals which displayed neither audiognic seizure nore running attack both pre- and postoperatively. Of these eight animals there were three hippocampus-ablated animals(A—2, A—7, A—32) and one neocortex-ablated animal(A—29) whose abilities of hearing were questionable throughout the experiment.

The latency of running attack tended to shorten and its duration to lengthen both after hippocampal and neocortical ablations. The latency of convulsion, however, tended to lengthen after hippocampal ablation, while no definite tendency in the change of latency of convulsion could be ascertained after neocortical ablation. Both the duration of convulsion and that of succeeding coma became lengthened after ablation(Table 3). No spontaneous convulsion was noted throughout pre- and postoperative observation periods.

Discussion

Beach and Weaver[1] observed increase in the frequency of audiogenic seizere after cerebral injury in the albino rats. Weiner and Morgan[5], on the other hand, found decrease in the frequency of the same activity following cortical lesions. Under strong sounds, the result of the present work is in accord with that of Beach and Weaver as to the effect of neocortical ablation.

In addition, rats in this experiment became increasingly susceptible to weak sound following hippocampal ablation, but this was not the case with neocortex-ablated rats. Thus it appears that both hippocampal and neocortical ablation cause increased susceptibility to audiogenic seizure.

Recently Green et al.[4] observed similar augmentation in motor seizure following hippocampal damage in cats. Though they did not see seizures when the hippocampus was not involved, and the seizures their cats displayed were not particularly audiogenic in nature, the result seems to agree with the present one as to the effect of hippocampal damage.

When one works on brain ablation, especially when the ablation of the structure in question is not complete, one has to ponder whether the symptomes he encounters is caused by the gross removal of the structure or due to the stimulatory effect of scars formed in the remaining tissue. This question also arises in the present study, where the removal of the hippocampus is far from complete. As far as the motor seizure is concerned, however, the increase in this activity following hippocampal ablation may be an expression of deficient rather than augmented functional state of this structure. What one gets by stimulation of the hippocampus, according to the experience of the author, is mostly freezing of the behavior, not an increase in movement. Should we infer then from the present results that the hippocampus is inhibitory to the motor seizure?

The latency of convulsion tended to lengthen following hippocampal ablation. Though the data are not impressive, they may be suggestive of hippocampal involvement in the audiogenic seizure in much more complex manner than in a simple inhibitory capacity.

Summary

Rats in which the hippocampus was ablated through overlying neocortex(hippoocampus-ablated rats) and rats in which only the portion of neocortex over the hippocampus was ablated(neocortex-ablated rats) were prepared and their susceptibility to the sound produced by one bell("weak" sound, 105~107 decibels) or two bells("strong" sound, 110~114 decibels) to induce audiogenic seizure was tested before and after brain ablation.

The susceptibility to the sound increased both in hippocampus-ablated rats and in neocortex-ablated animals. While in neocortex-ablated rats the increase in the frequency of audiogenic seizure was manifest only under strong sound, hippocampus-ablated animals showed increased susceptibility to both weak and strong sound.

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국 문 초 록

Hippocampus를 떼어버린 흰쥐의 Audiogenic Seizure

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32마리의 흰 쥐들에서 약한 소리(105~107 decibels) 및 강한 소리(110~114 decibels)에 각각 2분동안 노출함으로서 일어나는 audiogenic seizure의 출현빈도를 hippocampus 또는 neocortex 제거 전후에 2회식 관찰하여 다음과 같은 결과를 얻었다.

1. Audiogenic seizure가 나타나는 빈도는 hippocampus 제거군과 neocortex 제거군에서 모두 수술전에 비하여 증가하였다.

2. Neocortex 제거군에서는 강한 소리에 노출될 때만 audiogenic seizure를 일으키기 쉽게 되었는데 hippocampus 제거군에서는 약한 소리와 강한 소리에 노출되었을 때 모두 audiogenic seizure의 출현빈도가 증가됨을 보았다.

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