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THE MARCH OF FOCAL MOTOR EPILEPSY*

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AN APPRECIATION

During my career in neurosurgery, I have had the pleasure of meeting many of your leaders in the speciality of brain surgery both at our clinics in America and at International scientific meetings. It has been a pleasure in the past 2 weeks to renew acquaintances and to meet many more of your Japanese colleagues.

In your country, clinical and scientific neurology has evolved about the neurosurgical clinic; accordingly the Japanese Neurosurgical Society, (the largest national organization of the neurological specialty in the world) brings together members from all the disciplines interested in the nervous system. This common forum ensures a cross fertilization of the subspecialities and broadens the interests of all. For this reason, I am particularly honored by your invitation to visit your universities and to address this distinguished organization.

During the weeks that I have been your guest I have come to appreciate the beauty of your landscape, the fascination of your cultural traditions and the bounteous hospitality and sincere friendship of you and your colleagues. When I return, I shall take with me many pleasant thoughts of my visit and shall cherish the memories that will constantly remind me of Japan.

In selecting my subject I was not unmindful of the great amount of work which had been done in your country on the chemical and anatomical basis of epilepsy. In view of the tremendous interest in this subject and the fundamental contributions which have been made in Japan, it seemed that our studies on epileptic mechanisms might be of interest.*

* During the past 6 years a number of my associates have participated in this research. It is a pleasure to acknowledge the stimulating assistance of:
Dr. O. Andy, Dr. W. H. Faeth, Dr. D. LaFia, Dr. G. Poggio,
and Dr. G. Udvarhelyi.
Without the help of the electroencephalographer-in-charge of the Johns Hopkins Hospital, Dr. C. Marshall, the electronic recording could not have been accomplished.

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Introduction

In this discussion only the focal motor seizures will be mentioned; possibly the principles of their pathogenesis are applicable to the generalized types of epilepsy—the petit mal and idiopathic grand mal but too many gaps exist in our knowledge at the present time to attempt a discussion of the mechanisms in the latter epilepsies.

During the past two decades a considerable amount of work has been devoted to the mechanisms of initiating a focal epilepsy. These have been aided by the introduction of experimental methods of producing such an epilepsy by the cortical application of alum, convulsive drugs such as penicillin, metrazol, etc., and by local trauma isolating areas of the cerebral cortex. These studies have shown that, exposed to these insults, the cortex becomes hyperexcitable, although the precise biochemical mechanisms have yet to be demonstrated. However, the existence of a hyperexcitable cortex is not sufficient to produce an epilepsy. The neuronal discharges must be propagated through channels until subcortical centers are fired to induce a muscular response. It is the study of the phenomena associated with the cortical and subcortical activation to produce an overt convulsion that will be discussed in this paper.

There has been a growing body of evidence, both clinical and experimental, that the propagation of epileptic discharges from a cortical focus to other areas within the central nervous system is upon an orderly arrangement rather than a wild haphazard discharge or a widening circle of excitation such as the ripples produced in a body of still water when an object is dropped onto its surface. Although it is possible that the epileptic discharge may spread from a given point of the cortex to practically any other point of the central nervous system, the likelihood of such an occurrence between any two given points is a function of their anatomical and physiological relationship. A discussion of the pathways of epileptic discharges requires a consideration of operational mechanisms rather than solely structural lines of communication.

In an attempt to determine these pathways some years ago a series of experiments on macaque monkeys were begun using a technique by which the electrical activity of multiple cortical areas and subcortical ganglia could be examined simultaneously and continuously after electrical or chemical stimulation of any portion of the nervous system. This discussion will be confined to the data developed from this research.

Experimental Techniques

The animals were prepared after chemical block of the appropriate nerves of the head, and local infiltration of the scalp and anterior part of the neck with 0.1% procaine. A tracheotomy was carried out and the animal was then arti-

ficially ventilated as d-tubo-curarine or succinyl choline chloride was administered in sufficient doses to abolish respiratory and somatic movements. A slow intravenous drop of dextran and isotonic saline was maintained.

After placing the animal in a stereotactic instrument, small holes were drilled through the calvarium over selected areas of the cortex and phonograph needles, to serve as electrodes, inserted to the dura mater. A plate of bipolar concentrical electrodes each having an outside diameter of 0.65 mm. was positioned in a carrier, which was lowered so that the needles penetrated the convexity of the brain to a predetermined depth which put the tips of the needles in selected subcortical nuclear masses (fig. 1). At the conclusion of the procedure the animals were killed, and the vascuar system was profused with isotonic saline to wash out the blood, and then injected with a 10% solution of formalin to fix the brain.

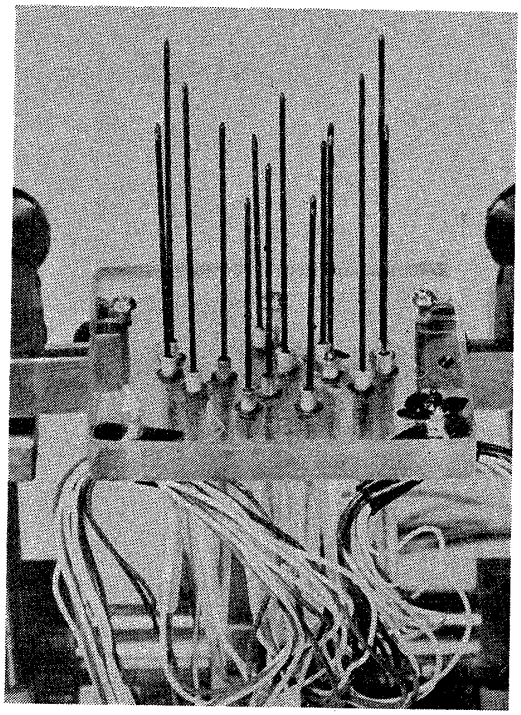

Fig. 1. Photograph of the plate of electrodes so positioned that their recording tips are in predetermined subcortical structures.

The brain of each animal was embedded in celloidin and cut at 30 micra and every third section was saved and routinely, every eighth preserved section was stained for myelin and an alternate section for cells by Nissl's technique.

At the time of the experimental procedure a sketch was made of the cerebral cortex to indicate the position of the cortical electrodes and this was verified at the postmortem examination. Serial sections of the brain were studied to determine the precise location of the electrode tip and a point approximately 1½ mm. above the tip of the depth electrode which represented the points of electrical contact.

The recording was made on two 8 channel electroencephalographs connected

by their motor drives so that they could be engaged simultaneously. Most of the records were taken with a time constant of 0.1 seconds, and a filter reducing the voltage of the high frequencies 50% at 70 CPS. In later experiments a 16 channel Gilson electroencephalograph connected with a Grass 8 channel electroencephalograph was used so that 24 traces could be recorded simultaneously.

The brain was stimulated electrically using a thyratron discharge or a square wave pulse having a duration of 1-2 milliseconds. The rate of stimulation was usually 30 cycles per second. The voltage varied from 2-20 volts. The stimulus was applied for 5 seconds. Stimulation of the cerebral cortex and subcortical structures was carried out seriatim, with an interval between each excitation of at least one minute or until the electrical state of the tissue had returned to its prestimulation level, which sometimes required a waiting period of five minutes.

The preparatory procedures ordinarily took about 3 hours following which excitation and recordings were carried on for 6 to 20 hours depending upon the condition of the animal. During this period of time the threshold of excitation did not vary greatly.

In some animals an epileptogenic agent such as penicillin, strychnine, or metrazol was applied to the cerebral cortex to induce a repetitive excitation of the cortex. With the latter techniques it was possible to follow the discharges throughout the central nervous system over a prolonged period of time. By this means the propagation of the discharge was somewhat easier to trace than when the cortex was stimulated electrically.

Although it is generally assumed that after-discharge or runs of spikes imply an epileptic phenomena it must be admitted that such electrical changes may occur without overt convulsive movements even if the experimental animal is not under anesthesia or the effect of a paralysing agent. Consequently, it should be understood that, although for the purpose of this discussion, spiking is equated with epilepsy, the issue is not so simple.

At the beginning of this work, a visual analysis was made of the records. To appreciate the activity of the various cerebral centers in time, the pages of record were processed to show by histograms the number of spike discharges per unit of time, usually 10 seconds. As the number of experiments increased—now more than 100 monkeys—it became obvious that some other analytic technique would be necessary. Accordingly a coding system was devised for use with International Business Machine punch cards. The detailed techniques involved need not be given other than to say that a code was evolved for the type of animal, previous operative procedures, number of stimulation, type and degree of stimulus used, the site of stimulation, the type of response, its duration and its propagation. A detailed analysis of the type of response to 3,350 stimulations of some 53 cortical and subcortical areas was coded.

Results

Electrical stimulation of the cerebral cortex and subcortical structures may give rise to one of four types of response. First, with stimuli of low intensity there may be no response at the site of stimulation or at points distant from it. The strength of these subliminal stimuli gives some idea of the threshold of the cortex although it should be recognized that over a period of time the threshold of excitation may fluctuate depending upon the condition of the animal and the previous state of excitation or inhibition of the local area. Second, a local after-discharge may occur at the point of stimulation and persist for seconds or minutes without any evidence of propagation of the discharge to other areas. This local discharge is particularly apt to be seen in such areas as the hippocampus or occipital cortex, but less likely to be observed in the motor or sensory cortex. A third possibility is a local after-discharge with propagation to other parts of the brain. This propagation may occur immediately with the electrical stimulation or may build up gradually over a period of time during the local after-discharge. The fourth type develops if the excitation is intense; the discharge may be generalized immediately or may diffusely propagate. In this experimentation, electrical stimuli were preferred which were just sufficient to give rise to an after-discharge lasting for a few seconds to perhaps a minute. Intense stimulations which might induce a generalized convulsive seizure were deliberately avoided because of the subsequent depression of the activity of the cortex and the possible modification of the paths of propagation of subsequent epileptic discharge. If a generalized seizure eventuated, the experiment was discontinued until the cortical activity had returned to its normal frequency and amplitude (table 1).

Table 1. Types of Response to Electrical Stimulation of Face Motor Area 0.5—5.0 volts

No response	49	26%
Local response	14	5%
Local with propagation	111	58%
Generalized response	15	8%
Total	188	

In this analysis, the responses which caused propagation to some other part of the nervous system are considered. Ineffectual or stimuli producing after-discharge confined to the site of excitation are not considered.

Pathways of Propagation

To illustrate the pathways of propagation of epileptic discharge during a focal motor seizure, a convulsion beginning in the face representation will be studied. The progression of an attack induced by the application of penicillin to the cerebral cortex will be the main source of data for this presentation; addi-

tional material obtained from electrical stimulation will be used when appropriate.

Within a minute or two of the application of a few thousand units of penicillin, spikes begin to appear locally. These electrical evidences of epileptic activity may remain confined to a small area of cortex but usually they spread to (1) the adjacent arm and leg representation, (2) the contralateral face area and (3) the ipsilateral putamen. At about the same time, but some period after the spikes begin, if the animal is not entirely paralysed, twitches are seen in the facial musculature opposite the irritated cortex. If the cortical and sub-cortical activity is sampled at 30 second intervals, the spread of the cortical spike from the site of application of penicillin may be followed along the precentral gyrus (fig. 2). As the spiking develops in the entire motor cortex the subcortical ganglia begin to participate in the discharge at approximately the same time as the clinical seizure appears. In the next few minutes, the spikes become more

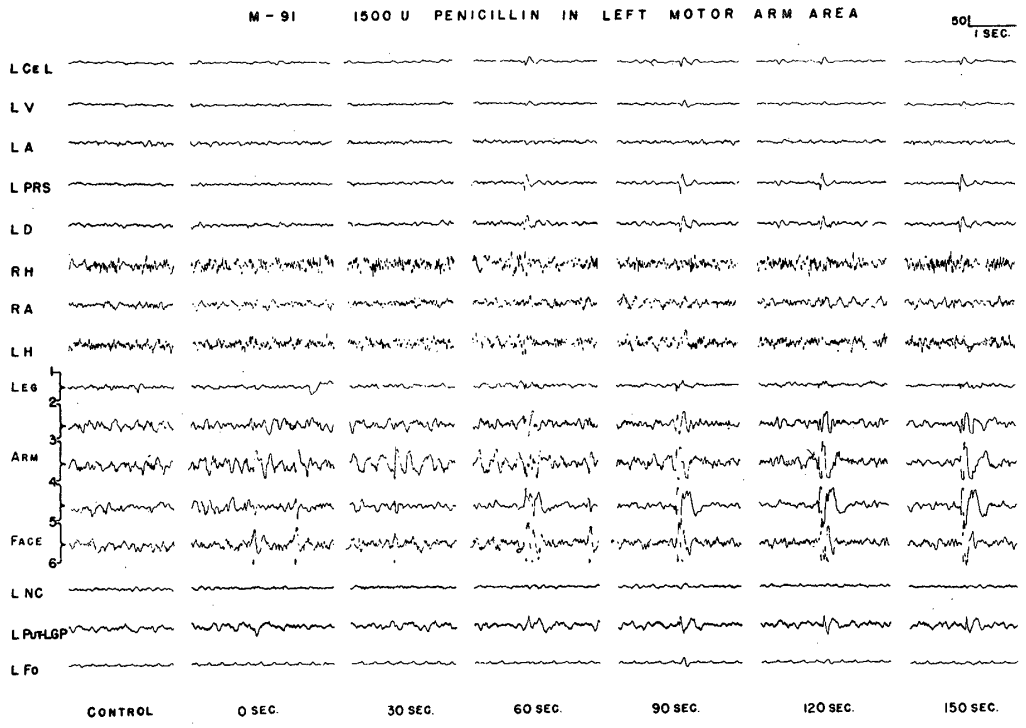

Fig. 2. Propagation of a seizure induced by the subpial injection of 1500 units of penicillin at the junction of the face and arm areas (between electrodes 4 and 5). The time is dated from the appearance of the first cortical spike; the clinical manifestation—jerking of the shoulder—occurred 60 seconds later as the discharges appeared in subcortical nuclei. The cortical electrodes 1 to 6 were placed along the precentral convolution from just to the right of the longitudinal sinus to the superior part of the left face area. The abbreviations are as follows:

LA—left amygdaloid nucleus LCel—left cerebellar cortex LD—left dentate nucleus LFO—left fornix LH—left hippocampus LNC—left caudate nucleus LPRS—left pontine reticular substance LPut, LGP—left putamen and globus pallidus LV—left lateral ventricle RA—right amygdala RH—right hippocampus

prominent in the subcortical structures. With the spread of the clinical seizure from the face and shoulder to the arm and leg, the spiky activity extends to the entire central gyrus but does not usually implicate the frontal agranular, temporal or occipital cortex. It is to be noted that the spread of the convulsion is accompanied by both cortical and subcortical extension of the spiky discharge. In

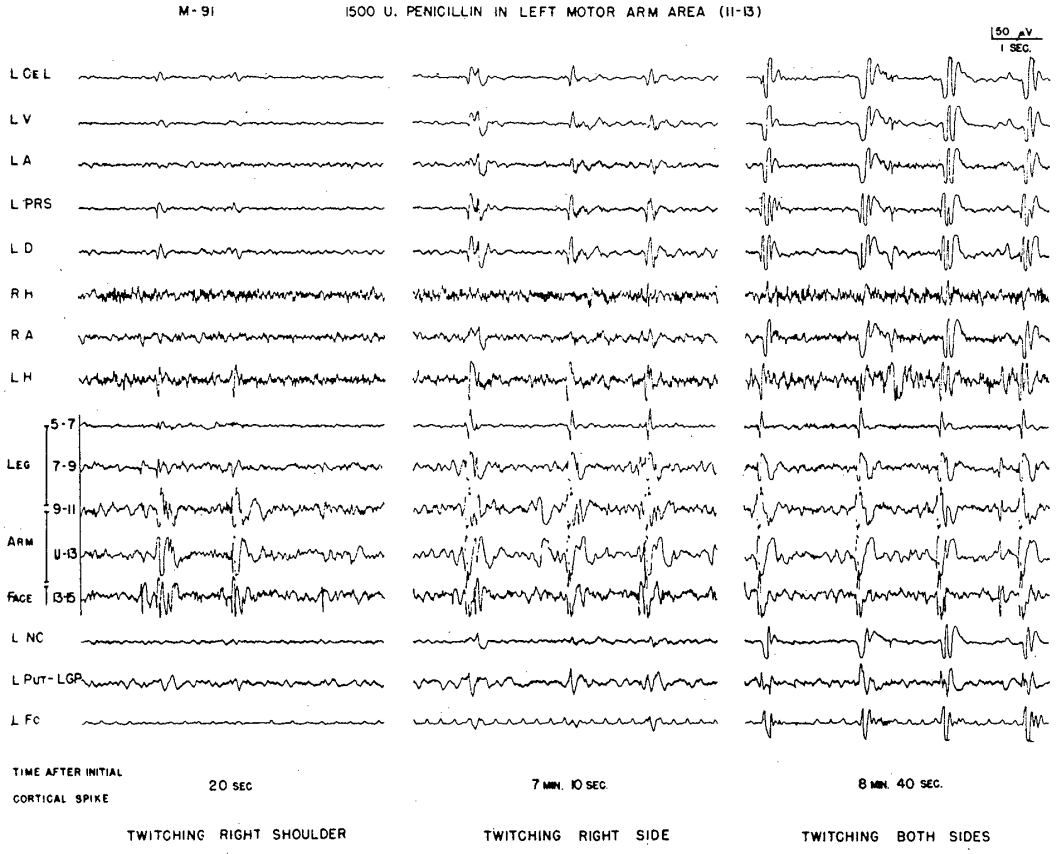

Fig. 3. Penicillin, 1500 units (0.01 cc.) was injected into the left motor arm area between the electrodes 11 and 13. Penicillin spikes appeared in the cortex four minutes after the injection. The section of the record taken at 20 seconds after the initial cortical spike shows the spread of the epileptic activity to adjacent cortical regions and the subcortical responses in the ipsilateral cerebellum, reticular substance of the pons, hippocampus, and basal ganglia. At this time, the clinical manifestations were twitching of the contralateral shoulder, synchronous with the cerebral discharges. Subsequently, the twitching progressed to involve the entire contralateral side of the body, the middle tracing (taken seven minutes after the initial cortical spike) shows discharges present in the ipsilateral motor cortex and subcortical structures. When the twitching became generalized, all the cortical and subcortical regions sampled exhibited discharges of high amplitude. It is noteworthy that the progressive involvement is more evident in the subcortical than in the cortical regions. The seizure took much longer to spread from the initial site of twitching (right shoulder) to the entire side (seven minutes), than to extend from the one side to both sides of the body (one and a half minutes).

fact, it appears in many instances that the subcortical propagation is more extensive and intensive than the cortical. With the clinical seizure confined to one side, the spiking is marked in almost all subcortical structures being sampled from that side. An exception is the caudate nucleus. When the attack becomes bilateral, practically all cortical and subcortical structures are spiking. It is to be noted that the cortical spike is not increased in size, although the clinical myoclonic jerks involve more and more of the skeletal musculature.

The spread of the clinical convulsion may be correlated with the electrical pattern. As the attack begins, the spikes are confined to the contralateral face motor cortex. The subcortical structures do not participate except for a spike in the putamen which becomes somewhat more pronounced as the clonic seizure commences and as the opposite face area participates in the spiky activity. As the spike discharges spread into the arm area, the spikes become more prominent in the medial part of the putamen, and the ventrolateral nucleus of the thalamus participates in the activity. With the progression of the attack in the motor cortex, almost constant spike activity is seen in the putamen, the contralateral cerebellar hemisphere, the ipsilateral ventrolateral nucleus of the thalamus and globus pallidus. The attack may be arrested at this point, or may become generalized by involvement of other structures, usually the hippocampus and amygdala (fig. 3).

We may inquire as to how preferential these pathways of propagation really are? To answer this question the responses of the motor face area, and many

Table 2. Frequency of Cortical and Subcortical Propagation from Face Motor Area

	Same Side	%	Opposite	%
Cortical zones				
Prefrontal	34/60	57	25/58	42
Face Motor	95/95	100	76/80	95
Anterior Temporal	21/47	44	11/43	26
Posterior Temporal	5/8		1/4	
Cingulate Gyrus	0/13		0/5	
Subcortical structures				
Caudate Nucleus	14/59	24	2/37	5
Globus Pallidus	7/12	59	1/11	9
Thalamus VL	24/36	67	7/32	22
Putamen	68/75	92	36/60	60
Amygdala	21/45	47	5/32	16
Hippocampus	11/38	29	6/37	16
Cerebellum	10/33	30	23/34	68

The figures give the number of times the specified structure exhibited spiky discharge in the number of effective stimulations of the face motor area; thus the ipsllateral; prefrontal area showed a discharge in 34 of 60 stimulations (57%) of the motor face area.

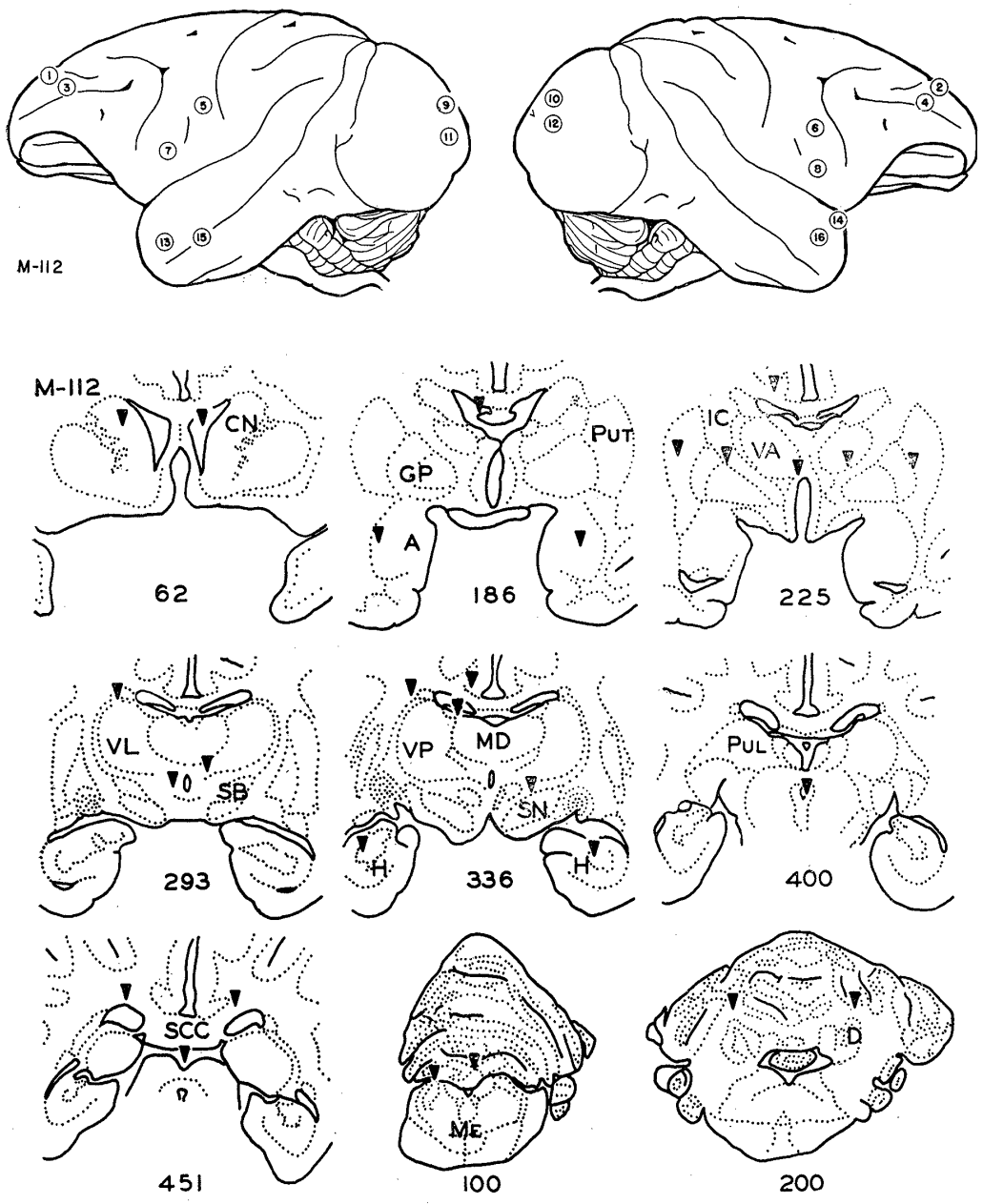

Fig. 4. (M-112) Sketches to show the position of the cortical electrodes and the subcortical electrodes as determined by the examination of serial sections. The abbreviations are:

A—amygdala CC—corpus callosum CE—cerebellum CN—caudate nucleus GP—globus pallidus H—hippocampus IC—internal capsule MD—medial dorsal nucleus ME—medulla oblongata PC—posterior commissure Pul—pulvinar Put—putamen SB—subthalamic body SCC—splenium SN—substantia nigra VA—ventral anterior nucleus VE—ventricle VL—ventral lateral nucleus VP—ventral posterior nucleus WM—white matter

subcortical nuclei were analysed from a number of experiments (table 2). It is apparent that, at times, the discharges from the motor face area are propagated to each nucleus sampled, but that certain nuclei are much more frequently activated than others. In a biological system as complicated as the motor, it is not surprising that many pathways are used in epileptic activity. Since through a few circuits, all nuclei of the central nervous system may be involved, it is understandable that every large nucleus will be at sometime involved on a chance basis, if a stimulus is repeated sufficiently often. In fact, a difference of 70% in the responses between caudate nucleus and putamen under these circumstances is particularly significant.

To this point, the subcortical propagation has been emphasized but the transcortical spread to the same and opposite hemisphere is equally important. The discharges pass through the corpus callosum to the opposite homologous motor cortex as soon as they become well developed on the primary side. However, this spread occurs while the clinical attack is unilateral and the limbs on the

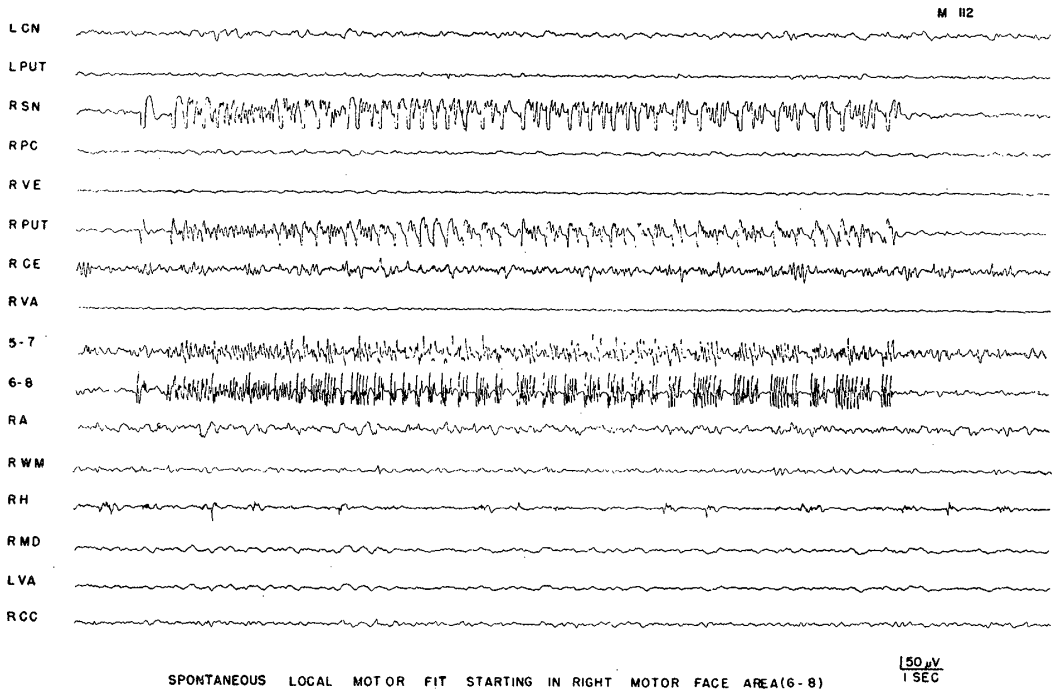

Fig. 5. (M-112) Spontaneous focal discharge of right face motor cortex, ipsilateral putamen, and substantia nigra and slight activation of contralateral homologous cortex. Other subcortical structures are not affected. The abbreviations are as follows:

A—amygdala CC—corpus callosum CE—cerebellum CN—caudate nucleus GP—globus pallidus H—hippocampus IC—internal capsule MD—medial dorsal nucleus ME—medulla oblongata PC—posterior commissure Pul—pulvinar Put—putamen SB—subthalamic body SCC—Splenium SN—substantia nigra VA—ventral anterior nucleus VE—ventricle VL—ventral lateral nucleus VP—ventral posterior nucleus WM—white matter

non-convulsing side are being used for voluntary activity. It seems probable that the spiky activity of the contralateral cortex is due to evoked potentials from afferent bombardment of the outer cortical layers without activation of the lower efferent layers of the cortex.

If the opposite motor cortex is "hypersensitive" due to the previous application of a convulsant agent, it may be fired into continuous discharge by a short volley of afterdischarge from a normal motor cortex. In figure 5 the electrical concomitants of a spontaneous focal seizure of the face area several hours after the application of penicillin are demonstrated. Subsequent electrical stimulation of the opposite (left) face area (fig. 6) induces a brief local afterdischarge but sustained seizure activity in the right motor area which activates the same subcortical structures as a spontaneous fit of that cortical area.

This transcallosal transmission is not necessarily the mechanism by which

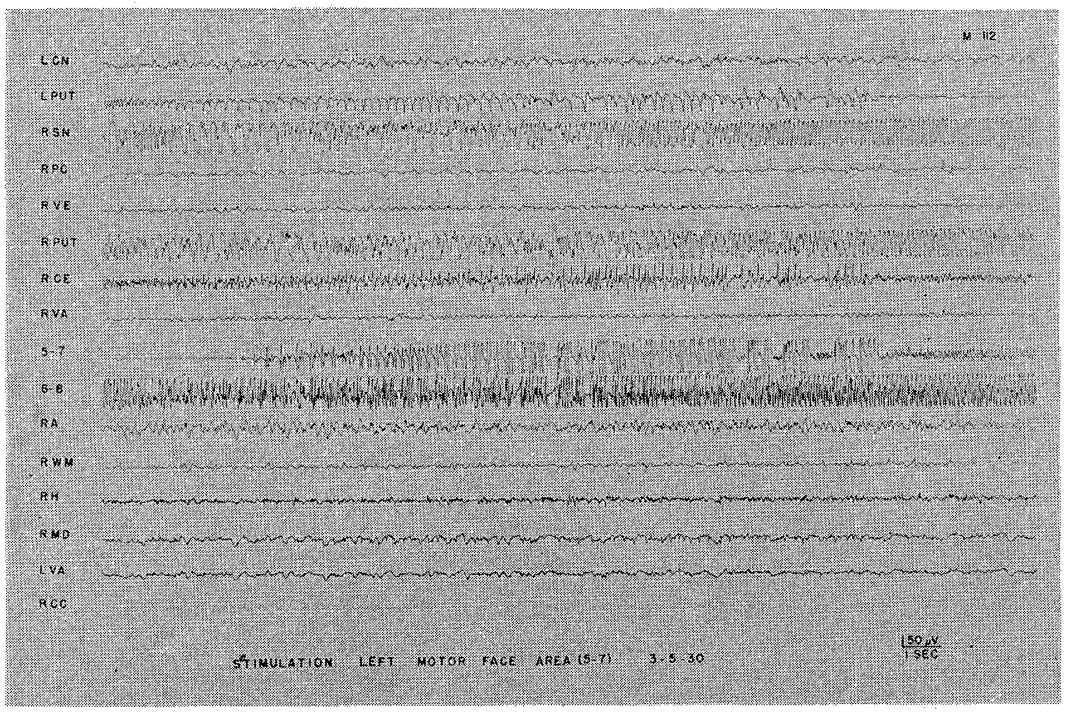

Fig. 6. (M-112) Stimulation of the left motor face cortex induces an afterdischarge in the ipsilateral putamen and contralateral cerebellum, lasting approximately 12 seconds and an afterdischarge in the homologous contralateral motor cortex, putamen, substantia nigra which persists after the first side has ceased. The right side had previously been activated by the local application of penicillin to the face cerebral cortex. The abbreviations are as follows:

A—amygdala CC—corpus callosum CE—cerebellum CN—caudate nucleus GP—globus pallidus H—hippocampus IC—internal capsule MD—medial dorsal nucleus ME—medulla oblongata PC—posterior commissure Pul—pulvinar Put—putamen SB—subthalamic body SCC—splenium SN—substantia nigra VA—ventral anterior nucleus VE—ventricle VL—ventral lateral nucleus VP—ventral posterior nucleus WM—white matter

the second side becomes involved in the seizure. The convulsion may become generalized through brainstem mechanisms, for after a hemispherectomy the intravenous injection of metrazol or bitemporal electrical shock will produce bilateral practically symmetrical convulsions. Possibly the pathway described by Hayashi[8] may be implicated. This subject has recently been studied by Morrell[12] who emphasized the development of secondary epileptic foci "mirror foci" at homologous points to an experimental cortical discharging focus. He considered the callosal pathway the major one but found that extracallosal pathways played a facilitatory role.

The transcortical ipsilateral spread has also been studied by many investigators. It has been known since the time of Unverricht[14] that linear incisions across the cortex will not prevent the spread of a seizure from one extremity to another. Moreover, Gerard[7] has demonstrated that caffeine excitation waves will cross such cuts. There has been the suggestion that the cortical spread is due to a feed-back mechanism from subcortical structures. Gastaut[4] in particular has emphasized the role of thalamic sectors in epileptic propagation. To test the hypothesis of a feed-back from subcortical structures as the mechanism by which the ipsilateral cortical spread of a seizure occurs, a series of 8 experiments were carried out in which the arm representation of the motor cortex was removed so as to eliminate the transcortical connections between face and leg motor areas. Some weeks later in an acute experiment, penicillin was applied to the face or leg area or serially to both.

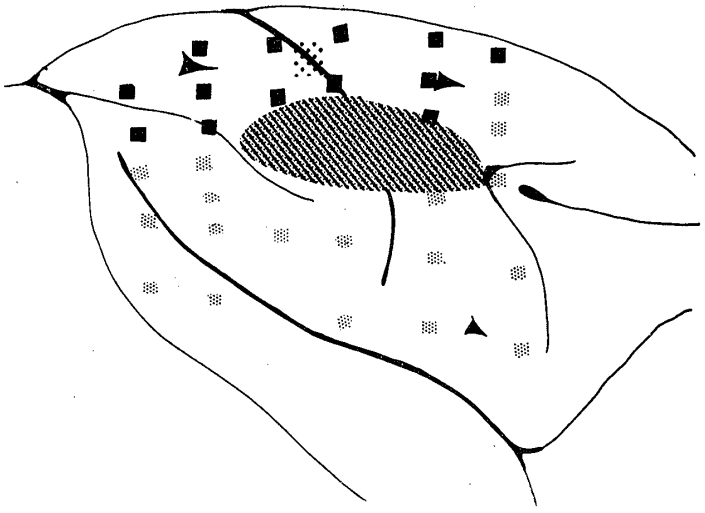

Fig. 7. (M-22) Sketch of the right hemisphere of a macaque monkey to show the site of a previous ablation of the motor and sensory cortex. Along the leg area of the central sulcus, penicillin was applied (square dotted) and spiking occurred by the electrodes indicated by solid black, but normal activity in the electrodes indicated by stippling.

As may be seen in fig. 7 the application of penicillin above the central ablation induced local spiking from the pre-and post-central gyri above the lesion but none below the lesion, although electrodes were sampling the activity of most of the convexity of the hemisphere. Moreover, if penicillin is subsequently placed below the lesion the induced spiky activity above and below the lesion bears no relationship one to the other (fig. 8).

It would thus seem that subcortical feed-back is not essential, and probably is not an important factor in the cortical spread of a seizure.

The Generalization of a Focal Seizure

The spread of a focal motor seizure through subcortical centers has been discussed in some detail. Many focal seizures, however, develop into a generalized convulsion. What is the mechanism by which this transition occurs? A number of theories have been proposed. That which has received the most attention recently is Penfield's centrencephalic system[13] which presupposes a functional diencephalic center symmetrically modulating cortical activity. According to this theory the cortical discharge fires this center, which then activates the entire cortex. Gastaut, impressed by the rhombencephalic strychnine fit, has added substance to this centrencephalic system, concluding that it, anatomically, is the reticular formation of the brainstem.

Gostaut and Fischer-Williams[5] believe that the partial epilepsies become generalized by the transmission "to the centrencephalic structures from the thalamus to the medulla, and from there be generalized to the rest of the brain". (5, p. 353). In support of this view they cite the work of Jasper et al[10] which showed that the majority of cortical post-discharges are transmitted to the reticular formation

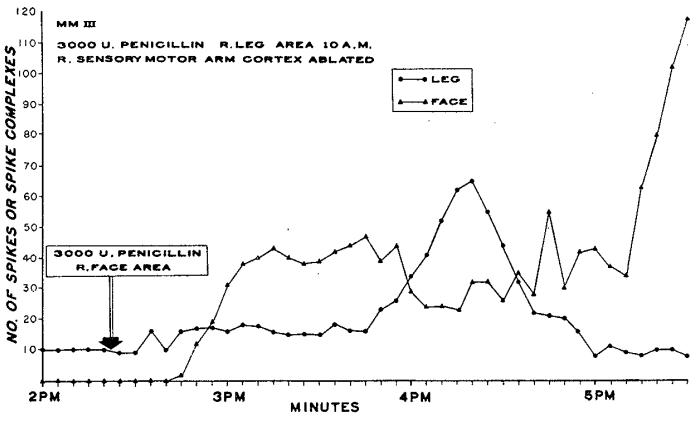

Fig. 8. (MM-111) Preparation as illustrated in figure 7. The number of spikes or spike complexes per 5 minute interval is plotted for the leg and face area. At the arrow 3,000 units of penicillin are applied to the right motor face area. The dissociated curves for the two areas are evident.

of the thalamus and brainstem. Moreover, French et al[3] stated that persistent afterdischarge seems "to have the capacity secondarily to excite certain diffusely projecting subcortical structures, (reticular formation, septal region and amygdala) which are capable of disseminating the induced discharge widely". But not all authors concur in such a subcortical center. Haynes et al[9] believe the cortex is the critical structure; Andy and Akert[1] thought that transcortical involvement of the parietal association areas on both sides was associated with generalization of the seizures.

By means of multiple subcortical recording we have attempted to answer this question. To understand our findings, one must appreciate that there are several systems of preferential propagation originating in the cerebral cortex other than the motor system. Seizures beginning in the prefrontal granular cortex propagate to the contralateral homologous cortex, to the ipsilateral caudate nucleus, and ipsilateral temporal pole, and eventually to the medial thalamus. Seizures of the temporal cortex propagate to the contralateral homologous cortex, the amygdala, hippocampus and the hypothalamus. Thus, a seizure beginning in the motor face area which fires the prefrontal granular cortex (as it does 70% of the time) will induce discharges propagating to the anterior temporal region, the ipsilateral caudate nucleus and medial thalamic structures. At the same time the face seizure may propagate directly to the temporal pole as it does in about 50% of cases and set up discharges in the amygdala, hippocampus and

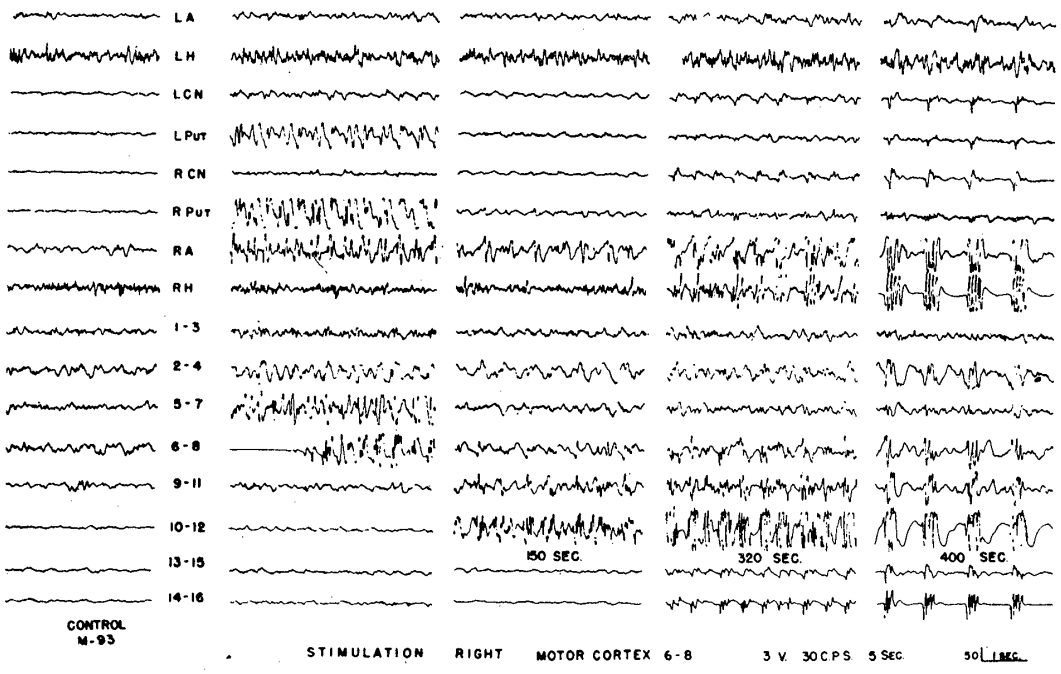

Fig. 9. (M-73) Following electrical stimulation of the right motor face area the seizure discharges may be traced during a period of 7 minutes until they become almost generalized.

hypothalamus. Although not all of these structures may be in a state of self-sustained discharge, they are being facilitated, so than an additional stimulus from another structure may be adequate to induce the self-sustained discharge of epilepsy (fig. 9).

If the course of a seizure is followed for some time after cortical stimulation (fig. 10) one notes the progressive involvement of cortical and subcortical structures along the systemic pathways mentioned until practically all parts of the brain are participating in the seizure—i.e. until it has become generalized.

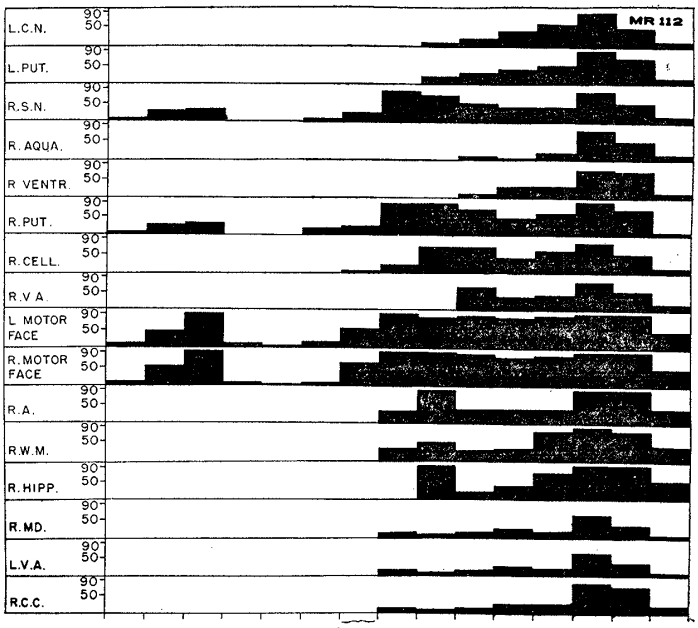

Fig. 10. (M-112) Activation of penicillin focus in right motor face area by intravenous metrazol. The number of spikes or spike complexes in the cortical or subcortical structures per 10 second period is indicated by the histograms. The gradual but irregular generalization of the seizure may be followed from the left to the right of the histograms. At the point of the record where the histogram begins at the left, an abortive seizure, represented by spiky activity is building up in the right and left motor face areas, the right putamen and right substantia nigra. About one minute later, the activity in these structures increases, and the right amygdala and cerebellar cortex become activated. In another ten seconds, the right hippocampus, the left putamen and caudate nucleus are beginning to fire. In the next 10 seconds in addition to these structures, the right nucleus ventralis anterior is firing and other structures are showing occasional spikes. Within another half minute all nuclei being sampled are discharging (generalized seizure) and continue to do so for 20 seconds when the fit, almost stops, simultaneously in all leads.

From these studies, the generalization of a focal seizure would seem to be related to the progressive involvement of subcortical and cortical neurones until a critical mass has been involved which causes a synchronous discharge of many parts of the nervous system. It should be noted that the progressive steps in the epileptic march may not be associated with overt manifestations of the participation of another nuclear mass. Consequently, it may appear that the seizure suddenly changes its character at the time the critical mass of discharging neurones has been reached. This may be the pathogenesis of the convulsive attack occurring without warning for much subcortical epileptic activity may be present without clinical comcomitants both in experimental animals and man.

As this spread occurs the synchronization of the bursts in cortical and subcortical structures seems to be a function of the primary discharging zone but if the primary zone stops its activity, the role of pace-maker may be assumed by some other structure.

The lower brainstem and spinal pathways by which the focal seizures are exteriorized have been studied by a number of authors. The situation is too complex to discuss at this time, except to say that the pyramidal tract seems to play an important, although not essential, role. There seems no doubt that the reticular formation participates in the spiky discharges associated with focal generalized epileptic seizures. However, it is not more active or longer lasting in its discharges than other parts of the brain. Its threshold for afterdischarge to electrical stimulation is several times higher than that of the motor cortex. The elimination of the mesencephalic part of the reticular formation with the resultant akinetic state does not seem to modify greatly the pattern of either the focal cortical or generalized induced seizure. This does not deny nor confirm the results of Miyasaka et al[11] who found that stimulation of the reticular formation just before direct excitation of the neocortex of cats lowered the threshold of seizure. However, this study has not supported the hypothesis of Gastaut[4] regarding the essential role of the reticular formation in the generalization of the seizure.

Nor does this reflect in any way upon the observations of Gellhorn et al[6] that high frequency stimulation of the reticular formation (90-100 c/sec.) may aggravate local cortical discharges. That the problem is very complex is indicated by Andy and Mukawa's[2] report that lesions of the reticular formation produced pronounced but erratic prolongation of seizure activity of the forebrain structures. Much investigation is necessary to clarify the role of the reticular formation in the mechanisms of convulsive activity.

Summary

With multiple subcortical bipolar electrodes sampling the activity of most of the basal ganglia and brainstem, the propagation of a focal epileptic seizure

originating in the face motor area has been followed. Both cortical and subcortical spread of discharge has been observed and statistically evaluated. The contralateral homologous cortex and ipsilateral putamen are most frequently activated, then the prefrontal cortex, ipsilateral thalamus and globus pallidus and contralateral cerebellum.

The generalization of a focal seizure seems related to the progressive involvement of cortical and subcortical structures until a critical mass is involved, when a generalized attack ensues. The reticular formation does not seem essential to this generalization.

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