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Excitation of Wide-Field Ventralis Posterolateralis Neurons by Contralateral Thalamic Stimulation

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Interconnections between the nuclei ventralis posterolateralis (VPL) of the thalamus were studied using single-unit recordings from chloralose-anesthetized cats. Responses to stimulation of the contralateral VPL (cVPL) were evoked in 28.9% of the 218 neurons sampled. Those neurons responsive to cVPL stimulation were almost exclusively those with an ipsilateral component to their receptive fields, i.e., *s*b (receptive fields on both fore- or hind limbs) and *m* neurons (receptive fields on all four limbs), but not all neurons of either of these sets responded. Only 2 of 127 neurons with receptive fields on either the contralateral fore- or hind limb, *s*a neurons, responded to cVPL stimulation. cVPL-Responsive and -unresponsive *m* neurons differed little in the properties of their responses to skin stimulation and no differences were found in their distribution within the nucleus. Corticopetal neurons were found among both cVPL-responsive and -unresponsive neurons. VPL neurons were shown to exhibit coadunate behavior, like cortical neurons, but no evidence was found of modulation of *m* neuron excitability by local *s*a neurons. Responsiveness of *m* neurons to cVPL stimulation was blocked by application of ice or KCl crystals to the contralateral, but not the ipsilateral cortex. The possibility is considered that some responses to cVPL stimulation are antidromically conducted.

INTRODUCTION

Harris (21, 22) and others showed that the thalamic nucleus ventralis posterolateralis (VPL) contains neurons excited from receptive fields

Abbreviations: VPL—ventralis posterolateralis, VPM—ventralis posteromedialis, VL—ventralis lateralis, CF, CH—contralateral fore-, hind paw, IF, IH—ipsilateral fore-, hind paw.

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restricted to one contralateral paw (*s*a neurons), neurons excited from fields on two paws (*s*b and *s*c neurons), and neurons excited from all four paws (*m* neurons). These sets of neurons have much in common with sets of neurons in the pericruciate cortex that have been given the same names (32, 44, 46). In the cortical pericruciate forepaw focus, *s*b neurons (responding to stimulation of the contralateral and ipsilateral forepaws only) depend on the contralateral homotypical cortex for their ipsilateral receptive fields (32, 48). Almost all *m* neurons respond to stimulation of the contralateral cortex, but unlike the *s*b neurons, they do not depend on the contralateral cortex for their ipsilateral fields and the pathway for their excitation does not appear to involve the corpus callosum (32, 48). In the forepaw focus, few, if any, *s*a neurons (responding to contralateral forepaw stimulation only) respond to stimulation of the contralateral cortex (32).

The question arises whether thalamic neurons of the same names and responsiveness to peripheral inputs are related to the contralateral VPL (cVPL) in the same way as their cortical counterparts are to the contralateral cortex. A series of experiments by Bava, Fadiga, and associates (4–11, 16) demonstrated intercommunications between neurons of opposing nuclei of the VPL, ventralis posteromedialis (VPM), and ventralis lateralis (VL) that do not require an intact corpus callosum, but seem to involve fibers in the region of the posterior commissure. Excitatory effects on VPL neurons from stimulating the cVPL were observed in chloralose-anesthetized and chronically decorticated cats, but not in unanesthetized, paralyzed cats (5, 16). Inhibitory effects were seen in unanesthetized as well as chloralose-anesthetized preparations (8).

Bava *et al.* (5) termed the neurons excited by stimulation of both the cVPL and the medial lemniscus, group II, and those excited only by medial lemniscus stimulation, group I. According to Bava *et al.* (8), "transversal excitation . . . becomes effective only in VPL neurones exhibiting extralemniscal properties." Yet their earlier work showed that 10% of their extralemniscal cells were placed in group I and 6% of their lemniscal cells were placed in group II in chloralose-anesthetized cats (5). Furthermore, Carreras *et al.* (13) found that 29 units of 75 tested were driven by cVPL stimulation in decorticate cats, and yet their entire tested-unit sample contained only five modality-place-unspecific (presumably extralemniscal) ventrobasal neurons; the number of extralemniscal neurons responding to cVPL stimulation could not have exceeded five. Thus, the majority of units excited by cVPL stimulation must have been modality-place-specific, presumably lemniscal neurons.

Although these observations shed some light on the nature of thalamic intercommunication, it is not clear how the lemniscal and extralemniscal appellations can be related to the classification of neurons by location and

extent of their excitatory receptive fields, i.e., to *s*a, *s*b, and *m* sets. Jabbur *et al.* (27) attempted to excite neurons in the VPL using cVPL stimulation and found that none of the small-field or *s*a neurons tested could be driven. On the other hand, they could drive some bilateral- (*s*b) and wide-field (*m*) cells from the cVPL, but the sample of driven neurons numbered only 18. The present study presents a larger sample of identified VPL neurons upon which the effectiveness of cVPL stimulation has been tested; the response properties of cVPL-responsive and -unresponsive neurons are compared. It will be shown that thalamic neuron sets behave much like cortical neuron sets of the same names with respect to contralateral stimulation, but, unlike cortical neurons, none of the thalamic neuron sets appears to depend on cVPL for its ipsilateral input.

METHODS

Single units were isolated in the thalamus of adult cats anesthetized with α-chloralose (Sigma, 50 mg/kg, i.p.) and paralyzed with decamethonium bromide (Syncurine) or gallamine triethiodide (Flaxedil) as needed. The animals were artificially ventilated using a positive pressure respirator to maintain end-expiratory CO_2 concentrations at 3.5 to 4.0%. Atelectasis was prevented by blocking the expiratory port of the respirator for two cycles every 5 min. Rectal temperature was monitored and maintained at 38.5°C using a servo-controlled DC heating pad.

The preparation was stabilized for recording by enlarging the foramen magnum and draining the cerebrospinal fluid, and by creating a double pneumothorax. Additional stability was achieved by suspending the animal from clamps applied to the spinous processes of a thoracic and a lumbar vertebra. The cranium was removed over the sensorimotor cortex [fields 1, 2, 3, 4, 6, and 2 pri of Hassler and Muhs-Clement (25)], and over the thalamus. Dura mater was removed and replaced, on the anterior opening, by a thin polyethylene film and, on the posterior opening, by Ringer's–agar. The polyethylene sheet was removed for antidromic testing.

Units were isolated, using stereotaxic coordinates (28, 29, 40) on a 1-mm grid covering the VPL nucleus (A11 to A8, L5 to L8), with 3 M NaCl-filled glass microelectrodes of 1- to 5-MΩ tip impedance, measured at 1 kHz. A hunting stimulus, consisting of 1/s stimulation alternating periodically between the contralateral forepaw (CF) and the contralateral hind paw (CH) at 0.1-ms duration and intensity supramaximal for the compound action potential recorded from the superficial radial nerve (25 mA), was used to isolate VPL neurons from both the forepaw and hind paw foci. The hunting stimuli were delivered through bipolar needle electrodes in the central pad of each paw. Similar stimulating electrodes were also placed in

the ipsilateral fore- (IF) and hind paws (IH). The same supramaximal stimulus of 0.1-ms duration delivered at 1/s was used for paw stimulation throughout this experiment.

A concentric bipolar electrode (David Kopf Instruments, NE100) was placed in the cVPL in the same frontal and sagittal planes as the recording microelectrode and in the horizontal plane where there was the largest response to stimulation of the CF, for medially placed tracks, or the CH, for laterally placed tracks. Attempts were made to excite neurons in the VPL using 0.05-ms duration pulses of constant current repeated once per second. The intensity of the stimulus was gradually raised from 0 mA until the cell fired or the maximum output of the stimulus isolation unit—30 mA—was attained. Threshold was taken to be the current at which the neuron responded to 5 of 10 stimuli. When threshold was determined, stimuli of at least two times threshold intensity were used to determine latencies and spikes per response.

The sensorimotor cerebral cortex ipsilateral to the recording site was stimulated using a movable silver ball electrode. The electrode was moved over the entire exposed sensorimotor cortex and an attempt was made to drive the neurons antidromically. Antidromic responses were identified using latency variation and frequency-following capability as described by Harris (21) and, when these criteria were not convincing, collision was demonstrated between antidromically and orthodromically conducted spikes. For cortical stimulation, 0.05-ms duration pulses of constant current were used.

Extracellular unit spikes were amplified, using a Grass P-15 preamplifier with 30-Hz and 10-kHz filter settings, and displayed on a Tektronix 565 oscilloscope. Photographic records were made using a Grass C-4 kymograph camera. The photographic images were enlarged 7 to 10 times for measurement of spike latencies.

In early experiments electrode tracks were marked by iontophoresis of fast green dye and in later experiments the Prussian blue method of Humphrey (26) was used. After each experiment the position of the cVPL electrode was marked by passing current through the electrode. The animal was perfused with saline followed by 10% Formalin (containing 2% ferrous ammonium sulfate for the Prussian blue reaction) and 50-μm frozen sections were stained with cresyl violet. Sections of the cVPL were also treated with potassium ferrocyanide after being washed, to make the lesion site more obvious. Neurons in electrode tracks that did not appear to traverse the VPL were not included in this analysis. The cVPL electrode was always in the intended position.

Each neuron was classified according to its response to electrical stimulation of the four paws, following the scheme of Jabbur *et al.* (27).

Neurons that responded to stimulation of all four paws were classified as *m* neurons; those that responded to stimulation of both forepaws or both hind paws were termed f,*s*b and h,*s*b, respectively; those that responded to stimulation of both CF and CH were termed *s*c neurons; and those that responded only to stimulation of CF or CH were termed f,*s*a and h,*s*a, respectively. The other sets defined by Jabbur *et al.* (27) were not seen in this sample. For this experiment, a neuron was said to respond to a particular stimulus if it discharged in at least 5 of 10 trials. For units with high rates of spontaneous discharge larger numbers of trials were used and regularity of latency after the stimulus artifact became an additional criterion. The same procedures were used for peripheral inputs and cVPL inputs.

Responses of neurons to natural stimulation were determined by moving hairs with puffs of air or touching, pressing, or tapping the skin with a glass probe. A neuron that responded to hair movement was called a hair neuron; one that responded to touch, but not hair movement, a touch neuron; one that responded to tap, but not touch, a tap neuron; and one that responded to hair movement and gave an additional discharge to touch, a mixed neuron.

RESULTS

Responses to Contralateral Ventralis Posterolateralis Stimulation. A total of 218 VPL neurons was tested for responsiveness to stimulation of the cVPL. Table 1 shows the distribution of responsiveness for all neuron sets. Only 28.9% of the VPL neurons responded to single stimuli applied to the cVPL. This percentage is similar to those reported by previous investigators whose values were from 24 to 39% (5, 13, 27). When the VPL

TABLE 1

Neurons Responsive to Contralateral Ventralis Posterolateralis Stimulation

Neuron set	Response		No response		Total
	N	%	*N*	%	*N*
f,*s*a	1	1.0	95	99.0	96
f,*s*b	5	71.4	2	28.6	7
h,*s*a	1	3.2	30	96.8	31
h,*s*b	1	33.3	2	67.7	3
*s*c	3	21.4	11	78.6	14
m	52	77.6	15	22.4	67
All	63	28.9	155	71.1	218

neurons were partitioned by sets, it was seen that more than three-fourths of the *m* neurons responded to cVPL stimulation. In contrast, among the *s*a neurons, only one f,*s*a and one h,*s*a neuron responded to cVPL stimulation. This occurred in spite of the fact that these *s*a sets constituted 58% of the tested neurons.

It is possible that these two responsive *s*a neurons were simply misclassified, having undetected, subthreshold excitatory influences from the other paws (37). No interaction studies were done to detect such subthreshold effects, but the one responsive f,*s*a neuron did have a first-spike latency in response to supramaximal CF stimulation (22.0 ms) that was more than two standard deviations above the mean for f,*s*a neurons (10.72 ± 5.08 ms) and more like that for cVPL-responsive *m* neurons (19.08 ± 7.37 ms). The one responsive h,*s*a neuron, on the other hand, did not differ in latency from other h,*s*a neurons.

More than 70% of the f,*s*b neurons tested responded to cVPL stimulation, resembling the *m* neurons in this characteristic. Only one of three h,*s*b neurons and 3 of 11 *s*c neurons responded. The sample sizes for all three of these sets were small, together making up only about 11% of the total, and the predictive power of these results for the populations of these sets is unknown.

Threshold values for excitation of 20 VPL neurons by cVPL stimulation averaged 2.59 ± 1.85 mA (mean ± SD). For 51 additional neurons, precise thresholds were not determined, but an upper limit was determined. All were excited at less than 13.0 mA, 48 were excited at less than 8.5 mA, and 41 were excited at less than 5.0 mA.

The mean first-spike latency of responses to cVPL stimulation (at, at least, two times threshold current) for the 58 neurons, whose distribution is shown in Fig. 1, was 17.29 ± 7.85 ms. When thalamic *m* neurons were considered alone (cross-hatched bars of Fig. 1), the mean latency lengthened to 17.68 ± 8.31 ms; the range for all neurons was 6.0 to 38.5 ms and for *m* neurons was 7.1 to 38.5 ms. Distributions of latencies for all neurons and for *m* neurons alone had modes in the 15.5 to 20-ms bin. Latencies did not shorten significantly at higher stimulus intensities to as much as four times threshold. Calculations from Fig. 5C of Bava *et al.* (5) yield a mean first-spike latency of 8.58 ± 4.88 ms, a significantly smaller value than that observed here (Student's $t = 7.2934$, df = 156, $P < 0.01$). Those authors reported both shorter minimum and maximum latencies, with none longer than 20.5 ms; they did not specify their stimulus parameters. Jabbur *et al.* (27) did not report cVPL response latencies, but noted that the responses were of longer latencies than those of Bava *et al.* (5), perhaps more like those of the present study.

The latency of the first spike in response to cVPL stimulation at, at least,

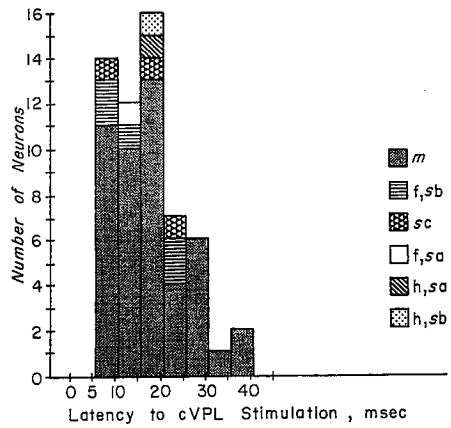

FIG. 1. Distribution of latencies of responses to stimulation of the contralateral ventralis posterolateralis in sets of neurons. Latencies are presented in 5-ms bins and sets are encoded by bar shading. Stimulation was at least two times threshold current.

two times threshold current was measured in photographed records for 45 *m* neurons. The percentage variation in latency was calculated from the following equation: % variation = 100 − (minimum latency/maximum latency) × 100. In addition, the coefficient of variation of first-spike latency was calculated for responses to both cVPL and CF stimulation for 51 cVPL-responsive neurons. The percentage variation in cVPL response latency varied from 7 to 84%, with a mean of 33.38 ± 20.56 (mean ± SD). When the percentage variation was plotted against the average conduction velocity of the pathway from the cVPL, estimated by dividing twice the lateral Horsely–Clarke coordinate of the cell by the latency, this scatter was apparent (Fig. 2A). There was no clear relationship between variability in latency and conduction velocity, although the highest variability did occur for the slowest velocities. Note that the conduction velocities, assuming that this was a direct pathway, were extremely slow, from 0.3 to 2 m/s and averaging 0.93 ± 0.50 m/s.

Figure 2B shows the variability of response latency in another way. The coefficient of variation for first-spike latency for cVPL responses was plotted against that for CF responses. It is seen that the variability of latency for CF (10.34 ± 8.58) was less than for the cVPL (14.25 ± 10.83), but there was a significant ($P < 0.01$) correlation between the two variables ($r = +0.38$, df = 49, Student's $t = 2.8993$). Also plotted in the figure is the least squares regression line for these data, which does not appear to be highly descriptive. Rather, it appears that two lines may better fit the points: CF = 2.99 + 0.19 cVPL and CF = 1.80 + 0.79 cVPL.

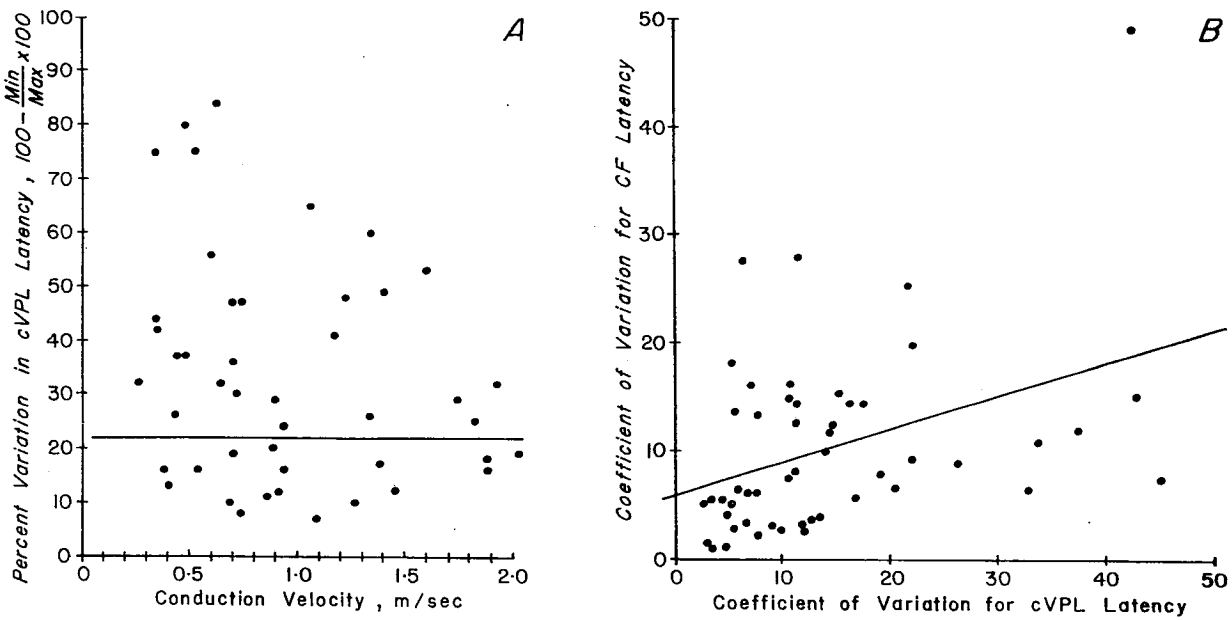

FIG. 2. A—The percentage variation in contralateral ventralis posterolateralis (cVPL) latency on the ordinate is plotted against the average conduction velocity on the abscissa for each of 45 *m* neurons. Values computed as described in the text. The line plotted at 22% variation marks the largest variation in antidromic latency observed by Swadlow and Waxman (42). B—the coefficient of variation for first-spike latency of responses to contralateral forepaw (CF) stimulation (ordinate) is plotted against that for cVPL stimulation (abscissa) for 51 thalamic neurons. The least squares regression line for the plotted points has the equation CF = 6.0 + 0.30 cVPL. CF stimulation was supramaximal and cVPL stimulation at least two times threshold current.

TABLE 2

Average Response Properties of Thalamic *m* Neurons[a]

	N	CF	IF	CH	IH
		First-spike latency (ms)			
cVPL-Responsive	44	19.08 ± 7.37	22.40 ± 11.73	26.75 ± 11.06[b]	29.64 ± 10.14
cVPL-Unresponsive	14	14.94 ± 9.40	17.70 ± 9.29	16.22 ± 6.58[b]	27.16 ± 10.48
		Spikes per response			
cVPL-Responsive	44	2.12 ± 1.36	2.01 ± 1.26[b]	2.25 ± 1.34	1.83 ± 1.18
cVPL-Unresponsive	14	2.87 ± 2.23	1.04 ± 0.07[b]	3.02 ± 2.50	1.54 ± 0.85

[a] Values are means ± SD for supramaximal paw stimulation.
[b] Difference significant, $P < 0.01$, Student's t test.

Response Properties of Contralateral Ventralis Posterolateralis-Responsive Neurons. Neurons excited by stimulation of the cVPL were overwhelmingly members of the non-*s*a sets, primarily the set of *m* neurons, but not all *m* neurons were cVPL-responsive neurons. Perhaps differences between cVPL-responsive and -unresponsive neurons can be found in their discharge properties. Table 2 summarizes the discharge properties of *m* neurons, both cVPL-responsive and -unresponsive. There was a tendency for cVPL-unresponsive *m* neurons to discharge earlier and with greater numbers of spikes for contralateral and fewer numbers for ipsilateral cutaneous inputs, but, except for CH latency and IF spikes per response, these trends were not statistically significant.

Towe *et al.* (46) noted a similarity in latency and number of discharges in the response to the various inputs to cortical *m* neurons. A neuron that responded late with respect to its fellows with a particular number of spikes per response to CF stimulation also discharged late to stimulation of the other paws and tended to discharge the same number of spikes for each input. This characteristic was termed coadunate behavior. Towe *et al.* (45, 46) used this behavior to deduce interactions between cortical *s*a and *m* neurons. Inputs from the pudendal nerve and from splanchnic nerves also discharged *m* neurons in a coadunate manner (39, 47).

Thalamic *m* neurons may also show coadunate behavior. Table 3 shows Pearson's product moment correlation coefficients for pairs of inputs to 39 thalamic *m* neurons for which measurements of first-spike latency were made for at least four inputs. There was a statistically significant correlation between each pair of inputs and the values were as high as or higher than those reported for cortical *m* neurons (45). This is more remarkable considering that the cortical neuron sample came from a single topographic focus, whereas the thalamic sample was drawn from both fore-

TABLE 3

Correlation Values by Pairs of Inputs for (A) Initial Response Latency, and (B) Mean Spikes per Response[a]

	A					B			
	CF[b]	IF	CH	IH		CF	IF	CH	IH
IF	0.59				IF	0.70			
CH	0.65	0.58			CH	0.61	0.79		
IH	0.52	0.77	0.75		IH	0.49	0.66	0.86	
cVPL	0.59	0.55	0.37[c]	0.57	cVPL	0.36[c]	0.58	0.39[c]	0.46

[a] Values for supramaximal paw stimulation and contralateral ventralis posterolateralis (cVPL) stimulation of at least two times threshold current.

[b] Abbreviations: CF, IF—contralateral, ipsilateral forepaw; CH, IH—contralateral, ipsilateral hind paw.

[c] Significant correlations (t test): $P < 0.05$; all other values $P < 0.01$.

and hind limb foci. Correlations were nearly as high between cVPL and paw parameters as they were for parameters among paws. This was an admittedly small sample, but the data suggested that coadunation was also a thalamic phenomenon. On the other hand, there was no indication of a local *s*a modulation of thalamic *m* neurons as would be deducible from a lowered correlation between CF and IF latencies and CH and IH latencies compared with the IF-IH correlations (45, 46).

Thalamic *m* neurons responded to stimulation of the cVPL with slightly less than two spikes per response (1.83 ± 1.14), nearly the same as for paw stimulation (Table 2). In fact, there was a significant correlation between spike numbers for the cVPL and for each of the paw inputs. The significant correlations, typical of coadunate sets, are presented in Table 3B.

Neurons responsive to cVPL stimulation have hair (48%), touch (29%), tap (10%), and mixed (7%) receptive fields. These proportions were computed for a sample of 29 *m* neurons for which natural receptive fields were determined. Of seven cVPL-unresponsive *m* neurons, all were classified as having hair receptive fields.

The question of whether or not the cVPL is necessary for the ipsilateral responsiveness of VPL neurons is answerable, in part, from data collected in this experiment. Not all neurons responsive to ipsilateral stimulation required the cVPL to be intact because not all these neurons responded to cVPL stimulation (Table 1). Of 41 *m* neurons responsive to cVPL stimulation, 28 had mean latencies of IF responses longer than their mean cVPL latencies. The other 13 could not require cVPL because the cVPL latencies were longer than the IF latencies. Of the 28 neurons, 19 had

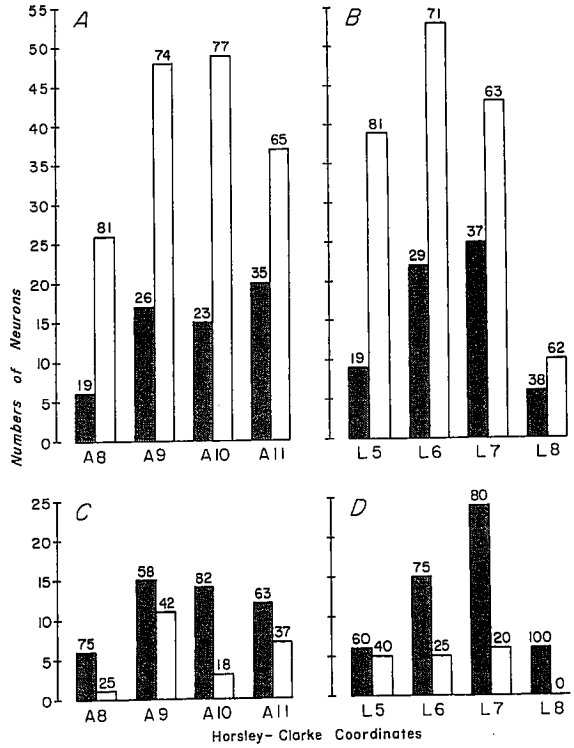

FIG. 3. Distribution of contralateral ventralis posterolateralis (cVPL)-responsive (cross-hatched bars) and cVPL-unresponsive (open bars) neurons in frontal planes (A and C) and sagittal planes (B and D). Comparisons for all VPL neurons together are shown in A (frontal) and B (sagittal) and for VPL *m* neurons alone in C (frontal) and D (sagittal). Number above each bar is the percentage of neurons at that position that were in that category, i.e, either cVPL-responsive or -unresponsive.

latency differences (IF minus cVPL) greater than the minimum f,*s*a latency (5.6 ms) observed in this study and could conceivably respond to ipsilateral stimulation via cVPL. Of *s*b neurons responsive to cVPL, five of six had longer latencies for IF or IH responses than for cVPL and all these were longer by more than the minimum latency of f,*s*a or h,*s*a (10.2 ms) neurons. Thus, although it was possible that *individual neurons* could depend on the cVPL for their ipsilateral inputs, none of the *sets* of neurons appeared to do so.

Distribution of Contralateral Ventralis Posterolateralis-Responsive Neurons. If cVPL-responsive and -unresponsive neurons do not differ in their discharge properties, then perhaps they differ in their locations within the nucleus. The distributions of both cVPL-responsive and cVPL-unresponsive neurons in the three Horsley–Clarke planes are shown in

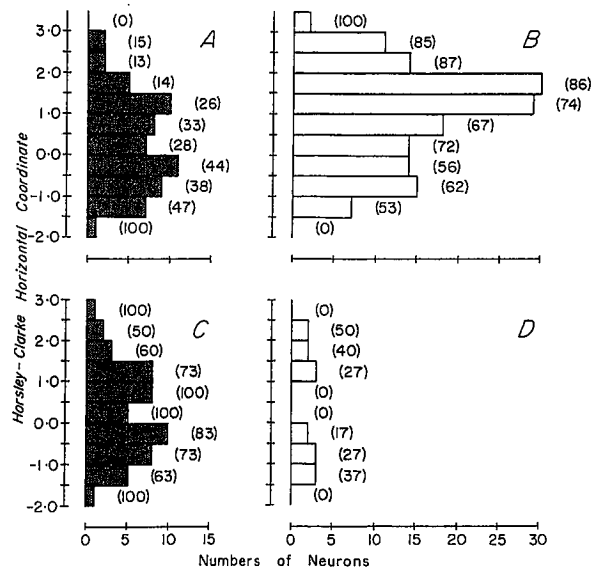

FIG. 4. The distribution of contralateral ventralis posterolateralis (cVPL)-responsive (cross-hatched bars) and cVPL-unresponsive (open bars) neurons in depth within the thalamus, expressed in Horsley–Clarke horizontal coordinates. Comparisons for all VPL neurons together are shown in A and B and for VPL *m* neurons alone in C and D. Numbers in parentheses are percentages of neurons at that depth that were within that category, i.e., either cVPL-responsive or -unresponsive. Horizontal coordinates are grouped into 0.5-mm bins.

Figs. 3 and 4. It appeared that cVPL-responsive neurons were more frequently seen in the anterior (Fig. 3A) and medial (Fig. 3B) parts of the nucleus, but there were no statistically significant differences in either place ($\chi^2 = 3.396$, 4.819, df = 3). Among *m* neurons, there was no anterior–posterior trend apparent in the distribution (Fig. 3C), but the proportion of cVPL-responsive neurons was larger in the more lateral parts of the nucleus (Fig. 3D). Even this trend failed to reach statistical significance ($\chi^2 = 3.251$, 3.646, df = 3). Neurons responsive to cVPL stimulation did appear more often deeper in the nucleus (0.395 ± 1.080 mm) than those not responsive to cVPL stimulation (0.917 ± 1.141 mm, Student's $t = 3.1404$, df = 214, $P < 0.01$). This is seen in Figs. 4A and B. The opposite trend for *m* neurons considered alone (Figs. 4C and D), did not reach significance (0.337 ± 1.048 mm, 0.310 ± 1.348 mm, $t = 0.0696$, df = 64).

Other Observations. Axon projections to the sensorimotor cortex were determined by antidromic testing in neurons whose activity was observed for a sufficient time. Two cVPL-responsive *m* neurons were driven

antidromically by cortical stimulation at 1.2- and 1.3-ms latencies; 11 others were not driven antidromically, though the whole of exposed fields 1 through 4, 6, and 2 pri was searched. The remaining neurons were not held long enough for a complete search to be made. Two cVPL-unresponsive *m* neurons were driven antidromically with latencies of 0.7 ms; two others were not driven antidromically. The f,*s*a neuron driven from the cVPL was also driven antidromically with a latency of 0.4 ms, but the h,*s*a neuron was not, though the entire exposed cortex was searched for an antidromic site. One cVPL-responsive *s*c neuron was corticopetal (latency 0.7 ms). In short, it appeared that at least some cVPL-responsive and cVPL-unresponsive neurons were corticopetal.

In four preparations, the sensorimotor cortex opposite the thalamic recording site was also exposed. In three of these, a wax dam was built around each cortical exposure to hold Ringer's ice cubes. Thalamic *m* neurons were isolated and tested for cVPL responsiveness. For two cells, the changes in cVPL responsiveness after application of KCl to the contralateral cortex were observed. In both cases, the initiation of a spreading depression was verified. For five cells, the changes in cVPL responsiveness after application of Ringer's ice cubes were observed. For two of the five cells, the ice was applied to contralateral and ipsilateral cortex in succession, with a recovery period between applications. The results were the same for contralateral application of ice or KCl; typical recordings are shown in Fig. 5. The control responses to cVPL, CF, IF, CH, and IH stimulation are illustrated in column 1, rows A–E. After application of ice to the contralateral cortex, the response to the cVPL was abolished (A2), but responses to paw stimulation were unchanged (B2 to E2). Recovery of the cVPL response after ice removal and application of warm saline is shown in A3. The action potential changed configuration after application of ice to the ipsilateral cortex, but the lack of effect on the various responses of the cell is obvious in column 4.

After application of the ice to the contralateral cortex the response to cVPL stimulation gradually lengthened in latency, the discharge frequency decreased, and the probability of a response decreased until, in most cases, it reached zero. The sequence of events was reversed upon rewarming. Where the cooling has its effect is unknown, but it is unlikely that the effect was directly on the thalamic neuron. No change in responsiveness to paw stimulation was seen in any of the neurons tested.

DISCUSSION

There can be little doubt that the nucleus VPL contains neurons with small receptive fields—*s*a neurons—and neurons with large, bilateral

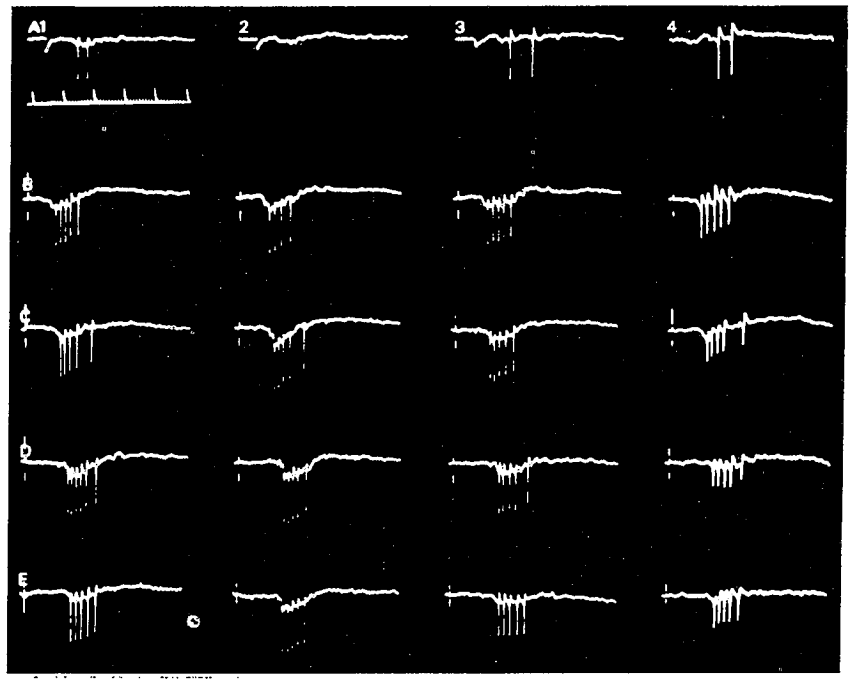

FIG. 5. Influence of "icing" pericruciate cortex on contralateral ventralis posterolateralis (cVPL) responsiveness. The responses of a VPL *m* neuron to, respectively, cVPL, contra-, ipsilateral forepaw, contra-, and ipsilateral hind paw stimulation are shown before (column 1, rows A–E); 5 min after application of ice to the contralateral pericruciate cortex (column 2, rows A–E); after removal of ice and rewarming the cortex (column 3, rows A–E); and 15 min after application of ice to the ipsilateral pericruciate cortex (column 4, rows A–E). Although spike configuration changed between the records of columns 3 and 4, it is clearly the same unit. The time-base in A1 is 1 and 10 ms and applies to all records. All paw stimulation was at supramaximal strength and cVPL stimulation at 1.2 mA. The threshold for the cVPL for this unit was 0.5 mA.

receptive fields—*s*b and *m* neurons. Both groups of neurons were clearly seen in chloralose-anesthetized (5, 21, 22, 27), barbiturate-anesthetized (12, 17, 23, 38), chronically decorticated (7), and unanesthetized (3, 19) animals. Furthermore, bilateral and wide receptive fields were described for cells in the cat gracile nucleus (15, 20) and many of these cells projected to the thalamus (15). Bilateral receptive fields were also described for widely scattered axons in the medial lemniscus (14, 24). Those wide-field neurons in the region of the VPL are clearly within the nucleus, as established by their thorough admixture with small-field, or *s*a neurons, and by histological reconstructions, and not inadvertently recorded residents of nearby posterior group nuclei (33, 34). It should not be

surprising that the characteristics of neurons change with the state of the nervous system and that this shows itself as a change in receptive field size or responsiveness to particular inputs (3, 45).

The data of Bagshaw and Evans (2) suggest that stimulating current, applied through concentric bipolar electrodes, spreads less than 1.80 mm at 10 mA and 1.03 mm at 5 mA. Those values were calculated for their largest electrodes, having exposed tips of the central electrode of 100 μm. The areas of the exposed surfaces of their electrodes were less than 0.08 mm^2, whereas the exposed surface of the Kopf electrodes used in the present study was 0.34 mm^2, more than four times greater. If the results of Bagshaw and Evans (2) can be applied to stimulation within gray matter and if the distance of current spread continues to decrease with even larger electrodes than they used, then effective stimulating currents in the present study usually spread over less than 1 mm (for 5 mA).

This estimate of effective current spread should be reduced even further because of the much shorter duration of the stimulus pulses used in the present experiments. Bagshaw and Evans (2) used 0.25-ms pulses, five times the duration used here. The conversion factor, calculated from the strength–duration curve in Fig. 6 of Stoney *et al.* (41), is 0.55. This value is close to that calculated by Ranck (35) and it suggests that the estimated current spread should be reduced to 0.71 of the value above.

In some cats, a second bipolar electrode was positioned 2 mm lateral to, but in the same frontal and horizontal planes as the cVPL electrode, as a control for stimulus spread to the internal capsule. The threshold intensity for excitation of VPL neurons was always higher at this internal capsule electrode than at the cVPL electrode; furthermore, the threshold at the cVPL electrode itself always increased if the electrode was raised or lowered to a new horizontal plane. Thus, it is unlikely that current was exciting axons of the internal capsule; however, it is likely that whatever was stimulated, leading to excitation of VPL neurons, was within the cVPL.

The larger sample of this experiment confirmed the preliminary observation of Jabbur *et al.* (27) that thalamic *sa* neurons are not driven by cVPL stimulation. Furthermore, it showed that it is primarily the thalamic *m* neurons that are driven by cVPL stimulation. Whether the results are seen to be in accord with those of Bava *et al.* (5) depends on the meaning attributed to the term lemniscal.

The precise significance of the terms lemniscal and extralemniscal was never made clear by Bava *et al.* (5), who said they were using the terms "primarily in their anatomical meaning, as defined by Mountcastle." Yet, Mountcastle's (31) lemniscal-extralemniscal classification scheme is physiologic rather than anatomic for it depends only on the discharge properties of the neurons. Furthermore, *all* neurons studied by Bava's

group responded to stimulation of the medial lemniscus and *must* be considered lemniscal in the anatomical sense. In the study by Jabbur *et al.* (27), all but one neuron in a sample of 232 VPL neurons responded to dorsal column stimulation, implying that perhaps all VPL neurons should be considered lemniscal in this sense. Thus, an anatomical relationship with the medial lemniscus does not seem to determine responsiveness to cVPL stimulation.

Bava *et al.* (5) also varied their usage of these terms, saying of group I and group II neurons: "as far as can be inferred from tests of cutaneous electrical stimulation, the former can be said to be lemniscal, the latter extralemniscal in nature." Continual references to receptive fields as defining characters of lemniscal and extralemniscal neurons lead the reader to believe the terms were being used in a physiological sense. In fact, Bava *et al.* (8) later referred to use of the terms in their functional rather than their anatomic meaning, writing of the "lemniscal mode of operation."

The partitioning of thalamic neurons into *s*a and *m* sets depends only on the size and distribution of their excitatory receptive fields as estimated by electrical stimulation of the paw pads. On the basis of this criterion alone, the *s*a neurons would be classified as lemniscal neurons and the *m* neurons as extralemniscal neurons (31), apparently confirming the notion of Bava *et al.* (5) that the excitatory influence of the cVPL is exerted upon extralemniscal neurons. But according to Mountcastle (31), lemniscal neurons also must have modality specificity, low thresholds for peripheral activation, faithful following of high rates of peripheral stimulation, and topographic organization, whereas extralemniscal neurons also must have mixed modalities, higher thresholds, lesser ability to follow iterative stimulation, and a nontopographic distribution. Mann (30) recently reviewed the concept of lemniscal neurons as it applies to sensorimotor cortical neurons and concluded that no set of cortical neurons qualifies as lemniscal by the above criteria. It can be reasonably asked whether thalamic *s*a and *m* neurons qualify as lemniscal and extralemniscal by the same criteria. Clearly *m* neurons have larger receptive fields. But Harris (21) noted that mixed touch and hair receptive fields (multimodal) occurred in 5% of *s*a neurons and 5% of non-*s*a (including *m*) neurons. In the present experiment, only 11 neurons with mixed receptive fields were seen. Of these, nine were *s*a neurons and only two were *m* neurons. Thalamic *m* neurons have poorer frequency-following ability, averaging only 29 stimuli per second, compared with the 42 stimuli per second of *s*a neurons, but they have lower thresholds (averaging 5.5 mA) than *s*a neurons (averaging 6.5 mA) (21). The *s*a neurons appear to be roughly topographically organized; f,*s*a neurons are isolated more often in medial tracks; h,*s*a neurons in lateral ones. Whether the *m* neurons are topographically organized cannot be

determined with the small samples available. They can be isolated throughout the nucleus [(22, 27) and this study], but Harris (21) pointed out that a topographic organization of sorts may be discernible if one compares the responses to stimulation of the paws. Thus, near the forepaw focus *m* neurons discharge in a particular pattern in response to CF stimulation but in different patterns to the other paws. If the same observation were to apply to *m* neurons near the hind paw focus, a rough topographic organization, much like that described previously for cortical *m* neurons (46), could exist. In summary, thalamic *s*a neurons have small receptive fields, higher (not lower) thresholds, modality-purity and mixed modalities, better frequency-following ability, and a topographic organization, whereas *m* neurons have larger receptive fields, lower (not higher) thresholds, modality-purity and mixed modalities, poorer frequency-following, and possibly a topographic organization. Thus, if all criteria must be fulfilled, *s*a neurons are not lemniscal neurons, nor are *m* neurons extralemniscal. Like cortical neurons, no set of thalamic neurons is either lemniscal or extralemniscal. Yet, in the anatomical sense both *s*a and *m* sets are lemniscal neurons (5, 27).

The relationship between thalamic *s*a and *m* neuron sets and groups I and II of Bava *et al.* (5) is also unclear. Those authors attribute a wider range of latencies, a greater number of spikes per response, and poorer frequency-following ability for lemniscus stimulation and wide, bilateral receptive fields to group II neurons, whereas group I neurons have circumscribed contralateral receptive fields. It was already noted that thalamic *m* neurons have poorer frequency-following ability, and they discharge greater numbers of spikes per response (21), but it should be noted that these are statistical statements. In fact, the range of frequency-following ability of *s*a neurons completely overlaps that of *m* neurons, and the range of number of spikes per response of *m* neurons completely overlaps that for *s*a neurons. The range of first-spike latencies of the two sets is almost exactly the same, although the mean for *m* neurons is greater (21). All these comparisons are for CF stimulation (21), but Jabbur *et al.* (27) pointed out the similarity of CF responses and those to stimulation of the dorsal columns. Presumably, responses to lemniscal stimulation would also be similar. It appears that group I corresponds to thalamic *s*a neurons in the present study and group II corresponds to thalamic *s*b, *s*c, and *m* neurons in these properties, yet not all *s*b, *s*c, or *m* neurons responded to cVPL stimulation, a property of *all* group II neurons.

According to Bava *et al.* (5) neurons activated by cVPL stimulation were concentrated in the VPL caudal to frontal plane A10 and mainly in planes A8.5 and A9. Furthermore, they said that only stimuli in planes A9.5 through A8.5 of the cVPL were effective in activating VPL neurons. The

cVPL-responsive neurons in the present study did not concentrate in the posterior part of the nucleus, but were spread throughout the anterior–posterior extent. Fewer tracks were made through the posterior parts of the nucleus, because experiments were always begun with tracks in the anterior portion, working backward. However, this does not account for the failure to observe a caudorostral gradient. More than half of the thalamic *m* neurons were isolated in A9 to A8. Carreras *et al.* (13) also failed to find any such gradient.

Neurons in this study were not driven from a fixed point within the contralateral nucleus, but from the same frontal and sagittal planes in which they resided. There was no tendency for neurons in the anterior part of the nucleus to have higher thresholds for activation, as would be required if the observation of Bava *et al.* above were also true here. Again, the observations of this experiment are consistent with those of Carreras *et al.* (13).

An explanation for the observed decrease and, finally, abolition of cVPL responsiveness by blocking activity in the contralateral cortex either with KCl or with ice is not readily at hand. Bava *et al.* (5) reported that cVPL responsiveness of VPL neurons was unaffected by transection of the corpus callosum; however, transection in the region of the posterior commissure abolished it. Furthermore, responsiveness to cVPL stimulation is resistant to ablation of sensorimotor cortex, either ipsilateral (7, 13) or contralateral to the recording site (5). This is not to say that the commissural transmission is not modulated by cortical circuits. That responsiveness of the VPL neurons to cVPL stimulation was altered without altering responses to peripheral stimulation suggests that the influence is exerted upon neurons in the cVPL or upon some interneuron in the pathway from the cVPL to the VPL.

The pathway for excitation of VPL neurons by cVPL stimulation is unknown. Bava *et al.* (5) asserted that the activation was in all cases orthodromic and synaptic because of the poor frequency-following ability of the pathway and the long latency, but poor frequency-following of *antidromically* conducted spikes occurs elsewhere (1). Direct connections from one VPL to the other have been described in various species and these connections involve "moderate" to "comparatively fine myelinated fibers" (18, 36). If the responses observed here were conducted directly to VPL neurons over such fibers, they must be extremely fine, as estimated from conduction velocities of Fig. 2A. They are even smaller than those of the corpus callosum interconnecting the visual cortices (42, 43). This latter group also contains some unmyelinated fibers; whether any of the interthalamic fibers are unmyelinated is unknown. However, the system is presumably symmetrical and some antidromic responses should be expected.

As pointed out by Swadlow and Waxman (42, 43), in such fine fibers antidromic latencies can be highly variable. They reported a variation of as much as 22% in latency at various times after a previous spike. In Fig. 2A, the horizontal line is plotted at this upper limit of variability. Responses represented by points below this line could be antidromic rather than orthodromic. Similarly, it could be argued that neurons that show smaller variability in latency of responses to cVPL stimulation than for known synaptic CF inputs are perhaps antidromically excited from the cVPL. Thus, responses represented by points above and at some distance from the regression line in Fig. 2B may be antidromic. However, as pointed out by Swadlow *et al.* (43), only collision or invariant latency for the second of two suprathreshold stimuli delivered at the appropriate interstimulus interval are reliable indicators of antidromic conduction. Future research into interthalamic conduction should examine these properties. On the other hand, it is possible that cVPL stimulation excites fibers of passage (36) leading to VPL excitation, thus explaining the lack of obvious antidromic responses. The origin of these fibers, if they are involved, remains obscure; control stimulation procedures indicate that they do not come from dorsal, ventral, or lateral aspects of the nucleus.

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