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Effects of brainstem and subcortical lesions on corticogenic epileptic convulsion with special reference to Forel h-field

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Abstract

An experimental study was attempted to make an analysis of the subcortical and brain stem lesion effect on the Metrazol-induced corticogenic epileptic convulsion based on EEG-discharge and EMG-convulsion as indicators. utilizing 42 adult cats. 1. A definite threshold increment of eliciting the seizure was found in the case of bilateral lesion of the Forel H-field. In contrast to it, no variation in the threshold was found in the case of the lesions at the other parts of brain stem, thalamus, red nucleus and its neighborhood, and lenticular nucleus. 2. There was a parallel relation between EEG discharge and convulsion. Dissociation could be obtained in none of the cases. 3. It is, therefore, to be concluded that the Forel H-field is composed of the main axis of cortico-subcortical reverberating circuit and that the lesion causes a decrement of the excitability at cortex and an inhibition of the corticogenic epileptic convulsion.

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EFFECTS OF BRAINSTEM AND SUBCORTICAL LESIONS ON CORTICOGENIC EPILEPTIC CONVULSION WITH SPECIAL REFERENCE TO FOREL H-FIELD

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Disease of epilepsy is believed to be primarily due to abnormality of metabolism, especially of amino acid metabolism in brain, whatever the cause may be.

JINNAI[23,24] has proved that enzymes such as glutamic decarboxylase, transaminase and others which participate in the synthesis of γ-aminobutyric acid are decreased in activity at epileptic focus compared with the areas out of the focus, generally in the epileptic brain compared with the nonepileptic. According to his hypothesis, such an enzyme deficiency may cause abnormal metabolism at epileptic focus or in epileptic brain, and accumulation of some substances to a certain level suffices to cause an epileptic attack. These accumulated substances may be swept away during the attack and normal cerebral excitability returns. However, the deficiency of enzymes would again elicit the accumulation of such substances and create another cycle. It may, therefore, be harmless and yet essential for epileptic patients to maintain the cycle of the intracerebral biochemical changes regulated by the epileptic attack.

An attempt has been made to find out the conduction path-way of convulsion, one of the most disturbing manifestions of epilepsy and to interrupt it with the cases in his laboratory[2,35,36]. Metrazol stimulation of the motor cortex did not elicit convulsion in cat, when the Forel H-field was bilaterally lesioned at the upper level of the midbrain. This is interpreted to be due to interception of the conduction pathway of the convulsion[13,14,22,26].

There is, however, an unsolved question in these experimental analyses about convulsion not being elicitied whether it is due to an interception of the efferent pathway of convulsive impulses on the way from the upper centre down to the manifestant, or due to an interruption of the reverberating circuit at the excitation centre which secondarily causes a decrement in the excitation state of the centre for manifestation. In the former case, convulsion can not be brought

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about even though epileptic discharge in EEG is to be elicited at the upper level of the lesion; that is, there should be a dissociation between epileptic discharge in EEG and concomitant convulsion. In the latter case, there should be an increment in the stimulus threshold for eliciting epileptic convulsion. It is furtheremore to be analyzed, if the latter is the case, whether such an interruption at the H-field is of a component of extrapyramidal systems such as subcortical ganglia, cerebellum and others[18,38,48] or brainstem activating systems such as reticular, hypothalamic and others[3,10,11,15,16,17,25,29,30,40], or their combination.

This experimental study was physiologically attempted to clarify the effect and machanism of the Forel H-field and other brainstem lesions on corticogenic convulsion in cats.

MATERIALS AND METHODS

Forty-two cats were utilized in this study; 11 for control, 5 for lenticular nucleus lesion and 26 for brainstem lesion. After tracheotomy, they were unmobilized on head and four extremities to a stereotaxic apparatus under ether anaesthesia. Two pairs of concentric needle electrodes were bilaterally inserted into the posterior sigmoid gyrus and also into the ventrolateral nucleus of the thalamus for EEG and fixed at the skull with screw nails and dental cement. Another pair of electrodes was inserted in flexor muscles of the bilateral hindlegs for EMG. Convulsion in bilateral hindlegs always accompanied that in bilateral forelegs, and therefore the EMG set was sufficient to check the pattern of the convulsion. The electrode was composed of a stainless steel tube, 0.5 mm in outer diameter and an insulated cupper wire in it. It was electrically insulated with Tygon paint (U. S. Stoneware, Akron, Ohio) except the tip. It had about 100 KΩ in cerebral tissue. Recording was made by 8 channel San'ei's inkwriting oscilograph; 0.1 for EEG and 0.05 for EMG in time constant, and 100 μV/5 mm for EEG and 100 μV/1 mm for EMG in calibration, in the majority of the cases. Anodal coagulation was done to make lesions bilaterally at the brain stem or at the lenticular nucleus with 4 mA constant DC for 45 sec through a 0.5 mm diameter steel needle, which was electrically insulated except the tip. The lesion was a football-shaped, 1.5—2.0 mm in horizontal diameter and 2 mm in height. It was composed of two parts; the inner part was a coagulated defect and the outer part was an absolutely necrotized hard shell. It was surrounded by an area 0.5—1 cm wide, in which glia cells conglomerated. Large lesions were made in some of the lenticular nucleus group by means of several needle tracts in order to destroy most part of the nuclear components. Eight- in minimum, 102- in maximum and 304-days in average survival period were postoperatively allowed for the subsequent stimulation experiment. Stimulation

was applied usually 3 hours after the preliminary anaesthesia with ether inhalation. A specially-made tuberculin syringe (0.25cc/34mm/25 scales) was used for this procedure with a tiny injection needle. A progressively increased dosage of the Metrazol (ranging 10—80% in concentration and 0.01—0.06cc in volume) was injected in each side of G. sigmoideus anterior alternatively through open skull window and intact dura with 5—10 minutes in interval until a typical epileptic convulsion could be obtained. Although recording was occasionally disturbed by movement artefact in the course of the experiment, an elicited epileptic convulsion was recorded in apparently characteristic pattern. At the end of the experiment, a large dosage of Metrazol was intraperitoneally applied to elicit the major epileptic episode, of which the record was evaluated in comparison with the one elicited at the stimulation of the cortex. Animals were sacrificed immediatly after the experiment and perfused with 10% formalin solution through bilateral carotid arteries. Brains were histologically verified by the Haemtoxylin-Eosin method. The cat atlas of Snider and Niemer was mainly referred to[42].

RESULTS

1) Control group :

An attempt was made to determine the stimulus threshold for eliciting epileptic convulsion when it was applied on motor cortex. Stepwise increasing amount of 10% Metrazol solution such as 0.01, 0.015 and 0.02 cc was intracortically injected. The detailed procedures in several cases are illustrated in Table 1. It was found that the stimulus dosage less than 0.02 cc could not always elicit corticogenic epileptic discharge and convulsion.

The responses to the stimulation with 0.02 cc of Metrazol in 11 cases of the control group are summarized in Table 2, termed as the 6th group in Table 3. Bilateral synchronous discharge was elicited in 8 cases, which had no dominance at either side of the motor cortex, and localized discharges at the stimulated site in 3 cases. According to EMG, clonic convulsion was elicited at bilateral hindlegs in 10 cases, and at unilateral hindleg in one. Discharge duration ranged between 60 and 320 sec, with 150 see in average. Convulsion was usually concomitant with the discharge from onset to end with exception of C-56 and C-58, in which great continuation of the discharges did not go together with convulsion in the later half stage. Discharge activity was spike, or spike and wave pattern, and the amplitude was over 300μV and over 140μV at the stimulated cortex and the contralateral cortex respectively. There was over 400μV of spike activity in the convulsive muscle contralaterally or bilaterally. Two types of the beginning patterns of elicited epileptic convulsion are illustrated

Table 1

Time	Metrazol		Site	EEG	EMG	Duration (sec)
C-27—3—6—62						
500	5%	0.01 cc	R-cortex	—	—	—
537	5%	0.01 cc	L-cortex	—	—	—
621	10%	0.01 cc	R-cortex	—	—	—
637	10%	0.015cc	L-cortex	localized discharge	—	330
652	10%	0.02 cc	R-cortex	localized discharge	unilateral clonic	180
C-29—4—14—62						
025	10%	0.01 cc	R-cortex	—	—	—
043	10%	0.01 cc	L-cortex	—	—	—
056	10%	0.015cc	R-cortex	—	—	—
107	10%	0.02 cc	L-cortex	localized discharge	unilateral clonic	117
115	10%	0.015cc	R-cortex	—	—	—
120	10%	0.02 cc	R-cortex	—	—	—
125	10%	0.02 cc	L-cortex	localized discharge	bilateral clonic	150
C-30—4—17—62						
238	10%	0.01 ce	R-cortex	—	—	—
244	10%	0.01 cc	L-cortex	localized discharge	—	35
249	10%	0.02 cc	R-cortex	localized discharge	unilateral clonic	265
303	10%	0.02 cc	L-cortex	—	—	—
311	10%	0.02 cc	R-cortex	—	—	—
319	10%	0.02 cc	L-cortex	generalized discharge	bilateral clonic	145
C-31—5—1—62						
849	10%	0.02 cc	R-cortex	generalized discharge	bilateral clonic	106
901	10%	0.02 cc	L-cortex	localized discharge	—	69

Table 2

Case	EEG	EMG	Duration (sec)
C-27	unilateral dominant	unilateral clonic	180
C-29	unilateral dominant	bilateral clonic	120
C-30	generalized	bilateral clonic	145
C-31	unilateral dominant	bilateral clonic	106
C-43	generalized	bilateral clonic	80
C-56	generalized	bilateral clonic-tonic	300
C-57	generalized	bilateral clonic	60
C-58	generalized	bilateral clonic-tonic	320
C-62	generalized	bilateral clonic	122
C-79	generalized	bilateral clonic	105
C-80	generalized	bilateral clonic	96
			mean 150

Table 3

Group 1	2	4	6	8	10	12	14	16	18/mg Metrazol
C-92	−	−		(±)		((±))			
C-63	−	−	−	(±)		(±)			

Group 2	2	4	6	8	10	12	14	16	18
C-87	−	−		−		(±)			
C-48			−					(±)	
C-74	−	−	−			((±))			
C-41	−	−			−				
C-75	±	−	−			±		−	

Group 3	2	4	6	8	10
C-89	((+))				
C-40	(±)	(±)			
C-39	±	±			−
C-35	((+))				
C-33	(±)	((+))			
C-99	−	((+))			

Group 4	2	4	6	8	10	12
C-84	(±)	((+))				
C-85	((+))					
C-82	((+))					
C-71	+					
C-34	±	(±)			(±)	
C-45	±		(±)			
C-81	−	(±)	((+))			
C-70	((+))					
C-69	((+))					
C-72	(±)	−		−		
C-66	±	((+))				
C-96	((+))					
C-78	((±))	((±))				((+))

Group 5	2	4
C-90	((+))	
C-91	−	((±))
C-93	(±)	(±)
C-94	((+))	
C-65	((+))	

Group 6	2	4	6
C-27	(±)		((+))
C-29	((±))		
C-30	((+))		
C-31	((±))		
C-43	((+))		
C-56	((+))		
C-57	((+))		
C-58	((+))		
C-62	((+))		
C-79	((+))		
C-80	((+))		

−: no EEG discharge
±: localized EEG discharge
+: generalized EEG discharge
( ): focal convulsion
(( )): general convulsion

Group 1: Bilateral lesions were totally involved in the H-field.
Group 2: Bilateral lesions were located in the H-field but one of them was partially involved.
Group 3: One of the lesions was totally or partially involved in the H-field but the other was absolutely out of it.
Group 4: Bilateral lesions were absolutely out of the H-field.
Group 5: Bilateral lesions were totally or partially involved in lenticular nucleus.
Group 6: Control.

in Figure 1; generalized EEG discharge and bilateral clonic convulsion which converted later to tonic convulsion (in the left), and localized or unilateral dominant EEG discharge and bilateral clonic convulsion (in the right).

The stimulation of the cortex with 0.02cc of 10% Metrazol could obviously elicit the epileptic discharge in EEG, either unilaterally dominant (localized) or bilateral (generalized), and also concomitant clonic convulsion in EMG, mainly bilateral (general), which was also ascertained in visual observation. The dosage

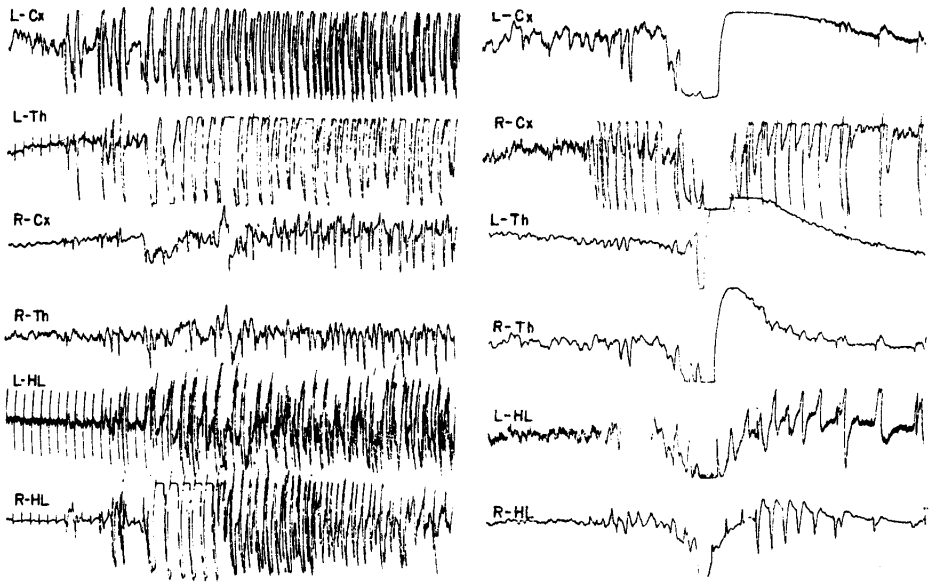

Fig. 1 Two types of the beginning patterns of Metrazol elicited corticogenic epileptic convulsion.

was then called the threshold stimulus in this experiment and was applied on the lesion group for the first stimulation trial.

2) Lesion group:

Three types of responses were obtained on stimulating the cortex in each of EEG and EMG. The first type of EEG response which was bilateral cortical discharge activity without remarkable dominance in either side is called generalized discharge. The second which was unilaterally dominant cortical discharge activity is called localized discharge. The third or no discharge activity at any lead is called no discharge. The first type of EMG response which was convulsive activity at bilateral hindlegs is designated general convulsion. The second type which was convulsive activity at unilateral hindleg is designated focal convulsion, and the third no convulsion.

a) Brain stem lesion group (Groups 1, 2, 3, and 4 in Table 3): There were 52 brain stem lesions located at the levels between A-11.5 and A-3.0. Most of them were in and around the subthalamus and red nucleus.

The threshold stimulus was applied on the motor cortex in these groups. The elicited three types of EEG responses are mapped in Figure 2 in accordance with the anatomical location of the lesions. In those animals which had the lesions at thalamus and ventral midbrain tegmentum (A : 5.0-A : 3.0) various types of responses could be elicited. In contrast, animals which had lesions at the medial part of subthalamic region between A : 8.5 and A : 6.5, anterior to

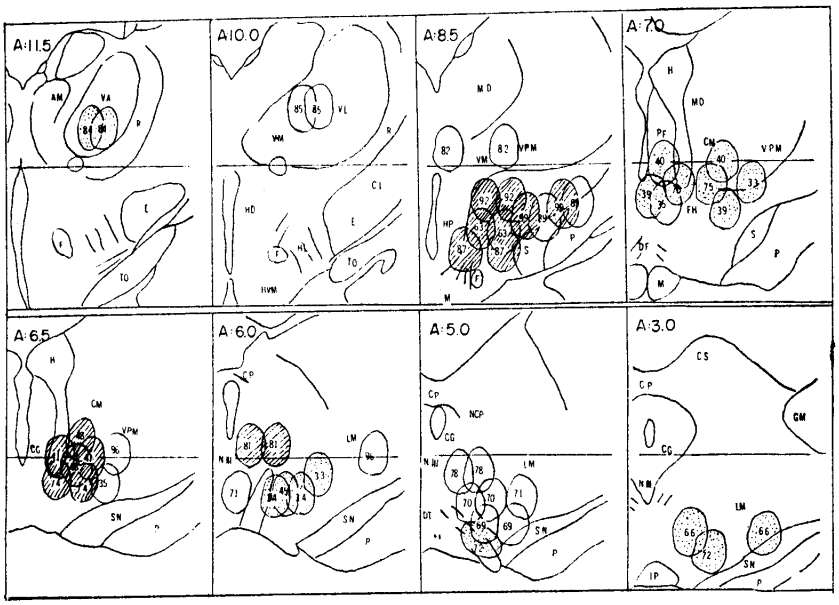

Fig. 2 EEG response to the threshold stimulation (2 mg Metrazol) The number in each circle represents the cat number, which has two circles or a pair of lesions, one in each side of the brainstem.
○: generalized discharge ◐: localized discharge ◍: no discharge
Nomenclature for abbreviation.
AM: N. anterior medialis, CI: Capsula interna, CG: Subatantia grisea centralis, CM: Centrum medianum (N. centralis centralis), CP: Commissura posterior, CS: Colliculus superior, DF: Decussatio Foreli, DT: Decussatio tegmenti, E: N. entopedunc-ularis, F: Columna fornicis, FH: N. campi Foreli (H), GM: Corpus geniculatum mediale, H: N. habenulae HD: N. hypothalami dorsalis, HL: N. hypothalami lateralis, HP: Area hypothalami posterior, HVM: N. hypothalami ventromedialis, IP: N. interpedun-cularis, LM: Lemniscus medialis, M: Corpus mamillare, MD: N. medialis dorsalis, NCP: N. commissurae posterioris, NIII: N. n. oculomotorii, P: Pedunclus cerebri, PF: N. parafascicularis, R: N. reticularis, S: N. subthalamicus, SN: Substantia nigra, TO: Tractus opticus, VA: N. ventralis anterior, VL: N. ventralis lateralis, VM: N. ventralis medialis, VPM: N. ventralis posteromedialis

red nucleus, did not respond to the stimulus. In other words, the group of no response was concentrated at the Forel H-field anterior to the red nucleus.

To make a detailed analysis of it, these animals were divided into the following four groups: The first group in which both lesions were totally involved in the Forel H-field; the second with the lesions also located in the H-field but one of them partially involved; the third with one of the lesions totally or partially involved in the H-field; and the fourth with the ones absolutely out of the H-field.

In the first and second groups, no response could be obtained both in EEG

and EMG. Epileptic discharge in 5 and convulsion in 4 out of 6 cases could be elicited in the third. The fourth group had epileptic discharge in 12 and convulsion in 9 out of 13 cases. It was found that generalized epileptic discharge could always be obtained with general convulsion, and convulsion could not be elicited without epileptic discharge. It is also interesting to note that in C-99 no response could be elicited as compared with C-89 in which generalized discharge and general convulsion was induced by the stimulation. Both animals had lesions at the same ventrodorsal level of the lateral part of subthalamic region but in the former lesions were located 1 mm each medial to the latter as compared to the bilateral lesions. The discharge duration ranged between 40 and 1215 sec, with 313 sec in average in the third group, and between 17 and 275 sec, with 160 sec in average in the fourth. C-35, one of the third group, had 1215 sec of the duration of a peculiar pattern of the epileptic convulsion, which was not found in the control group; localized discharge and general convulsion for the first 180 sec followed by sporadic spike discharge without convulsion until 945 sec, and then 100 sec of generalized discharge and general convulsion, followed by successive 200 sec of discharge without convulsion. When this was excluded as an exception, the discharge duration both in the third and fourth groups was almost the same as in the control irrespective of discharge pattern.

When the threshold stimulus was found to be insufficient to elicit the epileptic convulsion as seen in the control group, another trial of the stimulation was attempted with 4 mg or double dosage of Metrazol. The response tended to increase by the stimulation in cases of C-84, C-81, C-66 and C-34 of the fourth group, and in C-99 and C-33 of the third group. No response, in contrast, remained in the second group. as well as in the first group. They were absolutely silent in response of both EEG and EMG.

Furthere increment of the stimulant dosage was made for successive stimulation. The pattern of the epileptic discharge elicited on the stimulation below 6 mg of Metrazol was mapped according to the anatomical location of the lesions in Figure 3. No response group in EEG discharge as represented by the shaded figure was obviously concentrated in the area rostral to the red nucleus, the medial part of the subthalamus.

In sequence of the stimulation experiment, especially in the first and second groupe, in which it was difficult to elicit epileptic convulsions on stimulation with the threshold stimulus as well as on stimulation with double or triple dosage, the injection trial of each dosage was repeated several times and caused variation of the sensibility of the cortex due to mechanical injury by the needle tracks and accumulation of the injected stimulant. It seems reasonable therefore not to interpret that the response elicited on stimulation of the successive trial is the same as the one elicited at the first trial with the corresponding dosage.

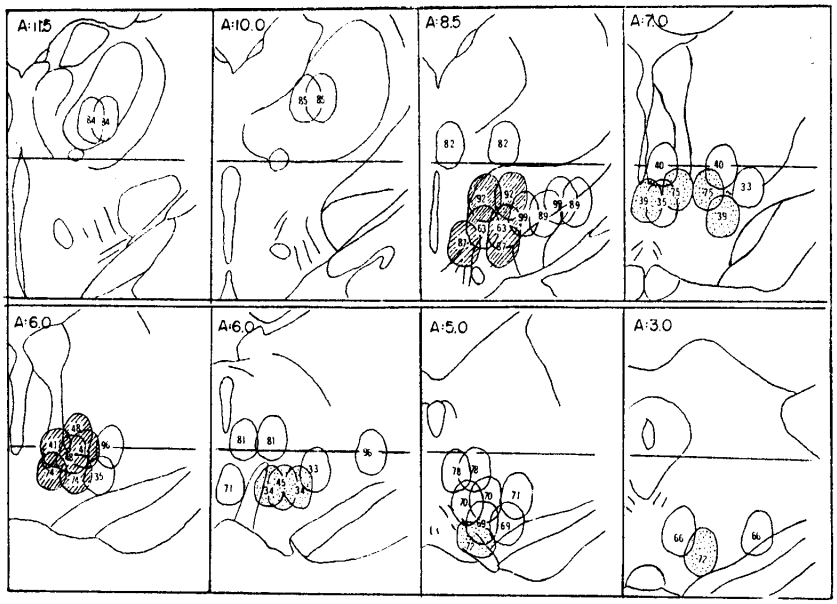

Fig. 3 EEG response to the stimnlation (6 mg Metrazol) Refer to Fig. 2.

Furthermore, there could not be found any rule in anatomical correlation of the laterality between the responded cortex and the brain stem lesion because of the alternatively repeated stimulation at each side of the motor cortex. For example, C-92 had 5 stimulation trials (38 mg in total dosage) at left cortex and 4 trials

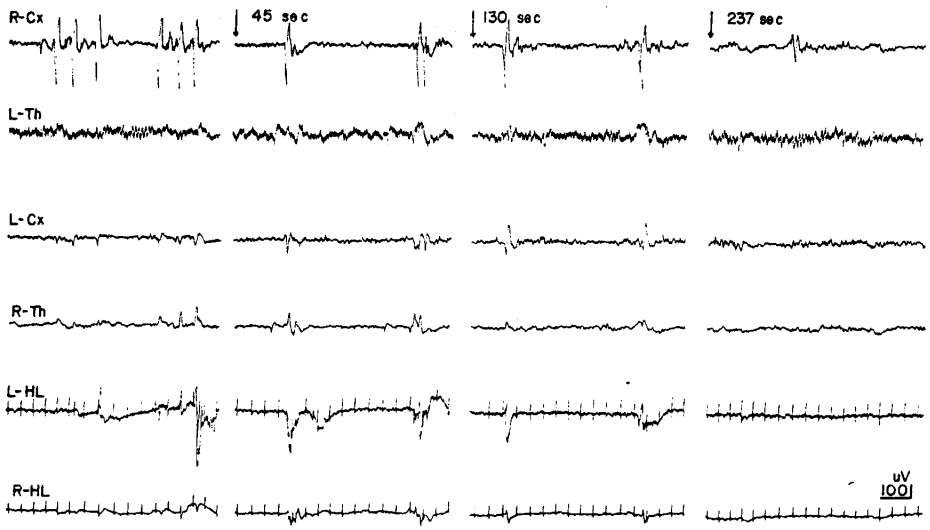

Fig. 4 Response of the right cortex to the stimulation of 12 mg Metrazol in the Forel H-field lesion cat, C-63. Cx: cortex Th: thalamus HL: hindleg

(16 mg in total) at right cortex, and C-63 had also 5 trials (32 mg in total) at left cortex and 4 trials (20 mg in total) at right cortex before the stimulation of 12 mg of the Metrazol was tried.

On stimulating with 12 mg Metrazol, localized discharge and general convulsion were elicited for 300 sec in C-92. Localized discharge and contralateral clonic convulsion were elicited for 240 and 356 sec in C-63 and C-87 respectively (Fig. 4 and 5). In case of C-75, localized discharge was obtained only at the injected site for 150 sec without concomitant convulsion (Fig. 6). Peculiar was

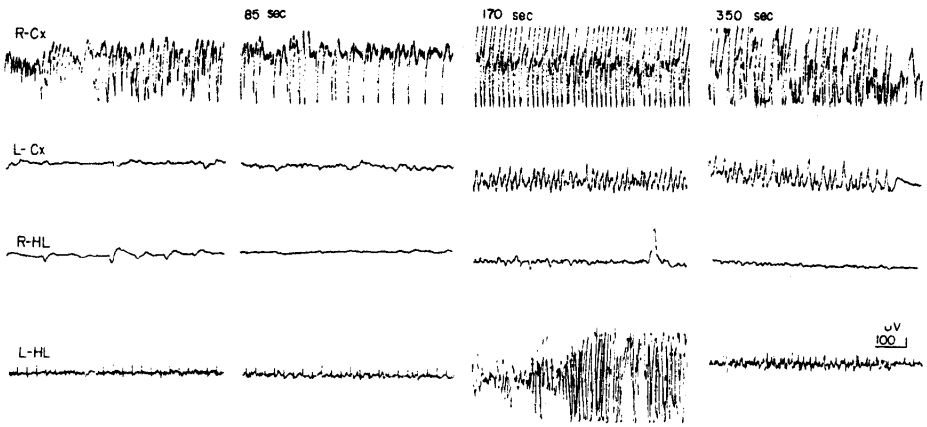

Fig. 5 Response of the right cortex to the stimulation of 12 mg Metrazol in the Forel H-field lesion cat, C-87.

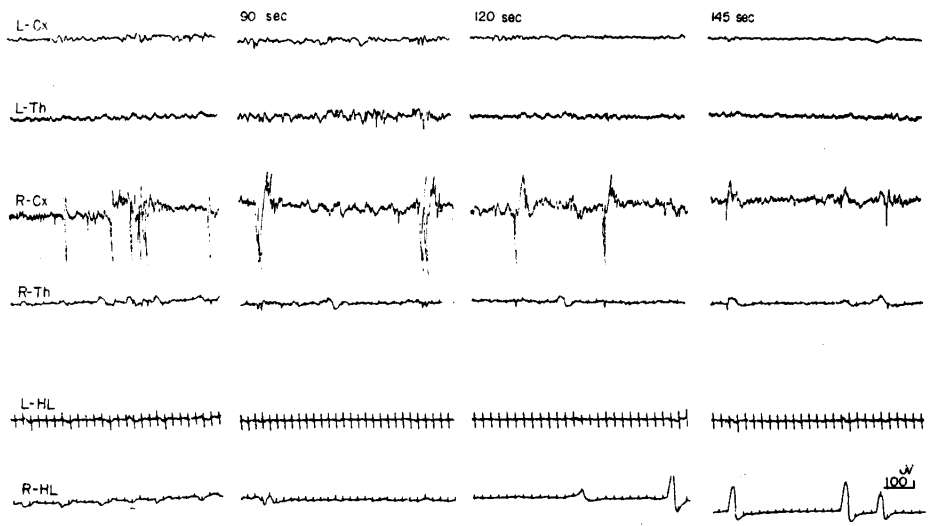

Fig. 6 Response of the right cortex to the stimulation of 12 mg Metrazol in the Forel H-field lesion cat, C-75.

the case of C-74; about 150 uV of low voltage spike activity was recorded for 180 sec on both sides of the motor cortex and thalamus, and bilateral hindlegs were found in convulsion (Fig. 7). This appears to be an abortive type in comparison with the discharge pattern elicited by intraperitoneal injection of Metrazol at the end of the experiment (Fig. 8). In contrast to the discharge pattern of

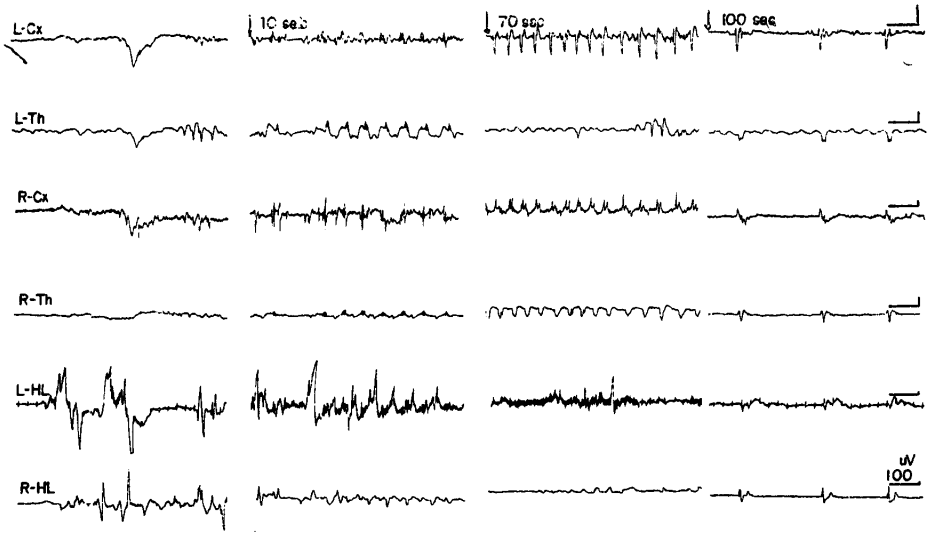

Fig. 7 Response of the right cortex to the stimulation of 12 mg Metrazol in the Forel H-field lesion cat, C-74.

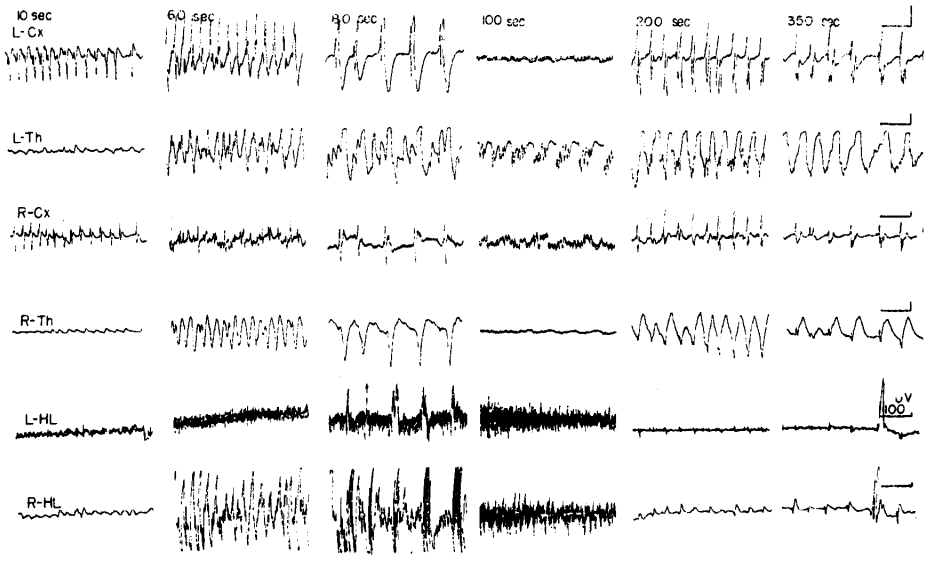

Fig. 8 Major convulsive seizure elicited by the intraperitoneal injection of Metrasol in C-74.

the control group, one of these cases was of a long latency at the onset and of progressive course of build up and end up, discharge, that is, nonexplosive character, the duration being almost twice as long. In all of the cases convulsion was elicited concomitantly with discharge activity in EEG, except C-75 which had no convulsion in the entire course of sporadic localized discharge.

It is thus concluded that when the Forel H-field was fairly completely destroyed, (Fig. 9), convulsion could be elicited concomitantly with epileptic discharge on the stimulation of the cortex, with the stimulus intensity being increased up to six times as great as the threshold stimulus.

Fig. 9 Histology in C-92, illustrating the Forel H-field lesion.

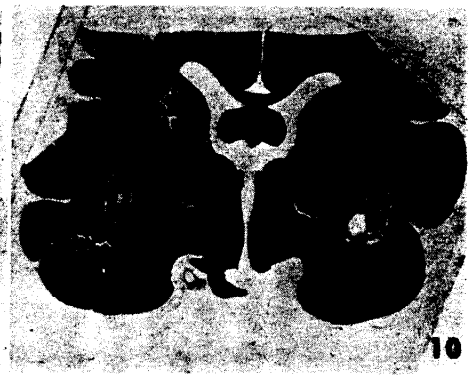

Fig. 10 Histology in C-90, illustrating the lenticular nucleus lesion.

b) Lenticular nucleus lesion group (Group 5 in Table 3): Lenticular nucleus, that is composed of globus pallidus and putamen, was bilaterally coagulated partly or fairly extensively by means of one or several needle tracts. In three out of 5 cases, generalized epileptic discharge and general convulsion could be elicited on stimulation with the threshold stimulus; the duration ranged between 125 and 280 sec, with 195 sec in average. Figure 10 illustrates histologically one of them, C-90, in which lenticular nucleus and its neighbouring structure was bilaterally extensively lesioned through the three pairs of coagulation electrodes, and epileptic convulsion was elicited on stimulation of the motor cortex with the threshold stimulus 17 days after the operation (Flg. 11). It is obvious that the nuclear lesion did not have anything to do with the epileptic convulsion at stimulation of the cortex, and the nucleus does not seem to play any important role on corticogenic epileptic convulsion in cats.

The relations between EEG discharge and convulsion in Groups 1, 2 and 3, of which the lesions were totally or partially involved in the Forel H-field

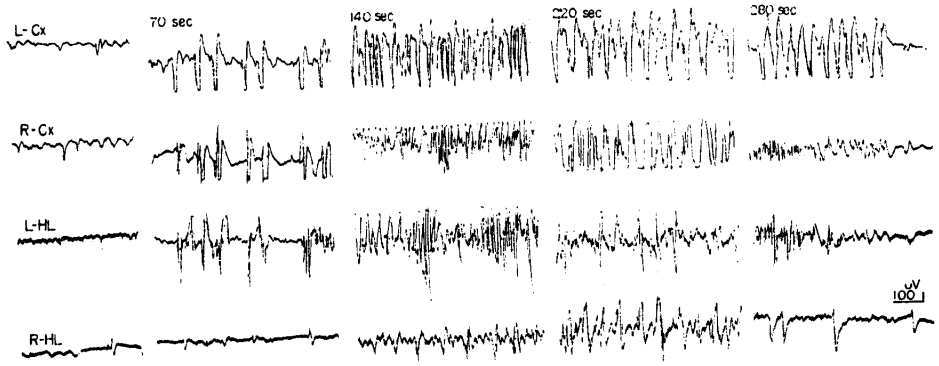

Fig. 11 Response of the right cortex to the stimulation of 2 mg Metrazol in the lenticular nucleus lesion cat, C-90.

Table 4 Relation between EEG-discharge and convulsion

conv. / EEG	general convulsion	focal convulsion	no convulsion	total
generalized discharge	5	0	0	5
localized discharge	1	8	7	16
no discharge	0	0	17	17
total	6	8	24	38

are summarized in Table 4. No discharge was associated with convulsion; in other words, convulsion conld not be obtained without EEG discharge. Convulsion could neither be obtained in half of the cases with the localized discharge. All of the focal convulsion could be obtained under localized discharge. General convulsion could be obtained under generalized discharge except one obtained under localized discharge. All generalized discharge was accompanied by general convulsion. It is, therefore, concluded that there is a certain parallel relation between EEG discharge and convulsion and no dissociation can be found between them.

DISCUSSION

This experimental study was made in an attempt to clarify the physiological phenomena of epileptic convulsion which had long been studied by JINNAI and his co-workers.

FUNAKI[13] attempted to cut the brain stem at the level of capsulopeduncular border bilaterally symmetrically in desired direction by means of his synchro-symmetro-encephalotome during the Metrazol-induced corticogenic convulsion under semi-anaesthsia. Bilateral transection of the area corresponding to the

Forel H-field was found to interrupt the existing convulsion. He believed that there was a conduction pathway of the convulsive discharge in the H-field.

KAMBAYASHI[26] subsequently tried to stimulate the motor cortex of cats with Metrazol under anaesthesia, whose Forel H-field was bilaterally lesioned several weeks prior to the stimulation, but failed to obtain convulsion. It was interpreted to be due to interception of the pallidofugal fibers which were believed to be the common pathway of the convulsive discharge[14,18].

There were, however, no analyses of the phenomena by means of EEG correlating with convulsion whether the Forel H-field lesions were to intercept the conduction pathway of the convulsinve discharges or to interrupt the circuit of the central excitation system of the epileptic convulsion. This problem has led me to this study in order to clarify the phenomena and analyze the mechanism by means of EEG and EMG in addition to the visual observation under unanaesthetized conditions.

The minimum dosage of Metrazol for eliciting corticogenic epileptic convulsion is 2 mg (10%, 0.02 cc) in cats in this experiment, which corresponds well with fhe data reported by ISHIZUKA[21], 3 mg (10%, 0.03 cc) in dogs, both under the unanaesthetized conditions. As it has been proved that stimulus strength is dependent on its concentration rather than on its volume at stimulation of cerebral tissue with a chemical stimulant[18], a progressive increment of the concentration in stead of the volume change was applied in this study. It is apparent that the dosage, 0.1 cc of 10% Metrazol, used by KAMBAYASHI[26], even though all of it can be injectcd in the cortex in spite of the technical difficulty, was less than 12 mg which was the minimum dosage to elicit epileptic convulsion in the Forel H-field lesion in this cat experiment.

Although the lesions located at the lenticular nucleus, thalamus, red nucleus and its neighboring structures did not cause any change in corticogenic epileptic convulsion elicited with the threshold stimulus, the one localized at the Forel H-field, medial part of the subthalamic region caused a remarkable effect on its inhibition. In the latter case, the Metrazol dosage less than six times of the threshold stimulus could not elicit the convulsion concomitantly with epileptic discharge in EEG.

Generalized epileptic discharge was always accompanied with general convulsion, and no discharge, in contrast, with no convulsion. Localized discharge was accompanied with three types of convulsive phenomena; no, focal or general. There was, however, no definite rule to be found between the types of convulsion and EEG discharge, in spite of the EEG analysis, except a certain tendency of parallelism between them. This counteracts to the interpretation that the lesion of the Forel H-field is an interception of the conduction pathway of the convulsive discharge. It is, therefore, to be coucluded that the

Forel H-field lesion causes an increment of the threshold for eliciting seizure activity at the cortex.

Now, discussion will be led to various literatures on the experimental and clinical observations concerned with subcortical and brainstem lesion effect on corticogenic epileptic convulsion.

Pyramidectomy has been attempted experimentally at the level of peduncle in various kinds of animals by a number of investigators[8,18,19,27,28,42,33,39,43,44,45,46,49,50]. It has been found that convulsion can be elicited on the stimulation of cortex or cerebrum in all of the cases. MELTLER[33], HOEFFER[19] and WALKER[49] found an increased threshold for eliciting the convulsion, but WALKER noted that the interpretation is hard to accept because of the technical difficulty and inaccuracy.

HAYASHI[18] stimulated motor cortex of dogs whose brain stem was completely transected and pyramis intact, but failed to obtain any motor manifestations. In contrast, when the transection was incompletely done, remaining the area of 1—2 mm^2 irrespective of the site, various motor manifestations could be elicited. He explained his findings by saying that there was a certain cooperation of the conduction pathways between the pyramis and other parts of the brain stem in spite of the fact that the conduction pathways all belong to the extrapyramidal pathway. This seems to mean that there is no localization but functioual compensation of the conduction pathways of the motor manifestation in anatomical and physiological sense.

HAYASHI[18] and NISHI[34] attempted to destroy the bilateral lenticular nucleus in dogs, which was believed to be the common conduction pathway of the convulsion and succeeded in abolishing the convulsive phenomenon. Clinical application was done on idiopathic and focal epileptic patients, and abolishment of the convulsive seizure and also inhibition of the unconscious fit were reported by TAKEDA[47]. In the present experinent with cats no such phenomena were observed, and it was found that the lenticular nucleus and its neiboring structures had nothing to do with the cortical sensitibity for the epileptic convulsion and they were not the sole common pathway of conducting convulsive discharges. It is furtheremore, to be noted that extensive lesions of the nucleus, several times as large as the Forel H-field lesion could not cause any change in the corticogenic epileptic convulsion, and no variation in epileptic convulsion was found in the bilateral lesion of H2, one of the major p pallidofugal fiber groups (C-88, C99).

In contrast, there are numbers of the reports dealing with ascending influences to the corticogenic seizure since Magoun's brain stem reticular activating system[31] and Gellhorn's hypothalamic activating system[15–17] have drawn attention.

MIYASAKA[29,30] found the fact that the mesencephalic reticular formation and

posterior hypothalamus had a fascilitatory influence on the neocortex and an inhibitory influence on the limbic system in seizure discharge. STARZL[41] noted that the reticular formation was only secondarily involved in Metrazol induced convulsion, and FRENCH[12] noticed that the reticular formation was chiefly responsible for spread of electrically induced corticogenic convulsion. GELLHORN[15,17] proved experimentally that an increased hypothalamic excitation state aggravated and generalized an existing convulsive discharge and also precipitated a seizure under subconvulsive condition in animals.

FREEDMAN[10,11] found a threshold increment of corticogenic convulsion on electrical stimulation and also a moderate increment of the seizure threshold induced by Metrazol intravenous administration in cat whose rostral mesencephalon was lesioned. It was concluded that the integrity of the rostral mesencephalon was essential not only for the maintenance of cortical electrical activity of the form, but also for the occurrence of the sustained hypersynchronous activity associated with major convulsive episodes. It is interesting to note that in one of his cats, no alteration of the seizure for sustained seizure activity resulted in an extensive destruction of both the thalamus and the posterior hypothalamus. ANDY and MUKAWA[1] could not find threshold variations for electrically induced forebrain seizure within a few hours after mesencephalic reticular formation was lesioned in cat, but observed an erratic prolongation in the elicited seizure duration. SANO[40] tried to destroy the most rostral part of mesencephalic reticular formation around aqueduct (reticulotomy) on patients and analyzed the effects on various types of the epileptic seizures. Such a treatment exerted favorable influences on behavioral problem but not on limbic seizure. A definite result could not be obtained in neocortical fit. In the present study the lesions were made at the area ventrolateral to the oculomotor nucleus and dorsomedial to red nucleus to interrupt the concentrated ascending reticular fibers (Forel's tractus fasciculorum) (C-48 and C-81), but no notable change could be obtained in comparison with the Forel H-field lesions. It seems obvious that an interception of the ascending reticular system does not give any significant influence as to increase the threshold for corticogenic seizure.

Penfield and Jasper's specific projection system[25,35,36,37], composed of dentorubrothalamic and basal ganglionic pathways believed to play an important role in maintaining cortico-subcortical excitatory state, was lesioned at the ventrolateral nucleus of the thalamus, red nucleus or lenticular nucleus (C-84, C-85, C-45, C-34 and C-70). Variation in eliciting corticogenic seizure was obtained in none of them.

There are a number of unsolved questions concerned with the relations between pyramidal and extrapyramidal systems, the localization of the conduction pathway of the convulsive discharge, the reverberating circuit at cortico-

subcortical level[4–7]. Based on the finding of threshold increment or decreased sensitibity at cortex caused by the Forel H-field lesion in this study, it is to be proposed that the H-field composes the main axis of cortico-subcortical reverberating circuit, and its destruction causes a decrement in the seizure susceptibility at the cortex which makes secondarily an inhibition of the convulsive manifestation.

Histological study of fiber connections of the Forel H-field by Marchi preparations was made in conjunction with this physiologieal study. (in press) Based on the anatomical observation, the H-field is the cross-road of numbers of ascending and descending reciprocal fiber connections of extrapyramidal system and brain stem activating system, which may justify the physiological observation in this study.

CONCLUSIONS

An experimental study was attempted to make an analysis of the subcortical and brain stem lesion effect on the Metrazol-induced corticogenic epileptic convulsion based on EEG-discharge and EMG-convulsion as indicators. utilizing 42 adult cats.

1. A definite threshold increment of eliciting the seizure was found in the case of bilateral lesion of the Forel H-field. In contrast to it, no variation in the threshold was found in the case of the lesions at the other parts of brain stem, thalamus, red nucleus and its neighborhood, and lenticular nucleus.
2. There was a parallel relation between EEG discharge and convulsion. Dissociation could be obtained in none of the cases.
3. It is, therefore, to be concluded that the Forel H-field is composed of the main axis of cortico-subcortical reverberating circuit and that the lesion causes a decrement of the excitability at cortex and an inhibition of the corticogenic epileptic convulsion.

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