CHANGES IN THE ELECTROENCEPHALOGRAM IN CASES OF DIFFUSE AND FOCAL DAMAGE TO THE BRAIN: A CORRELATED CLINICAL AND EXPERIMENTAL STUDY.

by

GEORGE A. ULETT, B.A., M.S.

A THESIS

Presented to the Department of Anatomy
and the Graduate Division
of the University of Oregon Medical School
in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy

September 1944

APPROVED:

[redacted]

(Professor in Charge of Thesis)

[redacted]

(Dean, Graduate Division)

Sept 9, 1944

The author wishes to give thankful acknowledgement to:

Dr. Robert Dow, under whose friendly guidance and direction the present work was undertaken;

Dr. Knox Finley, who trained the author in the science of electroencephalography and assisted in the interpretation of the neuropathological material;

Dr. John Raaf, who placed clinical material at the disposal of the author and thus made a great part of this study possible;

Mr. Fred Clausseen, without whose mechanical achievements the various technics utilized would have been impossible;

Mrs. Marsha Scott for assistance with microtechnique.

TABLE OF CONTENTS

INTRODUCTION

This investigation is concerned with a study of the disturbances in pattern of spontaneous brain potentials recorded electroencephalographically from man and dog in cases of diffuse and focal injury to the brain.

In part the problem is an evaluation of the electroencephalograph as a diagnostic procedure in cases of head trauma and space-occupying lesions; for despite the large literature upon the subject of clinical electroencephalography there is still considerable uncertainty as to the importance of its role as an indicator of the severity, type and location of intracerebral pathology.

The controlled reproduction in laboratory animals of the electroencephalographic phenomena observed clinically has seemed a logical approach towards understanding the abnormal potentials in terms of altered brain physiology and anatomy.

PART ONE.

DIFFUSE DAMAGE TO THE BRAIN

A. CLINICAL STUDY

B. EXPERIMENTAL STUDY

CLINICAL STUDY

1. REVIEW OF THE LITERATURE

Previous studies concerning electroencephalographic changes resulting from head injury have for the most part dealt with severe cases of head injury examined days or weeks after the injury. Jasper, Kershman and Elvidge (1940), Glaser and Sjaardema (1940), Williams (1941) and Marmer and Savitsky (1942) all agreed that there is a correlation between electroencephalographic abnormality and severe head injury and that, to a degree, the clinical recovery of the patient is accompanied by a change of the electroencephalogram from abnormal activity to a more normal pattern. Williams (1941) studied records taken within a few hours of the injury in a few patients who had sustained mild head injuries and observed that such records might be normal. It was felt that electroencephalographic examination of a large number of patients with mild head injuries within a few minutes of their injury might be of value in determining the onset and duration of the electroencephalographic changes and might throw some light on the mechanism of concussion.

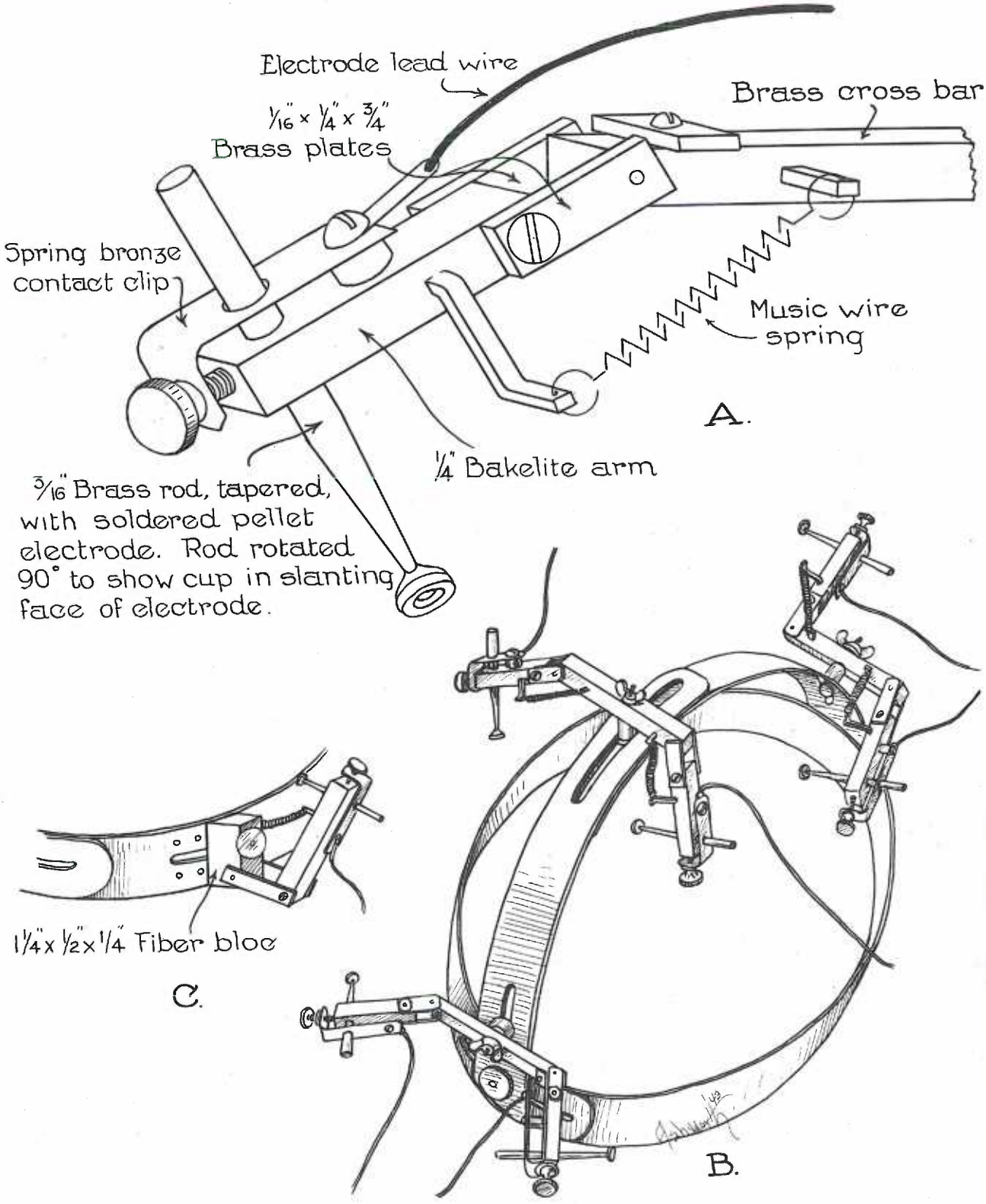
2. MATERIAL AND METHODS

The report presented here is an electroencephalographic study of two hundred and thirteen persons who sustained head injuries at the three shipyards operated by the Kaiser Corporation [1] in or near Portland, Oregon. Records were taken

---

1. We are indebted to the Kaiser Company and to the Oregon State Industrial Accident Commission for their excellent cooperation throughout this study.

Fig. 1. Headband electrode holder. (A) Shows detailed construction of spring-pressure-arm holding electrode for contact with scalp. (B) Shows total six electrode assembly on headband. (C) Detailed drawing of an individual side electrode unit such as is used in a sixteen electrode assembly.


Electrode lead wire
1/16" x 1/4" x 3/4"
Brass plates
Brass cross bar
Spring bronze
contact clip
Music wire
spring
A.
1/4" Bakelite arm
3/16" Brass rod, tapered,
with soldered pellet
electrode. Rod rotated
90° to show cup in slanting
face of electrode.
1 1/4" x 1/2" x 1/4" Fiber bloc
C.
B.

upon one hundred and ninty seven patients at the First Aid Station of the Oregon Shipbuilding Corporation. The remainder of the electroencephalograms were obtained on sixteen patients who were more severely injured, as soon as possible after they had been admitted to local hospitals. There were one hundred and eighty five men and twenty eight women in the group studied. The age range was from sixteen to eighty-seven years, the mean age being thirty-six and three-tenth years.

A push-pull amplifier with a three channel ink-writing oscillograph, manufactured by Grass was used to obtain the electroencephalographic records. In order to eliminate electrical interference, a wire shielded cubicle was built at the First Aid Station. The records were taken while the patient, with his eyes closed, was in a semi-reclining position on a bed within the cubicle. The placement of six electrodes on the scalp was such as to allow bipolar recording from frontal to parietal and parietal to occipital areas on both sides of the head. Inasmuch as the application of electrodes to the scalp with collodion is tedious and time-consuming, a more rapid method of application was sought. During the course of study, a head band electrode holder with six spring pressure contacts was developed. (Ulett and Claussen, 1944). (Fig. 1) With this device, it was occasionally possible to start taking a record within ten minutes after the patient had been struck on the head. All but twenty-eight of the two hundred and thirteen patients had records taken within twenty-four hours of injury. Most of the records upon the

more severely injured patients, who were hospitalized, were taken within the first twenty-four hours and a few were taken less than eight hours after the accident. The same methods of recording were employed in all cases. Follow-up records were taken on eighty-six of the series of two hundred and thirteen patients.

A history was elicited in each case when the patient was brought to the First Aid Station or hospital. Opinions of the patient, witnesses of the accident, ambulance men, safety inspectors, and attending physicians were recorded and evaluated in an attempt to obtain an accurate account of the accident. The scene of the accident was visited in almost all instances (by G.U.) and an attempt made to evaluate the physical factors responsible for the injury. When the patient had been struck on the head by a falling object, that object or an identical one was found and weighed and the distance of the fall was measured. When the patient fell his weight was estimated and the height of his fall measured. In eighty-three of the cases studied some approximation of the velocity of either the falling object or the person at the moment of impact in foot-seconds was calculated and the force involved in foot-pounds was determined. Other pertinent facts concerning the accident were obtained from an efficient and highly organized staff of safety engineers.

A general examination was performed on all patients immediately after the electroencephalographic record had been taken. The blood pressure, pulse, temperature, and respira-

tion were recorded and all patients were examined for evidence of injury. Of the two hundred and thirteen patients studied, two hundred and one had laceration and (or) contusion about the head. Two of the patients had tender painful necks and one had a fracture of the seventh cervical vertebra. Two had x-ray evidence of skull fracture. In only seven patients was there no external evidence of head injury but the history and statements by wittnesses that these patients had been struck on the head were so definite that they were included in the series. A neurological examination was likewise conducted and the patients sensorium evaluated. The account of events at the time of the accident as told by the patient enabled us to make some estimate of the period of amnesia during which he was mentally out of contact with his environment. In those cases in which there was impairment of sensibility at the time of examination the term"unconsciousness" was avoided and the state of the patient's insensibility was graded as (1) coma, (2) semicoma, (3) mild, moderate, or severe confusion. In defining these terms we followed the useage outlined by the Medical Research Council Brain Injuries Committee of Great Britain. [2]

As a control, records were taken during the course of the study on two hundred and eleven persons who were considered "normal" subjects. Most of these records were taken on workers

---

2. From "A glossary of psychological terms commonly used in cases of head injury", by the Medical Research Council Brain Injuries Committee, published by H. M. Stationery Office, London, 1941.

who came to the First Aid Station for ambulatory treatment of some minor condition other than head injury. Some records were also taken on foremen, office workers, nurses, or any others who happened to be near the laboratory and would submit to an electroencephalographic examination. There were one hundred and seventy one men and forty women in the control series; their age range was sixteen to seventy-seven years, the mean age being thirty-four and three-tenths years.

In order to evaluate the factor of old cerebral trauma both the control subjects and the patients with head injuries were asked whether they had experienced a previous head injury severe enough to have produced definite amnesia. Fifty-eight out of the two hundred and thirteen patients in the head injury series and seventy out of the two hundred and eleven persons in the control series gave the history of having had such a blow on the head. In both the injury series and the control series the electroencephalographic records of those who had had a previous injury showed no increase in abnormality as compared with those who had not sustained a previous injury.

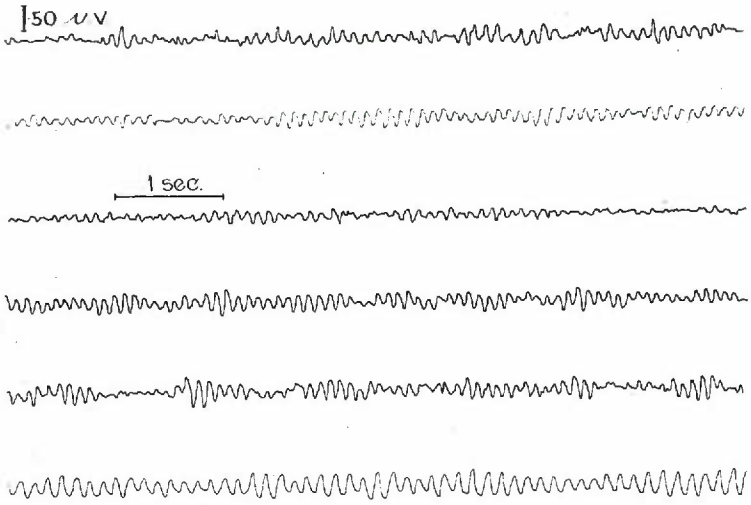
To insure uniformity within this study all records which were taken were graded by the same persons. [3] The records were classified as "normal", "borderline", or "abnormal". A range of dominant activity from and including eight to twelve cycles per second was considered normal. Slow waves below eight per

---

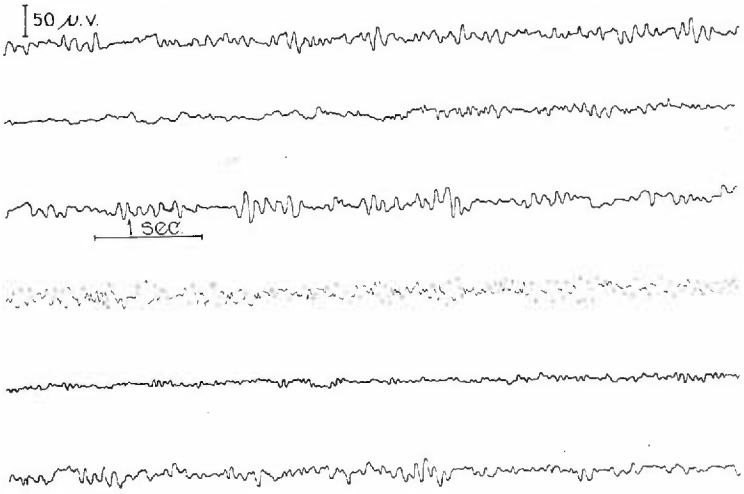
3. We are indebted to Doctor Knox Finley for his aid in record interpretation.

Fig. 2. Examples of normal, borderline and abnormal electroencephalographic records. There are six cases in each group and each record is from the left parieto-occipital lead.

SAMPLE NORMAL RECORDS



SAMPLE BORDERLINE RECORDS



SAMPLE ABNORMAL RECORDS

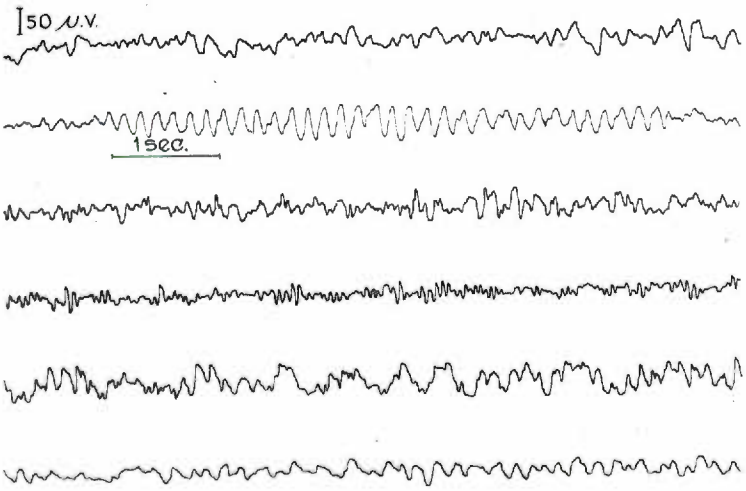
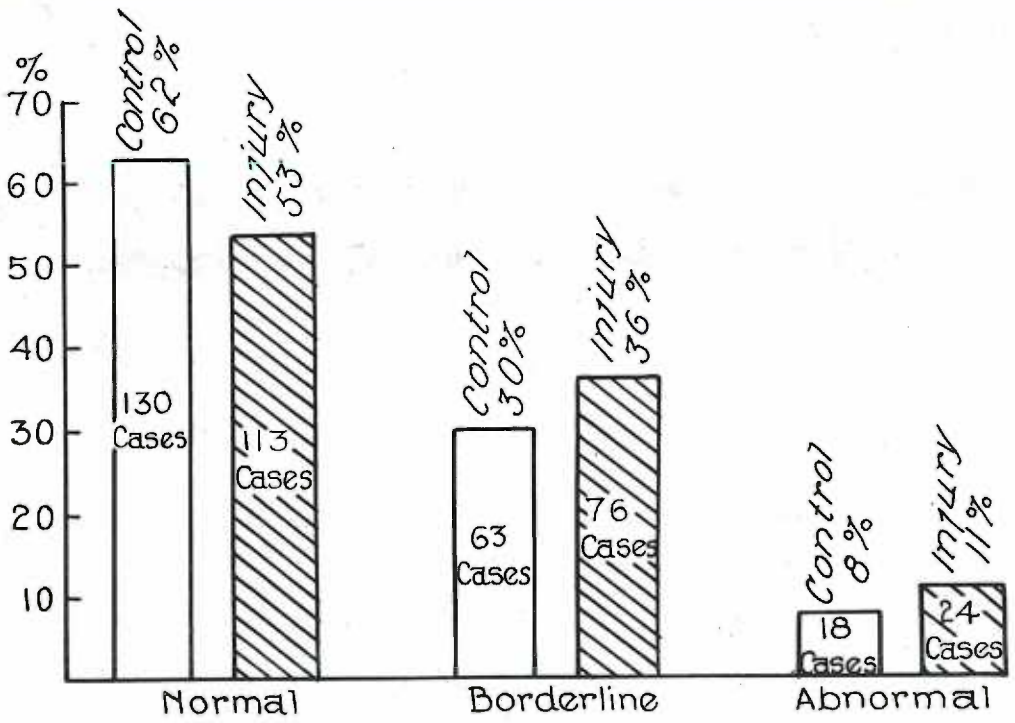


Fig. 3. Comparison of the total number of control cases with the total number of cases of head injury.

COMPARISON OF TOTAL NUMBER OF CONTROL CASES (211) WITH TOTAL NUMBER OF CASES OF HEAD INJURY (213)



second were called abnormal. Lack of definite pattern despite high amplification and bursts of high voltage activity against a normal background were considered indicative of abnormality. The greater the amount of slow or fast activity in a given record the more the normality of the record was held in question. (Fig. 2.)

3. RESULTS AND DISCUSSION

Comparison of the electroencephalograms of the head injury patients and controls: When the electroencephalograms on all of the two hundred and thirteen patients in the head injury series were compared with the electroencephalograms on the two hundred and eleven patients in the control series it was found that 62% of the control patients had normal electroencephalograms whereas 53% of the electroencephalograms from the head injury patients were normal. (Fig. 3). 30% of the control series had "border-line" records as compared to 36% of the head injury series with this type of record. Distinctly abnormal records were found in 8% of the control series and in 11% of the head injury series. It is thus evident that when the electroencephalograms of the entire group of head injury patients were compared with the electroencephalograms of the entire control group very little difference could be detected.

Correlation of electroencephalographic findings with clinical evidence of concussion: Upon the basis of severity of symptoms, we divided into groups the patients upon whom we took electroencephalographic records within twenty-four

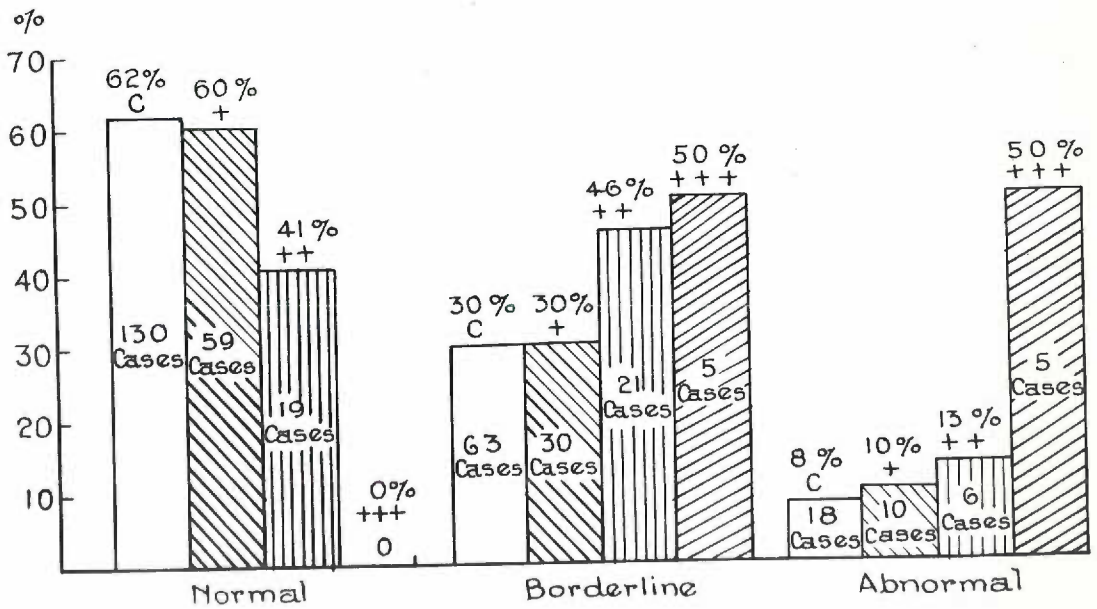
Table I.

Fig. 4. Relation between electroencephalographic abnormality and the clinical severity of the cerebral trauma.

CLINICAL CLASSIFICATION OF SEVERITY OF CEREBRAL TRAUMA

DEGREE	NO. OF PATIENTS WITH RECORD WITHIN 24 HRS.	SYMPTOMS
0	30	Scalp laceration and/or contusion. No cerebral symptoms.
1+	99	Dazed feeling, dizziness, "saw stars," diffuse headache, nausea, no amnesia for the accident, no impairment of conciousness when E.E.G. was taken.
2+	46	Definite amnesia of some duration. No impairment of conciousness when E.E.G was taken.
3+	10	Mild, moderate or severe confusion when E.E.G. was taken.
4+	0	Coma or semicoma at time that E.E.G. was taken.
	Total — 185	

RELATION BETWEEN E.E.G. ABNORMALITY AND THE CLINICAL SEVERITY OF THE CEREBRAL TRAUMA

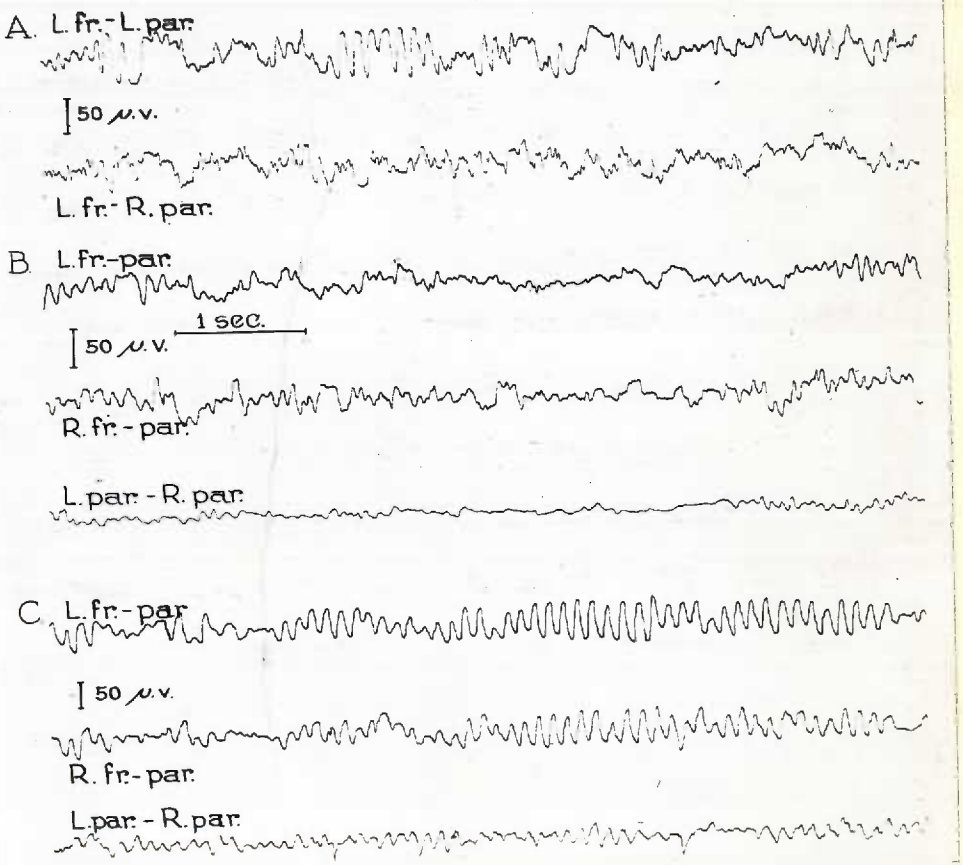


hours of injury. Out of the total of one hundred and eighty five patients who came to the First Aid Station for scalp lacerations or blows on the head and upon whom electroencephalograms were run within twenty-four hours of the injury, thirty had no symptoms except pain at the site of injury. No degree of clinical concussion was thought to have existed in these patients. Ninty-nine patients had complained of symptoms, including "dazed feelings", "dizziness", "saw stars", diffuse headache, or nausea coming on immediately after the injury. There was, however, no definite period of amnesia and no impairment of consciousness at the time the record was taken. Patients in this group were considered to have suffered cerebral trauma of plus one severity. Forty-six patients gave a definite history of amnesia of some duration as a result of the accident but there was no impairment of consciousness at the time the record was taken. Patients in this group were considered to have suffered cerebral trauma of plus two severity. Ten patients exhibited mild, moderate, or severe confusion at the time the record was taken. They were considered to be more severely injured and were classed as plus three. A category of plus four severity was reserved for patients in coma or semi-coma. There were no patients in this group in our series. (Table I). Figure 4 shows the percentage of normal, border-line, and abnormal records in the patients suffering from these degrees of cerebral trauma. It will be noted that the plus one group, which falls short of true concussion as defined by Trotter, has very little

deviation from the normal control group. There is a slight but significant shift toward the abnormal in the cases of plus two clinical severity and a decided shift in the plus three category. No case which exhibited any degree of impaired consciousness at the time the record was taken had a perfectly normal electroencephalogram and five out of the ten were distinctly abnormal. In none of the ten patients who fell in the plus three group was there any history of a previous head injury with amnesia, or a family or personal history of nervous or mental disease. Although one is perhaps not justified in expressing in percentage a group of only ten individuals it is done here for comparison with the larger groups. Subsequent electroencephalographic records have been taken on four of these ten patients. Two records have returned to normal, in two the records have as yet not changed, and in six no rechecks have been run. The following case report illustrates one of the patients with concussion whose abnormal electroencephalographic record subsequently returned to normal.

Case C1. An eighteen year old welder's helper fell about ten feet striking his head upon a steel deck. A wittness said the patient was "unconscious" for about a minute. In the First Aid Station the patient seemed to be in a state of mild confusion. He had a two centimeter scalp laceration in the region of the left forehead but there was no evidence of depression in the skull. Examination at the First Aid Station revealed no abnormality in the routine neurological examination. The patient was seen by one of us (J.R.) about four hours later. At this time he had no memory of the accident or the events which had occurred at the First Aid Station. His blood pressure was 104/60, and his pulse 80. The neurological examination again revealed no abnormalities except that the right pupil was slightly larger than the left. Roentgenograms of the skull showed no fractures.

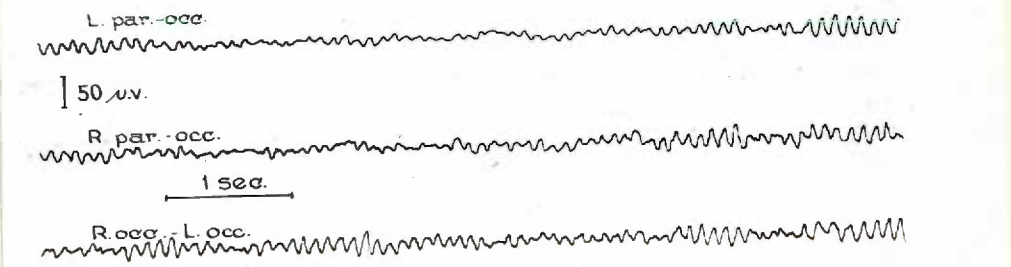
Fig. 5. Electroencephalographic records in Case 61. (A) Thirty minutes after the trauma. The record showed activity ranging from 4-9 per second, much of it above 50-60 uv made this record abnormal. (B) One hour and twenty minutes post-trauma. Decreased voltage except for occasional bursts. Disappearance of some of the slow, rolling activity. Occasional 5-8 per second waves still in evidence. The record was still considered abnormal. (C) Sixteen days after the trauma. Nine per second activity. Well organized pattern but high voltage. The record was now completely normal.


A. L. fr. - L. par.
50 μ.v.
L. fr. - R. par.
B. L. fr. - par.
50 μ.v.
1 sec.
R. fr. - par.
L. par. - R. par.
C. L. fr. - par.
50 μ.v.
R. fr. - par.
L. par. - R. par.

The clinical diagnosis was cerebral concussion. Figure 5 illustrates the electroencephalographic findings on this patient at various intervals following head injury. A completely normal record was obtained sixteen days after injury.

Time interval between injury and taking of the electroencephalogram: If the disturbance in the brain cells in concussion is a reversible process then it follows that the sooner after the injury one can take the electroencephalographic record the greater the chance of obtaining an abnormal record. We were able to start taking the electroencephalographic records on fifty-three patients within thirty minutes of the time of injury. Seventy-one patients had their electroencephalograms started within thirty to sixty minutes after the accident. Sixty-one records were obtained when the elapsed time was between one and twenty-four hours, the vast majority of these being obtained before two hours had elapsed. Records on twenty-eight patients were taken when more than twenty-four hours had elapsed since injury. It was found that the percentage of distinctly abnormal records was slightly greater in the patients examined within thirty minutes than in patients examined after thirty minutes. Nine out of the twenty-four patients having abnormal records in the injury series had their records taken within thirty minutes of the accident. It would seem, therefore, that if one is to detect a large percentage of abnormalities in the electroencephalogram in the patients with mild head injuries, such as those we have studied, one must examine the patients very early. The following case illustrates the fact that a normal electroencephalographic record may be obtained within

Fig. 6. Electroencephalographic record of case number 93. This record was started 15 minutes after cerebral trauma. This is a normal electroencephalographic record.


L. par.-occ.
50 μ.v.
R. par.-occ.
1 sec.
R. occ.-L. occ.

fifteen minutes of the time a patient sustained a true concussion as judged by his clinical symptoms.

Case 93. This twenty-eight year old painter was struck in the mid-occipital region and back of the neck by a fifteen pound piece of wood which fell fifty feet. The patient had on a felt hat but was not wearing a steel helmet. He was "knocked-out" for a few seconds and suffered an amnesia of approximately one minute's duration. At the time the record was started fifteen minutes after the accident he was not confused and he had no complaints. (Fig. 6). Neurological examination showed he had slight nystagmus and hypoactive tendon reflexes.

It is obviously impossible to demonstrate the time of onset of the abnormal waves in cases of human concussion. If information is to be obtained regarding the abnormality of the electroencephalographic record immediately after injury, the work must be done upon animals with the electrodes in place at the time the blow is struck. In their experimental work upon cats, Williams and Denny-Brown (1941) found that the time of onset of abnormally slow waves in all cases where concussion occurred was in the neighborhood of three minutes. They felt that concussion is associated with diminution or cessation of the electrical activity of the whole cerebral hemispheres and the appearance of these abnormally slow waves may represent a stage in the recovery from concussion.

Correlation between physical factors in the blow and abnormality of electroencephalographic record: Many difficulties were encountered in attempting to analyse the physical factors in a case of head injury. Steel helmets not only reduced the number of head injuries but also complicated the difficult task of estimating the force of the blow. Another

feature which at times hindered mathematical expression of the forces involved in a given accident was the difficulty of determining accurately how far an object fell. The weight of falling objects could usually be determined. Whether the blow was direct or glancing was often impossible to ascertain. When a board of some length fell it was impossible to know if the full weight struck the patient on the head. The forces involved when the patient fell were even more difficult to determine. The rapidity of movement of the head at the moment of impact might be greater or less than the acceleration of gravity because of muscular movement during the fall.

We have recognized that even under the relatively favorable conditions in which we were situated at the Oregon Shipbuilding Corporation it would hardly be possible to determine accurately the velocity at impact and the foot pounds of energy involved. However, in our series there were seventy-eight cases seen within twenty-four hours in which some estimate could be made of the physical factors. In seventy-seven the velocity of either the object striking the patient or the velocity of the patient's head at termination of a fall could be expressed in feet per second. In seventy-four cases it was possible to arrive at some kind of a figure for foot pounds of energy involved in the blow. Common experience has taught us all that the greater the force of a blow the greater the damage to the skull and cerebrum. The question whether concussion is related to the force of a blow or to the acceleration or deceleration of the head has been recently investigated by Denny-

Table II

COMPARISON BETWEEN ELECTROENCEPHALOGRAPHIC RECORDS AND THE PHYSICAL FACTORS IN THE INJURY

Normal		
32 cases	24.1 ft. sec. Range 8-56	324.2 ft. lb. Range 4-1650
Borderline 33 cases	25.8 ft. sec. Range 8-50	581.0 ft. lb. Range 5-2400.0
Abnormal 13 cases	34.2 ft. sec. Range 8-62	1077.2 ft. lb. Range 5-4500.0

Table III

COMPARISON BETWEEN THE CLINICAL SYMPTOMS AND THE PHYSICAL FACTORS IN THE INJURY

Clinical Severity of Injury	Average Velocity	Average ft. lb. of energy.
0	(6 cases) 18.4 ft/sec. Range 13-35	(6 cases) 38.6 ft. lb. Range 5-75
+	(44 cases) 21.5 ft/sec. Range 8-56	(42 cases) 321.8 ft. lb. Range 4-2,250
++	(25 cases) 31.2 ft./sec Range 11-62	(24 cases) 768.1 ft. lb. Range 20-8,400
+++	(6 cases) 31.5 ft/sec. Range 22-50	(6 cases) 1,028.3 ft. lb. Range 720-4,500

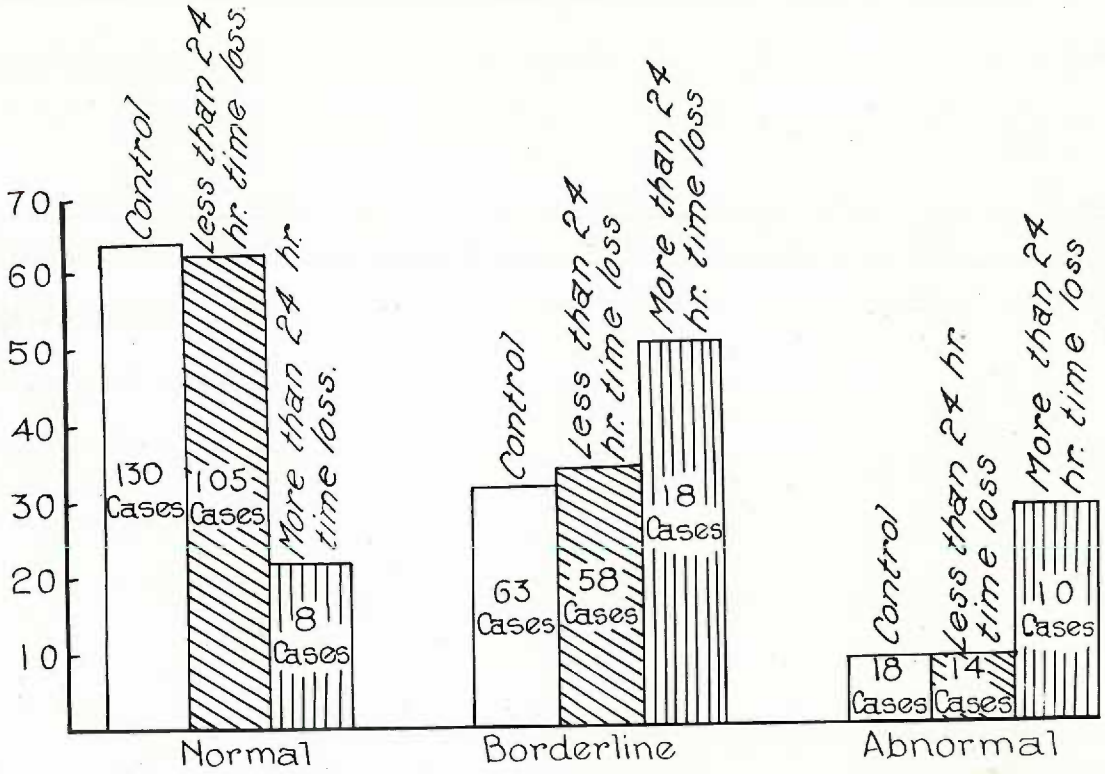
Brown and Russel (1941), Gurdjian and Webster (1943), Walker, Kollros and Case (1944), and Holbourn (1943). In our series the average velocity at the moment of impact was twenty-four and one-tenth feet per second in the group with normal electroencephalograms, twenty-five and eight-tenths in the borderline group, and thirty-four and two-tenths in the abnormal group. (Table II). It is of interest that the threshold velocity for concussion at the moment of impact in the cat and monkey, according to Denny-Brown and Russell (1941), is twenty-eight feet per second and this figure is between the average of the abnormal and borderline groups in our series. The average foot-pounds for the normal group was 324.2, for the borderline 581.0, and 1077.2 for the abnormal. The range within each group was extreme but this is expected in view of the difficulties of estimating physical factors in an individual accident. It is difficult to judge from our data whether it is the force as such or the acceleration or deceleration which is responsible for the electroencephalographic changes.

The relationship between the clinical severity of the symptoms and the average velocity of the head at the moment of impact is revealed in Table III. The relation between clinical severity and the energy involved was also tabulated. It is of interest that the average velocity of the two plus and three plus grades of clinical severity which represent true concussion, is well above the threshold of concussion as determined experimentally by Denny-Brown and Russell (1941). The average velocity for the zero and one plus injuries was well below this

Fig. 7. This figure shows a comparison of electroencephalographic records taken on persons in the control group with records of patients requiring less than twenty-four hours time off duty and with records of patients requiring more than twenty-four hours time off duty.

Table IV.

COMPARISON BETWEEN E.E.G. RECORDS IN CONTROL GROUP CASES REQUIRING LESS THAN 24 HOURS TIME OFF AND THOSE REQUIRING MORE THAN 24 HOURS TIME OFF



COMPARISON BETWEEN THE CLINICAL SYMPTOMS AND TIME LOSS FROM WORK.

CLINICAL GRADATION	LESS THAN 24 HRS. TIME LOSS	MORE THAN 24 HRS. TIME LOSS
+	84 cases 71 %	9 cases 25 %
++	31 cases 22%	20 cases 55 %
+++	3 cases 7 %	7 cases 20 %

threshold figure.

Head injury cases requiring more than twenty-four hours time off: In an attempt to survey more serious head injuries, cases requiring more than twenty-four hours time off were studied in contrast with those requiring less than twenty-four hours time off.

Figure 7 shows the differences in the two groups in respect to electroencephalographic records. It can be seen that the one hundred and seventy seven cases requiring less than twenty-four hours time off did not vary appreciably from the control group in respect to the percentage in the normal, borderline, and abnormal groups. In the other group of thirty-six patients only eight had normal records, eighteen borderline and ten (28%) had abnormal records. When patients in the two groups were compared as to the clinical severity of their symptoms (Table IV) it is seen that the more severely hurt required the most time off.

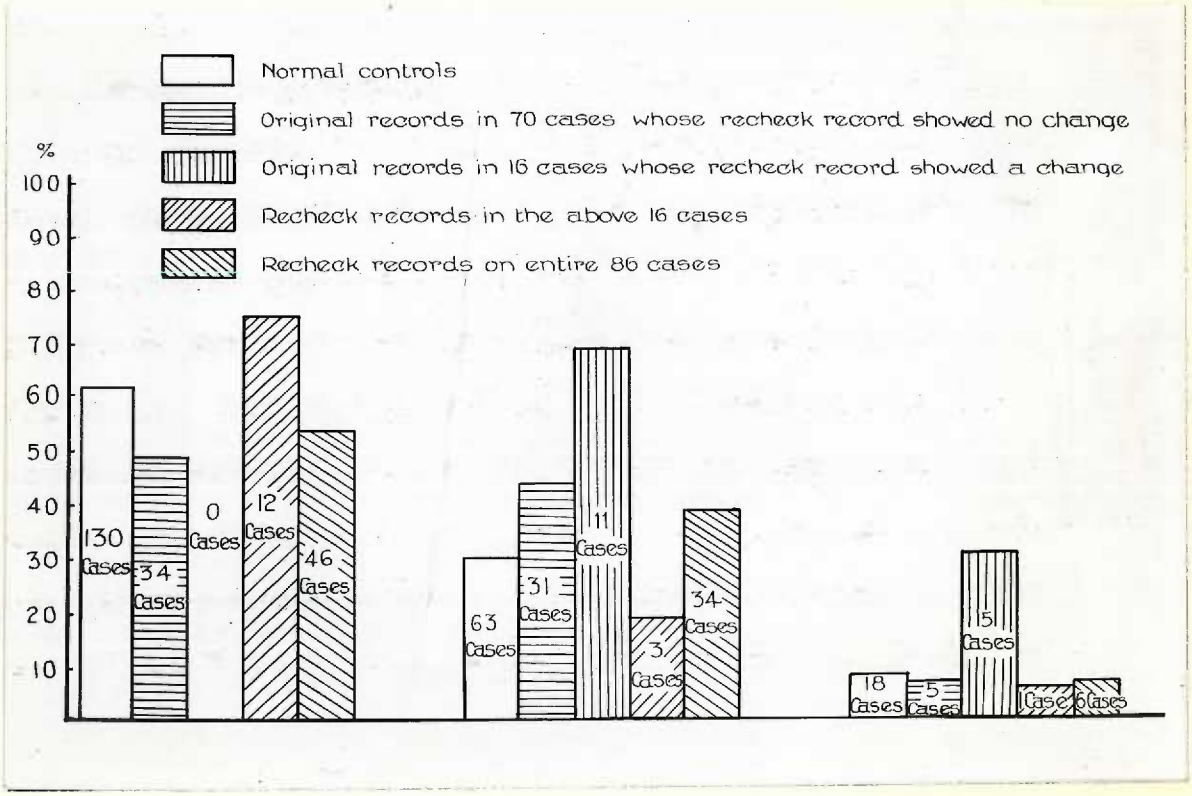
A study of Figure 7 and Table IV will reveal that if the electroencephalogram was used as a prediction of whether time loss will result from an accident it is rather inferior to clinical evaluation based on observation at the time the electroencephalogram was taken. For example, if it were predicted that all twenty-four patients in the head injury series with distinctly abnormal electroencephalograms would require more than twenty-four hours time off, one would have been wrong fourteen times and right ten times. If one should predict that the ten patients judged most severely injured, because of their mental confusion at the time the electroencephalogram was taken, would

require more than twenty-four hours time off one would have been right seven times and wrong three times.

A follow-up study of patients who had been studied electroencephalographically following acute head injury: This study consists of "recheck" records on eighty-six patients out of the total number of two-hundred and thirteen shipyard workers who were examined electroencephalographically following acute head injury. The first electroencephalogram was recorded within twenty-four hours of the time of injury in eighty-one of these eighty-six patients and in six the electroencephalogram was obtained within fifteen minutes of the trauma. The final electroencephalogram was not taken until the patient was able to return to work again or could be inducted to return to the laboratory for a "recheck" record. On the average these workers were seen about 8 weeks following the accident.

Sixteen of the eighty-six records showed a change between the first and last recording. Five records that changed were abnormal. Three of these changed to borderline and two to normal. Eleven borderline records changed, ten to normal and one from borderline to abnormal. It is felt that this last case might have been classified as abnormal at the time of the first electroencephalogram except that the reduction of amplitude of the record, a phenomenon seen frequently in head injury cases, caused this patient's record to appear more regular at the first recording than it did at the second recording. None of the thirty-four cases whose original record was normal changed when the record was repeated after clinical

Fig. 8. This figure shows the grouping of normal control records compared with the records of patients upon whom recheck records were obtained. The three major groups, reading from left to right are: normal, borderline and abnormal. The 86 patients upon whom recheck records were taken are compared from the standpoint of: (a) original records in the 70 cases whose recheck record showed no change, (b) original records in 16 cases whose recheck record showed a change, (c) recheck records in the above 16 cases and (d) recheck records on the entire 86 cases.


Normal controls
Original records in 70 cases whose recheck record showed no change
Original records in 16 cases whose recheck record showed a change
Recheck records in the above 16 cases
Recheck records on entire 86 cases
%
100
90
80
70
60
50
40
30
20
10
130 Cases
34 Cases
0 Cases
12 Cases
46 Cases
63 Cases
31 Cases
11 Cases
3 Cases
34 Cases
18 Cases
5 Cases
15 Cases
Case
6 Cases

recovery. Figure 8 shows that the seventy head injury cases which did not change after clinical recovery had a percentage of normal, borderline, and abnormal which closely resembled the normal control and that the recheck records after recovery also were very little different than the normal control. In fact the only group which is significantly at variance from the control group were the original records of the sixteen cases which showed a change on their second record. This group after recovery had records which were entirely comparable to the normal control group. This indicates that the electroencephalographic changes produced by head injuries of this severity are reversible.

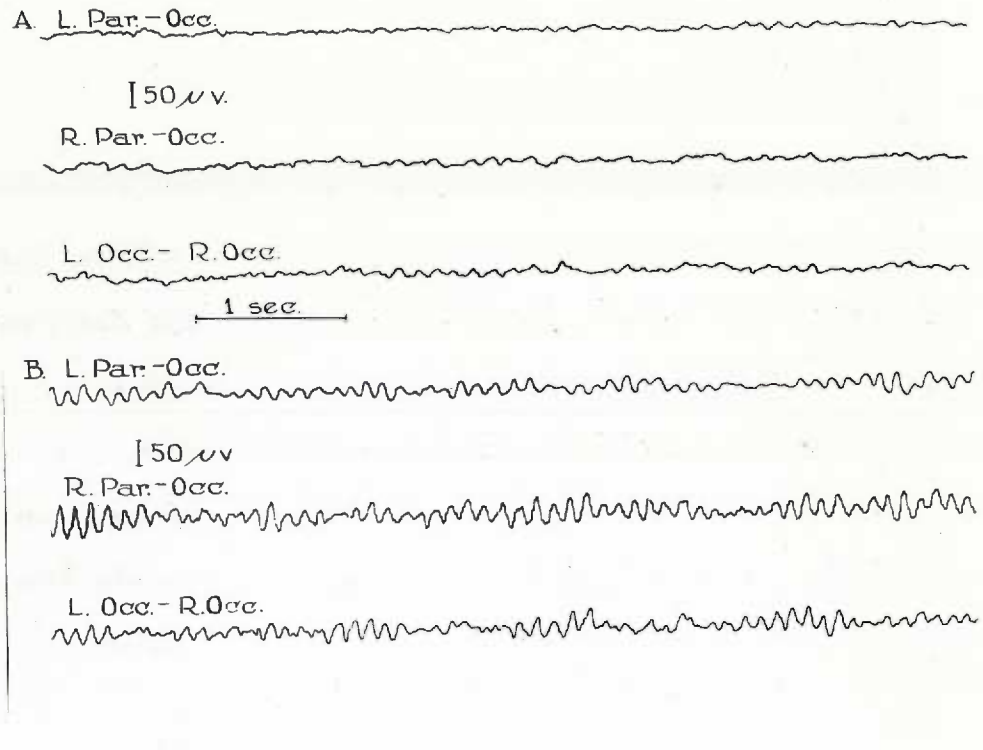
It might be expected that one would find a more severe type of head injury among this group whose electroencephalograms had shown a shift towards abnormality following head trauma. This view is seemingly supported by the fact that seven out of the sixteen workers in this group were to be found among the thirty-six injury cases (from the total of two hundred and thirteen cases) who required more than twenty-four hours time loss following the accident. An analysis of the physical factors in the blow also shows a trend towards a more severe injury among these sixteen patients. An average velocity of thirty-two feet per second at impact and an average force of seven hundred and seventeen foot pounds was present in this group of patients as contrasted with an average velocity of twenty seven feet per second and a force of five hundred and fifty six foot pounds for the cases whose

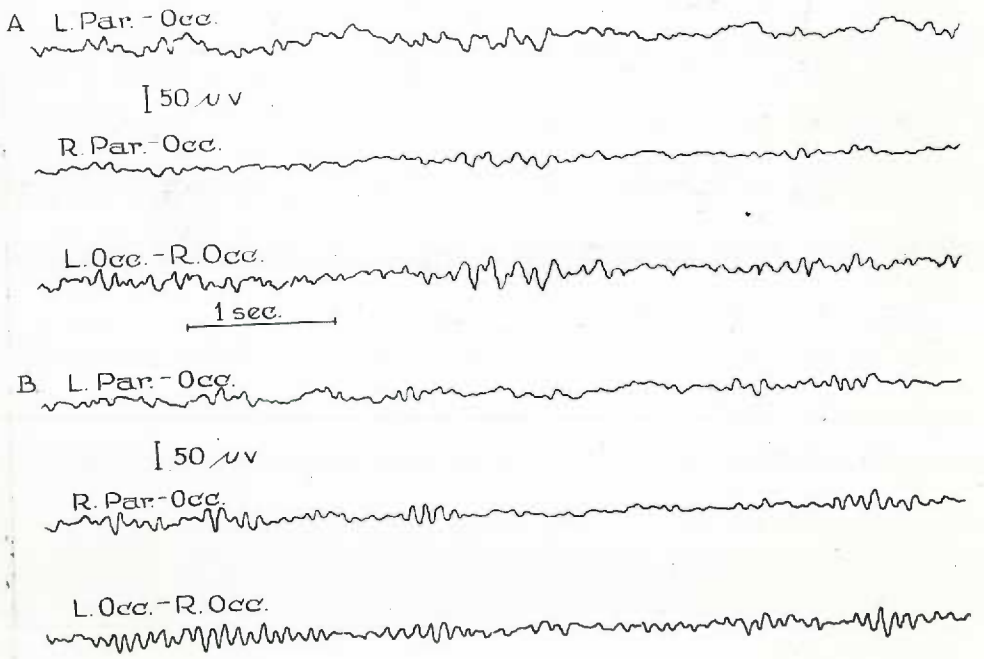
recheck record showed no change.

When the sixteen patients whose records shifted were compared as to the clinical severity of their symptoms there was a greater percentage of these patients in the two plus and three plus categories than in the entire group of two hundred and thirteen patients. However, two patients who clinically showed zero degree of cerebral trauma and five who suffered one plus degree of cerebral trauma exhibited a shift of electroencephalographic pattern to a more regular pattern upon recheck. On the other hand the patient (No. 93) in Figure C is an example of an individual whose electroencephalogram had already become normal within 15 minutes or was never altered by a blow of severe intensity. Possible individual difference in susceptibility to instability in the electroencephalogram may help to explain the wide range in the table where physical factors were correlated with electroencephalographic abnormality. It is well known that there is great individual variation in the effectiveness of over-breathing, alcohol consumption, and blood sugar reduction in the production of electroencephalographic abnormality. It is not unlikely that the effect of trauma on the electroencephalogram is likewise influenced by individual differences. That individual differences may play a role in the patient's reaction to concussion has been pointed out by Brown and Moore (1944) in a discussion of psychiatric casualties in battle, where blast concussion is an etiological factor. They state that "some soldiers who suffer from blast concussion return to battle and carry on". In this connection it is of interest

Fig. 9. (A) Electroencephalogram recorded from the left and right parietal-occipital leads and from the inter-occipital leads forty minutes after the accident in a case considered to have suffered a true concussion. This record showed six to nine per second activity and was almost flat in many places. (B) Electroencephalogram from the same patient and recorded from comparable leads two months after the day of the accident. This electroencephalogram was considered normal and showed well organized nine to ten per second activity at from forty to fifty microvolts.

Fig. 10. (A) Electroencephalogram recorded from the left and right parieto-occipital leads and from the inter occipital leads one hour after a sub-concussive blow. The record showed scattered bursts of four to seven per second activity against a background of low voltage activity. (B) Electroencephalogram from the same patient and recorded from comparable leads twenty-four days after the injury. The record at this time now showed normal bursts of ten to eleven per second activity at an amplitude slightly lower than that of the abnormal bursts in the original record.


A. L. Par. - Occ.
50 μv.
R. Par. - Occ.
L. Occ. - R. Occ.
1 sec.
B. L. Par. - Occ.
50 μv
R. Par. - Occ.
L. Occ. - R. Occ.


A L. Par. - Occ.
50 μv
R. Par. - Occ.
L. Occ. - R. Occ.
1 sec.
B. L. Par. - Occ.
50 μv
R. Par. - Occ.
L. Occ. - R. Occ.

to observe that nine out of the sixteen workers whose electroencephalograms showed a shift towards abnormality following trauma were back on the job the day following the accident. Yet one patient in this group of sixteen whose injury was of only one plus clinical severity required two weeks hospitilization and was complaining of constant headache when seen three months following injury.

An analysis of the types of change found between the initial and final electroencephalographic records reveals that non-specific phrases such as "better organization" and "fewer irregularities" best characterize the trend toward normalcy seen in the second or final record. In nine cases marked increase in voltage was seen in the second record. Such a change is illustrated by case number one hundred and seventeen.

Case 117. A thirty year old worker fell backwards. His head traveled approximately five feet to strike a steel plate. There was a post-traumatic amnesia of about fifteen minutes duration and a retrograde amnesia of two minutes duration. Neurological examination revealed no abnormalities although the patient was dazed until the time the electroencephalogram was started forty minutes after the accident. This record showed six to nine per second activity, and was almost flat in many places. (Fig. 9a) The highest voltage waves were about fifteen micro-volts. Two months later the patient was again seen. He had been clinically normal since the day of the accident and had lost no time from work. His amnesia remained unchanged. An electroencephalogram taken at this time showed well organized nine to ten per second activity with a voltage of from forty to fifty micro-volts. (Fig. 9b).

In eleven cases the frequency changed from a pattern of abnormally slow waves to one well within the normal range of eight to twelve per second. The increased frequency and

amplitude need not necessarily go hand in hand (Case 115) but usually appeared to do so.

Case 115. A sixteen year old shipfitter's helper fell backwards a distance of two or three feet striking his right mastoid process. He was dazed for about thirty seconds following the trauma and when first seen one hour after the accident had a normal neurological examination but complained of a diffuse headache. The electroencephalogram taken at this time showed scattered bursts of four to seven per second activity against a background of low voltage activity. (Fig. 10a) The patient was seen again twenty-four days after the injury. He reported that he had lost no time from work and had no complaints. The electroencephalogram taken at this time looked much like the previous record except that the bursts of waves now were from ten to eleven per second. The amplitude of these waves seemed to run about the same or a little lower than in the first record. (Fig. 10b).

In four cases more than two records were taken. In one of these (Case 61, Figure 5) the high voltage slow waves seen thirty minutes after trauma were replaced fifty minutes later by waves of lower voltage. A similar though less striking sequence was seen also in another patient who suffered a blow of like severity. The two remaining of the four cases, one of which suffered equally as severe an accident as the first two, failed to show this sequence.

In view of the highly variable changes which do occur and the finding of patterns which did not undergo alteration with clinical improvement in cases of equally and even more severe trauma, it is not possible to suggest an electroencephalographic pattern which could be said to be characteristic of a given series of pathological changes as the patient returned to normal.

EXPERIMENTAL STUDY

1. REVIEW OF THE LITERATURE

Two recent views concerning the physiological basis of concussion are in part based upon the electroencephalographic changes in experimental animals. In 1941 Williams and Denny-Brown described in detail the effects of blows in anaesthetized cats delivered manually to the freely movable head by means of a light hammer. They reported that in all instances in which concussion occurred there was an immediate reduction of voltage in the electroencephalogram which was especially selective for the faster frequencies. Slow waves of about three per second frequency appeared in the record in bursts after an interval of twenty-five to two hundred and five seconds following the injury. These reversible changes were interpreted as giving support to the theory that concussion is the immediate traumatic paralysis of the neurones of the central nervous system (Denny-Brown and Russel 1941) and that the slow waves seen in the recordings represented a stage in the recovery from this paralysis.

Walker, Kollros and Case (1944) produced experimental concussion by several methods including pendulum blows to the fixed, novocainezed head of cats, dogs, and monkeys. They propose the theory that trauma adequate for concussion causes first an initial excitation with massive discharge of the neurones of the central nervous system and is followed by an after-discharge. This is in turn followed by extinction of central nervous system activity with a decrease in

observable reflex phenomena. In support of their theory they report the occurence of an initial electrical discharge of several hundred microvolts to a milivolt in amplitude at the moment of concussion. This deflection is followed by rapid activity for ten to twenty seconds after the blow with a consequent gradual decrease to electrical inactivity which after a few seconds or minutes returns again to the preceding normal level. In addition to the changes in the electroencephalogram they enumerate other evidence of changes in reflex activity which occur immediately following a blow on the head and which they present in support of their theory.

It was felt that our observations on the electroencephalogram as recorded from animals with local or general anesthetic illuminate a greater uniformity to these divergent concepts of the nature of experimental concussion.

In order to have an index of the cerebral cortical function as many as possible of our animals were trained with a conditioned reflex technique described by W. F. Allen (1937) as correct conditioned differentiation, which Dr. Allen (1940) has shown, to be interfered with by lesions restricted to purely association areas of the cerebral cortex. It was thought that this might be the most delicate index of cortical function which could be obtained.

2. MATERIAL AND METHODS

Two cats and seventeen dogs were utilized in this study. One hundred and seven blows were delivered in the experiments here reported. Sixty-five separate blows were given to

twelve dogs and two cats anesthetized with nembutal (one cc of veterinary solution per five lb). Forty-two blows were delivered to nine dogs unanesthetized except for novocaine infiltration of the scalp. Five of the dogs anesthetized with nembutal were killed by the blow on the head while in the other seven we were unable to terminate the experiment by a fatal blow. In no instance was a dog that had only local anesthesia killed by a blow with our pendulum.

A pendulum with a rigid hitting arm to eliminate back lash and a coiled spring to increase acceleration was used. We obtained maximum velocity at impact of 39.7 feet per second and effective energy estimated at 52.1 ft. lbs. The dogs were placed in a leather harness which allowed them to stand but prevented too great movement. They were muzzled and their head fastened by rubber tubing in an appropriate position for the blow which was delivered to the occipital protuberance. The rubber tubing was of sufficient strength to decelerate the head after a movement of six to ten inches but not kept tight enough in the resting position to materially impede the original acceleration speed. By this method sufficient, gradual deceleration was obtained to avoid possible double concussion affects which might be produced when the head was allowed to strike a padded block of wood. Simultaneous records of respiration were taken in many of the experiments and electrocardiograms in all. Reflex changes and response to painful stimuli were noted. Changes in the animals behavior were recorded. Twenty-two blows were struck on six dogs previously

trained to react by lifting the right fore-paw to the sound of tapping at the rate of once a second, and to refrain from this act to the sound of tapping a board, a pipe, and the same bell at the rate of three taps per second. They were also trained to react positively to the odor of cloves and negatively to asafetida. Respiratory records were taken during this testing before and after the blows, to aid in interpreting the response according to the findings of Doctor W. F. Allen (1942). The animals were trained, until they reacted without error, before they were concussed. Eight thousand, two hundred and twenty-five separate test situations were used in training the dogs. After the blows the various clues were given until the animal was able to respond as correctly as it did before the blow was struck.

The electroencephalographic tracings in the dogs were always from multiple electrodes. In the early experiments several types of plugs were screwed into the skull with one or two embedded wires against the dura with leads between the wires or from one wire to the metal plug. Most of these proved unsatisfactory for chronic experiments. Only one of the dogs could be prevented from infecting his wound as a result of continuous scratching at the electrode plugs. Finally insulated phonograph needles were used, Hoagland (1940). The pattern of activity was identical with the various methods but muscle artifacts were somewhat more present in the latter method. The dogs were lightly anesthetized with ether for the few minutes necessary to place the electrodes and the scalp was liberally novocainized. The electrodes were removed after

each experiment and replaced when necessary for the next experiment. A four channel push-pull amplified and an ink writing oscillograph, manufactured by Grass, were used. One channel was used for electrocardiographic tracing. At the conclusion of each experiment, if the animal was not fatally injured by the blow he was anesthetized with nembutal, bled and the brain promptly removed, placed in 10% formalin and after fixation sectioned for gross pathological examination.

3. RESULTS AND DISCUSSION

A fatal result to the experiment was invariably sought by gradually increasing the severity of the blow. In five out of the twelve dogs anesthetized with nembutal a fatal blow was delivered, while in none of the nine dogs with local anesthesia was a fatal result obtained. In their ability to survive a blow to the head, there is a marked difference between the anesthetized and unanesthetized animal. We were incapable of delivering fatal blows to unanesthetized dogs with our apparatus even though some of these animals suffered blows of such intensity as to cause severe hemorrhages into the cerebral substance and the speed of the pendulum at the moment of impact in all was more than that necessary to produce severe concussion and death in cats both in our hands and in the experience of other workers.

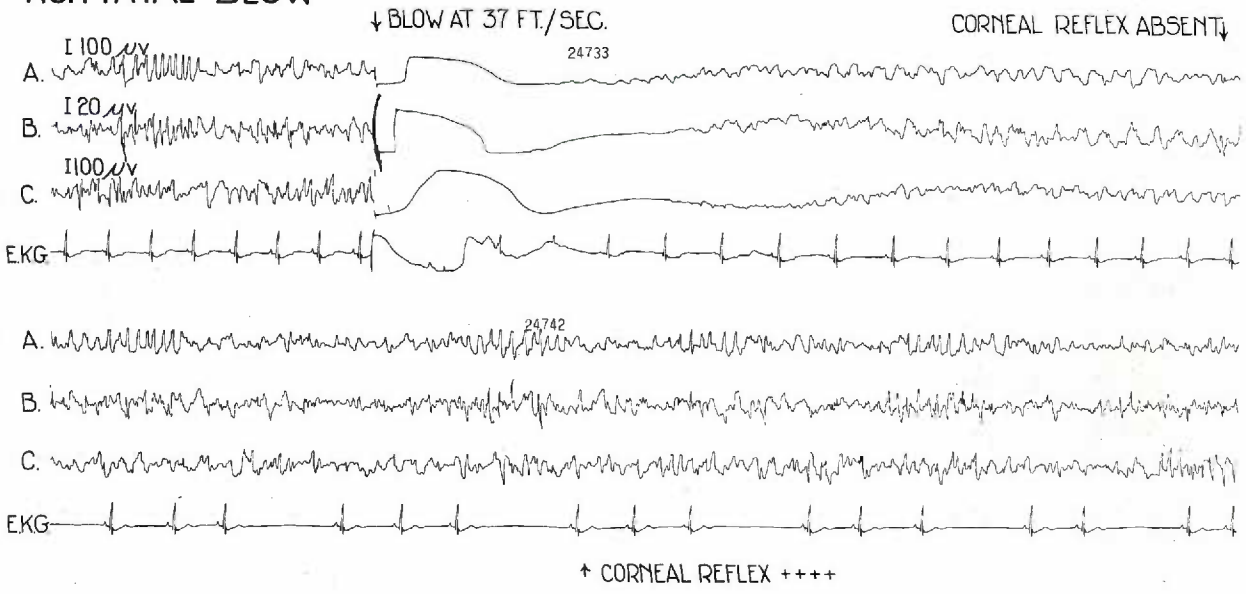
With our pendulum, blows at 30 to 35 ft./sec. regularly cause severe concussion in the anesthetized cat. One animal was killed by a blow at 35 ft/sec. The effects in the non-fatal blows were abolition of corneal reflexes for one to

three minutes with their gradual return in approximately five minutes, cardiac slowing with nodal rhythms and intermittent heart block and other arythmias. These cardiac effects may have been due to direct vagal effects or secondary to the hypertension known to be present after a blow of such severity. These frequently took ten seconds or longer to appear which makes it quite likely that they were secondary to the hypertension. The electroencephalographic changes which we observed were not as constant or predictable as the cardiac irregularities or the reflex abnormalities. However in the two cats studied a degree of diminution of amplitude was observed. In one it was unilateral, returning in ten minutes to its former level. Subsequent blows in each instance, one thirteen minutes after the first and in the other thirty minutes after the first blow caused the appearance of slow waves within the two to three seconds which was the earliest time the record could be interpreted because of unbalancing of the amplifiers. In the fatal case within twenty seconds a pre-concussion type record appeared which lasted one and one-half minutes and was followed by complete cessation of activity from asphyxia due to respiratory paralysis. In the other cat after the large sinusoidal activity at three per second had gone on for ten seconds there was a reduction in amplitude which lasted three and one-half minutes, followed by a pattern identical to the pre-concussion record. Except for the rapid appearance of slow waves after a second blow our records conformed quite well to the reports of Williams and Denny-Brown (1941).

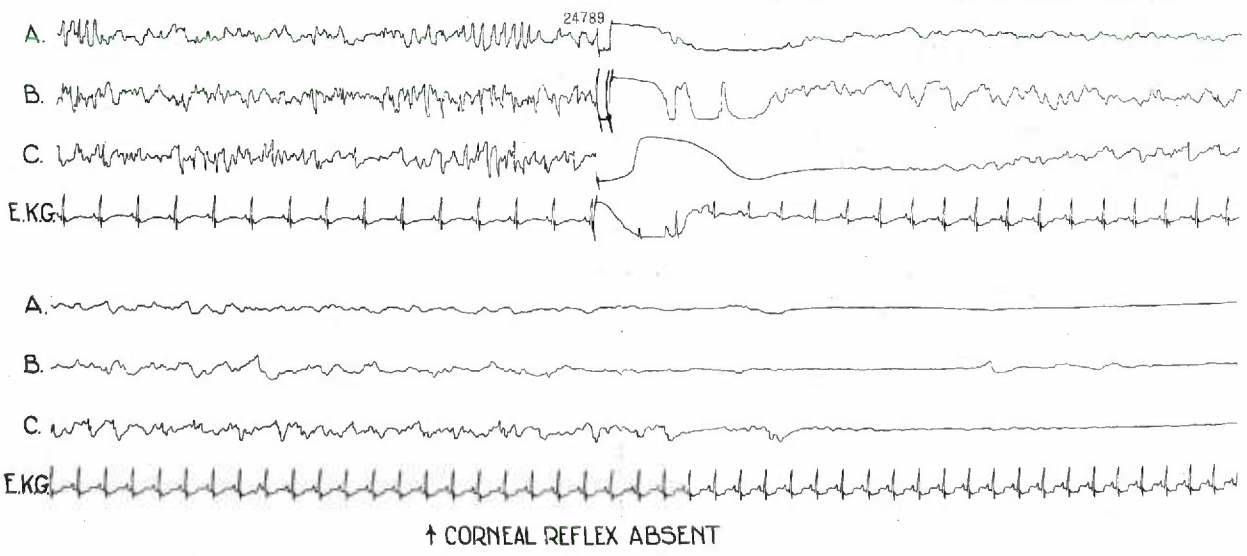
Fig. 10. Electroencephalogram and electrocardiogram recorded from a dog (5-27-43) before and after pendulum blows to the head delivered with a velocity of 37 ft. per second. Both non-fatal and fatal blows are shown. Lines A, B and C are recorded from bipolar electrodes two on the right, one on the left side of the head. In the case of the Non-Fatal Blow the first recorded strip taken before, during and immediately after the blow. The second was recorded 90 seconds after the blow. In the case of the Fatal Blow the first strip was taken just before, at the moment of and immediately after the blow. The second strip was recorded one and one half minutes after the blow (at the time of death).

1 second

NON-FATAL BLOW



FATAL BLOW



These results seemed to us to indicate that our equipment for the production of experimental concussion was in every respect comparable in its effects to that used in other laboratories. We are of the opinion that the high threshold necessary to produce concussion observed by White, Brooks, Goldthwait and Adams (1943) may have been due to back lash in the hitting arm which was not rendered completely rigid. This is an important precaution which must be taken in the construction of such apparatus in our opinion if results as to thresholds of concussion may be compared.

Results of experimental concussion which was fatal to nembutalized dogs: The five dogs in this series were subjected to a total of sixteen blows which were delivered at an average velocity of 36.9 ft./sec. with a range of from 34.2 - 39.7 ft./sec. In all animals in this group there were one to four blows prior to the fatal blow delivered during a period of one to three hours preceding. In some cases the non-fatal blows were equal in intensity to the fatal blow.

In every instance one or more of the preceding non-fatal blows caused a temporary cessation of respiration lasting from thirty seconds to two minutes and a temporary loss of corneal reflex lasting from twenty seconds to four minutes.

The pulse in practically all of the animals in this group showed a profound bradycardia from a preconcussion rate of one hundred and twenty-five (average) to eighty-five (average) (Figs. 19, 20). This bradycardia was usually at its height from thirty seconds to two minutes after the blow and diminished

gradually during the subsequent five to ten minutes. It was frequently preceded by a temporary tachycardia which lasted from five to ten seconds. In other instances the cardiac rate would be slower from the initial beat following the blow. During the period of bradycardia temporary and reversible changes in the cardiac rhythm were noted. Nodal rhythms, heart block and occasional ventricular extra-systoles were seen. These EKG changes were the most frequently observed changes following the blow in all groups of animals studied.

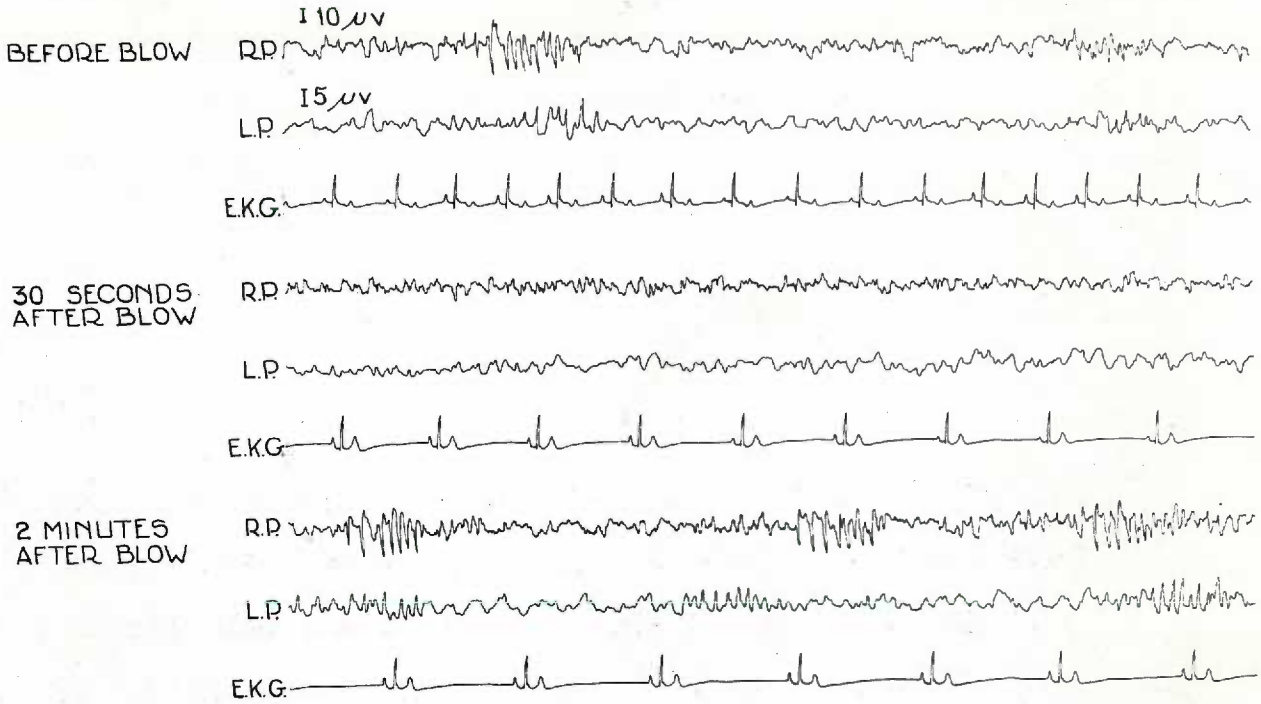
The fatal blows were characterized by the permanent loss of corneal reflexes except in one animal. In this case artificial respiration caused the corneal reflex to return only to be lost again. After the artificial respiration was stopped. The fatal blows, resulted in a tachycardia instead of bradycardia in four of the five animals. This tachycardia persisted until the effect of asphyxia manifested itself. The single instance of bradycardia following a fatal blow appeared two seconds after the blow and lasted only ten seconds in all. The rate dropped from one hundred and forty to ninety beats per minute during this interval.

The electroencephalogram in the dog anesthetized with nembutal characteristically consists of irregular waves of irregular amplitude at frequencies of from three to twelve per second. In addition groups of fairly regular waves lasting one to two seconds occur simultaneously in all leads at frequencies of nine to twelve per second. These spindles have been identified as dependent upon thalmic, cortical

Fig. 20. Electroencephalograms from bipolar right parietal (R.P.) and left parietal (L.P.) leads and electrocardiogram (E.K.G.). Fatal and non-fatal blows were struck while this dog (5-21-43) was under nembutal anaesthesia. In both instances the records were taken: (a) just preceding the blow, (b) 30 seconds after the blow and (c) two minutes after the blow.

1 second

NON-FATAL BLOW



FATAL BLOW

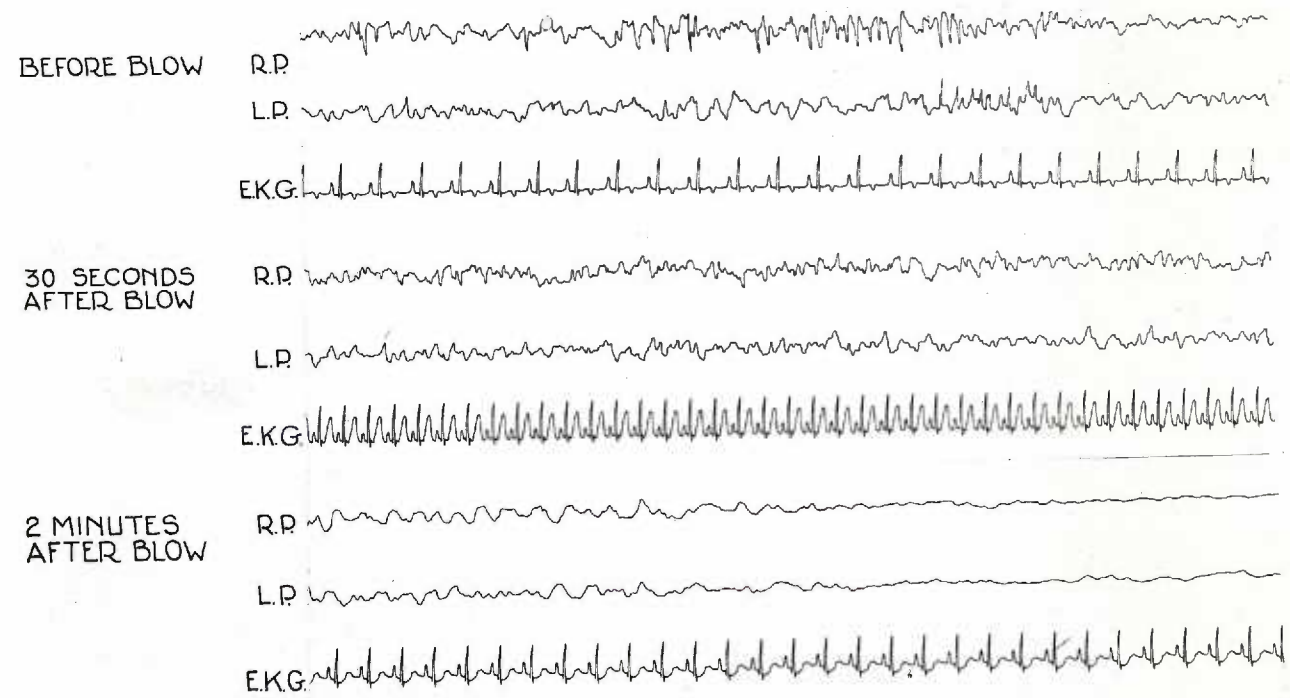
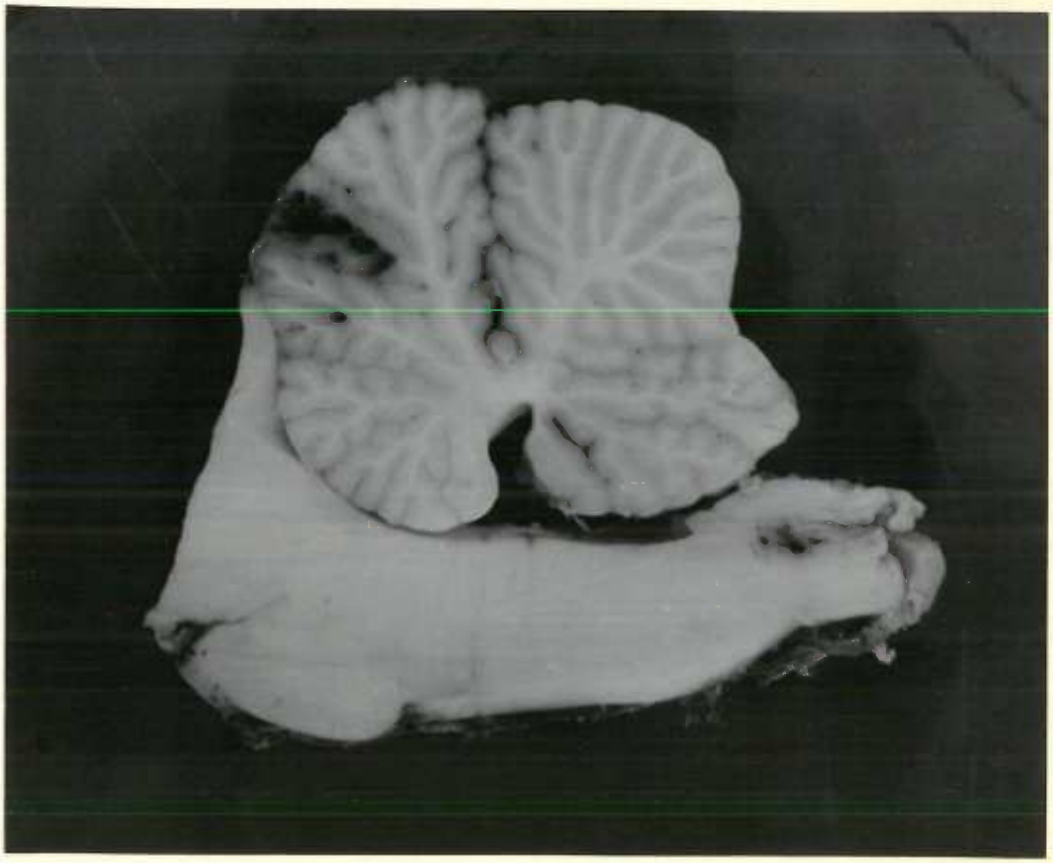


Fig. 22. Saggital section of the cerebellum of a dog that was struck a fatal blow while under nembutal anaesthesia. Hemorrhage is visible within the brain substance.



interconnections. (Morison & Dempsey, 1942).

Of the eleven non-fatal blows in these animals killed by a subsequent blow, there was a temporary abolition or decrease in the amplitude of the spindles characteristic of the electroencephalogram of dogs anesthetized by nembutal (Fig. 20) in six animals and in three there was a generalized decrease in amplitude of all types of activity (Fig. 19). This decrease in activity lasted from twenty seconds to sixty seconds. Slow waves were encountered in four out of a total of eleven non-fatal blows in this group. They lasted from one minute to thirty minutes following the blow and in one instance were exceedingly regular occurring synchronous with the "T" wave of each cardiac impulse. In only two instances was there an apparent increase in amplitude of waves after the blow. This came on some two minutes following the trauma. In one blow no change was noticeable.

The electroencephalographic changes with the fatal blows in these animals were in no way different from the preceding non-fatal blows except that instead of returning to the state present prior to the blow they disappeared probably as a result of respiratory failure and anoxia. (Figs. 19, 20). In one experiment in which artificial respiration was started after the electroencephalographic activity had ceased the activity returned to a state indistinguishable from that previous to the fatal blow only to disappear again when artificial respiration was discontinued.

In two of these animals skull fracture had occurred as a result of the blows to the occipital region. In both of these animals and in one animal in which skull fracture had

not occurred the tentorial face of the occipital poles and anterior surface of the cerebellum showed small (pinpoint to three mm.) hemorrhagic areas which on section were seen to extend into the superficial layers of the cortical substance. (Fig. 22). In two of the animals no gross lesions were to be seen.

Non-fatal nembutalized animals: The seven dogs in this series were subjected to a total of forty-five blows which were delivered at an average velocity of 38.1 ft./sec. it will be observed that the average velocity is higher in the non-fatal series than in the five animals previously described. The number of blows per dog was greater in this group because the experiment was always continued as long as good electro-encephalographic leads were available in an attempt to produce a fatal termination to the experiment.

About one-fourth of the blows caused temporary absence of the corneal reflex. In another fourth of the cases the corneal reflex following the blow was sluggish but not abolished. In one half of the cases the corneal reflex was unchanged by the blow.

After only one fifth of the blows was respiration temporarily arrested for periods of twenty to forty seconds.

All but five of the forty-five blows in this group caused some change in the heart rate or in the electrocardiographic tracing. The average heart rate previous to the blow was one hundred and forty-five. A bradycardia of some degree was produced in about half of the instances. The slowest rate

encountered was sixty and the average was ninety-nine. This bradycardia was preceded by an initial ten second tachycardia, in one instance. Tachycardia alone was noted after the blow in one-third of the cases. The average duration of this tachycardia was from ten to thirty seconds. The average rate of the tachycardia at its height was one hundred and fifty eight. Abnormalities in the electrocardiographic tracings were present most frequently during the phase of bradycardia and were present in approximately one-fourth of the blows in this group. Changes in the "T" wave were most frequently observed with extrasystoles in three instances, and nodal rhythm noted in only one. In general it may be stated that the changes in the pulse and electrocardiographic record were least frequently seen and were of less degree than were observed in the five animals who were fatally injured.

This suggests that differences in individual susceptibility to concussion was marked and greater than the limits of our apparatus for producing concussion. The cushioning effect of skin, muscles and hematoma formation over the occipital protuberance was controlled in over one half of these animals by surgical exposure and delivery of the blow directly on the bones of the cranial vault.

Approximately one quarter of the blows in this group showed no change in the electroencephalogram record. The most frequent changes present were: a decrease in the amplitude of the nembutal spindles and in a few instances their elimination for a period of thirty seconds to a minute, and an increase

in slow activity which occurred in twelve instances out of the forty-five blows delivered in this group. Isolated occurrences were: a decrease in amplitude of all types of activity in one case, an increase of all types of activity in one case, a speeding up of activity in two instances and in two instances an apparent return of the nembutal spindle activity to normal when it had been absent before the blow was struck. A possible explanation of this anomalous result was that the hypertension after the blow improved the cerebral circulation. It is obvious that although there is a slight tendency for reduction in nembutal activity followed by slow waves, this is by no means a regular occurrence and the changes produced are frequently quite unpredictable. It is possible that the absence of significant and constant changes is in part due to the fact that the threshold for true concussion was not reached in a large number of instances in these particular animals.

There were no skull fractures among the animals in this group. No gross changes were to be seen in the brains in five of the animals studied. In the remaining dogs small hemorrhagic discolorations were to be observed on the tentorial face of the occipital lobes, these extended one to two mm. into the cerebral tissue. The decreased effects of blows of greater intensity on the dogs in this series as compared to the five dogs previously described suggests differences in individual susceptibility to concussion. The cushioning effect of skin muscles and hematoma formation over the occipital protuberance was controlled in over one-half of these animals by surgical exposure

and delivery of the last blows directly to the bones of the cranial vault. Although the average weight of the dogs in this group was slightly greater than in the dogs which were killed by a blow on the head the variation was so extreme in the non-fatal dogs twelve lbs. to twenty-three lbs. that this is not an important factor.

Dogs with local anesthesia only: The dogs in this group were subjected to a total of forty-two blows with an average velocity of thirty-eight feet per second. The corneal reflex could not be tested in the unanesthetized dogs due to the fact that the dog was blindfolded. A study of respiration usually showed an increase in its rate and amplitude following the blows. This respiratory stimulation was sometimes accompanied by whining. In some cases spontaneous movement of the dog occurred just after the blow but at no time in our experience was a convulsion produced by a blow. In only three instances was respiration interrupted from periods of from twenty to thirty seconds following the blow.

The increase in respiratory rate and amplitude seen in the great majority of cases in this group of dogs is in contradistinction to the slowing and inhibition that has been frequently seen in the anesthetized cat by all workers and which was seen in approximately one half of the anesthetized dogs in this series. Here again it seems probable that had it been possible to deliver blows of greater intensity a stage of respiratory inhibition might have been produced even in the unanesthetized animal.

All but three of the forty-two blows in this series resulted in some changes in heart rate or electrocardiographic tracings. The average preconcussion pulse was one hundred and five. In thirty-four instances the initial effect upon heart rate was tachycardia. The increase might be three and one half times its preconcussion rate. The average heart rate at the height of this tachycardia was one hundred and ninety-four. The initial tachycardia lasted ten to twenty seconds and was followed by a bradycardia in nineteen instances. In five cases bradycardia without preliminary tachycardia was observed and in a few instances only tachycardia followed the blow. The bradycardia reached its maximum in thirty seconds to one minute after the blow was struck and lasted for a period of two to ten minutes. This phase of the cardiac change was marked by inverted "T" waves, heart block and nodal rhythms in about one quarter of the cases. The average rate at the depth of bradycardia was seventy-six. It is our opinion that the bradycardia and arythmias were due to reflex vagal effects secondary to a hypertension known to be a frequent effect of cerebral concussion in cats Denny-Brown & Russel (1941) and dogs Gurdjian & Webster (1943).

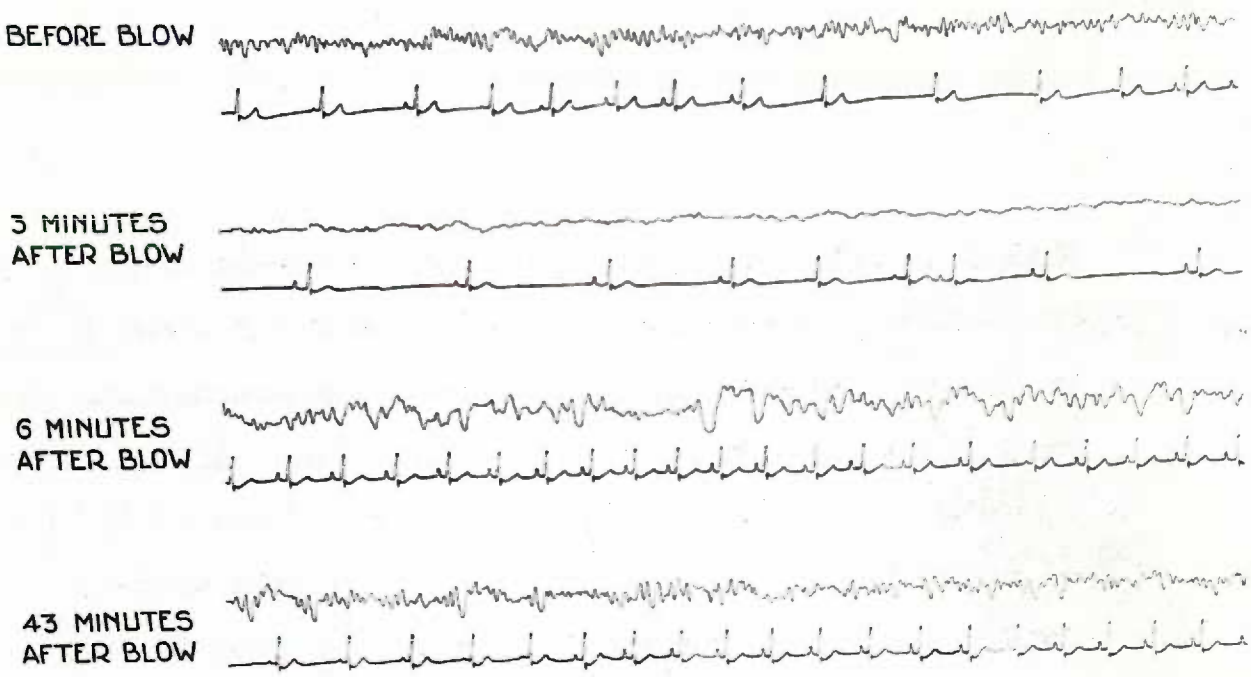
The electroencephalographic record in the unanesthetized dog is entirely different than in the dog anesthetized with nembutal. There is more variability than when anesthesia is used. Muscle artifacts are frequently troublesome in the unanesthetized animal particularly after the first blow was struck. Another factor which is difficult to control is the tendency

Fig. 21. Electroencephalogram and electro-cardiogram from two unanaesthetized dogs following non-fatal blows to the head. (A) Records from an untrained unanaesthetized animal. First strip recorded just before the blow. Second strip recorded three minutes after the blow. Third strip recorded six minutes after the blow. Fourth strip recorded forty-three minutes after the blow. (B) Records from a dog trained by the method of correct, conditioned differentiation. (This dog could discriminate almost perfectly between positive and negative mixed olfactory and auditory stimuli on tests given preceding the blow. He failed to respond to any stimuli until five minutes after the blow.) First strip recorded just before the blow. Second strip thirty seconds after the blow. Third strip three and one half minutes after the blow. Fourth strip twenty minutes after the blow.

A.

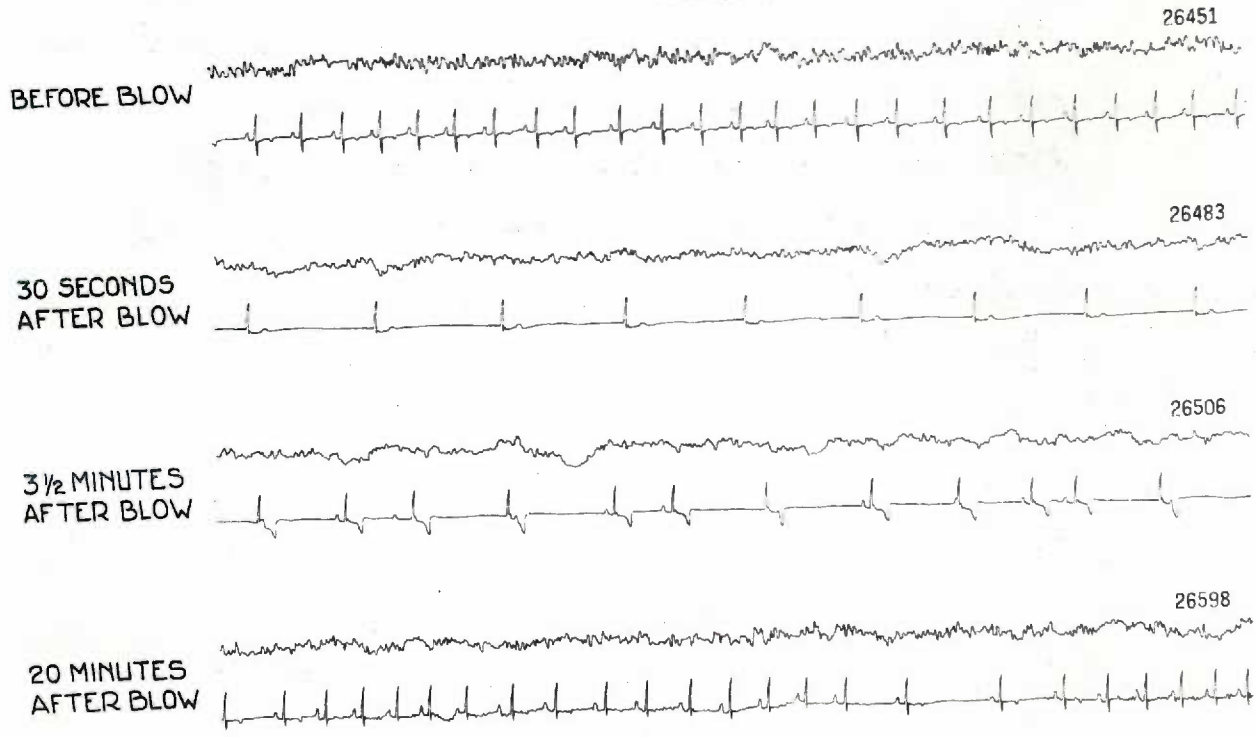
I 50 μv

1 second



B.

I 50 μv



for some dogs to go to sleep while standing in the harness. This causes the appearance of slow waves which are difficult to distinguish from the slow waves which were occasionally encountered after blows had been struck. The typical sleep potentials would disappear when the animal was stimulated or called but otherwise no distinction could be made between the two. In some animals after several blows the animal appeared sleepy and would show this tendency for slow waves in greater amount than before even though they could be eliminated by arousing the animal. It was difficult to decide whether this should be considered an abnormal electroencephalogram or not. In practice if the slow waves were persistent after the animal was obviously awake the activity was considered abnormal. Most dogs when awake have a low voltage, rhythmic activity occurring in small groups at a frequency of ten to twenty-eight per second. This is easier to pick up from leads on the posterior part of the head. A diminution of amplitude followed approximately one third of the blows in this group and in about one half of these this was combined with persistent slow waves. (Fig. 21). These seemed to occur simultaneously and no tendency was observed in the unanesthetized animal to exhibit slow waves following a period of diminished activity. The duration of this change in the electroencephalogram change varied from a period of two minutes to the remainder of the experiment, as long as two hours. As a rule the activity returned to its previous level in five to ten minutes. In no instance was there any increase in frequency or amplitude

of the activity as reported by Walker, Kollros & Case (1944) in the cat.

Effects on condition reflexes by the blows of this severity were evident in all instances except two blows in one animal. The effects observed were at first, no responses whatever followed by a period in which mistakes were frequent. The total effect lasted from three minutes to two days in one instance. Excluding two experiments one where the effect lasted several hours and another for two days, the average duration for the effect on olfactory clues was eighteen minutes, and for auditory clues, fourteen minutes. In an individual animal there was a definite trend for one or the other systems to be consistently more affected than the other. In view of the fact that no inhibition of reflexes and respiration was seen during the periods of deficient conditioned responses it is obvious that conditioned reflexes are more readily affected by these blows than are ordinary reflex activity and other vital functions. The defect in the responses was almost always purely a failure to respond to the positive clue responses, and only twice were incorrect positive responses noted in both instances an incorrect pull of the leg to asafetida. The possibility arose that this effect on the reflexes might be simply a strong negative reinforcement in as much as whipping was used to punish the animal after an incorrect positive response during the training period. The duration of the defect was against this interpretation as the inhibitory effect of a whipping rarely lasts more than a few tests separated by about thirty seconds

each. In order to further test this in one animal in whom a strong effect on the conditioned reflex by the head injury was observed, blows of equal intensity were delivered to the base of the tail. The average duration of the defect in the auditory clues in this animal after head injury was 41 minutes and for olfactory clues 38 minutes. It was further observed that following successive blows on the head there was a progressive increase in the duration of the effect after each blow. The effect of the conditioned reflexes following blows on the tail from the same height, which was an injury more nearly resembling the whipping used during training, caused an average duration of the defect of two minutes for the auditory clues and of three minutes for the olfactory clues but in each instance almost all the effect was noted after the first blow and practically none following subsequent blows.

A comparison of the electroencephalographic changes recorded after the blow was struck and the effect of the blow on the conditioned responses shows in general that the blows which we were capable of delivering effected the conditioned reflexes more regularly than they did the electroencephalographic record. Of the twenty blows in the trained animals only five showed readily recognizable electroencephalographic changes which lasted on the average of seventeen minutes as compared to eighteen blows which resulted in changes in the conditioned reflex lasting on the average about sixteen minutes. This figure for average duration does not include two animals affected for one and two days in their responses.

In order to test the validity of our opinion that the initial deflection and subsequent absence of any activity on the electroencephalographic record for the first three to five seconds was due to an artifact caused by the blow to the skull, a blow was struck with voltage dividers in the circuit before and after the death of the animal. The initial deflection appeared the same when the animal was dead or alive and in both instances the deflection was over seven mil. volts. So far as the conditions of our experiments are concerned a blow on the skull causes a movement artifact (Fig. 19) which is responsible for changes in the record for the first three to five seconds after the blow. In all statements above concerning negative electroencephalographic results it must be understood that we had no information of brain activity for the first three to five seconds of the blow due to this movement artifact.

In these three animals small effusions of blood which extended into the cerebral substance were seen on the tentorial face of the occipital lobes. In two cases there was some bruising of the anterior face of the cerebellum.

We have been unable to confirm the observation of Walker, Kollros, and Case that a blow on the head in an animal results in an increase in the frequency of the cortical activity for ten to twenty seconds after the blow. In our method of leading, the initial deflection observed is a movement artifact and we are not able to record activity during the three to five seconds after the blow because the amplifiers

are temporarily unbalanced. We have recorded electrical phenomenon accompanying a major convulsive seizure following electrical stimulation of the brain through electrodes applied to the skull. We have never observed any electrical phenomena comparable to that seen after blows on the head. Furthermore, the electrically induced convulsions were not accompanied by any pulse or E.K.G. changes which have been so consistently present following concussion in our experience. The two conditions seem entirely different phenomena in our experience.

The action potentials in the spinal cord and in peripheral nerves following cerebral trauma have not been studied here. The demonstration of such potentials by Walker and his associates are convincing evidence that there is a mechanical stimulation at the moment of impact. This has also been shown by Krems, Schoepfle and Erlanger (1942) and is undoubtedly responsible for the "stars" seen after blows on the head. The conclusion however that this excitation is responsible for the clinical manifestations of concussion seems unwarranted. Maximum electrical stimulation of peripheral nerves even if repeated many times over fails to cause reduction in muscle response seen following a single air blast to the nerve and indicates to us that something more happens to nerve tissue subjected to trauma than simply excitation. The fact that there is an increased susceptibility to the effects of concussion in the animal under general anesthesia with nembutal seems also to argue against any possible stimulating effects of the blow being responsible for the clinical manifestations of concussion.

Anesthesia should reduce the excitation and thus be a protecting influence just as it is a protection against convulsive seizures and post convulsive paralysis if the clinical symptoms of concussion were comparable to the changes which follow electrical or chemical stimulation as suggested by Walker, Kollros & Case.

Our results seem to show that the higher centers of integration are more susceptible to traumatic effects than are the more vital reflex mechanisms. It is also evident from our work that electroencephalographic records as we were able to record and analyze them are not as delicate an index of disturbance of cerebral activity as are conditioned reflexes such as we were using. It is possible that appropriate tests designed to show minimal changes in cerebral function would have brought out more changes than the electroencephalograph did in the clinical material recently reported. (Dow, Ulett, & Raaf, 1942). It was observed in this work that electroencephalographic changes were consistently observed only in the patient obviously confused at the time the record was taken. Our results suggest that, in evaluating the effects of head injury, it is necessary to test the patients ability to carry out relatively complicated mental processes if one is to detect minimal changes following head injuries. It is felt that our results fail to support the concept recently advanced that the "clinical manifestation of concussion...is the result of intense excitation of the central nervous system...". It is felt that the cerebral trauma has a direct effect of a temporarily paralyzing nature independent and beyond any mechanical stimulation of neurones which may or may not be produced by the blow.

PART TWO

FOCAL BRAIN INJURY

A. Clinical Study

B. Experimental Study

CLINICAL STUDIES

1. REVIEW OF THE LITERATURE

The presence of abnormal brain potentials arising from focal intracranial lesions was reported by Berger (1931) and by Foerster and Altenburger (1935). The practical significance of such foci was shown by Walter in 1936 when he used the electroencephalograph to correctly localize the pathology in five cases of brain tumor.

Studies of a larger number of clinical cases were soon forthcoming. Gibbs, Munro and Wegner (1941) found the electroencephalograph to give 73% of verified localizations in a series of fourty-four clinical cases. Their accuracy was 90% if only those cases were included in which there was involvement of the cerebral cortex. The accuracy of localization in this study corresponds to the earlier figure of 75% correct localizations in a series of fifty cases studied by Williams and Gibbs (1938). Yeager (1940) of the Mayo Clinic reports 86% successful localizations of cerebral lesions in a series of forty-three cases. Schwab (1941) reported from the brain-wave laboratory of Massachusetts General Hospital 84.5% correct localization in cases of intracranial pathology. Lambrose, Case and Walker (1943) studied ninety-seven cases with supratentorial lesions and found that the electroencephalogram, while abnormal in 83.5% of the cases, gave localizing findings in only 52.6%. This was a favorable statistic when compared with positive clinical localizing findings in 65.9% of cases and positive localizing skull X-ray findings in 28.8%.

TABLE V

Percentages of correct localization of supratentorial intracranial lesions by the methods of electroencephalography, roentgenography, pneumoencephalography, ventriculography and neurological examination, as reported in the available literature.

Worker	Cases localized	% of correct localization				
		EEG	X-ray	Enceph	Ventr.	Clinical
Gibbs et al.	44	73%				
Yeager	43	86%		82.3%		81.4%
Lambros et al.	97	52.6%	28.8%			65.9%
Schwab	115	84.5%				
Johnson	565		24%	68.8%	92.2%	

It is of interest that a ten year study at the University of Michigan Hospital (1943) including some five hundred and sixty-five cases showed an accuracy of localization of brain tumors by skull x-ray alone of 24%. Air encephalography gave correct localization in 68.8% and ventriculography in 92.2% of the cases so studied. One may conclude from the literature then, that in cases suspected of intracranial lesions, the electroencephalograph should, statistically, give localizing findings at least twice as often as routine skull roentgenograms and that it is about as accurate as either clinical observations or pneumoencephalography. Table V. Lambrose and workers (1943) included in their series fifteen cases in which the electroencephalograph localized tumors where the clinical findings alone were insufficient for localization. They concluded that, "Electroencephalography should be a routine procedure in every case suspected of harboring an intracranial tumor."

Electroencephalographic methods for the localization of intracranial lesions depend upon the detection of differences in amplitude and (or) frequency from comparable regions of the head and by comparison of the recorded brain wave patterns with established norms.

Commonly a focus of abnormally slow or delta [4] waves is seen over the region of cortical damage. A study of the

---

4. The term "delta wave" was first introduced by Walter (1936) to describe the slow waves arising from the vicinity of brain tumors. Since that time it has been widely used to describe all types of slower-than-normal brain waves.

reversal of phase relationships between pairs of scalp electrodes may also give a clue to focal cortical disturbance. This method of studying phase reversal was first used by Adrian and Yamigawa in 1935 in an attempt to determine the point of origin of the alpha rhythm and was found to be accurate in localizing ten per second potential oscillations of a few millivolts amplitude generated by artificial means within the skull of a cadaver. Walter (1936, 1937) adopted this method of studying phase relationships to the localization of brain tumors and found that the point of wave reversal was an indication of the site of the intracranial lesion. Williams & Gibbs (1938, 1938a, 1939) and Gibbs, Munro and Wegner (1941) popularized this method of localization in the United States, and Gibbs (1940) has described the procedure in some detail as a routine well adapted for use with the electroencephalographic equipment manufactured by Albert Grass. In the Gibbs Routine the head is treated as though it were a rectangle and 16 electrodes are spaced approximately equidistant in rows of four each, allowing for linear recording along the ordinates and abcissae. The focus of abnormality is located at the point of crossing of the two rows of electrodes which show the greatest abnormality.

Jasper and Hawke (1938) described a method of triangulation in which groups of three electrodes each, are placed over the scalp in the form of equalateral triangles thus permitting a study of the phase relationships of the waves as recorded from the pairs of electrodes forming the sides of the triangles.

In their hands this method has given localizations accurate to within a few millimeters.

Gibbs (1940) points out that he and other workers in the field have found such routine methods of value only in those cases in which the pathology involves the cerebral cortex. Other methods of recording, have therefore been attempted in order to localize lesions confined to the deeper portions of the brain. Such methods have included attempts at localization of lesions in the optic tract by observing differences in alpha activity (Lemere, 1937), simultaneous comparison of bipolar and monopolar records (Jasper 1941), and the utilization of leads on the base of the skull (Grinker, 1939).

Electroencephalographic techniques are less satisfactory for the localization of posterior fossa disturbances than for lesions above the tentorium. Lemere (1937) found no localizing difference in the recorded alpha rhythms in a case of cerebellar neoplasm, and Williams and Gibbs (1938) utilized the absence of a detectable electroencephalographic focus as a means of diagnosing a posterior fossa tumor in a case where the differential diagnosis lay between a supra-tentorial and infra-tentorial lesion. Gibbs, Munro and Wegner (1941) though reporting no cases of posterior fossa lesion state that, "In our experience such foci are usually lacking". Lamboros, Case and Walker (1943) in a study of twenty-nine patients with posterior fossa tumors were unable to localize the lesion by electroencephalography in any case.

It was first suggested by Smith and workers (1929) that

TABLE VI

SUMMARY OF THE RESULTS OF OTHER WORKERS IN THE LOCALIZATION OF POSTERIOR FOSSA LESIONS BY THE ELECTROENCEPHALOGRAPH

Author	Cases	Age Range	Comment
I. Cases in which no localizations were possible.			
Williams and Gibbs (1938)			No detectable focus
Gibbs, Munroe and Wegner (1941)		0	Occipital foci usually lacking
Lemere (1937)			No alpha differences on the two sides
Lambros, Case and Walker (1943)	29		No localizations possible. Diffuse abnormality in 18 cases.
II. Cases in which there was Frontal Lobe Localization.			
Witwer and workers (1943)	1	under 17 yrs.	Frontal and occipital foci.
Holland (1941)	1	"	Post-operatively only.
Smith and workers (1940)	1	"	Pre-central better than occipital localization
Rheinberger and workers (1942)	2	"	
Rheinberger and workers (1942)	8	over 17 yrs.	
Gibbs (in the discussion of a paper by Smith and workers 1940)	1	age not given	

Table VI Continued

III.	Cases in which there was localization in the mastoid region.			
	Walter (1938)			Delta focus just behind the mastoid region in a "few" cases.
	Rheinberger and workers (1942)	1	under 17 yrs.	Tumor has invaded lateral ventricle
	Rheinberger and workers (1942)	6	over 17 yrs.	
IV.	Cases in which there was posterior parietal and occipital localization.			
	Marinesco and workers (1938)	1	under 17 yrs.	
	Rheinberger and workers (1942)	1	"	Abscess
	Holland (1941)	2	"	
	Smith and workers (1940)	7	"	
	Lyman (quoted in article by Rheinberger and workers 1938)	7	"	
	Marinesco and workers (1938)	1	over 17 yrs.	Pontine angle tumor.
	Rheinberger and workers (1942)	5	"	Perineural fibroblastomas.

electroencephalographic localisation of posterior fossa lesions may be seen more frequently in patients of the younger age groups. He and his co-workers presented a series of eight patients ranging in age from four to nine years, in whom occipital foci were seen in conjunction with lesions below the tentorium. Further verification of this thesis is to be found in a study of the seventy-four patients with posterior-fossa lesions whose cases have been presented in the available literature. (Table VI). Twenty-four of these patients have been reported as having posterior-parietal or occipital foci of localization. Eighteen of these (75%) were below the age of sixteen years.

Although the placement of scalp leads directly over the posterior fossa has not been technically feasible, abnormal foci limited to the posterior parietal and occipital regions are of diagnostic value in infratentorial lesions particularly when, as occasionally occurs, a frontal lobe lesion must be included in the differential diagnosis. A disturbing factor, however, is the not infrequent appearance of frontal lobe disturbances in the electroencephalogram in cases of posterior-fossa tumors. Such disturbances have been reported by five different workers (Table VI). It should also be mentioned that posterior fossa lesions may also give a bilateral focus of abnormality and some have been described as giving an abnormal focus only on the side opposite to the lesion.

Focal lesions other than brain tumors are also localized by electroencephalography. Cases that have been studied by this method include; subdural hematomas (Jasper, 1940, Rogers 1941 and Sjaardema and Glaser 1942), cortical atrophy (Lemere

1937, Rubin 1939, 1940, Walter and Wyllie 1937), traumatic scars (Jasper and Hawke 1938, Case and Bucy 1939), areas of cortical excision (Marinesco, Sager and Kreindler 1938), contusions (Williams 1941), abscess (McDonald and Korb 1940), cerebral aneurysm (Woodhall and Lowenbach 1943), old vascular lesions (Yeager and Baldes 1942) and syphilitic gumma (Rheinberger and Siris 1940).

With such a variety of pathological lesions, some demanding, others contraindicating surgical interference, the question arises as to whether or not the electroencephalograph can give some clue as to the kind and amount of intracranial pathology. Lambros, Case and Walker (1943) feel that it is impossible to distinguish between the electrical changes produced by different kinds of intracranial lesions. In the case of both cerebral trauma and brain tumor the abnormally slow activity described has ranged from one to seven waves per second (Jasper, Kershman and Elvidge 1940, Marinesco, Sager and Kreindler 1938, and Case, and Bucy 1938). Walter and Wyllie (1937) report that the mode frequency of brain tumors is three waves per second whereas Case and Bucy (1938) maintain that one to two per second activity is most frequently seen. Yeager (1942) alone claims that it is possible to differentiate between such pathological types as are characterized by: (a) meningiomas, (b) gliomas and (c) non-neoplastic lesions. He fails however, to state the basis for such differentiation.

It seems agreed that the greater the amount of tissue damage the greater the amount of electroencephalographic abnormality

(Williams and Gibbs 1938, 1939, Walter 1938, Gibbs, Munro and Wegner 1941, Rogers 1941, and Scarff and Rahm 1941). Williams and Gibbs (1938) have stated that the most abnormal slow-waves are found at the periphery of large meningiomas, in cortex infiltrated by gliomata, in the edematous cortex overlying brain abscess and in cases of progressive idiopathic degeneration. Gibbs, Munro and Wegner (1941) write that as the lesion progresses in severity the waves become progressively slower, of higher voltage and have less superimposed activity. In Walter's (1938) series of proven brain tumors the three cases not detected by the electroencephalograph were either small meningiomas or astrocytomas. In cases of extreme brain damage with destruction of the overlying cortex (Scarff and Rahm 1941), over cystic cavities (Williams and Gibbs 1938, 1938a and Case and Bucy 1938) and where both electrodes are placed well within the boundries of a hematoma (Jasper, Kershman and Elvidge 1940) brain potentials are not recorded.

It has been suggested that with the electroencephalograph one may sometimes distinguish deep from superficial lesions. Williams and Gibbs (1939) feel that high voltage two to three per second waves are indicative of cortical damage whereas deeper lesions of the same severity give indefinite slow waves of a lesser amplitude. Jasper, Kershman and Elvidge (1940) have differentiated subdural from intracerebral hemorrhage by the presence of superimposed "cortical" activity in the latter. Similar evidence has come from the study by Smith, Walter and Laidlaw (1940) of occipital foci presumably produced by pressure

of posterior-fossa lesions against the tentorium. He has suggested that in cases where the lesion was deep and not destructive of cortex the delta waves were merely an elevation of the baseline with normal waves superimposed. In cases with more severe damage to the cortex the "alpha-wave-producing tissue" was damaged and only delta waves appeared.

Thus far we have mentioned only those abnormal records having slower than normal frequencies. Jasper (1941) has described faster than normal frequencies as "spike" foci in connection with meningo-cerebral cicatrix, focal atrophic lesions and from the cortical destruction of brain tumor and brain abscess. As a rule however, foci of high voltage cortical potentials of faster than normal frequencies are infrequently described in cases of space occupying intra-cranial lesions (Williams and Gibbs 1939). Such foci are seen more commonly in cases of arachnoiditis (Witwer, Derbyshire and Corrigan 1943) and in epilepsy (Jasper 1941).

2. MATERIAL AND METHODS

In this study one hundred and thirteen localizing, sixteen electrode, electroencephalograms were recorded from one-hundred and two patients seen on the neuro-surgical and neurological services of Dr. John Raaf and Dr. Robert S. Dow. All electroencephalograms were recorded by means of a portable push-pull amplifier, three-channel, ink-writing oscillograph manufactured by Mr. Albert Grass. Most of the records were recorded in the shielded electroencephalographic laboratory of the Good Samaritan Hospital. A few of the earlier records were recorded on the

TABLE VII

Forty two electroencephalograms showing evidence of focal abnormal disturbance.

No. Cases	Diagnosis	Verified		Not Verified
		Surgical	Clinical	
22	Supratentorial tumor	19	1	2
5	Subdural hematoma	2	3	
5	Cortical atrophy		2	3
3	Jacksonian epilepsy		3	
2	Infratentorial tumor	2		
1	Idiopathic epilepsy			1
1	Cardio-vascular accident	1		
3	No diagnosis			3
42		24	9	9

surgical floors of Good Samaritan and Saint Vincents Hospitals. All recording was bipolar, and electrode application was by means of a sixteen electrode model of the spring-pressure electrode headband (Fig. 1) designed by Ulett and Clausson (1944). The placement of electrodes as shown (Fig. 11) allowed for equal spacing of electrodes, a good sampling of activity of both hemispheres and an adaptability of the numbering system both to the ordinate-coordinate method of Walter (for which the automatic selector on the Grass built equipment is designed) and for the method of triangulation as described by Jasper and Hawke (1938).

All of the electroencephalograms used in connection with this study were taken and interpreted by Mr. George Ulett. The initial interpretations of the records were verified by Dr. Robert Dow. Record analysis was by simple scanning of the records in a search for abnormal waves and for focal disturbances in comparable sections of the record from homologous areas.

3. RESULTS

Evidence of a localized focus of intracranial pathology was found in forty-two of the one hundred and two cases upon whom localizing electroencephalograms were taken. (Table VII). Twenty nine of the one hundred and two cases came to either surgery or post-mortem examination. In twenty three (79.4%) of this group of verified cases the electroencephalographic findings were in keeping with the surgical or post-mortem diagnosis. In two other cases electroencephalographic foci

which had been considered as only "suggestive" were verified by surgical exposure. In twelve cases in which pathological confirmation of the results was not possible the electroencephalographic foci of abnormality agreed with the foci suggested by other clinical and laboratory procedures. Thus of the forty-two localizing electroencephalographic foci, thirty-five (83.3%) were substantiated by pathological and (or) clinical methods.

Value of the localizing electroencephalographic technic in different types of intracranial lesions: (a) Supratentorial brain neoplasms. There were twenty-four proven intracranial neoplasms in this series. The electroencephalograph correctly localized nineteen (79.1%) of these tumors. In addition there were two tumors in which the electroencephalographic localization was considered only as "suggestive". In three cases the electroencephalograph failed to detect any localizing focus and these records were graded respectively as diffusely normal, abnormal and borderline. In four other patients it seemed likely from clinical findings that a brain tumor was present. Three of these cases had borderline non-localizing electroencephalograms. The other case had a focally abnormal electroencephalogram. Additional laboratory studies, however, failed to substantiate the original clinical impression and so these four patients were dismissed to return for further study at a later date.

Several other methods of localizing intracranial neoplasms were used on this series of patients and hence may be compared with electroencephalography, these included: careful history,

neurological examination, routine roentgenography, pneumoencephalography and ventriculography. Of these the first two methods, namely history and neurological examination were available in every case. From the history of the case alone correct localization of the lesion was possible in thirteen of the twenty-four cases. In two cases the history alone would have led to incorrect localization of the lesion and in eight cases the history was non-contributory. The findings upon neurological examination were consonant with the final diagnosis in ten of the twenty-four cases. The findings of the neurological examination alone would have led to incorrect localization of the lesion in three cases and neurological examination was non-contributory in ten patients. Considering history and neurological examination together, that is from an opinion of the patient before any resort was had to laboratory procedured, correct localization was possible in fifteen of the twenty-four cases (65%).

Antero-posterior and lateral skull roentgenograms were obtained in sixteen of the twenty-four cases. Localization of intracranial lesions from such a procedure is most frequently made by observing calcification at the site of the tumor, by detectable erosion of the cranial vault or by shift of the calcified pineal body. Deviation from the normal in any of these specifications in even a slight degree was considered positive confirmitory evidence of a localized lesion. In seven cases (41.2%) such evidence was present. The method of pneumoencephalography was utilized in seven of the twenty-four patients

TABLE VIII

Percentage of correct localization by the methods of electroencephalography, roentgenography, pneumoencephalography, ventriculography and clinical examination of the patient in twenty four cases of verified supratentorial intracranial lesions.

EEG	X-Ray	Enceph	Vent	Clinical
79%	41.2%	71.4%	91%	65%

with intracranial tumor. In two patients there was insufficient filling for diagnosis. The percentage of correct diagnosis in these seven cases was therefore 71.4%. Ventriculography was resorted to in thirteen cases. It was satisfactory in all except one case. The percentage of correct diagnoses by ventriculography in this series is then 91%.

Table VIII summarizes the findings in this series of supratentorial lesions in such a manner that they may be compared with the results of other workers. (Table V).

(b) Infratentorial lesions. There were two infratentorial tumors in this study. Both of these cases were medulloblastomas. Both cases were correctly localized by the electroencephalograph (100%). These two cases fell within the age limit set by Smith and workers (1940) as the group in which electroencephalographic localisation is possible. In one of these cases, that of a seventeen year old girl, there was seen a bilateral posterior occipital five per second focus of abnormal activity with occasional three per second waves at an amplitude of fity microvolts. Localizing diagnosis was not possible from clinical findings and history by pneumoencephalographic studies indicated a posterior fossa lesion. The second case was that of a child of seven and one half years of age with a medulloblastoma which invaded the right cerebellar hemisphere. Clinical findings, history, ventriculography and electroencephalography all gave localizing evidence in this case.

(c) Subdural hematoma. Two cases of subdural hematoma in this series were proven by craniotomy. In both of these

cases the electroencephalographic lateralization was correct. In one case the disturbance was typified by one to four per second waves which were of higher amplitude and in greater abundance and showed frequent phase reversals on the affected side. In the other case slow waves were seen over a wide area on the normal side whereas the area about the lesion was characterised by slow delta waves of low voltage which gave the record the appearance of being almost flat. Three other cases were suspected of having subdural hematomas on the basis of history and clinical findings. In all three of these cases the electroencephalograms were abnormal. One showed a definite left sided occipito-parietal focus, one a right parieto-occipital focus and the other, although considered as only "suggestive" showed some evidence of preponderant left sided abnormality. It was not possible to prove the diagnosis in any of the last three cases.

(d) Miscellaneous localized lesions. Localizing electroencephalograms were obtained in three cases of Jacksonian convulsions, five cases of cortical atrophy, one case of idiopathic epilepsy and one recent, localized, vascular accident. In all of these cases the electroencephalographic localization agreed with the localization suggested by other methods of investigation.

(e) Cases with no electroencephalographic focus. There were sixty cases in which no electroencephalographic focus was found. Twenty of these had normal, eighteen borderline and twenty-two abnormal records. The clinical diagnoses accompanying

TABLE IX

Sixty cases in which the localizing electroencephalogram showed no focus of abnormal activity.

No. Cases	Diagnosis	Normal	Bord.	Abnl
7	Post traumatic cerebral syndrome	4	2	1
5	Post traumatic convulsive seizures	1	2	2
5	Grand Mal Epilepsy (idiopathic)	2		3
3	Brain tumors (proven)	1	1	1
3	Brain tumors (suspected)		3	
3	Psychoneurosis		2	1
3	Cerebro-vascular accident	1	2	
2	Spontaneous subarachnoid hemorrhage	1		1
2	Petit Mal Epilepsy			2
1	Epileptic equivalent			1
1	Subdural hematoma (suspected)			1
1	Hypertensive encephalopathy			1
1	Intra-cerebral hemorrhage basal ganglia (proven)			1
1	Migraine	1		
1	Hysteria		1	
1	Hysteria with unconscious attacks		1	
1	Convulsions secondary to typhoid encephalitis			1
1	Psychoneurosis (encephalitis?)			1
1	Central Nervous System Syphilis	1		
1	Narcolepsy and cataplexy	1		
1	Congenital bloc, aqueduct of sylvius			1

Table IX Continued

1	Alzheimer's disease		1
1	Multiple Sclerosis	1	
1	Tuberculoma of Pons with meningitis	1	
12	Cases in which final diagnosis was not reached at time of compilation.		
60			

these cases are shown in Table IX.

Type of electroencephalographic pattern as compared with type of focal pathology: To determine whether inspection of the electroencephalogram would enable prediction of the type of pathology to be disclosed at craniotomy the twenty-four cases of surgically verified electroencephalographic foci were subjected to analysis. In reviewing the records the following points were considered: (1) the slowest wave frequency recorded from the focus of abnormality was selected from a representative sample of tracing from each case; (2) the mode frequency of abnormality was selected as being the wave frequency most representative of the sample under consideration; (3) a figure representing amplitude was obtained by measurement, in microvolts, of the highest abnormal delta wave on the sample tracing; (4) the amount of superimposed normal and rapid activity was determined by counting all waves over eight per second on the sample; (5) a figure for comparison of the amount of brain tissue involved by the different types of tumors was determined by considering the number of lines of recording which showed waves of the mode abnormal frequency as a percentage of the total number of lines of recording (twenty-four) in the initial survey of each patient by the ordinate-coordinate method.

The samples of recording used in procedures 1-4 above were ten second samples selected as being free of artifact and typical of the total recording from the area under question. All estimations were made by scanning the records and counting waves against the one-fifth second time mark rulings of the

TABLE X

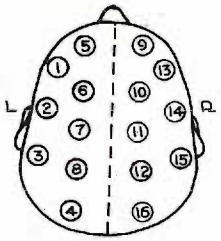
Analysis of a representative ten second sample of the electroencephalogram recorded from each of four cases of meningioma, six cases of astrocytoma and six cases of glioblastoma-multiforme.

Type	No.	Slowest wave	Mode abnl. frequency	Superimposed activity	Highest voltage	% of head involved
Meningioma	4	1.2/sec	1.6/sec	64 waves	34 mv.	41%
Astrocytoma	6	1.1/sec	1.6/sec	50 waves	53 mv.	66%
Glioblastoma	6	1.8/sec	3.2/sec	61 waves	88 mv.	54%

electroencephalographic paper. No attempt was made to utilize the more complex methods of record analysis that have been proposed in the literature. (Grass and Gibbs 1938, Engel, Romany, Ferris, Webb and Stevens 1944). It is true that this more or less subjective method of analysis may be open to just criticism, however, at present such criticism may also be leveled at the usual methods of grading clinical electroencephalograms. The type of patient studied and the conditions under which recordings were made did not allow for obtaining a record that was ideal for research analysis. Such ideal records (of greater length and uniformity and with complete freedom from artifacts) are the goal but not the usual achievement of the clinical electroencephalographic laboratory. It would seem, therefore, that the records and methods of analysis used here are probably more in keeping with those found in the field of applied electroencephalography and hence any conclusions from this study should have the value of clinical applicability.

Among the twenty-four localized and surgically verified lesions the only pathological entities represented by a sufficient number of cases to permit group comparison were sixteen intracranial neoplasms which included six cases of glioblastoma multiforme, six astrocytomas and six meningiomas. Table X lists the indices obtained by analysis of the records from each of these groups. From this table it can be seen that the numerical indices fail to reveal any very marked difference between the meningioma and the astrycotoma groups. The only noticeable differences seem to be a tendency for the astrocytomas

Fig. 11. Representative samples from each of the 16 cases of supratentorial brain tumor that was localized electroencephalographically. These tumors were classified pathologically into three groups: glioblastoma-multiforme, astrocytoma and meningioma.



1 second

GLIOBLASTOMA-MULTIFORME

P-128 6-2 I 20 μV

P-130 6-2 I 50 μV

P-98 1-5 I 20 μV

P-44 10-14 I 20 μV

P-47 1-5 I 20 μV

P-33 10-14 I 50 μV

ASTROCYTOMA

P-69 11-15 I 50 μV

P-15 7-5 I 50 μV

P-53 I 20 μV

P-95 9-13 I 50 μV

P-25 11-15 I 20 μV

P-18 12-16 I 20 μV

MENINGIOMA

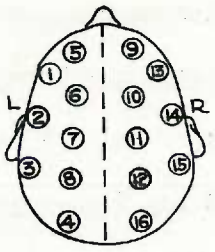
P-54 1-5 I 50 μV

P-97 1-5 I 20 μV

P-43 10-14 I 50 μV

P-58 9-13 I 10 μV

Fig. 12. Changes in the electroencephalographic record that may occur with variations in electrode placement, time of recording and mental state of patient. (a) Electroencephalograms taken from over the site of an intracerebral astrocytoma (electrodes 9-13), and from electrodes progressively removed from the abnormal focus (electrodes 10-14 and 11-15). The record from the abnormal focus (9-13) most closely resembles tumors of the astrocytoma group, that from 11-15 more nearly resembles the type of record from a case of glioblastoma-multiforme. (b) Representative samples of electroencephalograms which were recorded five days apart from over the site of an intracerebral tumor. Although no change was apparant in the patient's mental status the second recording shows delta waves of higher amplitude than those seen in the first recording. (c) Electroencephalograms taken at a single session to demonstrate the change in record that can occur with alteration in mental status of the patient. The first strip was recorded shortly after a Jacksonian convulsion and while the patient was in a post-convulsive state of confusion.



1 second

a

150 μV

9-13

Frontal

10-14

Fronto-Parietal

11-15

Parietal

b

150 μV

6-2

2-1-44

6-2

2-6-44

c

150 μV

1-5

Confused

1-5

Alert

to show a somewhat higher voltage and to have fewer rapid and normal waves superimposed upon the waves of abnormally slow frequency. Some indices of the glioblastoma-group, however, are quite different from those of the other two groups. These tumors seem to have an electroencephalogram in which the delta waves are of a faster frequency and higher voltage and carry superimposed fast and normal frequencies to almost as great an extent as do the meningiomas. With regard to the percentage of the head area showing abnormal changes in the recorded electroencephalogram the meningiomas seem to cause the least disturbance, the astrocytomas the greatest. [5]

Figure 11 shows representative samples from each case of the three groups. The activity shown is recorded from bipolar leads across the area of focal abnormality. The differences between the three groups are well illustrated here. A difference not clearly emphasized by analysis in numerical terms of frequency and amplitude is more easily detected as a pattern difference by inspection of the records.

Figure 12 illustrates the way in which a record may vary when recording conditions are altered. In (a) the typical changes recorded from a pair of electrodes over the site of the lesion in a case of astrocytoma are seen to be altered in such a way that the picture may resemble that of a glioblastoma multiforme as one records from areas more distantly removed

---

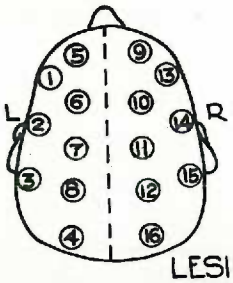
5. Because of the small group of tumors in this series the above findings must be considered only as observed tendencies until such a time as they can be verified by study of a larger number of tumors.

from a frontal focus. The findings in (b) demonstrate how the wave form from a similar area may vary from day to day and (c) the changes that can occur in a localizing record with alteration of the mental status of the patient. In this instance the record was begun shortly after a convulsion, while the patient was in a post-convulsive state of confusion. These variations in record pattern that occur apart from changes due to the pathological type of the lesion all tend to lend a note of caution to the interpretation of any particular electroencephalographic pattern as characterising a pathological entity.

The electroencephalograms were also studied with the patients grouped according to age. The findings here showed only the not unexpected tendency for higher voltage waves to appear in the younger age groups. A consideration of the records from the point of view of anatomical location of the lesion revealed that among the nineteen localized supra-tentorial neoplasms there were eight frontal lobe, two temporo-parietal, two fronto-parietal, six temporal and one parietal lobe lesion. The indices of superimposed activity ran respectively: 53, 47, 68, 72 and 178. This shows a slight trend towards a greater amount of superimposed activity as the posterior portion of the head is approached, a fact quite in keeping with the greater preponderance and higher voltage of the alpha activity normally recorded from the posterior regions of the head.

Only two surgically verified subdural hematomas were included in this series. One of these, cas P-36, had an electroencephalographic localization in the right parieto-occipital

Fig. 13. Electroencephalographic records from two cases of subdural hematoma (p-50 and P-36) and one case of cerebral vascular accident (P-150). In case P-50 the lesion was in the left parietal region (leads 3-7) and was localized by the relative flattness of the record taken from over the involved area. In case P-36 the lesion was on the right (leads 11-15) and was localized by the prevalance of delta waves over the focus, an abnormality seen to a much greater extent over the lesion than from other points on the same or opposite hemisphere. In case P-150 the first record (4-13-44) was taken six days after the onset of symptoms and showed abnormal out of phase slow waves over the lesion. A record taken two weeks later (4-27-44) showed considerable improvement.



1 second

SUBDURAL HEMATOMA

LESION ON LEFT

50 μV

P-50

3-7

11-15

LESION ON RIGHT

120 μV

P-36

3-7

11-15

CEREBRAL VASCULAR ACCIDENT

50 μV

4-13-44

P-150

2-6

6-7

4-27-44

50 μV

2-6

6-7

region which showed high voltage slow activity relatively restricted to this area whereas the other, case P-50, was localized in the left parietal region by a diminished voltage of activity on the affected side with slow waves generally distributed elsewhere over the head (Fig. 13). This patient was in semi-coma during the taking of the record. Although our experience with subdural hematomas has been limited, those we have seen have been difficult to localize due to the large percentage of abnormality seen from all parts of the head. However the focus can be discerned by a careful consideration of the total background of abnormality.

One case of left fronto-parietal intracerebral hemorrhage was suggested clinically by the rapid onset of progressive right hemiplegia with a partial motor aphasia and bloody spinal fluid. In this case the first electroencephalogram taken six days after the onset of symptoms showed a localization which verified the clinical impression. A second record taken two weeks later when the aphasia had disappeared, the paralysis had markedly improved and the patient was well on the way to recovery showed a change of the electroencephalogram in the direction of normality. Figure 13 shows sample records from bipolar electrodes placed over the involved area demonstrating the alteration in electroencephalographic pattern concommitant with recovery.

4. DISCUSSION

The percentage of successful electroencephalographic localizations of supratentorial, intracranial lesions obtained in

this study (79.1%) compares favorably with the figures achieved by other workers in the field (Table V). In our study it has seemed that successful localizations were greatly facilitated by: (a) routine use of both the ordinate-coordinate method (Gibbs 1940) and the method of triangulation in every case suspected of intracranial focal pathology; (b) interpretation of the record as it was taken, thus permitting more extensive survey of questionable areas; and (c) use of the spring contact electrode which has permitted easy re-application of electrodes and thus ruled out many electrode artifacts which might otherwise have been misleading in the interpretation of slow wave foci.

Inquiry into the nature of the five tumors in which no definite electroencephalographic localization was achieved reveals that three of these lesions were superficial parasaggital lesions; one was a three centimeter deep parasaggital tumor and the other tumor was deeply situated under the frontal lobe. Other workers (Finley) have noted the difficulty in locating parasaggital lesions and most workers agree (Gibbs 1940) that deeply situated lesions are not localizable by electroencephalographic methods.

Overcoming these two difficulties would theoretically raise our percentage of successful supratentorial tumor localizations to 100%. Practically however, it is probable that localization of deep lying lesions will not become a clinical reality until experimental work on laboratory animals has given us more insight into the production and control of abnormally slow potentials.

A critical examination of the placement of electrodes used in this study reveals that our method leaves uncovered a sagittal area some ten to twelve centimeters in width and running from nasion to inion. The significance of such an unexplored area is well shown by our experiments on animals in which an alteration of electrode placement a distance of but one centimeter can change the recorded electroencephalogram from a picture of apparent normality to one of gross abnormality. It is possible that a special headband fitted with midline electrodes for use in cases clinically suspected of tumor but in whom no lateralizing focus can be found would be well worth the additional trouble its usage would entail.

Our experience with infratentorial lesions has been limited to two cases. Fortunately localization was possible in both of these cases. They were both below the age of seventeen, and thus in the group in which Smith claims localization is possible.

Only two subdural hematomas were included in this study. Despite the paucity of material, however, it seems well to mention that neither of these cases were characterized by the one to two per second delta waves with superimposed sixteen to twenty-five per second activity that Sjaardema and Glaser (1941-2) have described as being typical of subdural hematomas in rabbits and in humans. It is only fair to point out, however, that in both of our cases there was an increase in the cerebro-spinal fluid pressure and marked impairment of consciousness. In one of these cases (P-50) the increased intracranial pressure was combated by the injection intravenously of 50cc of 50% glucose

solution. In this case the hematoma was localized by the relative flattness of the electroencephalographic tracing from over the site of the lesion, a finding quite in keeping with our own work on experimental animals. That the electroencephalographic localization of such lesions is fraught with difficulty, however, is apparant from figure 12 which shows that the recorded pattern from the side contralateral to the lesion in one case (P-50) closely resembles the pattern recorded from the side of the lesion in the other case (P-38).

It was a most unexpected finding that any grossly detectable difference existed between the records of three different types of intracranial neoplasm. Yeager (1942) alone has mentioned that there was a detectable difference in the electroencephalograms of different intracranial lesions and he neglected to publish the criteria by which such differentiation could be made. His claim to the differentiation of gliomas as a group from "non-neoplastic" intracranial lesions, however, does not receive support from our material, rather, the most striking difference we have found is within the glioma group. We have also recently observed several cases of non neoplastic lesion (not included in the present series) in which the electroencephalographic records are indetectable from those found in cases of glioma. It seems therefore that apart from placing the meningiomas in a group by themselves we fail to confirm the method of grouping proposed by Yeager.

That the pattern differences between the tumor groups in our material seems to defy detection by analysis in terms of

frequency and amplitude is not surprising when one considers the manner in which the spike and wave pattern so typical of petit mal epilepsy, might be obscured if considered only in terms of the numerical frequency of wave length and amplitude. But even as the spike and wave pattern is readily discernable upon casual observation of a strip of electroencephalographic recording in which it is present, so the difference in the patterns typified by the three kinds of tumors presented in figure 11 are best detected by scanning typical strips of record from over the tumor area.

It is probably fortuitous that the electroencephalographic records shown in figure 11 could be grouped, according to kind, into three groups representing the tumor types: astrocytoma, meningioma and glioblastoma. In any larger group there would certainly be found cases of grossly destructive meningiomas or of astrocytomas in the process of "de-differentiation" into glioblastomas (Cox 1933, Scherer 1940) which would have rendered the boundries between these groups less clear. Even within these small groups the range of variation between individual records is great and there are records in each group which despite a close resemblence to members of their own type tend to resemble certain records seen with tumors of another kind. Such variations within each of the groups may be accounted for by pathological variations in the tumor type. Such deviations within a given type of glioma have been pointed out by several workers (Bailey 1932, Roussy and Oberling 1932, and Scherer 1940). Until such time as it is possible to correlate the

electroencephalographic patterns with tumors whose purity of cell type and growth characteristics are pathologically verified we can not know the typical electroencephalographic tracing for a given type of tumor. Until that time the only way of attempting to predict the type of intracranial pathology in a given presurgical electroencephalogram is to compare the record in question with each of the groups of known records in figure 11.

In attempting to understand further the mechanism of production of the observed pattern types seen in this study it seemed logical to first consider the clinical characteristics described for these tumors. The meningiomas (in which high voltage delta activity was least in evidence) are notorious for slow, silent, circumscribed growth, measured in years (Cushing and Eisenhardt 1938). The astrocytomas (characterized electroencephalographically by the slowest, high voltage delta waves) are described by Bailey (1933) as having an average duration of growth of about sixty-seven months before surgery and freedom from symptoms for an indefinite period of time after surgery. The glioblastomas multiforme (whose electroencephalogram is characterized by a faster delta wave) develops rapidly in a period of about twelve months (Bailey 1935) and although Cushing feels that a certain proportion of such tumors are amenable to complete cure, the general feeling is that this is the most malignant tumor of the glioma group.

Considered from the standpoint of differences in pathology these tumors are not so readily placed into three well-defined

groups. In the case of the meningioma one can perhaps see why a lesion for the most part confined to the meninges and productive of cerebral pathology by pressure upon the cortex from above, would produce an electroencephalographic alteration differing from that seen in the case of tumors arising from within the cerebral substance itself. [6] The pathological basis for differences between the electroencephalographic patterns of two kinds of tumors both arising from within the brain substance is, however, more obscure.

In view of the electrical inactivity of the brain tumor itself (Foerster and Altenburger 1935, Scarff and Rahm 1941) it would seem that the small biopsy samples of tissue commonly removed for histologic diagnosis of the tumor type are worthless for analysis of this question. To be of any value in determining growth characteristics of tumor types the sections studied should include not only the typical region of the tumor itself but also large sections of the surrounding brain substance. The work of Scherer (1938 a, b, 1940 a, b, c) is almost alone in fulfilling these requirements yet we can find little comfort in his conclusions. Scherer for example points out that of all gliomas the astrocytomas are by far the most invasive. From the standpoint of the general pathologist (Cutler 1938) invasiveness is a sure criterion of malignancy, yet from the clinical standpoint it is not the astrocytoma but the glioblastoma that

---

6. It is conceivable that certain meningiomas may also produce a pattern like the gliomas when they greatly invade and destroy the underlying cerebral architecture. (Williams and Gibbs 1938)

is the most malignant. Perhaps the answer to this is that whereas the astrocytoma is by far more invasive, its invasiveness is not primarily of a destructive nature (Scherer 1940c). In fact both Scherer (1940c) and Cox (1933) have shown that within the substance of the astrocytoma, neurones and their axones may lie entirely undisturbed save for a greater spatial separation by the proliferating astrocytes. Carmichael (1928) has pointed out that grossly the astrocytoma may be indistinguishable from mere cerebral edema. This appearance certainly accounts for the falseness of the feeling of security of the neuro-surgeon after a presumably total removal of an astrocytoma, and it may be that this widespread, non-destructive, edematous-like alteration of tissue is responsible for the changes seen in the electroencephalogram ie. the production of high voltage, slow delta waves. The glioblastoma on the other hand is more rapid in its growth and although infiltrative over a narrow zone is rapidly destructive of the area it infiltrates. (Scherer 1940b) Its vascularity is much greater than that found in the case of the astrocytoma (Penfield 1931) and very few normal cell elements are to be found within the boundries of the tumor (Scherer 1938b). Furthermore there is a smaller amount of tissue rendered pathological by this tumor and although Greenfield (1939) has pointed out that the tendency to edema is greater in these tumors, this smaller area of involvment with tendency to multicentric growth (Scherer 1940b) would lead one to believe that the total amount of abnormal (altered though functioning) cerebral tissue would be less and

would be more irregularly distributed in the glioblastoma than in the astrocytoma.

Certainly we must keep in mind the possibility that despite the apparant classification of our electroencephalographic records into three separate groups of tumor pathology we may, in all electroencephalographic slow wave foci, be dealing with gradations of a single alteration of surrounding brain tissue. This change may eventually be demonstrated by histological or biochemical methods. If such is the case it could be hypothesized that wherever the process was at its maximum (ie. about astrocytomas and in three cases of recently observed brain abscess, not reported in this study) the production of slow delta waves was greatest, and that the narrower invading margin of the glioblastoma showed such changes to a lesser degree and hence produced delta waves whose frequency was not quite so slow and was mixed with and had superimposed upon it waves more nearly approaching normal frequencies. Such a concept would well embrace the transitional type records which contain some characteristics of both tumor groups.

Further evidence of the direction of alteration of this process from astrocytoma to glioblastoma, (ie. from most severe to least severe) is to be seen in a case of astrocytoma when one records from points successively distant from the point of maximum disturbance (Fig. 12) in which case the record shows fewer slow high voltage delta waves as the more normal tissue is approached.

The place of the meningioma in the above scheme is on the

side of the least pathological disturbance and with the smallest number of slow high voltage waves in the electroencephalographic recording.

Apart from theoretical considerations as to the underlying mechanism of the electroencephalographic alterations in the various tumors here studied, the practical significance of a possible method for the correct prediction of the type of intracranial lesion could be of inestimable importance to the neuro-surgeon. As with other clinical tests, however, the interpretation of the electroencephalographic recording is beset with many sources of error and it seems probable that the type of wave pattern seen will not always agree with the microscopic diagnosis that is made from a small section of tissue taken for biopsy directly from the tumor, but rather that the electroencephalographic changes will be indicative of some fundamental alteration in the physiology of the cerebral tissue which lies about the site of the lesion.

EXPERIMENTAL STUDY

1. REVIEW OF THE LITERATURE

Unfortunately for the experimental neuro-pathologist, naturally occurring brain tumors in animals are not frequently recognized (Slye, Holmes and Wells 1931). Jungherr and Wolf in a review of the literature through 1939 found only twenty-four apparantly authentic cases of glioma in dogs. The experimental production of gliomas by the introduction of carcinogenic agents into the brain of experimental animals has been successful in the mouse (Seligman and Shear 1939), an animal quite unsuited for electroencephalographic research. Similar attempts in the dog and cat have been unsuccessful (Scherer 1940a, Seligman and Shear 1939 and Bailey, Shimuzu and Davis 1944). Hence workers who would study the effects of space-occupying lesions in lower animals have been obliged to resort to the introduction of artificial tumor masses into the cranial cavity. Van Schulten 1885, Cushing and Bordley 1909 and Ward and Clark 1941).

Ward and Clark (1941) injected a mixture of lipiodal and beeswax intracerebrally in cats and produced a fibrous and leukocytic reaction with no change in the character and number of supporting cells of the brain tissue. Tschistowitsch (1898), and Hassin (1936) have described the production of a fibrous capsul about foreign bodies in the brain, the latter noting a pronounced gitter-cell response in the reactive zone and no change in ganglion or glia cells in the surrounding parenchyma. The reaction of brain tissue to puncture wounds has been

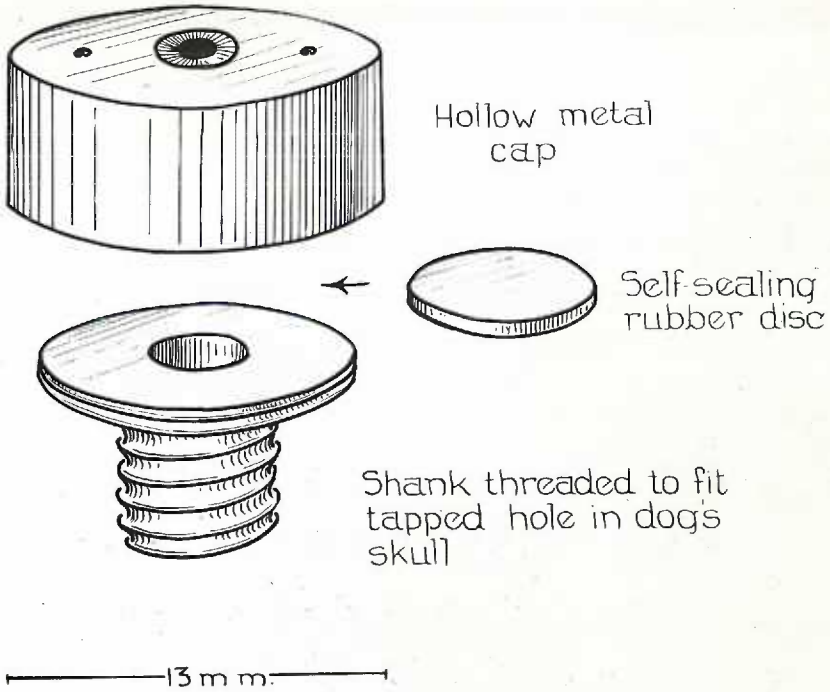
investigated by several workers (Macklin and Macklin 1920, Mortega and Penfield 1927, Penfield and Buckley 1928 and Lincll 1929). Such studies have shown that microglia gitter-cell production is prominant from the third to the sixth day and that astrocytic reaction is less marked in the early stages and reaches a peak somewhat later than the microglial response. Penfield and Buckley (1928), and Wilson (1926) have mentioned that astrocytes may play some part in the reaction but that such response is for the most part limited to the grey matter. Roussy, Lhermitte and Oberling (1931), have expressed belief that in injury to the nervous system the reaction of microglia and oligodendiroglia is of rapid onset while Rand and Courville (1932) have found such alteration within a few hours after generalized injury to the brain.

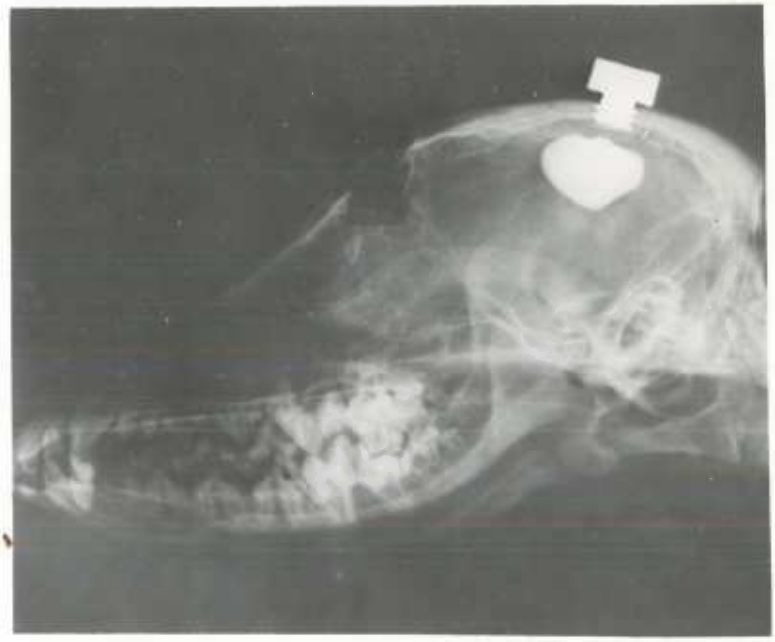
Alteration in the electroencephalogram with intracranial foreign bodies has been reported by Glaser and Sjaardema (1941) who placed gelatin capsuls, filled with citrated blood sub- and extra-durally in rabbits. They have described the immediate disappearance of four to six per second activity and the appearance of two to four per second slow waves with superimposition of a sixteen to thirty per second activity at increased amplitude. After removal of these artificial hematomas there was a return to the normal electroencephalographic pattern, the speed of recovery being inversely proportional to the length of time the lesion had been present.

As there have been no reported experimental studies on the electroencephalographic alterations in cases of artificial

Fig. 14. (a) Stainless-steel plug with rubber diaphragm. This plug was designed with coarse threads to screw into a tapped hole in the dog's skull.

(b) X-ray picture showing metal injector plug in place and beeswax iodochloral mass which has been injected into dog's brain.


Hollow metal cap
Self-sealing rubber disc
Shank threaded to fit tapped hole in dog's skull
13 m m.



brain tumors it was felt that such observations might give some insight into the mechanism of production of the electroencephalographic patterns which are of value clinically in the localization of cerebral neoplasms. The work of Foerster and Altenburger (1935) and Scarff and Rahm (1941) have shown that tumor tissue itself is apparently electrically inert and that the changes observed electroencephalographically come from the altered tissue surrounding the tumor. Hence it seemed logical to use a non-cellular material to simulate space occupying lesions.

2. MATERIAL AND METHODS

Electroencephalograms were obtained with a Grass four channel ink-writing electroencephalograph upon twenty-six adult dogs which were trained to lie quietly in a special holder, the muzzle of which prevented movements of the head. By the use of steel needle electrodes (Hoagland 1940) placed into the skull through the novocainized scalp it was possible to obtain records free from artifact. Under nembutal anaesthesia a scalp incision was made and a hollow, threaded, stainless steel plug with a self-sealing rubber diaphragm (Fig. 14a) was carefully screwed into a hole that had been drilled and tapped through the parietal skull of each dog without injury to the dura. Control electroencephalograms were taken both before and two weeks after surgery to insure that there had been no damage to the underlying brain. A sterile mixture of beeswax softened by iodochloral (radio-opaque oil) or mineral oil was aseptically injected into the brain by means of a twenty guage

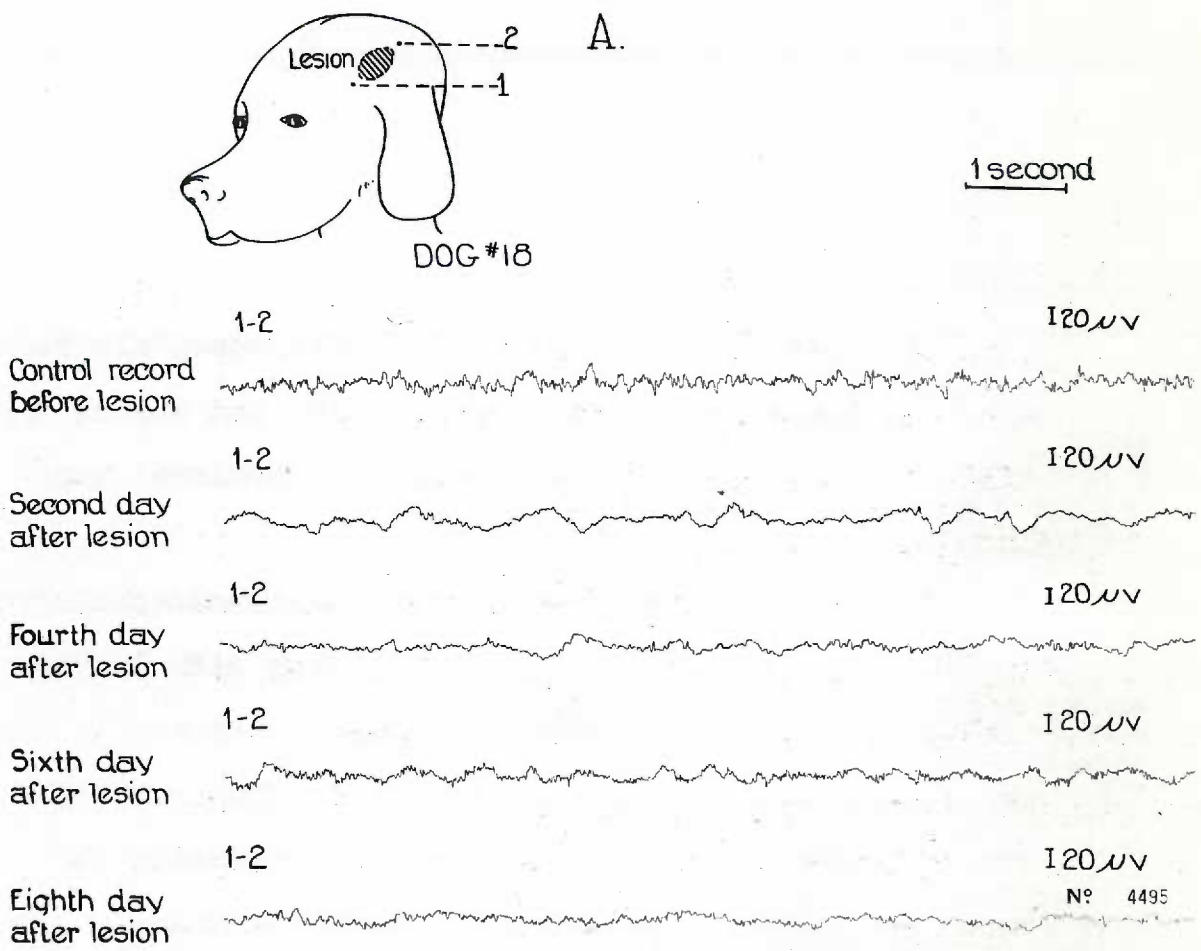
hypodermic needle thrust through the anaesthetized scalp and the rubber diaphragm of the hollow metal plug (Fig. 14b). The injection was accomplished by means of a metal syringe whose plunger was activated in "grease-gun" fashion by a threaded turnscrew. Following the injection, electroencephalograms were taken at frequent intervals until the experiment was terminated with a bilateral craniotomy performed under ether anaesthesia. At this time one millimeter, cotton-wick-core, steel tube electrodes were placed, four on each side of the exposed cortex. After liberal novocainization the ether anaesthesia was stopped and electrocorticograms taken over periods of up to three hours. The animals were then killed by an overdose of nembutal and the brain removed, fixed in 95% alcohol and in 10% formalin, imbedded in pyroxylin and in paraffine, cut at 20 mu and stained with hematoxylin and eosin and by the methods of Nissl and Weigert.

3. RESULTS

The electroencephalogram of the unanaesthetized dog: The electroencephalogram as recorded from forty normal unanaesthetized dogs in our laboratory is characterized by a dominant frequency of from twenty to thirty cycles per second (Gurdjian, Stone and Webster 1944) with occasional waves seen at lower frequencies. In a few young dogs, slower frequencies were more in evidence. In all animal recordings one must be constantly on guard for artifacts due to muscle potentials and from respiratory and other movements of the animal. In practice novocainization of the scalp served to eliminate the rapid spiking

Fig. 15. (a) Control record and electroencephalographic tracings taken on second, fourth, sixth and eighth days after injection of 1.50 cc. beeswax-iodochloral mass intracerebrally.

(b) Graphic representation of electroencephalograph frequency spectra from series of 19 dogs with intracerebral beeswax masses. The percentage graph is broken to emphasize the changes in the low end of the frequency spectrum. The NF column represents all normal frequencies above 5 waves per second and in all instances constitutes the greater percentage of the dog's electroencephalogram.


A.
Lesion
2
1
DOG #18
1 second
1-2
120 μV
Control record before lesion
Second day after lesion
Fourth day after lesion
Sixth day after lesion
Eighth day after lesion
Nº 4495
B.
%
100
90
60
%
5
4
3
2
1
Normal
1st.-2nd. day
3rd.-4th. day
5th.-6th. day
7th.-14th. day
1 2 3 4 5 NF
FREQUENCY PER SECOND

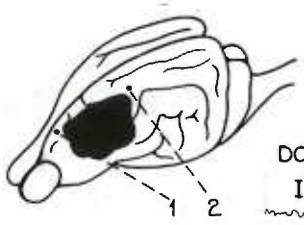
activity due to muscles and constant surveillance of the animal together with rigid fixation of the head made it possible to record for relatively long periods of time without troublesome movement artifacts.

Dogs with intracerebral lesions: Successful intracerebral injections of beeswax mixture were made in nineteen dogs, and electroencephalographic tracings were taken from one minute to four months after the injection. In every case post-surgical control records were compared to records taken before the surgical placement of the metal plug. Only three revealed a slight diminution of amplitude of the spontaneous activity on the side of operation. In all other cases the surgical procedure caused no change in the record at the time injection was made. Records were taken in three instances within ten minutes of the time of injection, two of these being recorded sixty seconds after the injection. In twenty-four instances records were made on the first or second day, eleven records were taken on the third and fourth days, eight on the fifth and sixth days and eight records were taken after the sixth day. The electroencephalogram was recorded on one animal four months after the injection. Figure 15b summarizes the findings seen in the records of all nineteen of the dogs studied. The indices were obtained by counting thirty second samples free from artifact and selected as being representative, in each case, of a much longer total recording.

The most noticeable alteration in the recorded electroencephalogram was the appearance of large delta waves (one to three

Fig. 16. (A) Electroencephalographic record from a dog with an extradural lesion as compared to electroencephalogram from a patient with a meningioma.

(B) Electroencephalographic record from a dog with an intracerebral lesion as compared with electroencephalogram from a patient with intracerebral astrocytoma.



A

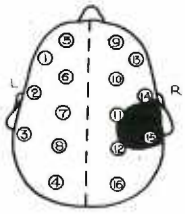
1 second

DOG No. 1

I 20 μv

36935

Normal side



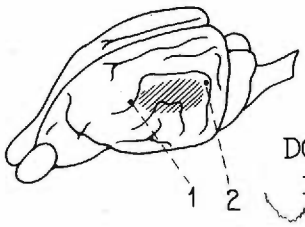
PATIENT 97

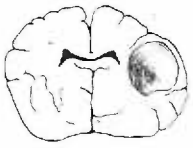
I 20 μv

11-12

7-8

B





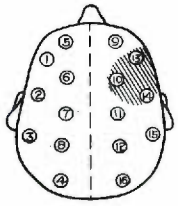
1 second

DOG No. 19

I 20 μv

Nº 4361

Normal side



PATIENT 95

I 50 μv

41525

14-10

2-6

per second at 30 to 60uv) and the disappearance of the normal fast frequencies. This change was seen as soon as thirty seconds after the injection and was very noticeable in records taken on the first and second days after the lesion was made. Following this there was a gradual return towards the normal record with a decrease in amplitude of all abnormal activity and the progressive disappearance of the delta waves affecting the slowest waves first. After the seventh day the record appeared quite normal to casual inspection and in dogs seen from two weeks to four months after the injection the electroencephalogram could not be told from a pre-injection record. Figure 15a shows the typical sequence of electroencephalographic alteration as demonstrated by a dog in which 1.5cc of beeswax-lipiodal mixture was injected just below the cortex. In figure 16b the type of electroencephalographic disturbance produced experimentally in the dog by the intracerebral injection of wax is compared to a similar disturbance which may be seen with intracerebral neoplasm in the human.

In the early experiments some discrepencies in the sequence of electroencephalographic changes were observed. Thus a recording which on one day was abnormal might revert towards normality only to exhibit subsequent change to abnormality again on successive days. Later observations on the placement of electrodes through the scalp revealed that this phenomenon could be entirely explained on the basis of minor changes in electrode placement and that a shift of electrodes a distance as small as five millimeters could mean the difference between

a relatively normal or an abnormal record.

The initial injection of wax mixture [7] used in the nineteen dogs varied from one to two cubic centimeters in amount. In another dog who was given two and one half cubic centimeters the post-injection electroencephalogram showed a higher voltage delta activity than was seen in any of the eighteen successful dogs. This abnormal pattern continued unchanged for four days at which time the animal expired. Post mortem examination revealed that infection had developed around the wax mass which thus lay within a cerebral abscess. Three dogs were given additional injections after the original disturbance of electroencephalographic pattern had returned towards normal. In one of these in which the initial injection was two cubic centimeters the injection, eight days later, of one and one half cubic centimeters additional wax mixture brought about a similar cycle of electroencephalographic alteration. The second dog in this group expired twelve hours after the second injection of four cubic centimeters. In the third dog a one cubic centimeter injection which had caused only minimal changes in the electroencephalogram was followed five weeks later by the injection of two cubic centimeters wax mixture which spread anteriorly to encroach upon the right motor cortex. Twenty hours later this dog showed evidence of brain damage (unequality of pupils, spasticity of left limbs and vomiting.) He was

---

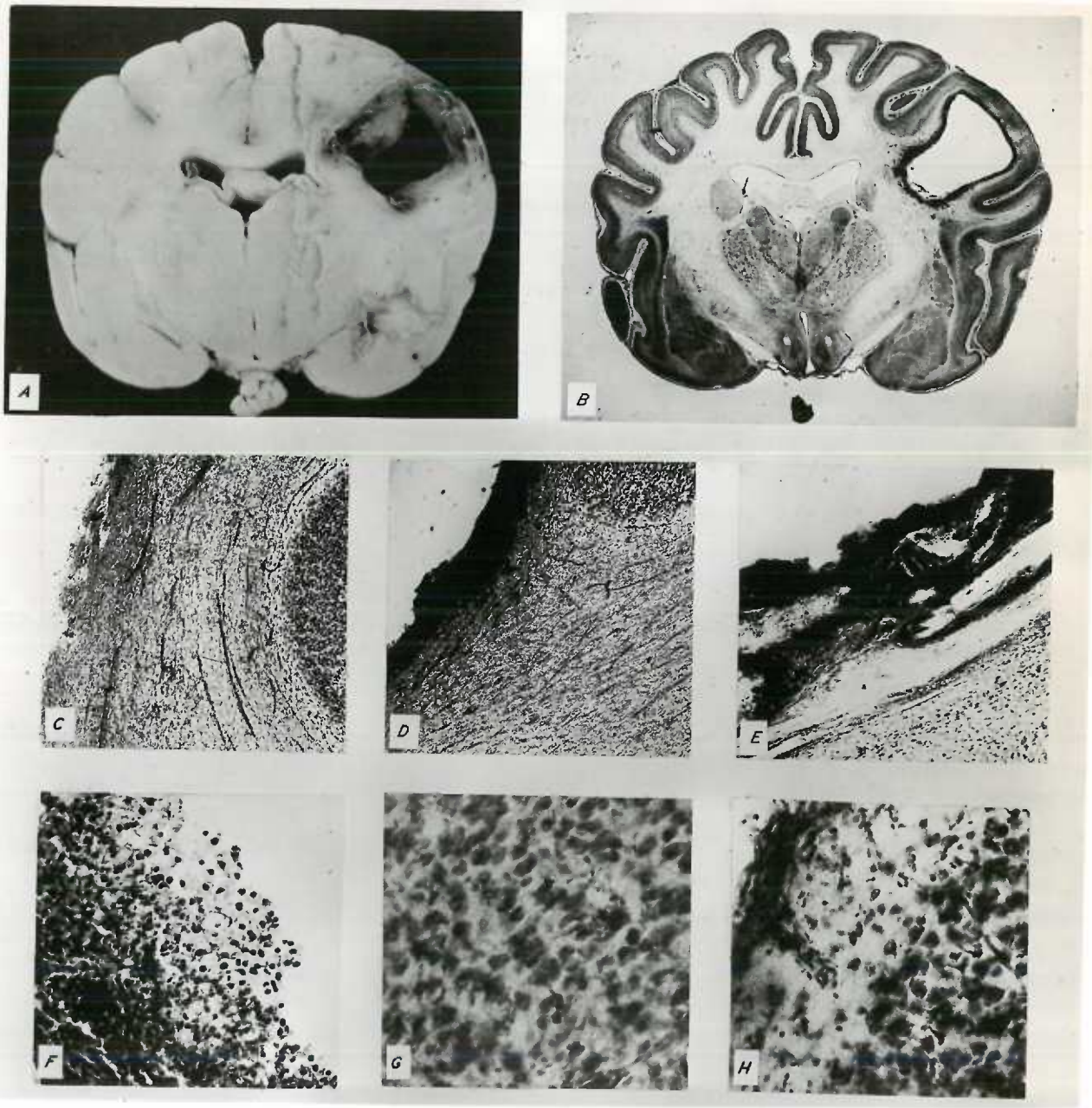
7. Although it had been pointed out (Ward and Clark 1941) that beeswax-lipiodal masses caused only "compression, displacement and distortion of the normal architecture of the brain" it was felt advisable to also use mixtures of beeswax and mineral oil to ascertain any possible irritant effect of the iodochloral. Results appeared identical with either mixture.

observed during the next six hours and during that time had recurrent convulsive seizures of some thirty to fourty seconds duration. Electroencephalographic records taken during this time showed a decrease in the normal fast frequencies and the appearance of fast spiking activity and of high voltage delta activity from one to six per second. The changes were most marked on the side of the lesion during the interseizure recording. Occasional bursts of rapid, high voltage spikes on the side of the lesion were frequently accompanied by twitching of the contralateral leg. With the advent of the seizures which first involved only the left side and later became generalized, spiking activity increased most markedly in the leads on the right side of the head but later spread to involve all leads. The post-convulsive record showed slow activity generally in all leads but most marked on the side of the lesion, and was interrupted by two to eight second periods of electrical inactivity.

Minor differences in the depth of injection beneath the cortex were not easily controlled by the method used and it was felt that any attempt to record differences in electroencephalographic records on the basis of varying depth and placement of lesions would be rendered inaccurate as a result of the differences that could result from an inability to achieve a placement of electrodes which did not vary a few millimeters from day to day.

The results of histological examination of the sections prepared at different stages of the reaction of the brain tissue

Fig. 17. (A) Cross section through cerebrum of dog with intracerebral tumor mass. (B) Nissl stained preparation of preceding section. (C) Margin of intracerebral lesion at second day (Nissl) (D) Margin of intracerebral lesion at sixth day, showing beginning gitter-cell-fibroblast capsul (Nissl) (E) Margin of intracerebral lesion after four months showing well developed fibrous capsul (Nissl). (F) Higher magnification of developing capsul showing gitter-cell reaction at eighth day (hematoxylin and eosin). (G) Pyknosis of nerve cells in cortex adjacent to lesion at second day. (H) Pyknosis of nerve cells in cortex adjacent to lesion at sixth day.


A
B
C
D
E
F
G
H

to the injected wax mixture do not differ widely from the reaction changes to foreign body that are described in the literature. It seems worthwhile, however, to point out the sequence of histological events in our material for comparison with alterations in the electroencephalogram at comparable periods of time.

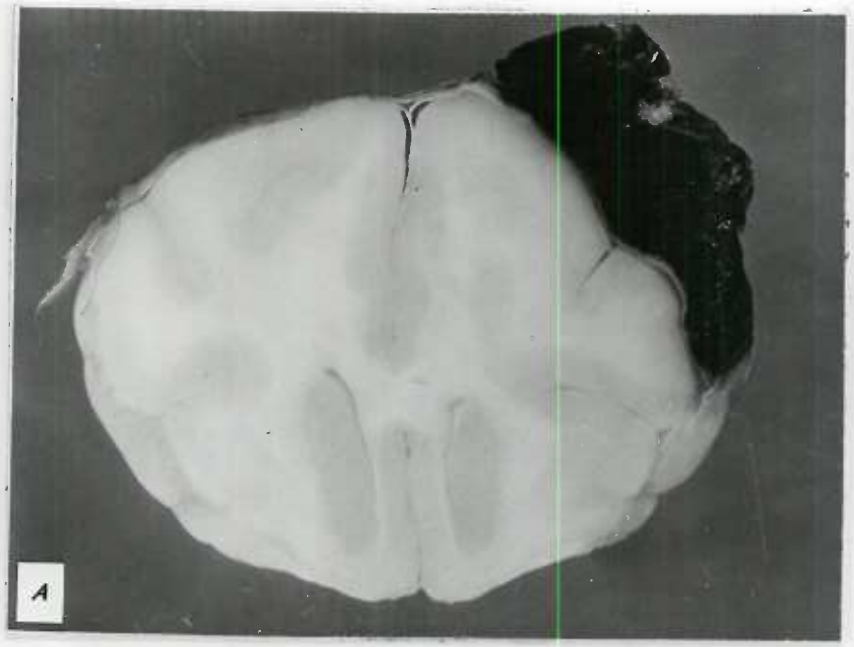
Under low power examination the most noticeable change seen was a gradual swelling of the surrounding tissue and the development of a ring of reaction about the wax-mixture (Fig. 17 c, d, e). This ring was first clearly in evidence by the fourth day at which time it was composed of a mixture of proliferated capillaries whose walls were thickened by a fibroblastic reaction, polymorphonuclear leukocytes, lymphocytes and a few gitter cells. From this time on there was a progressive increase in both gitter cells and in fibroblasts, the latter being seen in greatest abundance immediately adjacent to the blood vessels of the surrounding zone. These cells were bipolar and tended to arrange themselves in bundles placed parallel to the wall of the lesion. On the sixth to the eighth days the gitter cells were in greatest abundance and responsible for the great density of the reacting ring (Fig. 17 d, f). After this time the fibroblasts become increasingly evident until at four months (Fig. 17 e) the ring was composed entirely of fibrous tissue and gitter cells were no longer in evidence. In the first two days tissue debris, polymorphonuclear leukocytes, and lymphocytes were evident in the tissue immediately adjacent to the injected mass. The debris lessened in amount

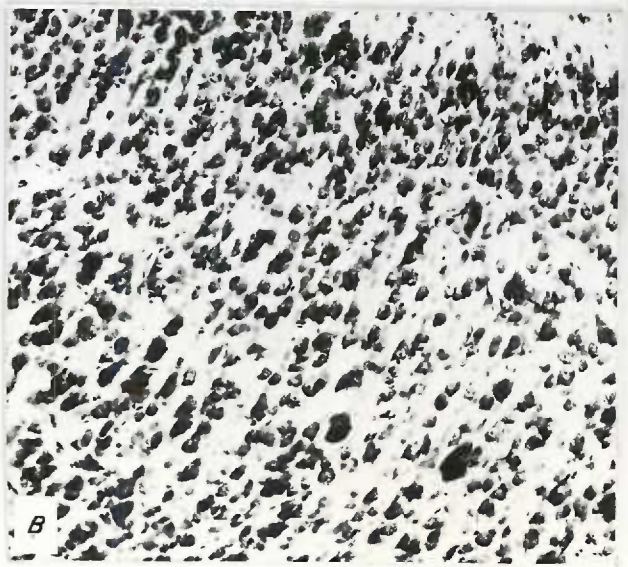
with the appearance of the gitter-cells, histiocytes and few giant cells that appeared after the second day, coincident with capillary proliferation and the perivascular response of the neighboring area. Changes in ganglion cells were seen only in the grey matter immediately adjacent to the lesion. Pyknosis, chromatolysis and mild vacuolation were seen in sections from the second to the eighth day with persistent alteration in architectonics of normal cells which remained after that time. It was not possible to determine if these changes were reversible as the number of damaged ganglion cells was small and evidence of dropping out of such cells at later stages of the process could not be detected. Some proliferation and swelling of astrocytes and increase in the number of microglia nuclei were seen in the neighboring grey matter particularly after the third day. Interfascicular oligodendroglia seemed most numberous about the lesion in the second and fourth days. Some myelin degeneration was seen by the fourth day in Weigert sections. The spread of demyelinization along the bordering fiber tracts was however more in evidence by the second week.

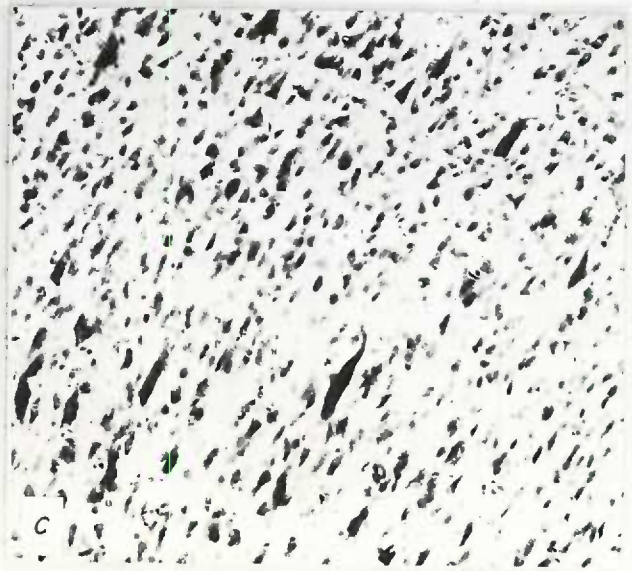
In summary then it can be stated that the most active histological response demonstrated by the methods here used was seen from the fourth to eighth days and that although histologically demonstrable alterations in ganglion cells were seen by the second day such changes were few in number and were seen with equal prevalance on the sixth day. (Fig. 17 g, h).

Dogs with sub- and extra-dural lesions: In five animals from one to three and one half cubic centimeters of wax mixture

Fig. 18. (A) Cross section of brain showing extradural mass in position. (B) Section of cortex from side of brain contralateral to extra-dural lesion. (C) Section of cortex from beneath extra-dural lesion showing pyknosis of ganglion cells.


A


B


C

was injected sub-durally (two cases) or extradurally (three cases). Records were taken on these animals from thirty seconds to two days after the injection.

In all cases the alteration in the electroencephalogram consisted of a flattening of the record on the side of the lesion. With this type of lesion slow delta waves were not produced, instead there was a selective loss of the normal rapid frequencies and a diminution of voltage of all normal frequencies, fast and slow. With such lesions the record appeared almost completely flat at an amplification that had previously been adequate for normal recording. In all cases the side opposite to the lesion was used for a control and showed no changes from the pre-injection records. The above described changes were seen at all times from thirty seconds after injection until the animals were sacrificed after the second day.

Naturally the question arose as to the possibility that the superimposition of a mass between the electrode and the cortical tissue would serve to lower the amplitude. However, definite changes of a slightly less noticeable degree were observed with the electrodes placed on the cortex after the lesion had been removed. Figure 16a shows the electroencephalogram as recorded from a dog with such an extradural lesion. For comparison the electroencephalogram of a patient with a similarly placed lesion (meningioma) is shown.

Histological examination of sections from these brains showed (Fig 18) that after the second day of the lesion, although such

difference was not marked, there was some increase in the number of pyknotic cells on the side of the compression as compared to the contralateral side. Swelling, vacuolation and chromatolysis were also to be seen on the side of the lesion. Grossly the tissue beneath the lesion showed indentation and deformity. No demyelinization was demonstrable in Weigert preparations and no glial or mesynchymal reaction in the brain substance.

Effect of focal abnormality on the brain potentials of sleep and nembutal anaesthesia: The electroencephalograms of unanaesthetized dogs during sleep have been recorded in the laboratory incidental to the investigation of other problems. Such records are characterized by the appearance of waves of slower than normal frequencies (three to five per second) at a somewhat higher amplitude with disappearance of much of the normal fast activity. Two dogs in the present study fell asleep during the recording of the electroencephalogram. One of these animals had previously had wax injected intracerebrally thirteen days previously, the other had an extradural wax mass injected two days before the record was taken. In both instances the characteristic sleep pattern was seen only on the normal side. In both the disturbance could be caused to disappear by awakening the animal (whistling, calling to him, etc.) only to reappear again with the advent of sleep.

The record of the nembutalized dog characteristically consists of irregular groups of three to twelve per second waves at a somewhat increased amplitude, interspersed by

spontaneous intermittent bursts of higher voltage five to ten per second activity such as has been described in the cat (Morison and Dempsey 1942). In seven dogs records were made under nembutal anaesthesia from two to twelve days after intracerebral injection of wax mixture. In two cases the record was from scalp leads and in five was from the exposed cortex and as a terminal procedure in the experiment. In all cases a difference was observed from the normal side and the side of the lesion. Differences between the side of the lesion and the control side were less marked with the animal under nembutal anaesthesia. However, the spontaneous bursts of activity were of considerably less amplitude on the affected side, and in some cases, particularly with cortical leading the side of the lesion showed generally a lower amplitude record.

Electrocorticograms: Records from the exposed cortex were obtained in sixteen dogs (twelve with intracerebral and four with sub- or extra-dural lesions). The electrocorticogram from an unaesthetized dog resembles the electroencephalogram in every way except that it is increased in amplitude some tenfold. In all cases studied the electrocorticogram substantiated the alteration in electroencephalogram seen from scalp recording.

In one dog records taken from tissue immediately adjacent to the point of injection one minute after injection exhibited alteration in the electro-corticogram with decrease in amplitude, slowing and disappearance of the rapid potentials. In another dog a record taken two minutes after acute injection showed a

similar although less marked change. In three cases electrocorticograms were taken from eight to twelve days after the injection of the wax mixture. In these cases scalp recording showed records that were almost normal whereas direct recording from the cortex showed that abnormality was still detectable from a limited area when this more exact method of electrode placement was used.

The extent of cortex producing abnormal potentials was determined by linear placement of electrodes. Monopolar and bipolar recordings were taken with similar type records. It was found that recording at progressively greater distances from the lesion produced records which more nearly resembled the normal control record from the opposite side. It was found however that definitely abnormal records could be recorded from areas distant from the injected mass, areas which appeared normal to both gross and microscopic inspection.

4. DISCUSSION

The mechanics of the production of abnormally slow brain potentials in cases of space occupying intracranial lesions is not known. That such potentials arise from the altered surrounding tissue and not from the tumor itself has been determined by leading directly from the exposed cortex (Foerster and Altenburger 1935, Walter 1937, Schwartz and Kerr 1940 and Scarff and Rahm 1941). The presence of occipital and posterior parietal delta waves in cases of tumors lying entirely within the posterior fossa (Smith, Walter and Laidlaw 1940) points to some mechanism other than the direct effect of neoplastic

cellular metabolism as responsible for slow wave production. Furthermore Murphy and Dusser de Barenne (1941) have demonstrated that products of tissue destruction (thermocoagulation) have the effect of lowering pH and bringing about the inhibition of cortical activity. Our present experiments illustrate well the ability of mechanical pressure alone to produce slow waves from cerebral tissue. The almost immediate appearance of these abnormal potentials in our experience and the comparatively delayed tissue reaction as demonstrated by the histological methods used make it seem reasonable to conclude that delta waves can occur apart from histologically evident inflammation or edema.

Although mechanical pressure from a foreign body lying within the white matter is an adequate stimulus for slow activity the abnormal potentials so produced will soon disappear provided that pressure remains static. Further increase of the pressure at a later date (ie after the dog's electroencephalogram has returned to normal) can reactivate the sequence of electroencephalographic alteration. This observation points to the necessity for continued activity (growth, inflammation etc.) of the causative agent as essential for the maintenance of abnormal electroencephalographic activity.

Walter (1936) and other workers (Gibbs 1940) have stated that injury to the overlying cortex is essential for focal electroencephalographic abnormalities. Were this the case it would seem that pressure entirely upon the cortical layers from above would be more likely to produce slow

waves than pressure from a mass lying almost entirely within the white matter and producing cortical pressure only indirectly. In our experience however, this has not been the case, and pressure upon the cortex from sub-and extra-dural experimental lesions and in certain clinical cases of meningioma (Fig. 16a) there was a noticeable absence of high voltage slow waves. This is in contrast to the marked delta wave production seen by us in cases of cerebral astrocytoma and in experimental lesions in dogs when the lesion was placed within the white matter of the brain (Fig. 16b).

One of the possible mechanisms for the production of the abnormalities seen in our experiments might be the interference with the blood supply to the cortex. However, the work of Pfeifer (1930, 1940), Campbell (1936) and Scharrer (1940) have shown that the blood supply to the cortex is mainly from without inward. The diminished amplitude of brain activity seen in our sub- and extra-dural lesions could be due to interference with the blood supply to the cortex. The intracerebral lesions which for the most part lay well below the grey matter produce little disturbance of blood supply to the cortex. Alterations in blood supply are therefore probably not an important part of the mechanism for the production of abnormally slow high voltage activity.

The low voltage slow potentials remaining in the electrocorticogram after thermocoagulation of the outer cortical layers (Dusser de Barenne and McCulloch 1936) have been termed by Walter (1936) a "delta-like" discharge. The potentials record-

ed by Dusser de Barenne and McCulloch (1936) and Murphy and Dusser de Barenne (1941) may well be the low voltage slow component of the normal electroencephalogram which, in the intact cortex, combines with faster frequencies presumably arising from more superficial layers of the cortex (Bishop 1936, Dusser de Barenne and McCulloch 1938) to give the full spectrum of the dog electroencephalogram. In our cases of sub- and extra-dural compression of the cortex leads from the periphery of the compressed area recorded low voltage five to ten per second activity. This activity was entirely different from the slow high voltage abnormal delta waves seen with deep lying lesions and appeared similar to the slow waves which are seen as a normal component of the electroencephalogram of the unanaesthetized dog. We believe that surface compression eliminates cortical activity and that the slow waves seen at the periphery may be the result of sparing of the deep cortical layers which presumably would be less affected near the borders of a surface compression. This resulting low voltage slow activity does not resemble the high voltage slow waves seen with intra-cerebral lesions.

Kennard and Nims (1942), and Kennard (1943a, 1943b) studied the effect of cortical ablation in monkeys and found a non-specific decrease in amplitude and frequency which she felt paralleled the development of post-operative edema. Her failure to find specific focal alterations may well have been due to the fact that her lesions were not of a space-occupying type and that, as she suggests, the cortical loading in acute

experiments was performed under anaesthesia. Anaesthesia, in our experience, makes it difficult to detect the focal changes resulting from injury, changes which are readily seen in the record of the unanaesthetized animal. From her chronic experiments Kennard concluded, "...lesions confined to cortical tissue do not alter it (EEG) even if an entire hemisphere is removed." This has not been our experience with lesions causing pressure upon the cortex. In one case of hemidecortication in the dog we found a noticeable difference in amplitude of the recordings from the normal and the decorticate sides. This finding was in keeping with the work of Ten Cate, Walker and Koopman (1939, 1940a, b, c) who found that the record from the normal side in hemi-decorticate dogs, cats and rabbits was several times greater in amplitude on the side opposite to the decortication. These workers demonstrated that the cortex was essential for the normal electroencephalogram as recorded from the scalp. Kennard has obtained characteristic eight to ten per second activity from the scalp of totally decorticate monkeys with basal ganglia intact. The only experiments reported on totally decorticate monkeys however were on preparations anaesthetized with dial. Grinker and Serota (1938) and Obrador (1943) who showed the seeming dependence of the electroencephalogram upon subcortical structures used anaesthesia. In our experience even light barbiturate anaesthesia has produced slower than normal rhythms and completely obscured the faster frequencies which are typical of the electroencephalogram of the unanaesthetized dog.

In the light of Kennard's work which showed that lesions in the basal ganglia were productive of abnormal slow waves in the electroencephalogram we must consider that the delta waves seen in our experiments could possibly have come from pressure on deeper-lying structures. Examination of histological preparations from the dogs in our experiments makes it seem unlikely, however, that such structures were directly involved. The absence or diminution of thalamic nembutal spindles (Morison and Dempsey 1942) and of sleep potentials from the side of the lesion, seen in our work with animals and noted in both dog and human material by Witwer and Derbyshire (1943) is probably the result of interference with afferent pathways to the cortex or of damage to cortical receptive structures rather than the involvement of the basal ganglia.

That disturbance in the white matter alone is responsible for delta wave production has been suggested by Williams (1939, 1941). Stewart (1941) has advanced the theory that tension on the subcortical nerve fibers may explain the production of slow waves seen in experimental hydrocephalus. In our experiments pressure from within the white matter produced abnormally slow potentials of high voltage and pressure upon the cortical layers from without did not. Although it therefore seems that some alteration in fiber connections to the cortex may favor the appearance of slow activity it does not necessarily mean that the white matter is the point of origin for these potentials. It is possible that slow activity could arise either as a result of disturbance of afferent pathways to the cortex

or from apparently reversible changes in cortical neurones, not demonstrable by present histological methods.

SUMMARY AND CONCLUSIONS

This investigation was concerned with a study of the disturbances in pattern of spontaneous brain potentials recorded electroencephalographically from man and dog in cases of diffuse and focal injury to the brain.

In part the problem was an evaluation of the electroencephalograph as a diagnostic procedure in cases of head trauma and space-occupying lesions; for despite the large literature upon the subject of clinical electroencephalography there is still considerable uncertainty as to the importance of its role as an indicator of the severity, type and location of intracerebral pathology.

The controlled reproduction in laboratory animals of the electroencephalographic phenomena observed clinically has seemed a logical approach towards understanding the abnormal potentials in terms of altered brain physiology and anatomy.

The clinical investigation of diffuse damage to the brain was carried on, for the most part, at the First Aid Station of the Oregon Shipbuilding Corporation; a few patients however, were followed into local hospitals. Electroencephalograms were recorded by means of a partable, Grass, three channel, push-pull amplified, ink writing oscillograph. Electrodes were placed by means of a spring-pressure-contact, six-electrode headband which was developed during the course of the investigation. Electroencephalograms were taken on a control series of 211 normal workers and upon 213 head injury patients. Records were taken on all patients as soon as

possible after concussion or minor injury to the head. All except 28 patients were seen within 24 hours of the injury and over half of all cases were seen within the first hour. The records were classified as normal, borderline, or abnormal in accordance with their deviation from the widely accepted, established norm of 8-12 per second basic "alpha" frequency.

Although the tendency was not marked, the head injury series showed a smaller percentage of normal records than the normal control series (53% as compared with 62%) and a greater percentage of abnormal records (11% as compared with 8%). When the records were grouped according to increasing intervals of time (up to 24 hours) from the moment of trauma to the time of electroencephalographic recording, it was found that there was a greater abnormality in the groups seen soon after trauma. Thus it was concluded that if mild cerebral trauma, such as was investigated in this study, produced change in the electroencephalogram, the abnormality disappeared within a period of minutes in the vast majority of cases. Such rapid disappearance of electroencephalographic abnormality seemed to point to some mechanism in concussion other than petechial hemorrhage, cerebral contusion or other histopathological change which must of necessity require several days to disappear. Patients with a history of true concussion (retrograde or post-traumatic amnesia) from head trauma whose consciousness was not impaired at the time the electroencephalogram was recorded showed only a slight trend toward abnormality of the

brain wave tracing, if however, there was any impairment of consciousness at the time of recording, abnormality in the electroencephalogram was the rule.

A careful evaluation of the physical factors was attempted in every case of head injury. Helmets, lack of wittnesses, broken falls etc. rendered such estimation difficult in many cases. As would be expected, the more severe injuries caused the greater disturbance of brain wave pattern. The forces and velocities at impact which appeared to be necessary to produce true concussion in humans seem to be of the same order as that found necessary to produce "experimental concussion" in animals.

A study was made to compare the amount of time loss, due to injury, with the abnormality of the electroencephalogram. Although the most severe injuries which necessitated the greatest time loss from work were frequently associated with abnormal electroencephalograms it was concluded from the total study that opinion based upon electroencephalographic records taken immediately following mild head injury was less reliable than clinical judgement in predicting time loss from work. In over one third of the patients (86) electroencephalography was repeated eight weeks (average) after the head injury. Of this group only 15 patients showed a shift of record towards normalcy. This group which showed a change in the record was on the whole a more seriously injured group than that in which no such shift occurred. Several individual patients, however, whose records demonstrated this shift to normalcy were found

to have received cerebral trauma which fell short of what is usually considered true concussion. This raises the possibility that there is a variable susceptibility to electroencephalographic change in different individuals, following trauma.

Analysis of the wave form, frequency and voltage of the brain activity encountered in the abnormal electroencephalograms which subsequently improved did not allow the designation of any particular activity which seemed characteristic of the electroencephalogram following mild cerebral trauma.

In the experimental investigation of diffuse cerebral trauma two cats and seventeen dogs were struck on the occiput by a pendulum capable of delivering blows of 39.7 ft./sec. maximum velocity with effective energy estimated at 52.1 ft. lbs. The animals were held upright in a halter and simultaneous electroencephalograms (needle electrodes into the skull) and electrocardiograms were taken. The animals were studied under nembutal anaesthesia and with only local anaesthesia of the scalp. The effect of head trauma upon cortical function was investigated by the method of correct conditioned differentiation (Allen) in six dogs who were trained to respond to olfactory, auditory and tactile stimuli by lifting the left fore-paw.

As with human, there was found in dogs to be an individual variation as to the effect of blows upon the head. The picture of concussion in the experimental animal (defined by Denny-Brown as consisting of "an immediate traumatic paralysis of reflex function" and an immediate reduction in voltage of

the electroencephalogram followed by the appearance of slow brain potentials), was seen regularly in cats but only inconsistently in dogs. It was found that blows of equal intensity caused more marked effects in animals under general anaesthesia, and that of all the elements of the electroencephalogram in the animal anaesthetized by nembutal the relatively high voltage "nembutal-spindles" (Dempsey and Morison) seemed most susceptible to the effects of trauma. Blows of an intensity capable of producing fatality, might, on the same animal in previous experiments, have caused little change in the electroencephalogram.

It was found that blows on the head affect conditioned reflex responses more easily and for a much longer time than they affect reflex activity and more vital functions. Just as in our head injury series among ship-yard workers it was found that clinical judgement was a more sensitive index of concussion than the electroencephalogram, so it seemed in dogs, that the conditioned reflex responses were a more delicate index of cerebral cortical function than the electroencephalogram as obtained at the present time.

Concerning the physiological basis for concussion, it is felt from our work that cerebral trauma has a direct effect of a temporarily paralytic nature independent and beyond any mechanical stimulation of neurones which may or may not be produced by the blow.

In a clinical study of focal damage to the brain localising electroencephalograms were taken on 102 patients by means

of a sixteen electrode model of the spring-pressure-electrode headband. In 42 cases there was evidence of focal electroencephalographic disturbance. Thirty five (83%) of these electroencephalographic foci were substantiated by pathological and (or) clinical evidence of brain disease at the site of this focus. In 19 cases of supratentorial tumor verified by surgery or autopsy the electroencephalogram gave a correct localizing diagnosis in 79% of the cases. This is to be compared with a 65% correct localizing diagnosis from clinical methods alone (history and neurological examination), 14% correct localization by routine skull x-rays, 71% correct localization by the method of pneumoencephalography and 91% correct localization by ventriculography. The 21% of intracranial, supratentorial tumors which were not localized by the electroencephalogram were either deep-lying lesions, or tumors in a parasaggital position.

Two cases (100%) of infratentorial lesions were correctly localized. Both of these cases were within the group (under 18 years) in which Smith, Walter and Laidlaw state that localization of posterior-fossa lesions is possible. Although the two cases of subdural hematoma in our series were both localized, it was felt that the criteria for diagnosis of this type of lesion are less certain than is the case with other space-occupying lesions.

It seemed possible to separate focally abnormal electroencephalograms into three groups on the basis of characteristic pattern types. In our series the pathological entities which were represented in sufficiently large number to warrant

consideration were represented by tumors of the meningioma, astrocytoma and glioblastoma multiforme groups. The variations in pathology and growth characteristics of these lesions seemed to suggest a possible basis for the observed electroencephalographic alterations.

Focal brain lesions in the experimental animal were produced by the aseptic intracranial injection of beeswax-iodochloral mixtures in the chronic unanaesthetized animal by means of a hypodermic needle. Such injection was made possible by a hollow, threaded stainless steel plug with a self sealing rubber diaphragm which was inserted into a tapped hole in the dogs skull, at surgery, several weeks prior to the beeswax injection. Control electroencephalograms were taken both before and after surgery. Following the injection of beeswax, electroencephalograms were taken at frequent intervals until the experiment was terminated with a bilateral craniotomy performed under ether anaesthesia. After liberal novocainization of the scalp, the ether anaesthesia was stopped and electro-corticograms were taken over periods of up to three hours. The animals were then killed, the brain removed and microscopic sections were prepared and stained with hematoxylin and eosin and by the methods of Nissl and Weigert.

High voltage slow waves (delta waves) were seen characteristically in the electroencephalogram of dogs with sub-cortical, space occupying lesions. Such changes at their height, resembled the electroencephalographic alterations that we have seen in our study of intracranial neoplasms (astrocytoma) in

man. A disappearance of normal rapid activity and flattening of the electroencephalogram was seen with sub- and extra-dural space occupying lesions in the dog. These changes resemble alteration we have seen in some cases of meningioma and sub-dural hematoma in human patients.

It was found that minor shifts in electrode placement could greatly alter the amount of abnormality seen in the electroencephalogram in cases of focal brain damage. This observation suggested that the application of mid-line electrodes in human cases might well enable the detection of the parasaggital type of lesion which was commonly missed in our series of clinical intracranial neoplasms. A histological study of the dogs brains showed that the reaction of cerebral tissue to a foreign body was at its height from the second to the eighth day. This was at a time when the electroencephalographic abnormalities are disappearing. Therefore it seemed that some change other than one demonstrable by histological methods was responsible for the alterations observed in brain wave pattern. The observation that a static lesion (i.e., one that was not increasing in size) caused only transient effect upon the electroencephalogram suggested that some active process (growth, inflammation etc.) was necessary to produce the sustained abnormality seen in the electroencephalogram with neoplasms in patients. It was shown experimentally in the dog that a space-occupying lesion within the white matter and exerting pressure below the cortex was capable of causing high voltage slow activity in the

electroencephalogram, whereas lesions pressing on the cortex from above were not capable of producing such (delta) activity. It seemed possible that such slow activity could arise either as a result of the disturbance of afferent impulses to the cortex or from apparantly reversible change in cortical neurones, a change not demonstrable by histologic methods.

Some evidence was obtained from this study which seemed to favor the cortical origin of the brain potentials seen in the electroencephalogram of the unanaesthetized dog and which suggested that certain potentials seen with sleep and with nembutal anaesthesia might be controlled by sub-cortical mechanisms.

BIBLIOGRAPHY

Adrian, E. D. and Yamigawa, K. The origin of the Berger rhythm. Brain, vol. 58, pp. 323-351, 1935.

Allen, W. F. Olfactory and trigeminal conditioned reflexes in dogs. Amer. J. Physiol., vol. 118, pp. 532-539, 1937.

Allen, W. F. Effect of ablating the frontal lobes, hippocampi and occipito-parietal-temporal (excepting pyriform areas) lobes on positive and negative olfactory conditioned reflexes. Amer. J. Physiol., vol.128, pp. 754-771, 1940.

Allen, W. F. Studies on irradiated cerebral differentiated excitation and inhibition as indicated and measured by respiration. Amer. J. Physiol., vol. 136, pp. 783-789, 1942.

Bailey, P. Histologic diagnosis of tumors of the brain. Arch. Neurol. Psychiat., Chicago, vol. 27, pp. 1290-1297, 1932.

Bailey, P. Intracranial tumors. Charles C. Thomas, Baltimore, 1933.

Bailey, P., Shimuzu, K. and Davis, E. W. Effects of implantation of methylcholanthrene in the brain of the dog. J. Neuropath. exp. Neurol., vol. 3, pp. 184-189, 1944.

Berger, H. Ueber das Elektrenkephalogram des Menschen. Arch. f. Psychiat., vol. 94, pp. 16-60, 1931.

Bishop, G. H. The interpretation of cortical potentials. Cold Spr. Harb. Monogr., vol. 4, pp. 305-319, 1936.

Brown, W. T. and Moore, M. Soldiers who break down in battle: some predisposing factors. Milit. Surg., vol. 94, pp. 160-161, 1944.

Campbell, A. C. P. The vascular architecture of the cat's brain. Res. Publ. Ass. nerv. ment. Dis., vol. 18, pp. 69-93, 1938.

Carmichael, E. A. Cerebral gliomata. J. Path. Bact., vol. 31, pp. 493-510, 1928.

Case, T. J. and Bucy, P. C. The localization of cerebral cortical lesions with electro-encephalography. Tr. Am. neurol. Ass., vol. 64, pp. 128-130, 1938.

Case, T. and Bucy, P. Localization of cerebral lesions by electroencephalography. J. Neurophysiol., vol. 1, pp. 245-261, 1938.

Cox, L. B. The cytology of the glioma group; with special reference to the inclusion of cells derived from the invaded tissue. Amer. J. Path., vol. 9, pp. 839-899, 1933.

Cushing, H. and Bordley, J. Observations on experimentally induced choked disc. Johns Hopk. Hosp. Bull., vol. 20, pp. 95-102, 1909.

Cushing, H. and Eisenhardt, L. Meningiomas. Charles C. Thomas, Baltimore, 1938.

Cutler, M. and Buschke, F. Cancer, its diagnosis and treatment. W. B. Saunders, Co., Philadelphia, 1938.

Denny-Brown, D. and Russell, W. R., Cerebral electrical changes in experimental concussion. Brain, vol. 64, pp. 93-164, 1941.

Dow, R. S., Ulett, G. and Raaf, J. Electroencephalographic studies immediately following head injury. Amer. J. Psychiat., September 1944 (in press).

Dusser de Barenne, J. G. and McCulloch, W. S. Some effects of laminar thermocoagulation upon the local action potentials of the cerebral cortex of the monkey. Amer. J. Physiol., vol. 114, pp. 692-694, 1936.

Dusser de Barenne, J. G. and McCulloch, W. S. Kritisches und Experimentelles zur Deutung der Potentialschwankungen des Elektrocorticogramms. Z ges. Neurol., vol. 162, pp. 815-824, 1938.

Engel, G., Romano, J., Ferris, E., Webb, J. and Stevens, C. A simple method of determining frequency spectrums in the electroencephalogram. Arch. Neurol. Psychiat., Chicago, vol. 51, pp. 134-146, 1944.

Finley, K. Personal communication.

Foerster, O. and Altenburger, H. Elektrobiologische Vorgange an der menschlichen Hirnrinde. Dtsch. Z. Nervenheilk., vol. 135, pp. 277-288, 1935.

Gibbs, F. A., Munro, D. and Wegner, W. R. A standard electroencephalographic technic for the localization of gross intracranial lesions. New Engl. J. Med., vol. 225, pp. 279-282, 1941.

Gibbs, F. A. and Gibbs, E. L. Atlas of electroencephalography. Lew Cummings Co., Cambridge, 1940.

Glaser, M. A. and Sjaardema, H. The value of the electroencephalogram in craniocerebral injuries. West. J. Surg. Gynaec. Obstet., vol. 48, pp. 689-696, 1940.

Grass, A. and Gibbs, F. A. A Fourier transform of the electroencephalogram. J. Neurophysiol., vol. 1, pp. 521-526, 1938.

Greenfield, J. G. The histology of cerebral oedema associated with intracranial tumours; with special reference to change in the nerve fibres of the centrum ovale. Brain, vol. 62, pp. 129-152, 1939.

Grinker, R. A method for studying and influencing cortico-hypothalamic relations. Science, vol. 87, pp. 73-74, 1938.

Grinker, R. and Serota, H. Studies on corticohypothalamic relations in the cat and man. J. Neurophysiol., vol. 1, pp. 573-589, 1938.

Gurdjian, E. S., Stone, W. E. and Webster, J. E. Cerebral metabolism in hypoxia. Arch. Neurol. Psychiat., Chicago, vol. 51, pp. 472-477, 1944.

Gurdjian, E. S. and Webster, J. E. Experimental head injury with special reference to the mechanical factors in acute trauma. Surg. Gynaec. Obstet., vol. 76, pp. 623-634, 1943.

Hassin, G. B. Reacting cells in the brain in the presence of a foreign body. Arch. Neurol. Psychiat., Chicago, vol. 36, pp. 231-247, 1936.

Hoagland, H. A simple method for recording electrocorticograms in animals without opening the skull. Science, vol. 92, pp. 537-538, 1940.

Holbourn, A. H. S. Mechanics of head injuries. Lancet, vol. 2, pp. 438-441, 1943.

Holland, C. Changes caused by cerebellar neoplasms in the electroencephalogram. Virg. med. Monthl., vol. 68, pp. 459-462, 1941.

Hortega, P. Del Rio and Penfield, W. Cerebral cicatrix. The reaction of neuroglia and microglia to brain wounds. Johns Hopk. Hosp. Bull., vol. 41, pp. 278-303, 1927.

Jasper, H. Electroencephalography. In Penfield, W. and Erickson, T. Epilepsy and cerebral localization. Chas. C. Thomas, Springfield, Ill., 1941.

Jasper, H. and Hawke, W. Electroencephalography: IV, Localization of seizure waves in epilepsy. Arch. Neurol. Psychiat., Chicago, vol. 39, pp. 885-901, 1938.

Jasper, H., Kershman, J. and Elvidge, A. Electroencephalographic studies of injury to the head. Arch. Neurol. Psychiat., Chicago, vol. 44, pp. 328-350, 1940.

Johnson, V. C. and Hodges, P. J. (Univ. of Michigan Hospital) Reliability of brain tumor localization by roentgen methods. Radiology, vol. 41, pp. 117-129, 1943.

Jungherr, E. and Wolf, A. Gliomas in animals. Amer. J. Cancer, vol. 37, pp. 493-509, 1939.

Kennard, M. A. and Nims, L. F. Effect on electroencephalogram of lesions of cerebral cortex and basal ganglia in Macaca mulatta. J. Neurophysiol., vol. 5, pp. 335-358, 1942.

Kennard, M. A. Electroencephalogram of decorticate monkeys. J. Neurophysiol., vol. 6, pp. 233-242, 1943a.

Kennard, M. A. Effects on EEG of chronic lesions of basal ganglia, thalamus and hypothalamus of monkeys. J. Neurophysiol., vol. 6, pp. 405-416, 1943b.

Krems, A. D., Schoepfle, G. M. and Erlanger, J. Proc. Soc. exp. Biol., N. Y., vol. 49, pp. 73-75, 1942.

Lambros, V. S., Case, T. L. and Walker, A. E. The clinical value of electroencephalography. Dis. nerv. Syst., vol. 4, pp. 202-206, 1943.

Lemere, F. Berger's alpha rhythm in organic lesions of the brain. Brain, vol. 60, pp. 116-125, 1937.

Linell, E. A. The histology of neuroglial changes following cerebral trauma. Arch. Neurol. Psychiat., Chicago, vol. 22, pp. 926-948, 1929.

Macklin, C. C. and Macklin, M. T. A study on brain repair in the rat by the use of trypan blue with special reference to the vital staining of the macrophages. Arch. Neurol. Psychiat., Chicago, vol. 3, pp. 353-393, 1920.

Marinesco, G., Sager, O. and Kreindler, A. L'electrencephalogramme dans certains etats pathologiques. Presse med., vol. 46, pp. 650-654, 1938.

McDonald, C. A. and Korb, M. Brain abscess with brain potentials. R. I. med. J., vol. 23, pp. 81-84, 1940.

Marmer, J. and Savitsky, N. Electro-encephalography in cases of head injury. J. nerv. ment. Dis., vol. 95, pp. 285-289, 1942.

Morison, R. S. and Dempsey, E. W. A study of thalamocortical relations. Amer. J. Physiol., vol. 135, pp. 281-292, 1942.

Murphy, J. P. and Dusser de Barenne, J. G. Thermocoagulation of motor cortex exclusive of its sixth layer. J. Neurophysiol., vol. 4, pp. 145-152, 1941.

Obrador, S. Effect of hypothalamic lesions on electrical activity of cerebral cortex. J. Neurophysiol., vol. 6, pp. 81-85, 1943.

Penfield, W. The classification of gliomas and neuroglia cell types. Arch. Neurol. Psychiat., Chicago, vol. 26, pp. 745-753, 1931.

Penfield, W. and Buckley, R. Punctures of the brain. Arch. Neurol. Psychiat., Chicago, vol. 20, pp. 1-13, 1928.

Pfeifer, R. A. Grundlegende Untersuchungen fur die Angioarchitektonic des menschlichen Gehirns. Verlag von Julius Springer, Berling, 1930.

Pfeifer, R. A. Die angioarchitektonische areale Gliederung der Grosshirnrinde. Verlag von Georg Thieme, Leipzig, 1940.

Rand, C. W. and Courville, C. B. Histologic changes in the brain in cases of fatal injury to the head. Arch. Neurol. Psychiat., Chicago, vol. 27, pp. 605-644, 1932.

Rheinberger, M. B. and Davidoff, L. M. Posterior-fossa tumors and the electroencephalogram. J. Mt. Sinai Hosp., vol. 9, pp. 734-754, 1942.

Rheinberger, M. and Siris, J. Resorption of intracranial gumma under electroencephalographic control. Arch. Neurol. Psychiat., Chicago, vol. 44, pp. 879-885, 1940.

Rogers, L. Electroencephalography in traumatic intracranial hemorrhage. Brit. med. J., vol. 1, pp. 510-511, 1941.

Roussy, G., Lhermitte, J. and Oberling, C. The neuroglia and its pathologic reactions. Arch. Neurol. Psychiat., Chicago, vol. 25, pp. 653-659, 1931.

Roussy, G. and Oberling, C. Histologic classification of tumors of the central nervous system. Arch. Neurol. Psychiat., Chicago, vol. 27, pp. 1280-1290, 1932.

Rubin, M. A. Electro-encephalographic localization of atrophy in the cerebral cortex of man. Proc. Soc. exp. Biol., N. Y., vol. 40, pp. 153-154, 1939.

Rubin, M. A. Electroencephalography in the psychoses. Localization of cerebral atrophy. Amer. J. Psychiat., vol. 96, pp. 864-875, 1940.

Scarff, J. E. and Rahm, W. E. The human electro-corticogram. J. Neurophysiol., vol. 4, pp. 418-426, 1941.

Scharrer, E. Arteries and veins in the mammalian brain. Anat. Rec., vol. 76, pp. 173-196, 1940.

Scherer, H. J. The frequency of gliomas having variable histological structure. J. belge Neurol. Psychiat., vol. 38, pp. 783-787, 1938a.

Scherer, H. J. Structural development in gliomas. Amer. J. Cancer, vol. 24, pp. 333-351, 1938b.

Scherer, J. J. A critical review: the pathology of cerebral gliomas. J. Neurol. Psychiat., vol. 3, pp. 147-177, 1940a.

Scherer, H. J. The forms of growth in gliomas and their practical significance. Brain, vol. 63, pp. 1-35, 1940b.

Scherer, H. J. Cerebral astrocytomas and their derivatives. Amer. J. Cancer, vol. 40, pp. 159-198, 1940c.

Schwab, R. S. The clinical application of electro-encephalography. Med. Clin. n. Amer., vol. 25, pp. 1477-1489, 1941.

Schwartz, H. G. and Kerr, A. S. Electrical activity of the exposed human brain. Arch. Neurol. Psychiat., Chicago, vol. 43, pp. 547-559, 1940.

Seligman, A. M. and Shear, J. J. Studies in carcinogenesis, (VIII). Amer. J. Cancer, vol. 37, pp. 364-395, 1939.

Sjaardema, H. and Glaser, M. The electroencephalographic diagnosis of subdural hemorrhage. Ann. Surg., vol. 116, pp. 452-460, 1942.

Slye, M., Holmes, H. F. and Wells, H. G. Intracranial neoplasms in lower animals. Amer. J. Cancer, vol. 15, pp. 1387-1400, 1931.

Smith, J. A., Walter, C.W.P. and Laidlaw, R. W. The electroencephalogram in cases of neoplasms of the posterior fossa. Arch. Neurol. Psychiat., Chicago, vol. 43, pp. 472-487, 1940.

Stewart, W. A. Electroencephalographic changes associated with different forms of experimentally produced increased intracranial pressure. Johns Hopk. Hosp. Bull., vol. 69, pp. 240-265, 1941.

Ten Cate. J., Walter, W. G. and Koopman, L. J. Electro-encephalography after removal of the occipital cortex. Arch. neerl. Physiol., vol. 24, pp. 153-168, 1939.

Ten Cate, J., Walter, W. G. and Koopman, L. J. Electro-encephalography in rabbits after removal of neopallium. Arch. neerl. Physiol., vol. 24, pp. 570-596, 1940a.

Ten Cate, J., Walter, W. G. and Koopman, L. J. Electro-encephalography on cats after removal of neopallium. Arch. neerl. Physiol., vol. 25, pp. 27-50, 1940b.

Ten Cate, J., Walter, W. G. and Koopman, L. J. Note on electroencephalography of brain stem and cerebellum of cats. Arch. neerl. Physiol., vol. 25, pp. 51-56, 1940c.

Tschistowitsch, Th. Ueber die Heilung aseptischer traumatischer Gehirnverletzungen. Ziegler's Beitrage, vol. 23, pp. 321-349, 1898.

Ulett, G. and Claussen, F. A spring-pressure-contact electrode for use in electroencephalographic recording. Science, vol. 99, pp. 85-86, 1944.

van Schulten, M. W. Untersuchungen uber den Hirndruck, mit besonderer Rucksicht auf seine Einwirkung auf die Circulation-verhaltnisse des Auges. Arch. f. klin. Chir., vol. 32, pp. 947-988, 1885.

Walker, A. E., Kollros, J. J. and Case, T. J. The physiological basis of concussion. J. Neurosurg., vol. 1, pp. 103-116, 1944.

Walter, W. G. Location of tumours by electro-encephalography. Lancet, vol. 2, pp. 305-308, 1936.

Walter, W. G. The electro-encephalogram in cases of cerebral tumour. Proc. R. Soc. Med., vol. 30, pp. 579-598, 1937.

Walter, W. G. The technique and application of electro-encephalography. J. Neurol. Psychiat., vol. 1, pp. 359-385, 1938.

Walter, W. G., Griffiths, G. M. and Nevin, S. The electro-encephalogram in a case of pathological sleep due to a hypothalamic tumor. Brit. med. J., vol. 1, pp. 107-109, 1939.

Walter, W. G. and Wyllie, W. The electro-encephalogram in the diagnosis of cerebral atrophy. Proc. R. Soc. Med., vol. 30, pp. 578-579, 1937.

Ward, J. W. and Clark, S. L. The production of artificial tumours in the brains of cats. J. Lab. clin. Med., vol. 26, pp. 1778-1784, 1941.

White, J. C., Brooks, J. H., Goldthwait, J. C. and Adams, E. D. Changes in brain volume and blood content after experimental concussion. Ann. Surg., vol. 112, pp. 619-634, 1943.

Williams, D. The abnormal cortical potentials associated with high intracranial pressure. Brain, vol. 62, pp. 321-334, 1939.

Williams, D. The electro-encephalogram in acute head injuries. J. Neurol. Psychiat., vol. 4, pp. 107-130, 1941.

Williams, D. and Denny-Brown, D. Cerebral electrical changes in experimental concussion. Brain, vol. 64, pp. 223-238, 1941.

Williams, D. and Gibbs, F. The localization of intracranial lesions by electroencephalography. New Engl. J. Med., vol. 219, pp. 998-1002, 1938.

Williams, D. and Gibbs, F. The localization of cerebral lesions by electro-encephalography. Trans. Amer. neurol. Ass., vol. 64, pp. 130-132, 1938a.

Williams, D. and Gibbs, F. Electroencephalography in clinical neurology, its value in routine diagnosis. Arch. Neurol. Psychiat., Chicago, vol. 41, pp. 519-534, 1939.

Wilson, R. Brain repair. Arch. Neurol. Psychiat., Chicago, vol. 15, pp. 75-84, 1926.

Witwer, E. R., Derbyshire, A. J. and Corrigan, K. E. Application of some new technics to study of brain tumors. Radiology, vol. 41, pp. 130-143, 1943.

Woodhall, B. and Lowenbach, H. Congenital cerebral aneurysms lateralized by electroencephalography. South. med. J., vol. 36, pp. 580-585, 1943.

Yeager, C. L., Baldes, E. J., Craig, W. McK. and Woltman, H. W. Electro-encephalography as an aid in localizing intracranial lesions. Proc. Mayo Clin., vol. 15, pp. 147-149, 1940.

Yeager, C. L. and Baldes, E. J. Differentiation of intracranial lesions by electroencephalography. (An exhibit) Tr. Amer. neurol. Ass., p. 168, 1942.

Fig. 19. Electroencephalogram and electrocardiogram recorded from a dog (5-27-43) before and after pendulum blows to the head delivered with a velocity of 37 ft. per second. Both non-fatal and fatal blows are shown. Lines A, B and C are recorded from bipolar electrodes two on the right, one on the left side of the head. In the case of the Non-Fatal Blow the first recorded strip taken before, during and immediately after the blow. The second was recorded 90 seconds after the blow. In the case of the Fatal Blow the first strip was taken just before, at the moment of and immediately after the blow. The second strip was recorded one and one half minutes after the blow (at the time of death).

require more than twenty-four hours time off one would have been right seven times and wrong three times.

A follow-up study of patients who had been studied electroencephalographically following acute head injury: This study consists of "recheck" records on eighty-six patients out of the total number of two-hundred and thirteen shipyard workers who were examined electroencephalographically following acute head injury. The first electroencephalogram was recorded within twenty-four hours of the time of injury in eighty-one of these eighty-six patients and in six the electroencephalogram was obtained within fifteen minutes of the trauma. The final electroencephalogram was not taken until the patient was able to return to work again or could be inducted to return to the laboratory for a "recheck" record. On the average these workers were seen about 8 weeks following the accident.

Sixteen of the eighty-six records showed a change between the first and last recording. Five records that changed were abnormal. Three of these changed to borderline and two to normal. Eleven borderline records changed, ten to normal and one from borderline to abnormal. It is felt that this last case might have been classified as abnormal at the time of the first electroencephalogram except that the reduction of amplitude of the record, a phenomenon seen frequently in head injury cases, caused this patient's record to appear more regular at the first recording than it did at the second recording. None of the thirty-four cases whose original record was normal changed when the record was repeated after clinical