EFFECTS OF LESIONS IN THE HIPPOCAMPUS AND AMYGDALA ON DURATION AND FREQUENCY PATTERNS OF SEPTUM AFTER-DISCHARGES

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Summary (1) In twenty-two adult cats, septum after-discharges were induced, following placement of lesions in the hippocampus, amygdala and temporal cortex. The duration and frequency patterns of the after-discharge were analyzed.

(2) The hippocampus, in contrast to the amygdala, is the main contributor to the duration of the septum after-discharge. Septum discharge durations are shortest following massive hippocampal ablation. Increased seizure duration occurs at a much faster rate with an intact hippocampus and lesioned amygdala.

(3) The dorsal hippocampus is the predominant contributor of the faster frequencies in septum after-discharge patterns, whereas the ventral hippocampus and amygdala contribute slower frequencies predominantly.

(4) Septum after-discharges were longest following cortical resection alone. This suggested the existence of a cortical inhibitory effect upon limbic system after-discharges.

The septum after-discharge system “is made up of two basic frequency patterns (fast and slow) which, in part, may be closely associated with, and dependent upon, hippocampal participation (ANDY and KOSHINO, 1967).” During simultaneously exciting seizures, the amygdaloid after-discharges were found to potentiate the slow frequency component of the septum discharges. The objective of the present study is to differentially evaluate the contribution of the amygdala and hippocampus by analyzing septum after-discharge frequency and duration patterns following the ablation of those structures.

TECHNIQUE

Twenty-two adult cats were utilized. Operative resections were performed.
under sodium pentobarbital anesthesia. Resections of the hippocampus were performed through an incision made in the posterior ectosylvian gyrus. Bilateral lesions were placed at the same sitting. Resections of the amygdala were performed unilaterally through the sylvian fissure. The ventral anterior tip of the hippocampus was visualized and used as a landmark for the posterior limits of the amygdala.

The following six groups of animals were prepared. (1) Unilateral transection of the posterior hippocampus in three animals: this consisted of removing a small segment in the posterior part of the hippocampus in order to isolate the dorsal from the ventral component on one side: (2) Unilateral resection of the dorsal hippocampus in four animals: the major portion of the dorsal component on one side was excised, leaving the caudal end of the hippocampal commissure intact: (3) Bilateral transection of the posterior hippocampus in nine animals: this left the bilateral ventral components isolated from the dorsal components of the hippocampus. (4) Total lesion group: these were massive lesions of the bilateral hippocampus in two cats in which most of the dorsal, posterior, and ventral components of the bilateral hippocampus were resected. (5) Resection of the unilateral amygdala was performed in two animals through the ectosylvian fissure. (6) A unilateral resection of the ectosylvian gyrus was done in two animals without resection of the amygdala or hippocampus.

The animals were allowed to recover for a period of one month before the implantation of electrodes in the septum. For the insertion of the electrodes, a local 1% Xylocaine anesthesia was utilized in order to alleviate pain in the scalp tissues. A similar anesthetic was utilized for a tracheostomy through which the animal was artificially ventilated while under the influence of anectine. Temperatures were maintained in the approximate range of 37°C and 10-20 ml of dextrose solution was given i.v. each hour. Bipolar electrodes with 1 mm bare tips and 1.5 mm apart were bilaterally placed in the septum for both recording and stimulation. Electrical stimulation was performed with a Grass stimulator using 1 msec square pulses at 50 c/sec in trains of 5 sec duration. Minimum voltages necessary for threshold stimulation to induce electrographic seizures (4-8 volts) were used. The total number of septum after-discharges elicited were 205. The intervals between stimulations varied from three to five minutes. The average duration of experiments was five to seven hours. Electrical recordings were made on a Grass electroencephalograph.

In each experiment, the electrographic seizures were ranked according to their durations. Duration and frequency patterns were analyzed for three seizures taken at three levels of rank: the three longest, three intermediate, and three shortest ranked seizures. Consequently, nine seizures were analyzed in each experiment. Seizure duration was measured from a sustained "tonic" or "clonic" after-discharge activity to that of a pre-discharge (control) or depressed EEG pattern. The mean duration was determined for the three longest, intermediate,
and shortest after-discharges obtained in each of the 22 experiments. In order to obtain the distribution of frequency patterns for each after-discharge, the total time-durations for a specific frequency were cumulated. Only those frequencies which were discernible by visual examination were counted. Those periods of time in which the frequency could not be determined or in which the amplitude was less than 50 µV were cumulated and recorded as the amount of discharge duration with undetermined frequency. For comparison of frequency distributions between groups, the percentage amount of each frequency was calculated in relation to the average seizure duration in the longest ranked seizures. All points of stimulation and recording were histologically verified.

Quantification of degree of hippocampal lesion in each of the groups

The percentage volume of remaining hippocampus in the lesioned animals was determined by the following technique. The average volume of the intact hippocampus was determined from 10 control animals (not used in these experiments) in which histological sections through the hippocampus were made using a similar technique. The average of the total volume of the hippocampus taken from those 10 animals was considered as 100%. In the resected animals, the remaining volume of the hippocampus was computed and percentages determined in relation to the control volume. Volumes were measured by projecting the histologic sections of the hippocampus on bond paper using 2× magnification. The outlined structure was then cut and weighed. The analysis was based upon comparing the weights from normal hippocampal animals with weights obtained from the resected hippocampal animals.

The histological localizations, stimulation parameters, time sequence, and characteristics of all after-discharges were punched on individual IBM cards in order to make possible computer analysis of the data. The changes in duration in relation to time were established for each group of operated animals.

RESULTS

Duration of after-discharges

It should be noted that the percentage amounts of hippocampus resected in the various groups were as follows: “total” hippocampus resection, 85%; bilateral hippocampal transection, 52%; unilateral hippocampal transection, 40%, and unilateral dorsal hippocampal resection, 22%. In the amygdala and cortical resection groups the hippocampus remained intact. The mean duration of the septum after-discharges for the various operated groups were: “total” hippocampus resections, 15 sec; bilateral hippocampal transected, 37 sec; unilateral hippocampal transection, 42 sec; unilateral dorsal hippocampal resection, 40 sec; amygdala reseaction, 62 sec, and unilateral cortical resection, 83 sec. The
Mean durations of the longest, intermediate and shortest seizure duration categories in each of the hippocampal lesioned groups are diagrammed in Fig. 1.

**Fig. 1. Septum seizure durations compared in the six lesioned groups as previously identified. Three ranks of seizure durations were observed in each group. Abbreviations: H, hippocampus; Unilat, unilateral; Bilat, bilateral; DH, dorsal hippocampus; Amyg, amygdala; Cort, cortex. Hippocampal sketches in black illustrate location and extent of lesions.**

*Durations of after-discharges in relation to the time sequence of their elicitation*

In all hippocampus lesioned groups, the durations of the discharges became progressively longer in relation to time (Fig. 2). It should be noted that the rate of progressively increasing duration was greatest in the group with the greatest amount of hippocampus remaining and the lowest rate of progressively increasing duration was in the group with the smallest amount of hippocampus (the bilateral massive hippocampectomy group). It is of interest that the mean slope of the curve for all hippocampus lesioned groups was 0.12 and that the mean slope of the curve for non-lesioned animals was 0.13 (Andy and Koshino, 1967). In animals having had a unilateral amygdala resection and those having had unilateral cortical resection alone, the slope of the curve was much greater than for each of the hippocampal groups. In other words, the presence of an intact hippocampus greatly facilitated the rate of the progressively increasing septal seizure duration.
Frequency patterns in septum seizures

In the presence of the bilateral massive hippocampal ablation, the septum discharge frequency pattern ranged from 1 to 15 cps with modes at 4 and 10 cps. A relatively small amount (only 6%) of the total discharge frequency was above 10 cps and a large amount (66%) below 6 cps. The group in which the dorsal hippocampus was left attached to the septum, following bilateral posterior hippocampus transection, possessed greater amounts of the faster frequencies (50% above 10 cps). A trimodal pattern was present at 7–8 cps, 15 cps and 20 cps. The group in which unilateral transections were performed possessed greater amounts of the slower frequencies than the bilaterally transected group and had a single frequency mode at 8 cps. (It should be emphasize that the posterior portion of the hippocampal commissure was left intact in the unilateral transection.) In the unilateral dorsal hippocampal ablation group there was a shift to a slower dominant frequency of 2 cps. However, frequencies in the higher ranges of 11 to 25 cps were present, although relatively small in amounts. This is of interest in view of the remaining dorsal hippocampus of one side. The amygdalectomy group had a broad frequency pattern of 4 to 25 cps with two dominant modes: one at 9 cps and the other at 15 cps. The cortical resection group had dominant modes at 8 and 12 cps (Fig. 3).
HIPPOCAMPUS, AMYGDALA AND CORTEX LESION EFFECTS ON FREQUENCY DISTRIBUTION PATTERNS (SEPTUM AFTER-DISCHARGE)

"TOTAL" HIPPOCAMPUS RESECTION
AV. SEIZURE DURATION 26 SEC
95% MEASURABLE

BILATERAL HIPPOCAMPUS TRANSECTION
78 SEC
91%

UNILATERAL HIPPOCAMPUS TRANSECTION
65 SEC
97%

UNILATERAL DORSAL HIPPOCAMPUS RESECTION
74 SEC
83%

UNILATERAL AMYGDALA RESECTION
115 SEC
98%

UNILATERAL CORTEX RESECTION
175 SEC
97%

Fig. 3. Frequency distribution patterns expressed as percentage amounts of a given frequency in relation to the average seizure duration in each group.
DISCUSSION

This study suggests that through analysis of frequency patterns it is possible to identify the structures contributing to an after-discharge. A marked reduction and even the absence of the slowest frequencies of the septum discharge occurred following ablation of the amygdala. The ventral hippocampus also contributes to the slow frequencies of the septum after-discharge. Fast frequencies are predominantly derived from the dorsal hippocampus. These findings are not surprising in view of the anatomical relationships of the septum with the hippocampus and amygdala. Furthermore, discharges induced in the amygdala are characterized by predominantly slow frequencies (Andy and Koshino, 1967) and discharges induced in the ventral and dorsal hippocampus are characterized by slow and fast frequencies, respectively (Andy et al., 1962).

The hippocampus and amygdala appear to have antagonistic effects upon the septum discharge durations; the former is facilitative and the latter, inhibitory. It is of interest to note that the neocortex also exerts an inhibitory effect upon the septum discharge durations. This finding is in accord with the clinical impression that seizures of subcortical origin, such as psychomotor seizures, are prolonged in the presence of diffuse cortical or brain damage.

REFERENCES
