EFFECTS OF LESIONS UPON THALAMICALLY INDUCED ELECTROCORTICAL DESYNCHRONIZATION AND RECRUITING[1]

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INTRODUCTION

Repetitive stimulation in midline and intralaminar regions of the thalamus causes widespread changes in ongoing cortical activity. Contrasting effects may be obtained from the same loci by low and high frequency stimulation. Thus, stimulation at 6–12/sec produces recruiting responses (Morison and Dempsey 1942), whereas high frequency stimulation at the same recruiting sites induces low voltage, fast activity, that is, desynchronization of spontaneous, ongoing activity, and blockade of recruiting responses (Moruzzi and Magoun 1949).

Thalamo-cortical pathways for recruiting appear to course rostrally to the frontal pole of the thalamus, *via* n. ventralis anterior and n. reticularis, before entering the internal capsule (Nauta and Whitlock 1954; Nashold *et al.* 1955). Lesions in these nuclei have been shown to prevent or attenuate cortical recruiting responses (Hanbery *et al.* 1954; Eidelberg *et al.* 1958; Chow *et al.* 1959). Less is known regarding the anatomical course of the desynchronizing effects and blocking of recruiting by high frequency stimulation. The present study has sought to determine whether thalamically induced desynchronization is mediated by the same pathways as those involved in recruiting.

METHODS

Experiments were performed on 18 adult cats, immobilized by high cervical transection (*encéphale isolé*) and maintained by artificial respiration. Surgical procedures were performed under ether anesthesia; recording began at least 2 h after cessation of ether. Local anesthesia was maintained at pressure points and wound margins by infiltration with procaine hydrochloride. Normal body temperature was maintained throughout by external application of heat. Normal EKG, partially miotic pupil, and electrocortical spindles and/or slower waves were used as indicators of a suitable preparation.

Concentric, stainless steel electrodes were used for stimulation. The tip to shoulder distance was 1 mm and the tip was bared for 0.5 mm. Electrodes were inserted, bilaterally, into intralaminar regions of the thalamus (Fr. 8 to 11, L. 2 to 4, H. 0 to +4: Jasper and Ajmone-Marsan, 1954). The stimuli were monophasic square wave pulses delivered by Grass S4 stimulators, through SIU-4 isolation units. Parameters used to elicit recruiting responses were 8/sec, 0.1–0.5 msec, 1.5–7 V. Placement of the electrodes was monitored by stimulation at various depths, the final locus being determined by production of consistent recruiting responses with minimal voltage. Responses were observed on a Tektronix 502 oscilloscope in conjunction with Tektronix 122 pre-amplifiers (t.c. = 0.2 sec). Recruiting responses were differentiated from other repetitive responses by their latency (15–50 msec), frequency, incremental nature and minimal or no response to the first stimulus.

Desynchronization and blocking effects were produced by stimulation at 150/sec, 0.5–1.0 msec, 2–13 V during the occurrence of (1) spontaneous spindle bursts, (2) triggered spindles or

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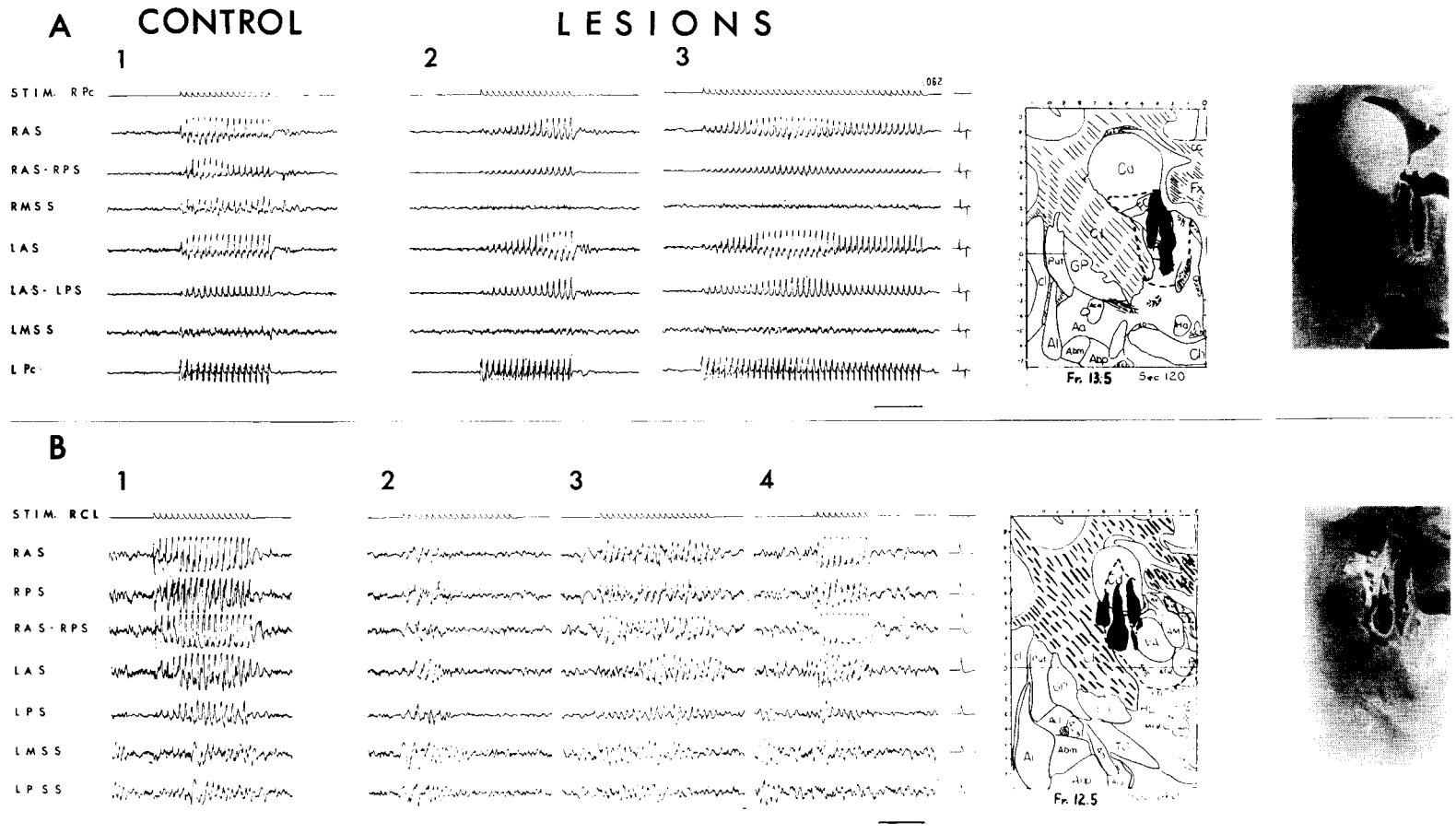


Fig. 1

ECoGs before and after diagrammed lesions showing changes in recruiting responses. *A*: Stimulation of right n. paracentralis, 8/sec, 0.5 msec, 4 V. *1*: Control; *2* and *3*: following lesions of pre-thalamic region, showing delayed development of recruiting. *B*: Stimulation of right n. centralis lateralis, 8/sec, 0.5 msec. *1*: Control, threshold at 7 V; *2*, *3* and *4*: following lesions of n. caudatus and adjacent n. reticularis; threshold for recruiting markedly increased. There is little response to control voltage in *2*; larger response to 9 V in *3* and to 12 V in *4*. Calibrations: 1 sec; 100 μV.

First channel: monitor of stimulus. Abbreviations in this and succeeding figures: R, right; L, left; A, anterior; M, middle; P, posterior. Gyri: L, lateral; S, sigmoid; SS, suprasylvian. Nuclei: CL, centralis lateralis; MD, medialis dorsalis; Pc, paracentralis; VA, ventralis anterior. In diagram black area shows extent of lesions; the surrounding dotted line, the extent of iron deposits.

(3) recruiting responses elicited by stimulation of the contralateral thalamus. Blocking or attenuation of these waveforms, served as indices of the effectiveness of high frequency stimulation.

The ECoG was recorded from stainless steel screws placed in the calvarium. Both monopolar and bipolar records were taken on a Grass model IIID electroencephalograph. In the case of monopolar recording, the reference was ordinarily the stereotaxic frame, and occasionally a screw electrode in the skull over the frontal sinus. Electrolytic lesions were produced by the passage of anodal current through a fine gauge stainless steel probe insulated except for 1–2 mm at the tip. Current flow was monitored on an ammeter, and was usually of 2–4 mA for 60 sec.

Following final placement of the electrodes in recruiting sites bilaterally, the electrode for making electrolytic lesions was stereotaxically positioned 3–5 mm rostral to the right "recruiting" electrodes. Threshold voltages were determined for triggering spindles by a single shock, and for producing recruiting responses by stimulation in the left thalamic recruiting site; also for blocking of these responses by high frequency stimulation of the right thalamic recruiting site. The threshold for recruiting from the right side was then determined immediately preceding and following the lesions. If recruiting could still be elicited at the threshold voltage, additional lesions were made. Following disruption of recruiting, the recruiting site on the left side was re-tested for the production of recruiting, and that on the right for desynchronization and blocking effects. Tests were repeated at intervals, up to 90 min later. Stimulation following the lesions was performed on the same general background as that during which the control records had been taken. In three experiments, bilateral lesions were made at the level of the posterior commissure (Fr. 5.0) following completion of the above procedures.

At the termination of the experiment, the animal was sacrificed with an overdose of barbiturate anesthesic. The superior vena cava was sectioned and the cat perfused through the heart with normal saline followed by 10% formaldehyde. While still mounted in the stereotaxic instrument, the brain was blocked in a plane parallel to that of the electrodes, and soaked in a solution of potassium ferrocyanide and formaldehyde. Serial frozen sections were made at 80 μ throughout the extent of the lesions and associated iron deposits, and the electrode tracks. The sites of electrode tips were located by the Prussian blue reaction. Final localization of the lesions was determined by projecting the brain sections on corresponding plates of the Jasper and Ajmone-Marsan Atlas.

RESULTS

I. *The effects of lesions on recruiting responses*

Unilateral lesions rostral to the sites of stimulation in the thalamic recruiting system (TRS) either altered, reduced, or abolished cortical recruiting responses, the effect depending upon the area destroyed. Destruction in the pre-thalamic area (Fr. 13.5) usually resulted in a slower development of recruiting without altering the form or amplitude of the recruiting responses.

For example, prior to lesions of n. prothalamicus and rostral n. reticularis, recruiting attained maximal amplitude by the fifth stimulus to the right n. paracentralis (Fig. 1, *A1*). Following these lesions, the maximum recruiting was not reached until the 16th stimulus (Fig. 1, *A2*). However, no such alterations were seen in the responses of contralateral n. paracentralis (Fig. 1, *A*; note tracing L Pc).

Unilateral lesions in the head of n. caudatus, often with slight damage to the adjacent n. reticularis (Fr. 13.0), increased the threshold of the recruiting response (Fig. 1, *B*), but did not prevent its elicitation. Bilateral electrocortical recruiting induced by right thalamic stimulation was altered bilaterally by ipsilateral pre-thalamic and caudate lesions.

Unilateral lesions slightly more caudal, involving the n. reticularis and n. ventralis anterior, abolished recruiting bilaterally (Fig. 2; 3, *A*). Thus, following lesions largely confined to n. ventralis anterior, recruiting could not be elicited by stimulation at the original threshold (4 V) nor at a much higher voltage (13 V), although the latter produced short latency evoked potentials which were not recruiting in nature (Fig. 2, *A*, *B*).

In order to control for the possibility that decrements in recruiting responses were a function of depressed excitability in the TRS due to passage of current, stimulation was repeated at

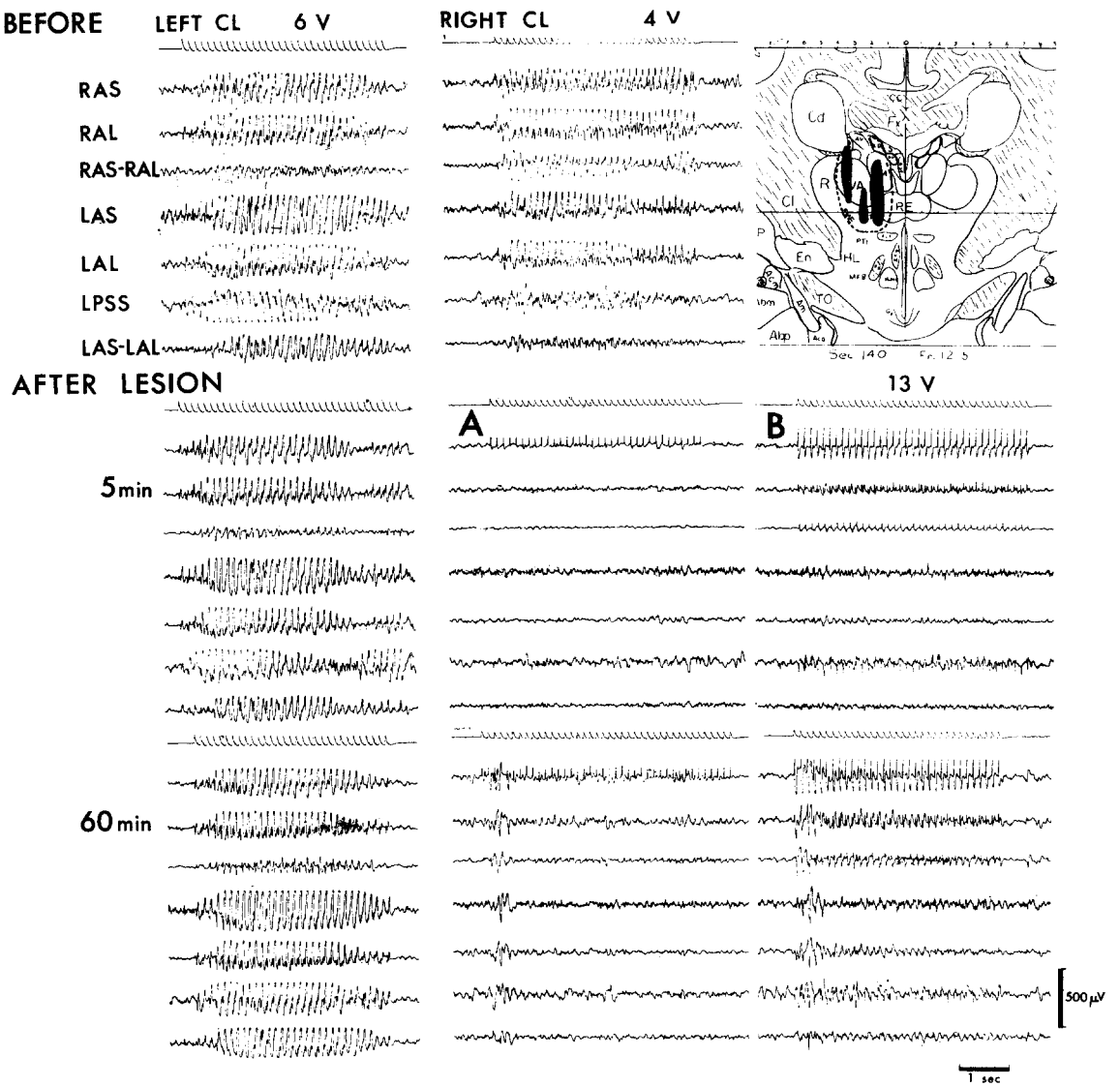


Fig. 2

ECoGs showing recruiting elicited by stimulation of left and right n. centralis lateralis at 8/sec, 0.5 msec, at voltages indicated, before and after lesions of right n. ventralis anterior and n. reticularis. First column shows maintenance of recruiting elicited from left CL; middle column shows abolition of recruiting elicited from right CL after lesions (*A*), and absence of recruiting by supramaximal stimulation at 13 V (*B*). Note no substantial recovery 60 min later. See Fig. 1 for other explanations.

irregular intervals for as long as 90 min after the lesions, but without eliciting typical recruiting (Fig. 2). These effects could not be attributed to destruction or injury to the site of stimulation. Histological controls indicated that the most caudal extent of iron deposit from the lesions was regularly 1–2 mm rostral to the stimulating electrodes. Furthermore, the effects of high frequency stimulation at the same electrode sites were unaffected by the lesions (see below). Finally, the abolition or attenuation of cortical recruiting was not, we believe, the result of long-lasting depression of the cortex due to partial deafferentation by thalamic lesion since lesions

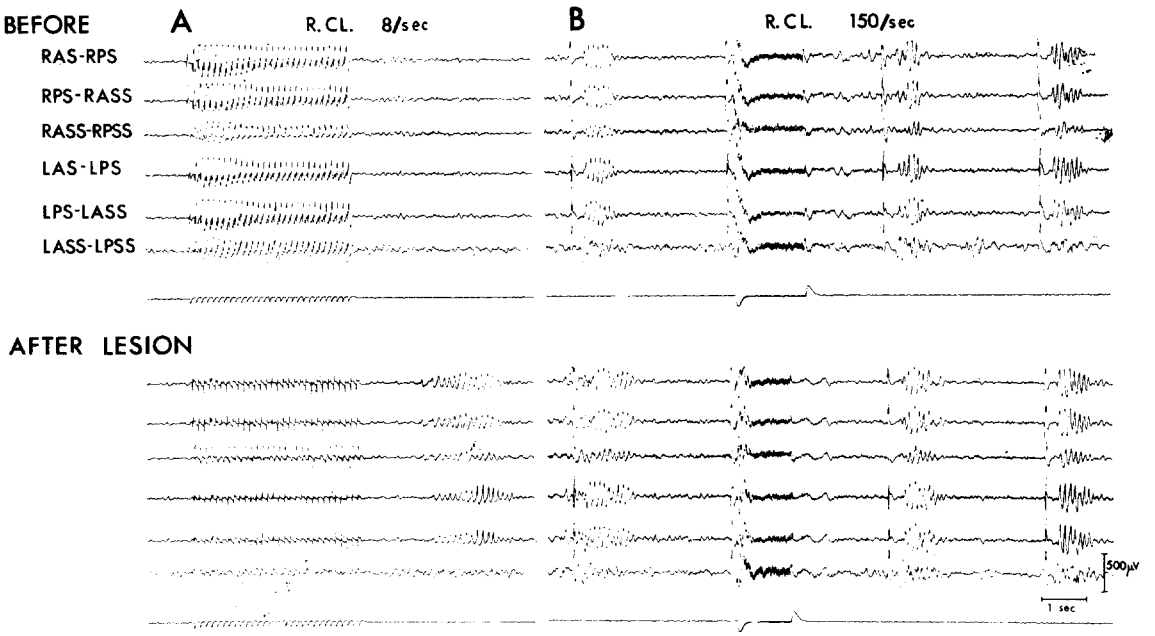


Fig. 3

A: Abolition of recruiting from right n. centralis lateralis (8/sec, 0.3 msec, 5 V) following lesions of right n. ventralis anterior (see Fig. 4). *B*: Spindles triggered by single shock to left n. centralis lateralis (1 msec, 13 V) blocked by high frequency stimulation of right n. centralis lateralis (150/sec, 1 msec, 5 V); this spindle blocking was unaffected following lesions. See Fig. 1 for other explanations.

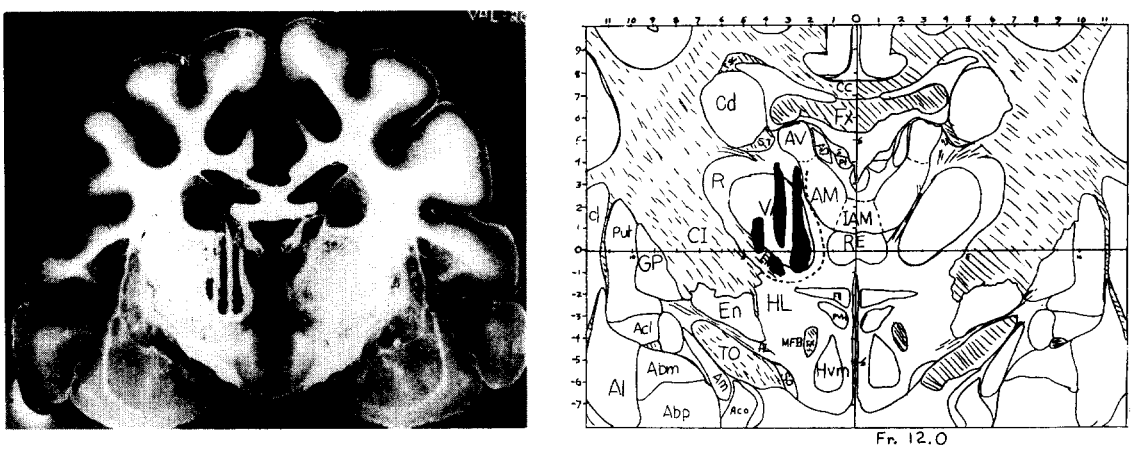
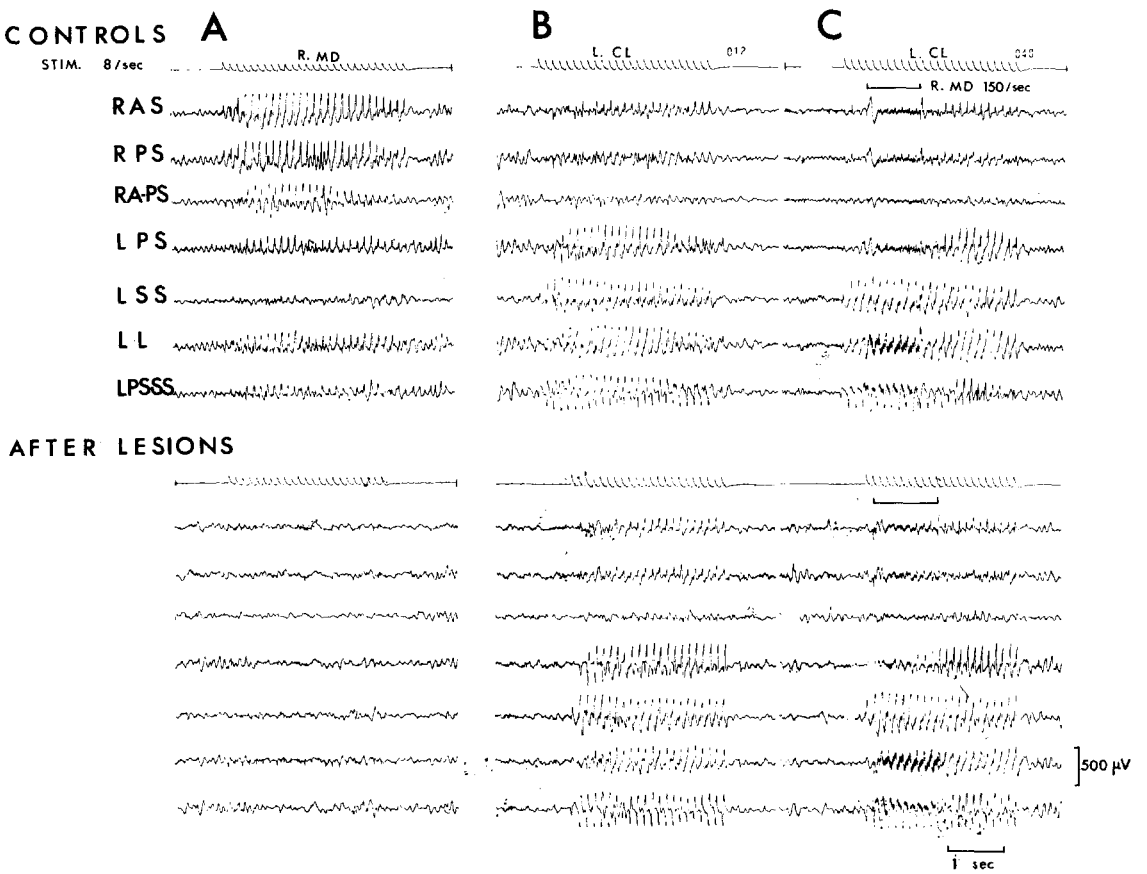
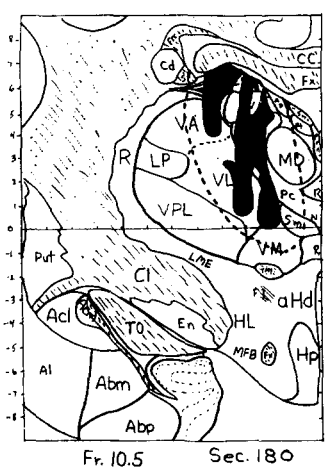


Fig. 4

Lesions of right n. ventralis anterior which prevented recruiting responses by stimulation of right n. centralis lateralis, but which did not modify spindle blocking by high frequency stimulation at the same site (see Fig. 3).

never caused "flattening" of the EEG (see also Starzl *et al.* 1951). Additionally, recruiting responses produced by stimulation of the left TRS were never altered following contralateral lesions (Figs. 2; 5, *B*). Furthermore, recruiting from the left TRS continued to be of "normal" amplitude in areas which no longer yielded recruiting from the right TRS.





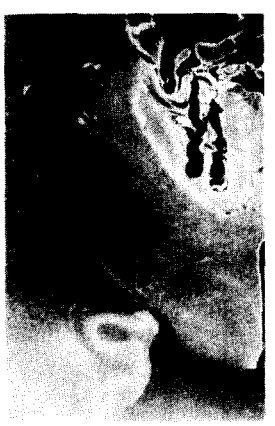


Fig. 5

A: Recruiting responses elicited from right n. medialis dorsalis (8/sec, 0.5 msec, 6 V) were prevented following ipsilateral lesions rostral to the site of stimulation. *B*: Recruiting responses elicited from contralateral n. centralis lateralis were unaffected by the lesions. *C*: High frequency stimulation of right n. medalis dorsalis (150/sec, 1 msec, 8 V) which blocked recruiting responses elicited from contralateral n. centralis lateralis was unaffected following the lesions. Note complete blockade of recruiting at LPS, partial blockade at LL, and absence of blockade at LSS. See Fig. 1 for other explanations.

II. *The effects of anterior lesions on desynchronization and blocking*

The desynchronization and spindle blocking effects of high frequency stimulation of the TRS were not altered by lesions rostral to the sites of stimulation, although such lesions attenuated or abolished recruiting responses elicited by low frequency stimulation at the same sites. For example, lesions restricted to the right n. ventralis anterior (Fig. 4) prevented recruiting from the right n. centralis lateralis (Fig. 3, *A*). However, high frequency stimulation at the same site continued to block spindles triggered by single shocks to the left n. centralis lateralis (Fig. 3, *B*).

Blocking of recruiting elicited by stimulation of the contralateral TRS was also used to measure the effectiveness of high frequency stimulation. Higher voltages were generally required to block recruiting than to block spontaneous spindles. Attenuation of recruiting was easier to obtain than complete blockade. Furthermore, the degree of blockade was not necessarily the same at all cortical loci. It was possible to have complete, partial, or no blockade simultaneously in various areas (Fig. 5, *C*). These differential effects, observed simultaneously in different regions of the cortex, are also noticeable in the records of Moruzzi and Magoun (1949) where recruiting blockade was produced by stimulation of the bulbar reticular formation.

In the experiment illustrated in Fig. 5, recruiting and recruiting blockade were elicited by stimulation of the lateral part of n. medialis dorsalis. Lesions caudal to n. ventralis anterior, but 3 mm rostral to the locus of the stimulating electrodes, abolished recruiting (Fig. 5, *A*). Attenuation and blockade of recruiting by high frequency stimulation were not diminished by these lesions (Fig. 5, *C*).

A third method of assessing the effects of high frequency stimulation was by blockade of spontaneous spindles and desynchronization of the background activity. As in the cases of blockade of triggered spindles and recruiting, lesions which abolished recruiting had no influence on the high frequency effects produced by stimulation of the same nucleus. Thus it was still possible to block spontaneous spindles by 150/sec stimulation of the right n. centralis lateralis following large lesions of n. ventralis anterior and adjacent subthalamic areas (Fig. 6, *A*, *B*).

III. *The effects of posterior lesions on desynchronization and blocking*

Schlag and Chaillet (1963) have reported that high frequency stimulation of a specific thalamic nucleus (VPL) may also block spindles, but that lesions at the level of the posterior commissure will prevent spindle blocking by high frequency stimulation of TRS without affecting spindle blockade from VPL. Because of the widespread bilateral blocking observed in the majority of our experiments, it was felt unlikely that the high frequency effects were mediated by current spread to specific nuclei. However, to control for this possibility, lesions were made bilaterally at the level of the posterior commissure in three animals following completion of the usual procedures outlined above. In each of these cases, it was no longer possible to block spindles by high frequency stimulation of TRS sites (Fig. 6, *C*, *D*). Thus, unlike recruiting responses which appear to ascend by pathways rostral to the stimulation sites, desynchronization and blocking due to high frequency stimulation of the same thalamic sites appear to follow a caudal course, presumably via the reticular formation.

DISCUSSION

The present findings are consistent with the position that recruiting responses from intralaminar regions of the thalamus pass rostrally to the cortex via the oral pole of the thalamus. Lesions in n. ventralis anterior and n. reticularis were maximally effective in abolishing cortical recruiting as were lesions slightly caudal to these nuclei (see also Hanbery *et al.* 1954). Lesions rostral to these nuclei had a less pronounced effect, thus supporting the view that electrocortical recruiting responses are relayed principally via n. ventralis anterior and n. reticularis (Nashold *et al.* 1955). The mechanisms underlying the delayed development of recruiting (Fig. 1, *A*), caused by pre-thalamic lesions, remain to be elucidated. However, it is known that recruiting from n. paracentralis can be recorded in this region (Hanbery *et al.* 1954). While this region does not appear to constitute a major

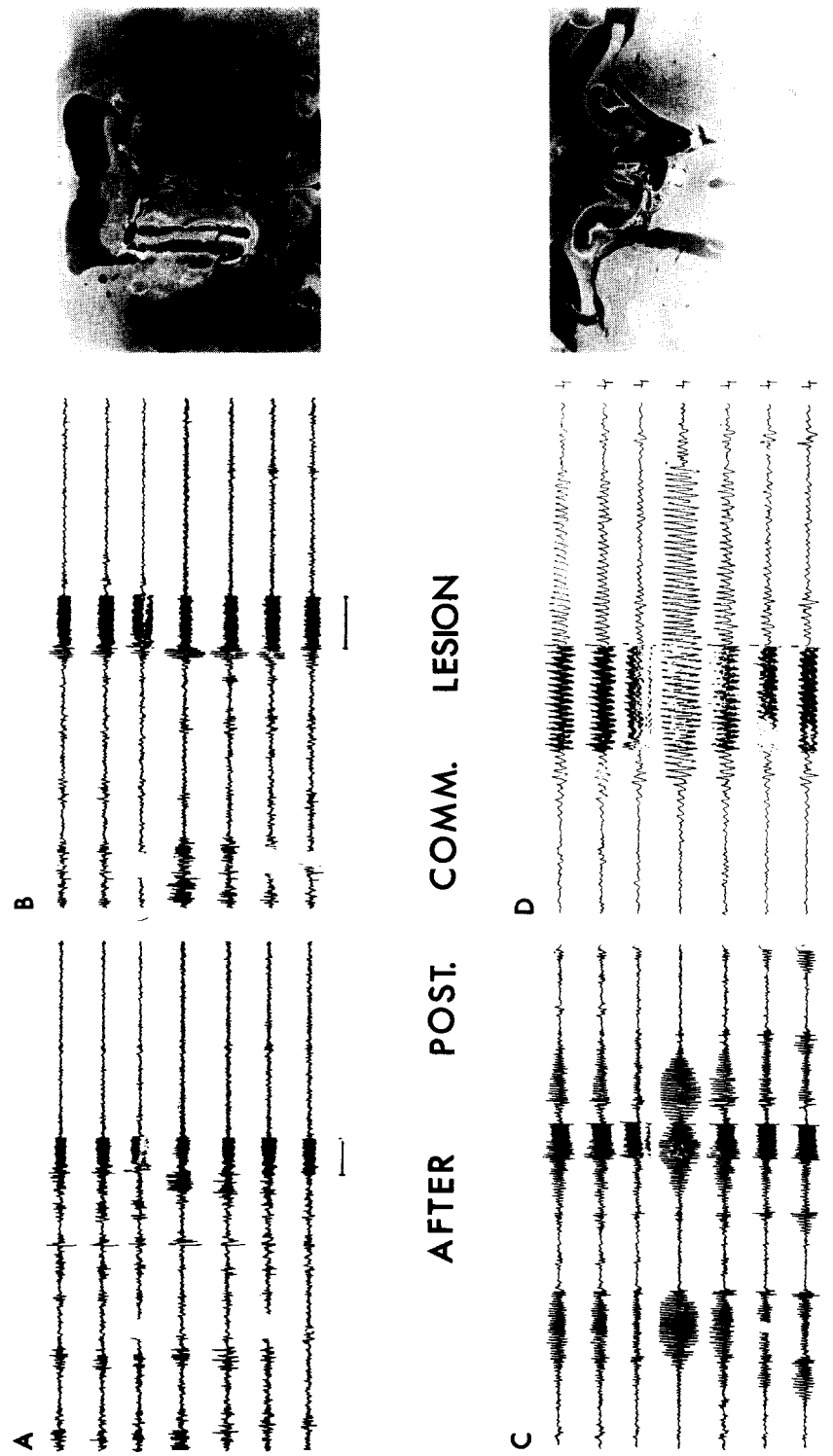


Fig. 6

High frequency stimulation of recruiting sites (right n. centralis lateralis; 150/sec, 0.5 msec, 4.5 V) which blocks spontaneous spindles before (*A*) and after (*B*) rostrally placed thalamic lesions (n. ventralis anterior) fails to block spindles following subsequent caudally placed bilateral lesions at the level of the posterior commissure (*C* and *D*). In this same preparation recruiting responses elicited by stimulation of right n. centralis lateralis were abolished following the lesions of right n. ventralis anterior. Calibrations: 2.5 sec for *A*, *B*, *C*, and 1 sec for *D*; 100 μV. See Fig. 1 for other explanations.

pathway for recruiting it may have facilitating effects upon thalamo-cortical recruiting.

The changes produced by high frequency stimulation of the TRS apparently do not traverse rostrally directed recruiting pathways, since rostral lesions which disrupted recruiting responses never altered blocking and desynchronization caused by high frequency stimulation of the same sites. Thus far only caudally placed lesions appear to block high frequency effects, for example, lesions in the mesencephalic reticular formation and in the region of the posterior commissure (Schlag and Chaillet 1963). It seems probable that these caudally directed influences are mediated by the mesencephalic reticular formation since one of its well known functions is activation and desynchronization of electrocortical activity.

SUMMARY

(1) Unilateral lesions rostral to thalamic recruiting sites altered, attenuated, or abolished cortical recruiting, bilaterally. Lesions involving n. reticularis and n. ventralis anterior were most effective in abolishing recruiting responses, while more rostral lesions including n. caudatus and n. prothalamicus either raised the threshold or delayed the development of recruiting.

(2) Desynchronization produced by high frequency stimulation of the same sites in the thalamus was not affected by such rostrally placed lesions, but was abolished by lesions caudal to the site of stimulation, at the level of the posterior commissure.

(3) The results indicate that pathways mediating recruiting responses (low frequency stimulation) and those subserving desynchronization (high frequency stimulation) are different; the former course rostrally, and the latter caudally, apparently via the mesencephalic reticular formation.

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