16342

Effects of Electroshock Convulsions on Chronic Decorticated Cats.

ABRAHAM WIKLER AND KARL FRANK.

From the Department of Research, U. S. Public Health Service Hospital, Lexington, Ky.

Masserman[1] has presented evidence that electroshock convulsions produce marked changes in the adaptive behavior of intact cats with experimental neuroses, comparable to the effects of electroshock therapy in man. In view of the evidence[2] that metrazol convulsions have excitant effects on autonomic centers of the hypothalamus, it was considered of value to investigate the possibility that electrically induced convulsions alter not only learned adaptive responses at the cortical level, but also non-learned, subcortically integrated responses which are closer to instinctive adaptive patterns. A study was therefore made of the effects of single and repeated electrically induced convulsions on the reactions of chronic decorticated cats to various stimuli, observations being limited to directly observable phenomena in the non-narcotized, non-curarized preparation.

In addition, this study afforded an opportunity to study the electroencephalographic patterns of electroshock convulsions in animals without neocortex. This was accomplished in terminal experiments on the decorticated cats after curarization.

Methods. Six cats were prepared by successive ablation of each cerebral hemisphere under nembutal anesthesia. Two operations were made, a week or more apart, under aseptic conditions without previous ligation of the carotid arteries. After recovery from anesthesia, all preparations exhibited the usual behavior and reactions of chronic decorticated cats and remained in good condition until terminal experiments were performed 29 to 147 days after completion of decortication. Observations were made on spontaneous behavior, posture, righting reflexes, licking reflexes, rectal temperature, pulse and respiratory rates, and sham rage responses to handling and to nociceptive stimulation. To evoke nociceptive responses, a device was employed which permitted the quick application of known pressures from 1.0 to 10.0 kg to a segment of the tail for one second. With this apparatus the pressure in kg per cm^2 necessary to elicit a given response is a function of the area over which the pressure is applied. Hence, in this paper, all references to "pressure" are expressed in kilograms, understood to be applied to the specific jaw area of the instrument (1 cm^2). Sham rage was also elicited in response to presumably non-nociceptive stimuli by holding the preparation by the loose skin around the back of the neck and alternately raising and lowering it rhythmically so that the hind footpads lightly touched the surface of the table on the downward movement. Control observations were made at intervals of 1 to 3 hours over a period of 8 hours on each of two successive days and before each experiment with electroshock convulsions.

Convulsions were produced by passing 200 to 450 milliamperes of 60 cycle A.C. for 0.2 to 0.3 sec. from vertex to palate. The electrode at the vertex consisted of a battery clip covered with saline paste attached to the scalp between the ears. The palate electrode consisted of a metal rod, one end of which was covered with gauze padding soaked in salt solution, and applied to the hard palate just behind the upper canine teeth. A commercial electroshock apparatus (Offner Type 735) was employed throughout. This device permits the delivery of a predetermined amperage regardless of variations in circuit resistance or size of the head. As will be shown below, the currents used appeared to exert no deleterious effects either physiologically or anatomically. From observations on conscious patients it is known that electroshock treatments are not painful.

1 Masserman, J. H., and Jacques, M. G., *Am. J. Psychiat.*, 1947, **104**, 92.

2 Gellhorn, E., *Am. J. Psychiat.*, 1941, **97**, 944.

Studies on the effects of electroshock convulsions were begun 7 to 37 days after completion of decortication in 5 of the preparations. The sixth was utilized only in the terminal experiment, 29 days after total decortication. After 48-hour observations on the effects of single electrically induced convulsions, 5 to 9 daily convulsions were induced, following which the preparations were observed during a 4- to 39-day period. One preparation was subjected to a second series of electroshock convulsions and observed for 7 days thereafter.

In terminal experiments carried out on 4 of the preparations, records were made of the electrical activity of the remaining brain immediately following passage of the current known previously to have induced convulsions regularly. This was accomplished by inserting, under ether, a tracheal cannula and screw electrodes into the calvarium and the body of the sphenoid bond (Fig. 1). The preparation was then immobilized by repeated intravenous injections of curare ("Intocostrin," 0.3 to 0.5 cc at ½ to ¾ hour intervals) and maintained on artificial respiration without anesthesia. Leads from the screw electrodes and one ear were connected to a capacity-resistance coupled amplifier-oscillograph system with optical recording on moving bromide paper. In all experiments the leads to the amplifiers were disconnected before and during the passage of the convulsing current and replaced as soon as possible (3 to 5 seconds) afterward, with simultaneous removal of the electroshock leads, to reduce amplifier blocking.

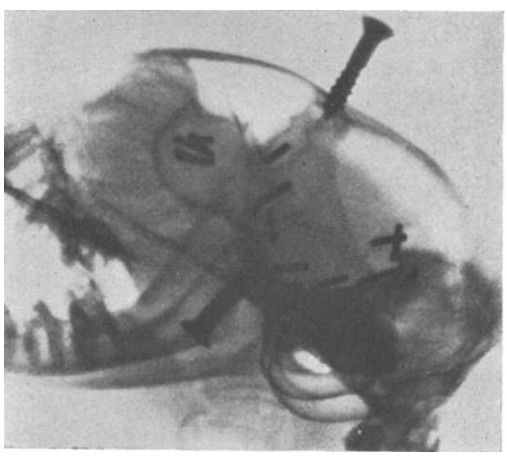

FIG. 1.
Cat No. 105 (chronic decorticate). X-ray of skull showing location of screw leads used for recording electrical activity of remaining brain in terminal experiments. Both screws are in the midline sagittal plane; the upper just penetrates the calvarium at the vertex and the lower extends to about 1 mm below the floor of the sella turcica in the body of the sphenoid bone.

After completion of these experiments the cats were sacrificed and the brain tissue was fixed *in situ* with formalin and removed for gross and microscopic study.*

Results. A. *Motor Pattern of Electrically Induced Convulsions.*

Immediately after electroshock the preparation assumed a posture of general semiflexion and for 15 to 20 seconds exhibited rapid rhythmic oscillatory movements of small amplitude involving the extremities, jaw and facial musculature. Frequently, several such paroxysms occurred, separated by quiescent periods lasting a few seconds. Finally, transient running movements of the hindlimbs appeared, after which all activity ceased for about 30 seconds. The preparation then righted itself or maintained the upright posture when so placed. During the seizure, apnea occurred, followed by transient hyperpnea. Occasionally, the preparation exhibited a burst of sham rage lasting 15 to 30 seconds, immediately after the seizure. One preparation circled for several minutes after each convulsion. With smaller currents greater variations were seen, such as sham rage without a preceding seizure or falling to one side in semiflexion without further motor activity. The motor pattern of the convulsions elicited by a given electroshock was remarkably constant for each preparation.

B. *Effects of Single and Repeated Electrically Induced Convulsions.*

Changes in temperature and pulse rate after single or repeated convulsions did not exceed spontaneous variations noted in control studies. No enduring impairment of righting re-

* The neuropathological examinations were made by Dr. I. Mark Scheinker, Assistant Professor of Neuropathology, University of Cincinnati College of Medicine.

flexes occurred after single or repeated seizures. In 4 of the preparations, vigorous licking movements of the tongue could be induced by tactile stimulation of the perineal region. The licking appeared to be directed to any object nearest the tongue, e.g., the forepaws, the experimenter's hand, etc. This response was abolished for from ½ to 3½ hours after each convulsion in 3 of the cats. In the fourth preparation, no change occurred. No additional or cumulative effects were noted after daily convulsions.

In control observations, the threshold for sham rage induced by rhythmically raising the cat from a table varied from one such maneuver in one cat to no reaction after 50 trials in another. The day-to-day variations were also considerable, except in the cat with the lowest threshold, which always exhibited sham rage after one maneuver. The rage pattern thus evoked consisted of springing or lunging, boxing and scratching movements of the forelimbs, extrusion of the claws, lashing of the tail, retraction of the angle of the mouth, dilation of the pupil, retraction of the nictitating membrane and piloerection. Vocalization, spitting or hissing did not occur. After each electrically induced convulsion, such rage reactions were either unaffected or increased as indicated by a reduction in the number of maneuvers needed to elicit the response compared with the control value for that day. After completion of a series of daily electroshock convulsions, there seemed to be some intensification of the rage response to handling, but this could not be confirmed by the threshold values which were not altered beyond the range of variation in the control studies.

In control observations the threshold for sham rage induced by graded pressure on the tail varied from 3.0 to 7.0 kg from cat to cat; in each preparation daily variations of about 1.0 kg were observed. The pattern of reaction to such stimuli was remarkably constant in each cat but varied in detail from one to the other. In general, the responses consisted of vocalization, spitting and hissing, struggling, lashing of the tail, mydriasis and retraction of the nictitating membrane. After each electrically induced convulsion, no reaction at all could be evoked even with maximum pressures of 10.0 kg, the limit of the instrument, for periods of from one to 2½ hours, and the thresholds in most instances did not return to the control level before 4 hours—*i.e.*, peak analgesic effects of over 50% to over 300% were observed. This was in marked contrast to the concomitant lowering of the rage threshold to handling described above. No significant changes occurred after completion of a series of daily electroshock convulsions.

C. *Electroencephalographic Patterns of Electroshock Convulsions.*

The electrical patterns of the seizures recorded in the terminal experiments varied in detail from one preparation to another, but the record illustrated in Fig. 2 A-C is fairly representative. After a single electroshock, several bursts of relatively high (75 to 100 microvolts) activity appeared, with frequencies varying from 2 to 21 per second. These paroxysms were separated by abruptly appearing silent intervals. In 3 of the experiments, a steady 15 to 18 per second rhythm appeared before cessation of the convulsive electrical discharge, which was followed by periodic isolated high voltage slow waves which were more prominent in tracings with a vertex lead. Such records could be obtained in each preparation several times by repeated electroshocks.

In places, a series of alternating fast and slow wave sequences was seen. Since in our laboratory typical "spike and dome" complexes have been observed in dogs following convulsant doses of morphine, we investigated the effects of this drug on the electrical patterns described above (Fig. 2 D-G). It will be noted that the slow and fast wave sequences after electroshock are more prominent in the morphinized preparation.

D. *Neuropathologic Findings.* On removal of the remaining brains after terminal experiments, the dead space left by removal of the cerebral hemispheres was found to be occupied by fibrous connective tissue which bound the dura to the underlying brain structures. Coronal sections revealed no evidence of neocortex; varying portions of the caudate

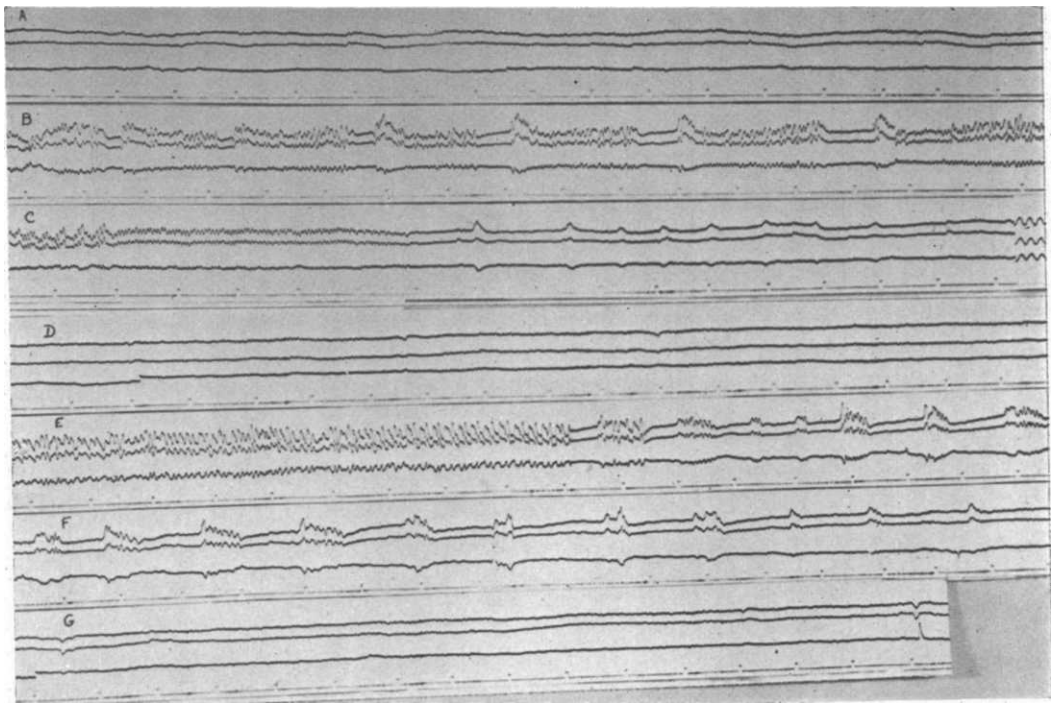

FIG. 2.

Cat No. 105 (chronic decorticate). Effects of electro-shock on electrical activity of remaining brain. Screw leads as in Fig. 1; clip lead on left ear. Preparation curarized and on artificial respiration. Time in seconds. Calibrations 23.8 microvolts peak-to-peak. In all records upper tracings are sphenoid to vertex, middle tracings sphenoid to ear, and lowest tracings vertex to ear. A, control. No significant electrical activity at this gain. B, 3 to 5 seconds after passing 450 milliamperes 60 cycle A.C. from vertex to palate for 0.3 sec. Note paroxysmal discharges of high voltage 6 to 21 per sec. waves originating in vicinity of the sphenoid lead. In places, a fast and slow wave occur in sequence, most often at the beginning of a paroxysm. C, continuation of preceding record. Note terminal regular 18 per sec. discharge of moderate voltage and random slow waves as record returns to control state. D, resting record 35 minutes after intravenous injection of morphine 20.0 mg per kg. No significant change from A. E, 3 to 5 sec. after electroshock as in B. Note paroxysmal discharges as in B, with greater tendency for fast and slow waves to occur in sequence. F and G, continuous with E. Note subsidence of electrical activity and return to control state.

nuclei, thalami and basal parts of the pyriform lobes were preserved. Microscopic study revealed evidence of degeneration with glial and connective tissue proliferation in the basal ganglia, especially in the periphery. In one specimen changes indicative of granular ependymitis were seen, and in another, evidence of mild subarachnoid hemorrhage. These changes did not differ in degree or kind from changes seen in the remaining brains of other chronic decorticated cats not subjected to electroshock or other convulsant agents in our laboratory.

Discussion. On comparison of our results with those of Masserman,[1] it is evident that, although transitory changes did occur in the licking and sham rage reactions of the former, recovery was rapid and no enduring effects comparable to those in intact neurotic animals were observed. It would seem, therefore, that the long-enduring effects brought about by electroshock in Masserman's neurotic cats were due to changes involving the cerebral cortex. This inference is supported by the observations on the electroencephalographic changes in intact cats subjected to repeated electroshock convulsions, reported by Rubinstein and Kurland.[3]

[3] Rubinstein, H. S., and Kurland, A. A., PROC. SOC. EXP. BIOL. AND MED., 1947, **65**, 348.

The differences between the immediate effects of electroshock convulsions on sham rage reactions to nociceptive tail pressure and to handling are also of interest in connection with the report by Pisetsky[4] of the disappearance of painful phantom limbs after electric shock therapy in a patient, who, though no longer complaining of pain, still displayed considerable effect. The observations on decorticated cats suggest that such analgesic effects may be partly subcortical in origin. However, since no cumulative or long-enduring effects were observed in decorticated cats it is inferred that the permanent disappearance of phantom limb pain in Pisetsky's subject was probably due to effects involving the cortex.

The striking features of the electrical activity recorded from sphenoid leads in chronic decorticated cats after electroshock are the recurrent paroxysmal hypersynchronous discharges, suggestive of "status epilepticus." The mixture of fast and slow frequencies during such paroxysms resembles the pattern seen in the clonic phases of convulsions in man, while the terminal steady 15 to 18 per second discharge is more like that occurring in tonic seizures. Also noteworthy, especially in the morphinized preparations, are the rhythmic fast and slow wave sequences which resemble to some extent "petit mal" spike and dome complexes. However, the "spike" frequencies in the decorticated preparations were not faster than 24 per second, perhaps differing in this respect from cortical seizure discharges in man. Further studies are in progress to determine more precisely the relationship of the subcortical convulsive electrical discharges to those recorded from the cortex and to the motor seizure patterns.

[4] Pisetsky, J. E., *Am. J. Psychiat.*, 1946, **102**, 599.

Summary. (1) The effects of single and repeated convulsions induced by electroshock were observed in 6 chronic decorticated cats. (2) The seizures were characterized by a posture of general semiflexion with small amplitude rapid rhythmic movements of the limbs, jaws and facial musculature, interrupted by one or more short quiescent periods, terminating in running movements after which a more prolonged quiescent phase preceded recovery. Apnea occurred during the seizures and was followed by transitory hyperpnea. (3) Body temperature and pulse rate were not affected significantly. Righting reflexes returned a few minutes after each seizure. Licking reflexes were abolished for from ½ to 3½ hours after each convulsion in 3 preparations. Sham rage in response to a non-nociceptive stimulus was unaffected or enhanced temporarily after each electroshock convulsion. Sham rage responses (chiefly facio-vocal) to nociceptive pressure stimuli applied to the tail were markedly reduced or abolished for from 1 to 2½ hours after each electrically induced seizure. (4) No changes other than those noted after single electroshocks were noted after repeated electrically induced convulsions. (5) The electroencephalographic patterns of electroshock convulsions in the decorticated preparations were characterized by bursts of relatively high voltage 2 to 21 per second rhythms separated by short silent intervals, frequently terminating in a steady 15 to 18 per second discharge before cessation of electrical activity. Slow and fast wave sequences appeared at times during the paroxysmal discharges and were more prominent in previously morphinized preparations. (6) Gross and microscopic studies of the remaining brains after completion of the experiments revealed no changes which could be ascribed to the electric currents used to evoke convulsions.