0270-6474/85/0511-2971$02.00/0

The Journal of Neuroscience
Vol. 5, No. 11, pp. 2971–2978
November 1985

Responsiveness of Ventrobasal Thalamic Neurons after Suppression of S1 Cortex in the Anesthetized Rat[1]

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Abstract

Corticofugal influences on the responses of ventrobasal (VB) thalamic neurons to repetitive stimuli were studied in anesthetized rats by suppressing primary somatosensory (S1) electrocortical activity with topically applied lidocaine. Effective concentrations of lidocaine were confined to S1 and immediately adjacent cortex and suppressed evoked S1 responses and corticofugal discharges. Suppression of S1 cortex reduced the average number of spikes discharged by 83 VB neurons in response to each of 25 electrical somatic stimuli delivered at frequencies ranging from 1 to 50 Hz. Of 20 units studied both before and after S1 suppression, 14 (70%) showed a similar reduced response to repetitive stimuli. Cortical suppression produced no consistent changes in spontaneous activity, somatic stimulus threshold, response latency, or size of receptive field. There was no significant difference in the effect of cortical suppression on the responsiveness of 8 VB neurons to repetitive medial lemniscal, as compared to somatic, stimuli. We conclude that, in the anesthetized rat, S1 corticofugal activity facilitates somatosensory transmission to VB neurons and that this facilitation is mediated, at least in part, by corticothalamic neurons.

Corticofugal control of somatosensory transmission has been investigated for many years (Frigyesi et al., 1972; Towe, 1973), and the anatomical and histochemical techniques developed during the past decade have led to new information about corticothalamic relations (Macchi et al., 1983). Nonetheless, there is a lack of agreement about how corticothalamic activity influences somatosensory processing at the thalamic level. Because chronic cortical ablation produces retrograde degeneration of thalamocortical neurons (Waller, 1934), focal cortical or pyramidal tract stimulation or temporary suppression of cortical function has been used to study corticofugal effects. The results have been interpreted as indicating predominantly excitatory (Waller and Feldman, 1967; Andersen et al., 1972; Albe-Fessard et al., 1983; Giuffrida et al., 1983), inhibitory (Ogden, 1960; Burchfiel and Duffy, 1974; Angel and Clarke, 1975), or mixed effects (Shimazu et al., 1965; Tsumoto et al., 1975; Angel, 1983) on somatosensory transmission in the thalamus.

Received January 21, 1985; Revised April 8, 1985;
Accepted May 3, 1985

[1] This work was supported by the Veterans Administration. We thank Drs. David Fink and L. Cass Terry for help with these experiments and for reviewing the manuscript. Mr. Avery Gottfried provided valuable technical assistance.

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Because stimulation of the cortex can antidromically activate recurrent collaterals of thalamocortical projection neurons (Andersen et al., 1964), focal cooling or cortical spreading depression (CSD) (Leao, 1944; Bures et al., 1974) has been used to inactivate corticothalamic neurons while studying spontaneous or evoked activity in the ventrobasal (VB) thalamus. Both CSD and focal cooling, however, have been shown to produce periods of excitation or seizure activity that precede cortical inactivation and may therefore complicate interpretation of the results (Gartside and Lippold, 1967; Moseley et al., 1972; Adey, 1974; Burchfiel and Duffy, 1974; Bures et al., 1974; Albe-Fessard et al., 1983). Furthermore, these methods often produce only brief periods of cortical depression, thus limiting the time available for testing thalamic neuronal excitability.

We applied lidocaine topically to the S1 cortex of anesthetized rats to produce a focal depression of corticofugal activity while testing the responsiveness of VB thalamic neurons. We report here that, in this experimental preparation, lidocaine focally suppresses S1 corticofugal discharge and attenuates the responses of VB neurons to repetitive stimuli, indicating a facilitatory influence of corticothalamic neurons.

Materials and Methods

Seventy-five male albino rats weighing from 250 to 450 gm were used in this study. All rats were anesthetized with chloral hydrate injected intraperitoneally at an initial dose of 40 mg/100 gm; supplemental doses of 40 to 50 mg were given to maintain suppression of flexion reflexes. A tracheostomy was done, the rat's head was mounted on a stereotaxic instrument, and the skull was exposed widely by a midline incision. Rectal temperature was maintained at 37 to 38°C by a feedback-controlled DC heating pad. If respirations were depressed, rats were paralyzed with gallamine triethiodide (10 mg/hr; i.p.) and artificially ventilated with a stroke volume of 5 to 6 ml at a rate of 70 to 80 cycles per minute.

A trephine opening was made in the skull on the right side to expose the entire S1 cortex for application of lidocaine or for recording or stimulating in this area (coordinates: AP 2.5 to −3.0; ML 2.0 to 7.5; Pelligrino et al., 1979). The dura mater in this area was removed and a piece of cotton soaked with normal saline was put on the surface of the cortex to prevent drying. Another trephine opening, which was about 3 mm in diameter, was made on the left side for inserting a recording microelectrode into the VB thalamus on the right side. In some rats, a third craniotomy was made on the right side for inserting stimulating and recording electrodes through the intact dura into the ipsilateral medial lemniscus and cerebral peduncle.

Teflon-coated stainless steel wires (0.2 mm diameter) were used for stimulating or for recording evoked responses. The local electrocorticogram was recorded on an ink-writing polygraph connected to bipolar electrodes (2 mm tip separation) on the cortical surface or on the dura. For monopolar recording of evoked responses, the indifferent electrode was placed on the margins of the scalp wound. The amplified potentials were displayed and photographed from a storage oscilloscope.

Stainless steel microelectrodes (8 to 12 megohms impedance at 100 Hz) were angled stereotaxically through the left hemisphere toward the VB thalamus on the right side to avoid the passage of cortically applied lidocaine along the electrode track. Extracellularly recorded unit spikes were monitored

with an oscilloscope and loudspeaker. When the tip of the microelectrode was near the VB complex, the face and body surface of the rat was brushed, pressed, and tapped to excite units that might not be spontaneously active. Single units were isolated by a window discriminator on the basis of amplitude and spike waveform. The peripheral receptive field and the sensory modality of each unit were determined by deflecting hairs and touching or pressing the skin with a probe. Joint movement, deep pressure, and noxious stimuli were not tested routinely.

The receptive field of each unit was stimulated with single electric pulses of 0.1 msec duration, delivered via bipolar needle electrodes inserted into the skin. After the stimulus threshold and the latency of the first spike had been measured and recorded, the receptive field was stimulated repeatedly at progressively increasing frequencies ranging from 1 to 50 Hz; 25 single pulse stimuli were delivered at each frequency. Post-stimulus histograms for each test frequency were constructed on line by microprocessor from window discriminator pulses triggered by each action potential. The number of spikes generated within 20 msec of each stimulus was determined from the histogram at each stimulation frequency so that frequency following curves could be constructed for each unit. The stimulus intensity was set between threshold and twice threshold to obtain a high response probability at a low stimulus frequency (1 Hz). The spontaneous activity of the unit was also recorded by leading the output of the window discriminator into a frequency-to-voltage converter connected to the polygraph. Changes in the frequency of spontaneous unit activity were determined by comparing measured integrals, obtained with a digital planimeter, of equal time periods of the analogue frequency record.

In some rats, a bipolar stimulating electrode (tip separation 0.5 mm) was inserted into the ipsilateral medial lemniscus in the pons. The response of VB neurons to stimulation of the medial lemniscus was tested in a manner similar to that used for peripheral stimulation. Lemniscal stimulation intensities were below twice threshold and did not exceed 70 μA.

Lidocaine hydrochloride (20%) (International Medication Systems Ltd., South El Monte, CA) was diluted with normal saline into desired concentrations. A piece of Gelfoam, cut to the size of the trephine opening, was saturated with lidocaine solution and put on the surface of the S1 cortex. The volume of the lidocaine solution applied was 0.04 ml. In one experiment, tritiated lidocaine (1 mCi/ml; New England Nuclear, Boston, MA) was used to determine the extent of diffusion of lidocaine. The radioactive lidocaine was added to the stock solution to give a final concentration of 2.5 mCi/ml of 10% lidocaine; 0.04 ml (0.1 mCi) of this solution was applied to S1 cortex in the usual manner. Approximately 30 min after the cortical application, the brain was removed and frozen on dry ice. Serial frozen sections (300 μm) were cut on a cryotome and placed on glass slides. Three fresh frozen punched samples (0.33 mm^3 each) were taken from each of several brain regions (Palkovits, 1973), pooled, and homogenized in 0.1 N NaOH, and aliquots of these samples were counted in a liquid scintillation counter.

At the end of each recording experiment, lesions were placed at two levels along each recording track by passing anodal DC current (20 μA for 20 sec) through the microelectrode. The animal was deeply anesthetized with chloral hydrate and perfused through the heart with 10% formalin in normal saline. After the brain was fixed in 10% formalin for at least 2 days, serial sections were cut at 50 μm in the coronal stereotaxic plane and stained with cresyl violet. Electrode tracks were reconstructed from drawings of projected images of the sections.

Results

Effect of lidocaine on spontaneous and evoked cortical activity. After a pledget saturated with 10% lidocaine was placed on the S1 cortex, the frequency and amplitude of surface electrocorticographic (ECoG) activity were markedly reduced within 5 min and nearly eliminated after 20 min. In five rats, 20% lidocaine was applied to the intact dura; this gave similar results. If the pledget was removed after 1 hr and the cortical surface was washed, ECoG activity gradually returned to a normal or nearly normal pattern over a 2- to 4-hr period. When lower concentrations of lidocaine were used (1 to 4%), the ECoG depression appeared more slowly and was less complete; concentrations less than 1% produced no discernible effect.

Lidocaine-induced ECoG depression was restricted to the cortical area immediately surrounding the site of application. This observation was made during experiments on six rats as illustrated in Figure 1. Eight pairs of ECoG recording electrodes were placed on the exposed cortical surface of one hemisphere at various distances

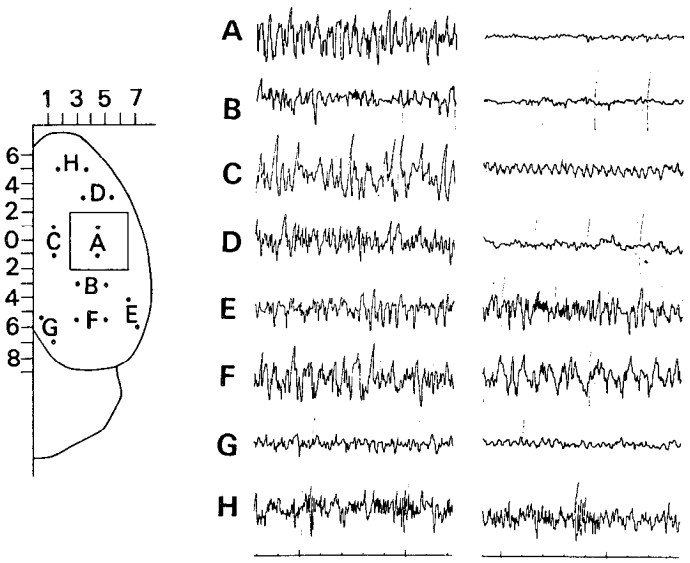

Figure 1. Localized effect of lidocaine on ECoG activity in an anesthetized rat. The *drawing* on the *left* shows the cortical surface of the right hemisphere, with the *square* indicating the placement of the lidocaine pledget (millimeters from bregma and midline) and *letters* showing the location of bipolar ECoG recordings (*dots*). The *column* of recordings *A* to *H* shows, on the *left*, records taken before and, on the *right*, 30 min after lidocaine application. *Time marks*, 1 sec.

from the site of lidocaine application. Within 30 min of the application, ECoG activity was markedly depressed at the site of application and at sites within 1 mm of the edge of the pledget (Fig. 1, *A* to *D*). Little or no effect was observed at sites 3 mm beyond the area of application (Fig. 1, *E* to *H*). The affected area corresponds well to the rat S1 map determined by the microelectrode recording of Chapin and Lin (1984), but it is impossible to be certain that the suppressive effect of lidocaine was strictly confined to the S1 cortex. Based on the results of the ECoG monitoring experiments, it is possible that portions of the posterior precentral, anterior retrosplenial, striatal, and temporal areas (as designated by Lashley, 1941) immediately adjacent to S1 were suppressed, even though more centrifugally placed ECoG recording from these areas showed no changes. Extension of depression throughout the ipsilateral cortex or to the contralateral cortex was never seen. Seizure activity was never observed.

In one experiment, we examined the effect of lidocaine on cortical unit activity. A small pledget of 1% lidocaine placed near the tip of a cortical recording microelectrode eliminated the spontaneous activity of multiple units over a time course of depression and recovery similar to that observed during ECoG recording. In this experimental arrangement, however, it was impossible to control adequately for the direct spread of lidocaine along the electrode track even when angular penetrations were used. Consequently, evoked potential recording methods were used to determine whether the surface application of lidocaine effectively suppressed cortical neuronal activity.

Lidocaine eliminated the surface S1 cortical postsynaptic response evoked by 1 Hz electrical stimulation of the ipsilateral medial lemniscus or the contralateral body surface (Fig. 2). The evoked response simultaneously recorded from the ipsilateral VB thalamus showed only a slight (10%) reduction in amplitude at a 1-Hz stimulus frequency. The cortical response recovered completely 90 min after removing the pledget and rinsing the cortical surface.

Lidocaine also nearly eliminated the direct corticofugal discharge recorded from the cerebral peduncle following stimulation of S1 cortex (Fig. 3*A*). The reflex corticofugal discharge evoked by stimulation of the contralateral face or forepaw or ipsilateral medial

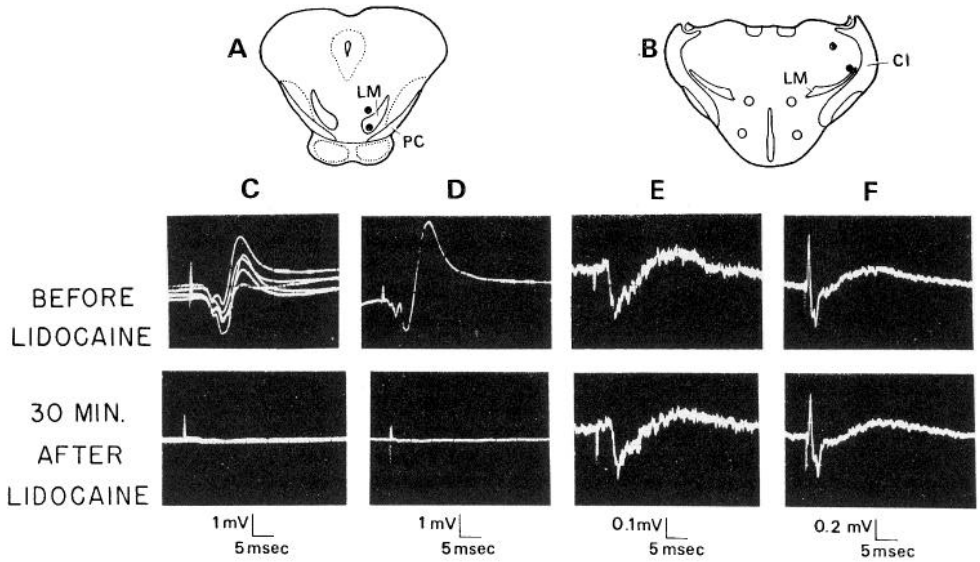

Figure 2. Effect of applying lidocaine to S1 cortex on cortical and VB thalamic responses evoked by somatic or medial lemniscal stimulation. *A*, Location of bipolar medial lemniscal stimulating electrodes. *B*, Location of bipolar VB thalamic recording electrodes. Lidocaine eliminates the cortical response to electrical stimulation of the face (*C*) and medial lemniscus (*D*), but leaves the thalamic responses to electrical facial (*E*) and medial lemniscal (*F*) stimulation nearly unchanged. Stimulation frequency, 1 Hz. *CI*, capsula interna; *LM*, lemniscus medialis; *PC*, pedunculus cerebri.

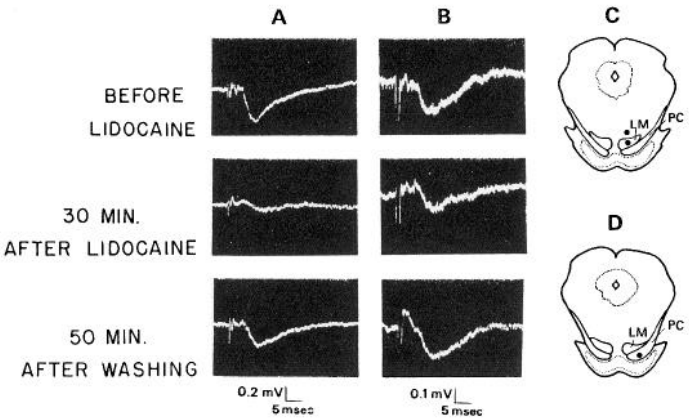

Figure 3. Effect of cortical (S1) lidocaine on evoked corticofugal discharge. *Column A*, Corticofugal response elicited by direct electrical stimulation of S1 cortex and recorded (monopolar) from cerebral peduncle (*D*). *Column B*, Recording as in *A*, but corticofugal discharge was elicited by bipolar medial lemniscal stimulation (*C*). Abbreviations are as in Figure 2.

lemniscus was only partially attenuated (Fig. 3*B*), consistent with a localized effect of lidocaine and a widely distributed cortical origin of the corticofugal reflex (Patton and Amassian, 1960; Patton et al., 1962).

Diffusion of lidocaine applied to S1 cortex. Tritiated lidocaine was applied to the cortex of one rat as described under "Materials and Methods" to determine the extent of spread to other cortical and subcortical tissues. The results (Table I) show that lidocaine, in concentrations sufficient to affect ECoG activity, was restricted to the treated cortical tissue and does not diffuse into adjacent cortical or subcortical areas that mediate or affect somatosensory function.

These results are supported by the observation that a pledget saturated with methylene blue solution and applied to S1 cortex for 30 min resulted in no spread of methylene blue beyond mid-parietal cortex or below 1 mm beneath the cortical surface.

The effect of S1 cortical suppression on the responsiveness of VB thalamic somatosensory neurons. Lidocaine-induced suppression of S1 cortex reduced the responsiveness of VB thalamic neurons as determined by their ability to respond to somatic stimuli delivered at frequencies ranging from 1 to 50 Hz. A total of 146 VB neurons was tested; 63 were tested only before the cortical application of lidocaine, 63 were tested only after lidocaine application, and 20 others were tested both before and after this treatment.

TABLE I

Distribution of total and percentage of mid-parietal disintegrations per minute of ^{3}H-lidocaine in regional samples of equal volume 30 min after application to mid-parietal cortex

Structure[a]	Ipsilateral	Contralateral
Mid-parietal cortex	58,268 (100)[b]	1,050 (1.8)
Anterior precentral cortex and olfactory bulb	1,380 (2.3)	106 (0.2)
Striate and posterior retrosplenial cortex	1,406 (2.4)	654 (1.1)
Dorsal hippocampus (below parietal cortex)	268 (0.4)	176 (0.3)
Lateral thalamus	220 (0.3)	288 (0.4)
Basal ganglia	290 (0.4)	158 (0.3)
Hypothalamus	352 (0.6)	112 (0.2)

[a] Cortical designations after Lashley (1941).
[b] Numbers in parentheses, percentages.

Table II shows the distribution of the receptive fields of these units. All units were recorded from the VB thalamus (see Fig. 4) and were activated by innocuous mechanical stimulation of skin, hair, or vibrissae within small contralateral receptive fields. Figure 5*A* compares the average frequency following curve of the 83 units tested before S1 cortical suppression with that of the 83 units tested after lidocaine-induced suppression in 46 rats. Although no significant effect was seen at stimulus frequencies of 1 Hz, the depressive effect of S1 cortical suppression became apparent as stimulus frequency was increased to 20 Hz, when the number of spikes per stimulus was reduced to approximately one-half the control value. Reduced neuronal responsiveness was still evident, although less pronounced, at higher stimulus frequencies.

Examples of the effect of S1 cortical suppression on the responses of several single units is shown in Figure 5, *B* to *D*. Neurons with frequency response curves that were somewhat steeper than the average of our sample population showed a more pronounced effect of cortical suppression at lower stimulus frequencies (Fig. 5*B*). Some units with flatter frequency response curves showed less depression of responses at 1 to 5 Hz stimulus frequencies than at frequencies of 10 to 30 Hz (Fig. 5*C*).

Figure 6 shows a similar comparison for the 20 VB units that were tested both before and 30 min after lidocaine-induced inactivation of S1 cortex. Five of these units showed no change in frequency following and one showed an increased response at low stimulus

frequencies (1 to 5 Hz) and reduced responses at higher frequencies. The remaining 14 units showed the usual reduction in responsiveness. Other indices of excitability of these 20 units were systematically examined. Cortical suppression produced no consistent changes in the frequency or pattern of spontaneous activity as determined for 18 units ("Materials and Methods"). Six units showed increases ranging from 65% to 315% (average, 174%), 6 units showed decreases ranging from 43% to 77% (average, 63%), and 6 others showed small increases or decreases averaging only 4%. The threshold of the peripheral stimulus increased from an average of 0.4 mA to an average of 0.6 mA in 4 units and the response latency increased by 1 to 3 msec in 5 other neurons. We observed no changes in the size or location of receptive fields following cortical suppression.

Differences in the frequency response curves among units could not be attributed to differences in receptive field location (Table II), modality of the adequate stimulus (hair versus vibrissae versus skin), response latency, or stimulus intensity. In preliminary experiments, 46 units in 11 rats were tested for frequency following at threshold and at twice threshold. The results (Fig. 7*A*) show no significant change in responsiveness at the higher stimulus intensity and no evidence for a change in the form of the frequency response curve. The stability of the frequency response curve of each unit was also examined in 6 units that were tested twice at 30-min intervals using the same stimulus intensity. As shown in Figure 7*B*, the response curves are stable during the period of testing used in this study.

TABLE II

Distribution of receptive fields of VB neurons

Condition	Total No. of Units	Face	Forelimb	Hindlimb	Trunk
Before lidocaine only	63	36	20	3	4
After lidocaine only	63	21	25	11	6
Before and after lidocaine	20	7	10	1	2

Comparison of lidocaine-induced cortical suppression with extirpation of S1 cortex and CSD. In two rats, 20 units were studied after suction removal of S1 cortex with the aid of a dissecting microscope. Subsequent histological examination showed that all units were recorded from the VB complex and that nearly all S1 cortex was removed with sparing of adjacent cortical areas and underlying white matter. The receptive fields of the units were located on the contralateral face (8 units) and forepaw (12 units). As shown in Figure 8, the frequency response curve of these units is quite similar to that of the sample of units tested after lidocaine-induced cortical suppression and was significantly depressed, compared to the normal control population ($p < 0.01$), at all stimulus frequencies above 1 Hz.

In seven rats, ECoG recording revealed nearly complete suppression of the surface electrical activity of one hemisphere within 10 min of applying 1 M KCl to the dura overlying S1 cortex. The frequency response curves of nine VB units were determined before and 10 to 30 min after CSD. The receptive fields were located on the contralateral face (three units) and forelimb (six units). During CSD, the frequency following curve showed a depression like that seen after cortical lidocaine in five units, increased at low (1 to 5 Hz) frequencies and decreased at higher frequencies in 1 unit, and was unchanged in three units. Although the size of this comparison sample was small, the proportion of units showing these effects following CSD was not significantly different from that of the 20 units tested before and after focal S1 suppression with lidocaine (χ^2 =

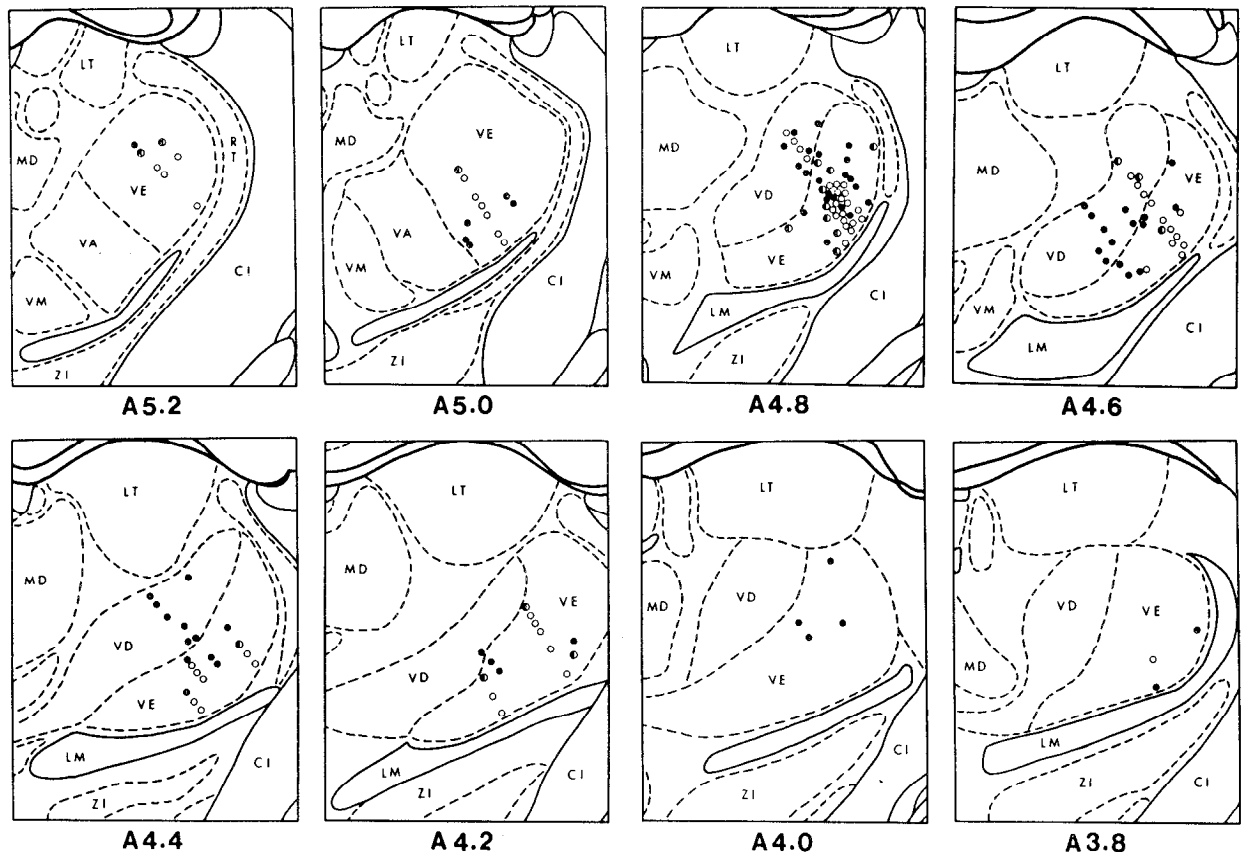

Figure 4. Location of recording sites for VB units plotted on atlas sections taken from Pelligrino et al. (1979). Locations are indicated for units studied before (●), after (○) and both before and after cortical application of lidocaine (◐). *CI*, capsula interna; *LM*, lateral lemniscus; *LT*, lateralis thalami; *MD*, nucleus medialis dorsalis; *PC*, pedunculus cerebri; *RT*, nucleus reticularis thalami; *VA*, nucleus ventralis anterior; *VD*, nucleus ventralis dorsalis; *VE*, nucleus ventralis externa; *VM*, nucleus ventralis medialis; *ZI*, zona incerta.

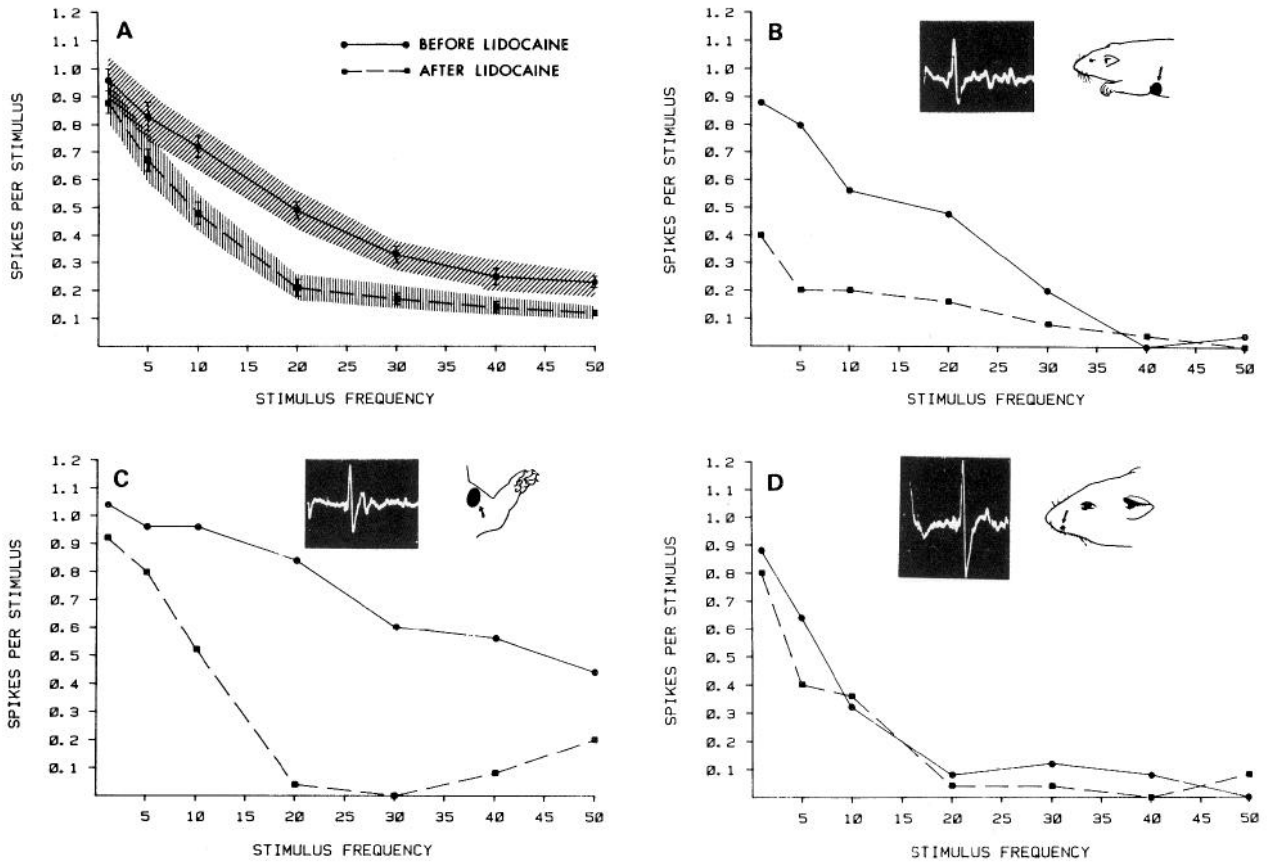

Figure 5. Frequency response curves of somatically excited VB thalamic neurons. *A*, Average (±SEM) responses at 83 VB neurons tested before (*solid line*) and of 83 neurons tested after (*dashed line*) applying lidocaine to S1 cortex. *Shading* shows 95% confidence limits. *B* to *D*, Examples of frequency response curves of single units (*insets*) obtained before (*solid lines*) and after (*dashed lines*) suppression of S1 cortex. Receptive fields are shown in *drawings*. Some neurons showed a maximum depression at low (*B*) and others at high (*C*) stimulus frequencies. Five neurons showed no changes in responsiveness (*D*).

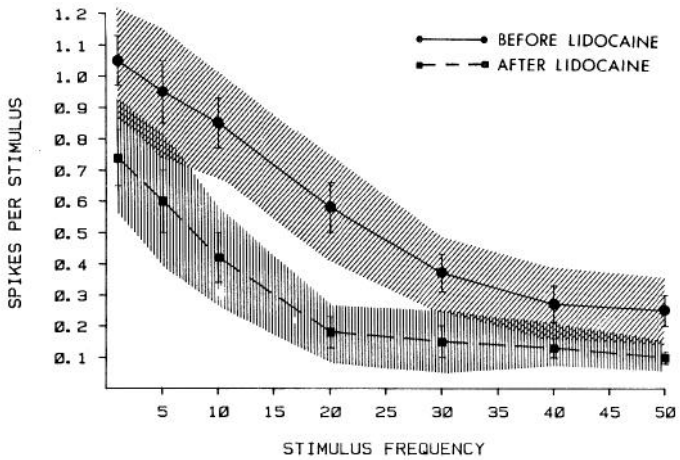

Figure 6. Average (±SEM) frequency response curves of 20 somatically excited VB thalamic neurons tested both before (●—●) and after (■- - -■) suppression of S1 cortex with lidocaine. *Shading* shows 95% confidence limits.

1.4; $p > 0.1$). However, as shown in Figure 8, CSD was not as effective as either lidocaine or S1 extirpation because only at stimulation frequencies of 10, 20, and 30 Hz was the average responsiveness below the 95% confidence limits of the control population mean.

Site of cortical influence. If the effect of suppressing S1 cortex is due to the removal of a facilitatory influence acting, at least in part, at a thalamic level, then cortical lidocaine should reduce VB neuronal responses to both medial lemniscal and somatic stimuli. Accordingly, we compared the responses of eight VB units to electrical stimulation of the receptive field and the ipsilateral medial lemniscus before and after applying lidocaine to the S1 cortex. As shown in Figure 9*A*, single shocks of suprathreshold intensity (35 to 70 μA, 0.1 msec) to the medial lemniscus in the pons elicited fewer spikes per stimulus than did somatic stimuli at stimulus frequencies below 20 Hz, resulting in a flatter frequency response curve. Nonetheless, the effect of lidocaine-induced suppression of S1 cortex was clearly seen in the responses of six units to either somatic or lemniscal stimulation. Two units showed no change in response to either stimulus. A direct comparison of the changes in responsiveness (Fig. 9*B*) showed no significant difference ($p > 0.10$; t test) in the effect of cortical suppression on VB neuronal responses to lemniscal, as compared to somatic, stimulation at any stimulus frequency.

Discussion

The use of a local anesthetic such as lidocaine to inactivate temporarily a focal area of the cerebral cortex has some advantages over other methods that have been used previously to investigate corticothalamic function. First, the duration of the cortical suppression can be prolonged sufficiently to permit more detailed studies than are allowed by brief waves of CSD or periods of focal cooling. Effective cortical suppression by cooling requires temperatures of approximately 25°C or below (Moseley et al., 1972; Adey, 1974; Burchfiel and Duffy, 1974; Kayama et al., 1984). In the cat, maintain-

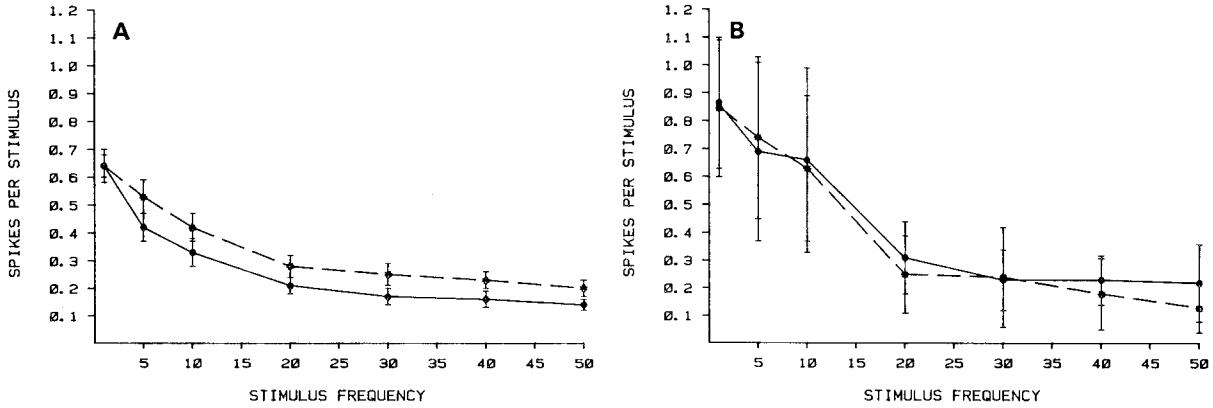

Figure 7. *A*, Average (±SEM) frequency response curves of 46 somatically activated VB units tested at threshold (*solid line*) and at twice threshold stimulus intensity (*dashed line*). *B*, Average (±SEM) responsiveness of six units tested initially (*solid line*) and 30 min later (*dashed line*) to examine stability of frequency response profiles.

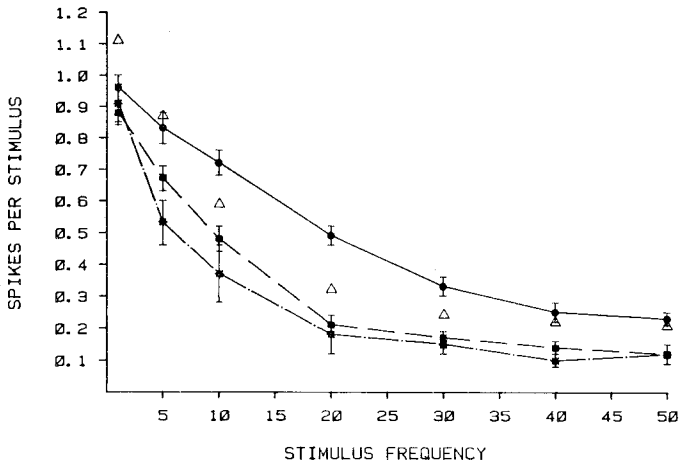

Figure 8. Comparison of the effect of lidocaine-induced suppression with the effect of removing S1 cortex. ●—● and ■– – –■, depression of frequency following produced by cortical lidocaine; data are identical to those shown in Figure 5*A*. *–·–, frequency following profile of 20 units studied after extirpation of S1 cortex. △, average responsiveness of 9 units during CSD.

ing a portion of the parietal cortex at that temperature for more than a few minutes produces focal seizures (Burchfiel and Duffy, 1974) and, in the rat, a 2 to 3°C temperature drop in the VB thalamus (B. Yuan, unpublished observations). Second, the maintained suppression is focal, unlike CSD. The tritiated lidocaine experiment showed that effective concentrations of lidocaine do not diffuse widely throughout the cortex or into subcortical areas. Furthermore, the agreement between the lidocaine and S1 lesion experiments supports the conclusion that our results are not due to the suppression of cortical areas outside S1. Third, in the anesthetized rat, there is no preceding period of cortical excitation as is seen with CSD (Leao, 1944; Bures et al., 1974; Albe-Fessard et al., 1983) or during moderate rates and intensities of cooling (Gartside and Lippold, 1967; Moseley et al., 1972; Adey, 1974). Finally, we have shown that local anesthetic effectively suppresses corticofugal activity, whether directly or reflexly evoked.

A possible complicating factor in the use of lidocaine in these experiments is that it may have blocked rapid axoplasmic flow from neuronal endings (Fink et al., 1972; Fink and Kish, 1976); the effect this might have on the excitability of thalamocortical neurons is not known.

The results of our experiments support the hypothesis that corticofugal activity from S1 cortex has the net effect of facilitating somatosensory transmission in the VB thalamus. This is consistent with the observations of Albe-Fessard et al. (1983), using CSD, and Waller and Feldman (1967), who used both CSD and focal cortical cooling to study spontaneous unit activity in the deafferented VB thalamus in cats. Cortical stimulation has been shown to have a frequency-dependent facilitatory effect on thalamic somatosensory transmission (Andersen et al., 1972), and a shift of ECoG activity from the synchronized to the desynchronized state has been associated with an increase in the responsiveness of VB neurons (Angel, 1983). The finding of a predominantly excitatory influence of corticothalamic activity is also in accord with the evidence that corticothalamic neurons, including those projecting to VB thalamus, use glutamate or aspartate as the neurotransmitter (Bromberg et al., 1981; Fonnum et al., 1981; Rustioni et al., 1983).

A predominant effect of excitation followed by depression of spontaneous VB neuronal activity was produced by pyramidal tract stimulation in the experiments of Giuffrida et al. (1983). Both excitation and inhibition were observed in similar experiments by Shimazu et al. (1965) and Tsumoto et al. (1975) with evidence for a predominant inhibitory effect on VB relay neurons receiving cutaneous input (Tsumoto et al., 1975). However, pyramidal tract stimulation activates synchronously a fraction of the corticofugal outflow, including that originating from cortical areas other than S1, so that the results of such experiments are not strictly comparable to ours, in which there was a focal suppression of all S1 corticofugal activity.

Several experiments have led to the conclusion that S1 cortex depresses somatosensory transmission in the VB thalamus. Ogden (1960) found that focal, penicillin-induced ECoG spike activity in S1 cortex produced a strychnine-reversible depression of evoked potentials in the VB thalamus. Subsequently, it was shown that antidromic stimulation of VB thalamocortical neurons activates inhibitory interneurons via recurrent collaterals of VB relay cells (Andersen et al., 1964) and that penicillin spikes can produce the necessary antidromic activation (Gutnick and Prince, 1972). Angel and Clarke (1975) were able to record from more VB neurons in a decorticated, as compared to an intact, hemisphere, but the responsiveness of these small samples of neurons was not compared.

The experiments of Burchfiel and Duffy (1974) provide perhaps the strongest evidence for corticofugal depression of VB responsiveness. They found that cooling S1 cortex to 20°C for approximately 5 min increased the amplitude of a potential evoked by medial lemniscal stimulation and recorded from the white matter under the S1 cortex of unanesthetized, paralyzed cats. Ablation of S1 cortex produced similar results except that the augmentation of the response decreased considerably after 30 min. Their single record of a recording within the VB thalamus (Fig. 3 from Burchfiel and Duffy, 1974), however, shows a much smaller effect of S1 cooling than that observed while recording from the subjacent S1

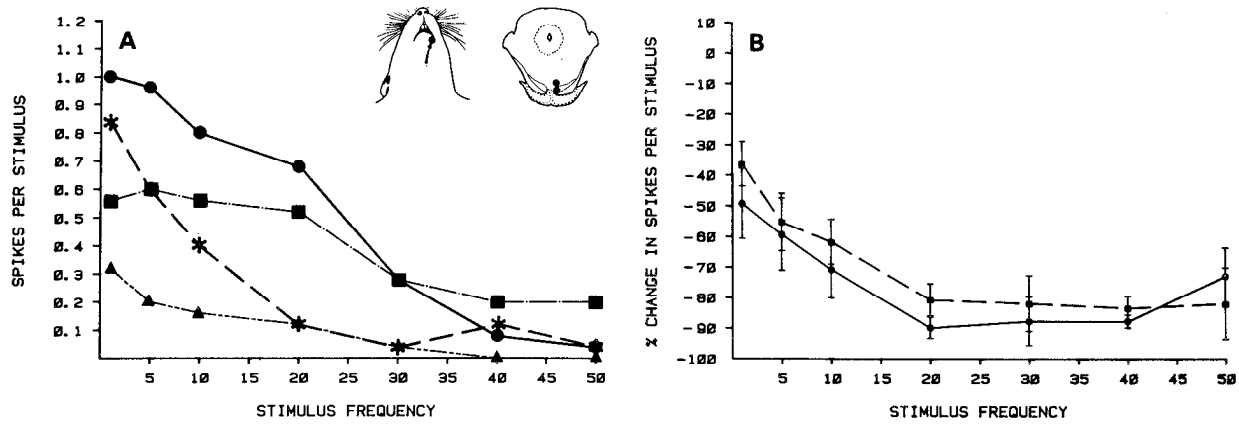

Figure 9. Depression of VB responses to somatic stimuli compared with depression of responses to stimulation of medial lemniscus. *A*, A VB unit with receptive field as depicted (*inset*) shows attenuation of responses to repetitive somatic stimuli after S1 cortical lidocaine (*) as compared with control responses (●). The control frequency following curve to bipolar stimulation of the medial lemniscus (■), in the *inset*, is relatively flat, but suppression of S1 cortex produces an attenuation of responsiveness (▲) similar to that seen with somatic stimulation. *B*, Average (±SEM) percentage of change in responses of six units to somatic (*solid line*) or medial lemniscal (*dashed line*) stimulation after suppression of S1 cortex.

white matter. To support their observations, the authors cite the experiments of Hosko and Helm (1969), who observed an increase in the amplitude of a VB potential evoked by radial nerve stimulation after 5 to 6 min of occlusion of both carotid arteries in cats with the basilar artery ligated. Because of these radically different experimental conditions, the observations of Hosko and Helm (1969) probably have little relation to our experiments or to those of Burchfiel and Duffy (1974).

Several important differences between our study and that of Burchfiel and Duffy (1974) may account for the conflicting results. First, there is the question of anesthesia. We studied the anesthetized rat rather than the unanesthetized cat. Second, there are significant species differences. In the rat, excitatory corticothalamic activity may act directly on thalamocortical neurons because inhibitory interneurons within the VB thalamus are lacking in this species but are present in cat and monkey (Ralston, 1983). However, we did not attempt to identify thalamocortical projection cells in our experiments. Third, we recorded the activity of single neurons within the VB thalamus rather than an immediately subcortical evoked potential. Finally, Burchfiel and Duffy (1974) recorded relatively short-duration, and possibly transient, changes in responses to single synchronous volleys. We recorded the responsiveness of VB neurons to repetitive inputs tested over periods of several minutes and at least 30 min after cortical suppression had been initiated. It is possible, therefore, that we might have overlooked an early, transient increase in VB neuronal excitability. It is also possible that a depression of corticofugal activity facilitates the response of some VB neurons to single synchronous volleys but simultaneously depresses their response to repetitive inputs. For example, a subthreshold depolarization of VB neurons might be superimposed on a disinhibition or facilitation of recurrent inhibitory mechanisms that selectively limit repetitive discharge.

Our results indicate that, in the anesthetized rat, a substantial fraction of the corticofugal influence on somatosensory transmission is facilitatory and is exerted at the thalamic level. Thus, we found that suppression of cortical activity attenuated VB neuronal responses elicited either by somatic or lemniscal stimulation. This observation, however, does not contradict the well established corticofugal influences on transmission through the dorsal horn and dorsal column nuclei (for review, see Towe, 1973). Our experiments may have revealed only the most prominent effect and site of action in the anesthetized rat.

In the rat, corticothalamic effects may be produced directly on VB neurons or indirectly via neurons of the adjacent thalamic reticular nucleus (TRN). The available anatomical evidence (Ralston, 1983) suggests that cortical suppression would remove an excitatory corticothalamic input to thalamocortical relay neurons. In addition, the experiments of Angel (1983) suggest that cortical suppression would disinhibit some TRN neurons because those TRN neurons that are most active during low voltage, high frequency ECoG activity are inhibited by cortical stimulation. Cortical suppression might therefore increase the effectiveness of some TRN neurons as possible mediators of recurrent inhibition of VB thalamocortical cells (Yingling and Skinner, 1976; Houser et al., 1980). Our results are consistent with both of the above possibilities.

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