MAPPING OF CENTERS SUSCEPTIBLE TO ELECTRICALLY INDUCED AFTERDISCHARGE IN THE CAT BRAIN.

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INTRODUCTION

Electrically induced afterdischarge from limbic and cortical areas is a phenomena closely related to epileptiform activity (1,2,3). Several investigators have implicated these areas (cortex, hippocampus) in clinical epilepsy (4, 5), while others (9) have shown the high susceptibility of these areas to afterdischarge, as well as the existence of gradients of threshold voltage within these anatomical structures.

Previous published results from this laboratory (6, 7) have indicated the presence of centers highly sensitive to electrically and mechanically induced afterdischarge in the cortex, amygdala and hippocampus of various species.

The main objectives of this investigation were (a) to determine the location and threshold of centers susceptible to electrically induced afterdischarge and seizure discharge in regions of the cat brain previously unexplored for such activity, and (b) to observe faradic properties of brain tissue as well as propagation characteristics of electrically induced afterdischarge.

METHODS

Twenty cats of either sex and ranging in weight from 1.5 to 4 kg. were used in this study. With the animal under preliminary ether anesthesia, the trachea and jugular vein were cannulated. Ether was then discontinued, the animal was immobilized with gallamine hydrochloride (5 mg/kg), and maintained on artificial respiration for the duration of the experiment. The animal was then secured in a Takahashi stereotaxic frame and prepared for electrode implantation. The surgical procedures, electrodes used, electrical stimulus recording techniques and histological procedures have been previously reported in a publication (7) from this laboratory.

The mapping electrode, mounted on the Takahashi micromanipulator, was gradually moved into the brain. At each millimeter the brain was stimulated with 0.6 V and the voltage increased (if necessary) by increments of 1.0 V until the threshold for response (afterdischarge) of a center was determined, and the procedure repeated until the bottom of the skull was reached. This procedure was repeated for Horsley-Clarke frontal planes 2 through 19 to the right of the mid-line of the skull at lateral positions 2, 4, 6, 8, 10, 12, 14, and 16.

The elicited responses were recorded on an 8-channel Alvar electroencephalograph. Monopolar recordings were obtained from the inner and outer poles of the concentric mapping electrode. Bipolar recording provided information concerning the electrical activity occurring between the inner and outer poles, as well as information about activity of neurons in the vicinity of the electrode tip.

Histological verification of the electrode traces was performed according to the method of Kolmer (8).

RESULTS

General Mapping. Horsley-Clarke frontal planes 2 through 19 were mapped on the right side of the mid-line. The existence of hyperexcitable centers as previously reported by Leclercq and Segal (6, 7, 9) was confirmed. These centers or pacemakers were observed to be present in all Horsley-Clarke planes investigated, but appeared to be localized chiefly in the cortex, amygdala, hippocampus, lateral geniculate body, and pyriform lobe. These observations were confirmed by histological examination of mapping electrode tracts and electrode tip placement.

The stereotaxic co-ordinates showing the location of susceptible centers found in a

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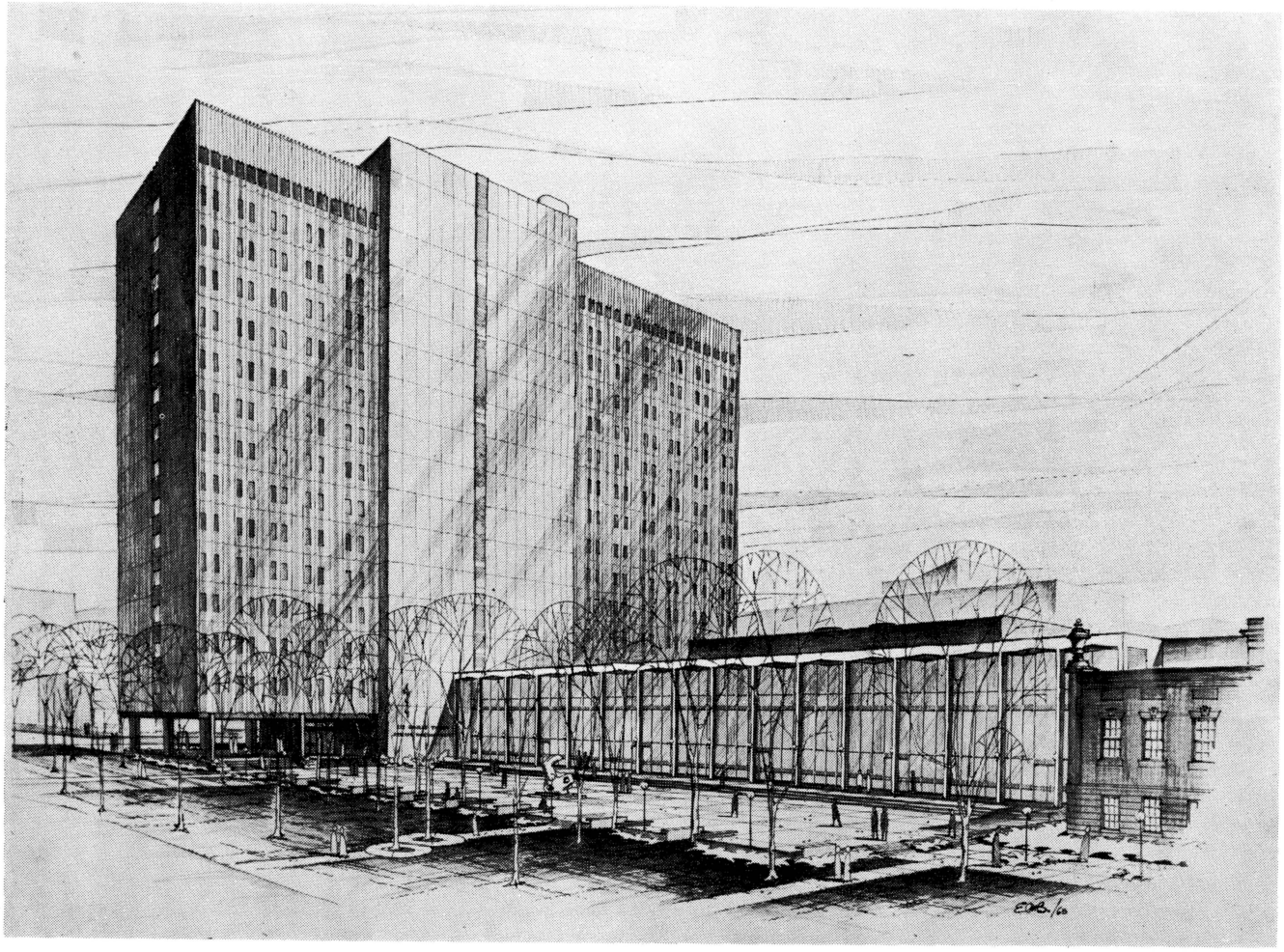

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typical mapping experiment (frontal plane 4) are summarized in Table I. As can be seen, several areas responded to low threshold stimulation (0.8-I.5 V).

Table I

Susceptible centers responding to 0.8-1.5V.

Area Responding	Co-ordinates		
	Frontal	Lateral	Vertical
Cortex	4	2	+10
	4	2	+8
	4	4	+10
Hippocampus	4	6	+8
	4	6	+5
	4	10	0
	4	10	—1
	4	12	+4
	4	12	—1
Lateral Geniculate Body	4	8	+4
	4	6	+4
	4	8	+3
	4	8	+2
	4	8	+1

The susceptible areas in this experiment were present in the specific regions of the cortex, hippocampus, and lateral geniculate body. Although many other regions in the cortex, hippocampus and mid-brain responded, thresholds greater than 1.5 V were required to elicit a response. The most sensitive centers in the cortex were observed to be deep below the cortical surface.

Histological examination of the area of these susceptible centers in sub-cortical or other regions showed an inverse relationship between the number of large nucleated cells present in the center and the threshold of stimulus. The larger the number of these cells in the area, the lower the threshold.

Propagation of Responses. It was observed that electrical stimulation at one point in the brain often elicited propagation of afterdischarge from another point or region. Figure 2 shows a mapping experiment at F12, L8 in which a response was elicited apparently at V + 2 by a 10V stimulus. Little or no activity was seen in the bipolar recording at this time. After the response had ceased at V + 2, the mapping electrode was moved downward to V + 1 for the determination of threshold there; however, a response was found already in progress in the vicinity of the bipolar electrode tip at V + 1. The electrode was quickly returned to V + 2 where it was seen that the response at V + 1 had propagated upward to V + 2 and was occurring in the bipolar recording. Upward movement of the electrode to V + 3 indicated that the propagated response had not reached that area. Movement of the electrode back to V + 2 showed the response continuing there. Movement to V + 1 indicated that the amplitude of the bi-polar recording was greatest at that point. Downward movement of the electrode to V0 confirmed that afterdischarge was not propagated in that direction. The electrode was returned to position V + 1 where the response in the vicinity of the bipolar electrode was still in progress. (See Figure 2). This position, then, appeared as

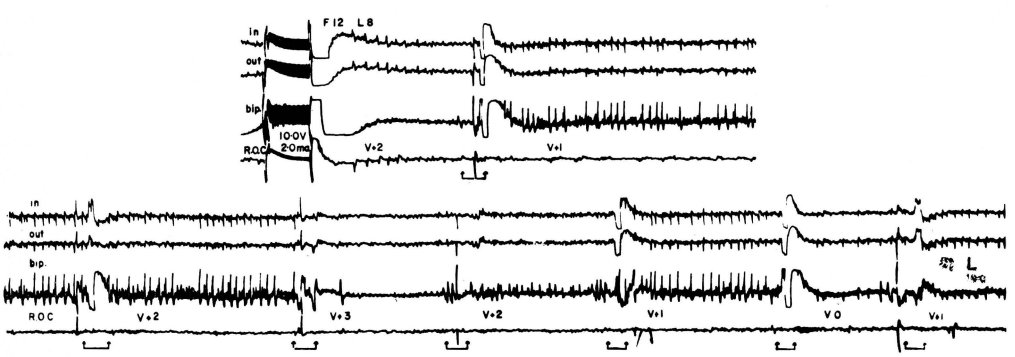

Figure 2. Record illustrating the propagation of afterdischarge response elicited from a susceptible center at F12, L8, V + 1, by a 10V stimulus applied at F12, L8, V + 2. Recording leads: bip., bipolar lead from outer and inner pole of the concentric electrode; in, inner pole; out, outer pole; R.O.C., right occipital cortex. ⅄⅄, indicates artifacts due to movement of the concentric mapping electrode. See text for further explanation.

the true site of origin of the afterdischarge response observed earlier.

It seemed feasible that afterdischarge from a hyperexcitable area or center had propagated to another part of the brain in an upward direction.

DISCUSSION

The results have indicated that many highly sensitive centers (threshold less than 1.5V) exist in the hippocampus, amygdala, cortex, and other areas that have been implicated in epilepsy. The fact that gradients of threshold voltage exist within the cortex, hippocampus, and lateral geniculate body, as well as other susceptible areas, indicated that these areas do not present a uniform susceptability to this type of activity.

The present results, combined with histological verification of electrode traces and placements, has led investigators in this laboratory (6, 7, 9) to conclude that the susceptible centers of the cortex are not at the surface, but are situated in the sublayer of the cortex at the limit between grey and white matter in the walls of sulci. Since a correlation appeared to exist between threshold and number of large nucleated cells present, it is possible that interneuronal spaces in these regions are reduced because of folding. This would increase the density of critical neurons and render the region more susceptible to afterdischarge response.

The presence of these highly susceptible centers in the sublayers of the cortex explained the necessity of the high threshold voltages required by earlier investigators (10, 11, 12) to elicit a response from the cortical surface. The high voltages are required to activate the susceptible centers by current spread.

The results of the propagation study have indicated that a susceptible center can be triggered from a distance probably by afferent connections between regions. The greater the distance of the stimulating electrode from a center, the scarcer the afferent connections become, necessitating a higher stimulating voltage to trigger it. Insensitive regions (threshold above 10V) probably respond because of stimulus current spread to a more sensitive region. Once a susceptible center has been triggered, the spread of hyperexcitability from that center may be toward a particular structure and in a selective direction. Further mapping studies are necessary to clarify the location of all the hyperexcitable centers in the brain. Once this is accomplished, more detailed studies on the propagation of afterdischarge can be undertaken.

Under normal conditions, the regions of the brain where susceptible centers or pacemakers have been found respond to incoming signals and stimuli. The role of the susceptible centers is probably of fundamental importance in controlling the overall excitability of the brain in response to afferent stimuli. A chemical or neurohumeral imbalance in the immediate environment of these centers could cause hyperexcitability resulting in the generation of epileptiform discharges.

The overall evidence, in summary, indicates that susceptible centers could play a role in the genesis of cortical or sub-cortical epilepsy.

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