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Authors

Swett, John E
Bourassa, Charles M

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DETECTION THRESHOLDS TO STIMULATION OF VENTROBASAL COMPLEX IN CATS

JOHN E. SWETT and CHARLES M. BOURASSA

Department of Anatomy, California College of Medicine, University of California, Irvine, Calif. (U.S.A.) and Department of Psychology, University of Alberta, Edmonton, Alberta (Canada)

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Key words: sensory detection — subcortical stimulation — detection threshold

SUMMARY

Cats were trained to indicate, by bar pressing for food rewards, their detection of stimulation of the ventrobasal (VB) complex delivered through implanted bipolar electrodes. By varying stimulus intensity it was possible to determine thresholds for detection. Scaling stimulus intensity relative to the appearance of a minimal evoked potential allowed comparisons between animals and also comparisons with results obtained by stimulation of peripheral nerve. Animals could detect VB stimulation, but only at stimulus intensities consistently stronger than those required for minimal appearance of an evoked response in ipsilateral primary somatosensory cortex. Results of VB activation differed from cutaneous nerve effects in that VB detection thresholds were markedly influenced by stimulus frequency. They were lowest at frequencies above 30 Hz and increased greatly at lower frequencies. Discomfort or pain did not seem to result even from relatively high stimulus intensities. The results compare well with observations obtained from stimulation of VB in humans. The appearance of an evoked cortical response is not necessarily correlated with behavior. Under appropriate conditions, behavior can be elicited predictably with minimal electrocortical activity; under other conditions detection may be absent even when large numbers of cortical neurons are activated. We suggest that regions of the cerebral cortex receiving thalamocortical projections from VB may not be essential in the detection process.

INTRODUCTION

The dorsal column–medial lemniscus (DC-ML) system, a major somatosensory pathway of the spinal cord, relays information from mechanoreceptors of skin, muscle and joints to the cerebral cortex in a well-organized somatotopic fashion. The functional properties of the neurons that compose this system have been intensively studied and appear to be well suited to subserve fine tactile discrimination and localization, vibra-

tory sensibility and kinesthesia^{1,13,34,38,61}. A number of studies have, however, raised serious questions concerning the role of the DC-ML system in sensory detection and discrimination of somatic stimuli because complete transections of the dorsal columns do not produce the marked sensory deficits that would have been expected from neurophysiological analyses^{6,47,48,60,61}.

Recent studies suggest, however, that the dismissal of the role of the DC-ML system in conscious sensation is premature. A series of experiments which tested the ability of cats to detect afferent signals which reached the brain exclusively by way of surgically isolated dorsal columns revealed that sensory detection thresholds were identical to those obtained from normal, intact animals³⁵. These results have been confirmed and extended to demonstrate that the isolated dorsal columns are able to convey some information about location and quality of tactile stimuli¹⁸.

In our previous work, the technique of measuring sensory detection thresholds involved stimulation of primary afferents exclusively^{12,35,53}. Knowing that selective excitation of an extremely small population of primary afferent axons caused behavioral detection^{12,23,35,58} it seemed likely that excitation of a numerically small and spatially restricted group of second and third order fibers along the DC-ML pathway to somatosensory cortex was causally related to detection. It then seemed reasonable to compare the behavioral effectiveness of a peripherally evoked sensory cue with one evoked centrally in the same pathway, i.e. stimulation of the medial lemniscus or ventrobasal (VB) complex in the region of the neuron population activated from the periphery, thereby influencing roughly the same thalamocortical projection system. It has been known for many years that an animal can be conditioned to respond predictably to stimulation of cortical or subcortical structures, but there has always been uncertainty as to the relative potency of CNS vs peripherally evoked sensory cues for eliciting behavior¹⁶.

The present study compares sensory detection thresholds to stimulation of peripheral and diencephalic portions of the somatosensory projection system. The data reported here allow comparison between sensory detection thresholds produced by stimulating two separate portions of the DC-ML system, the cutaneous primary afferent fibers and the medial lemniscus at its entry into VB. This comparison is made possible by using the minimal evoked cortical response as a marker, indicating the occurrence of a physiological response which serves as a reference point for relating stimulus intensity and behavioral detection thresholds.

METHODS

Operant conditioning procedures. The ability of an animal to detect thalamic stimulation was tested in 6 of 18 cats previously trained to lever-press for food rewards in response to sensory cues produced by direct electrical stimulation of peripheral nerve. The surgical, operant training procedures and apparatus do not differ significantly from those described previously¹². Briefly, cats learned first to lever-press for food rewards in response to auditory cues and to refrain from lever-pressing in the absence of these cues. When the animals demonstrated that they had learned this task by making con-

sistent short-latency responses to the stimulus presentation and few responses in the absence of the stimulus, they were anesthetized (Nembutal, 35 mg/kg i.p., Abbott) and recording and stimulating electrodes were surgically implanted. Three days following surgery the animals were returned to the test chamber and retrained by pairing peripheral nerve or thalamic stimulation with the auditory cues. The auditory cues were gradually withdrawn until the animals responded exclusively to sensory cues evoked from peripheral nerve or thalamus.

A behavioral trial consisted of a stimulus presentation for a duration of 15 sec. If the animal responded within that period it was assumed that the stimulus was supra-threshold for detection and the animal was allowed to continue to press until 4 or 5 pellets of food were received. Failure to respond indicated that the stimulus was not detected. Precautions, such as catch trials and random time intervals between trials, were introduced in order to eliminate the possibility of an animal responding to extraneous cues or temporal intervals. Numerous trials (40–80) were conducted every day for 2–3 weeks at stimulus intensities above and below an intensity at which the animal responded correctly in 50% of the trials. This intensity was defined as the threshold for sensory detection. Data for plotting behavioral response curves, from which sensory detection thresholds were measured, were accumulated if there was less than a 5% probability that the animal would lever-press during any catch trial. Although sensory detection thresholds were normally measured first with peripheral nerve stimuli, identical procedures were used later in the same animal when detection threshold for thalamic stimulation was measured.

Thalamic behavioral data were obtained in 2 animals in which no peripheral nerve electrodes were implanted. This was done to test the possibility that peripheral stimuli might in some manner influence VB detection thresholds. These animals were trained identically to the others. The absence of peripheral inputs made it difficult to obtain good VB placements. One animal had well-placed electrodes in VB and its behavioral response curves were very similar to those reported for the other animals.

Electrodes. Peripheral nerve stimulating electrodes of the type described in our previous work^{12,40}, were implanted on either one or both superficial radial nerves of the cat's forelimbs.

Several holes were drilled through the cranium in the region directly overlying the forelimb projection zone on the postcruciate gyrus. Each hole received a screw electrode and evoked responses were recorded from each site to confirm placement over the region of maximum responsiveness, i.e. the region providing the lowest threshold and shortest latency response. Recordings were made under deep barbiturate anesthesia and no signal averaging was used to ensure that the site of maximum responsiveness could be distinguished from surrounding 'off-focus' regions.

The thalamic stimulating electrodes consisted of a pair of insulated, stainless steel needles separated by 1.0–1.5 mm. Insulation was removed from the tips for a distance of 0.5 mm. The electrodes were positioned in the brain stereotaxically so that the medial electrode came to rest within the coordinates, anterior, 6.5–7.5; lateral, 6.0–7.0; and depth of zero to –1.5⁵⁰. This region encompasses the entry of the medial lemniscus into the posterior portion of the VB complex of the thalamus. Recordings were made from

these electrodes and their location was adjusted until a short-latency, large-amplitude response could be evoked by stimulation of the contralateral peripheral nerve. When, in turn, the thalamic electrode was used for stimulation, polarity was chosen so that the maximal cortical evoked response could be recorded from the same 'on-focus' cortical site responding to peripheral nerve volleys. The cortical site was generally found to be about 2–3 mm caudal to the postcruciate dimple and 2–3 mm lateral to it.

Finally, before electrodes were fixed in position, it was confirmed by recording simultaneously from cortical and VB electrodes, that minimal evoked potentials appeared at the same stimulus intensity to peripheral nerve stimulation. All electrodes were anchored in place with dental cement along with an electrical connector for mating cables with recording and stimulating equipment.

After completion of all behavioral trials the animals were sacrificed and VB electrode placements were verified with routine histological procedures. A 1.5 V positive charge was applied to the electrode that had served as the cathode of the stimulating electrode pair during the behavioral trials. The animal was then perfused with 10% formalin–1% potassium ferrocyanide mixture. The subsequent formation of a Prussian blue spot at the cathode tip allowed identification of the stimulus site.

Recording procedures. Unaveraged evoked waveforms in primary somatosensory cortex, produced by VB or peripheral nerve stimulation, were monitored daily during the behavioral training periods to ensure that stimulating and recording conditions remained constant. If any change was noted the animals were withdrawn from the study. Averaging of the evoked potentials was necessary in order to obtain an accurate value for the minimal evoked response. Recordings were made with a Tektronix 122 pre-amplifier, the output of which was led into one channel of a Tektronix 502 oscilloscope. The vertical deflection signal from the oscilloscope was digitized by a signal averager (Enhancetron 1024), and the averaged signal displayed on the other oscilloscope channel. No less than 256 responses were accumulated for each averaged record. Most of the averaging was done at high sampling rate to resolve high frequency components. The input band-pass filter was set at 10 or 40 kHz and the digitizing rate was 5–10 μ sec per channel for 1024 channels. The early components of the cortical evoked responses from peripheral nerve or VB were readily distinguished by this procedure. Each averaged record was photographed or written out on an x-y plotter. Averaged records were periodically obtained in the awake, unanesthetized animal to confirm threshold response values for the evoked cortical potentials from peripheral and thalamic stimuli and to obtain sample records of evoked waveforms associated with several stimulus intensities used during the behavioral trials.

After completion of the behavioral trials the animals were anesthetized so that activity from the peripheral nerve could be measured directly from the posterior division of the brachial plexus. It was verified that the minimal stimulus value inducing a response in peripheral nerve, also produced a minimal response from the electrodes in VB and somatosensory cortex. From this it could be inferred that minimal cortical evoked responses to VB stimuli represented minimal excitation of neurons near the tip of the VB cathode.

Three of the 6 animals in the experimental series failed to meet all necessary crite-

ria. One animal died from an unexplained cause just prior to the final control recordings; the other 2 revealed shifting thresholds due to nerve or electrode damage and were dropped from the series. Before these problems emerged data observed from these animals were, for all practical purposes, identical to the results reported from the 3 animals which successfully completed the series.

Stimulation. Rigid control of stimulus conditions was an essential aspect of these experiments. The reliability of the data points used for constructing the behavioral response curves was, mostly, determined by the accuracy and repeatability of the stimulus. The special stimulator used in this study has undergone minor design modifications and improvements but it has the same functional principles originally described by Mills and Swett³³. The stimulator, of constant-voltage type, assured linearity of pulse amplitude adjustment with electrode impedances as low as 50 Ω . Peripheral nerve electrode impedances were usually between 500–900 Ω . Thalamic electrodes had impedances of 2–5 k Ω . At evoked response thresholds stimulus current values at VB stimulus sites was 80–200 μ A and for nerve 250–500 μ A.

All stimulus pulses were rectangular and monophasic with a duration of 0.1 msec. Behavioral data were obtained with at least two basic stimulus frequencies, low-rate (4 Hz) and high-rate (100 Hz), and with some animals thresholds were also obtained at other pulse rates or pulse trains of varying frequencies and durations. All averaged evoked potential records were made at 4 Hz stimulus rates or less.

Stimulus intensities are expressed in values relative to an electrophysiological criterion (see refs. 12 and 53) in which the relative value of 1.0 T represents the intensity required to evoke a minimal cortical response to stimulation of VB or the contralateral superficial radial nerve. As the cortical response foci were made to be as congruent as possible, the minimal activity produced at 1.0 T from either stimulus site should represent comparable numbers, but not necessarily the same populations, of active neurons at the recording site. When stimulus intensity is raised to some multiple of 1.0 T, the electrophysiological and behavioral consequences will be nearly identical for the same stimulus site in different animals, but when two different stimulus sites are compared, as in the present study, one must recognize that the electrophysiological and behavioral consequences will be different. For example, doubling stimulus intensity (2.0 T) at 4 Hz rates at both sites will not produce the same reactions because the structures influenced by the two stimuli will be different.

RESULTS

After an animal learned to lever-press for food rewards in response to low-intensity cutaneous nerve or VB stimulation, data were accumulated for constructing behavioral response curves in order to compare sensory detection thresholds between the two stimulus sites. VB stimulation produced behavioral response curves which differed markedly in several respects from those obtained by cutaneous nerve stimulation. These differences are summarized in Fig. 1.

Sensory detection thresholds occurred with cutaneous nerve stimulation at intensities of, or slightly below, 1.0 T, an intensity which produces barely measurable

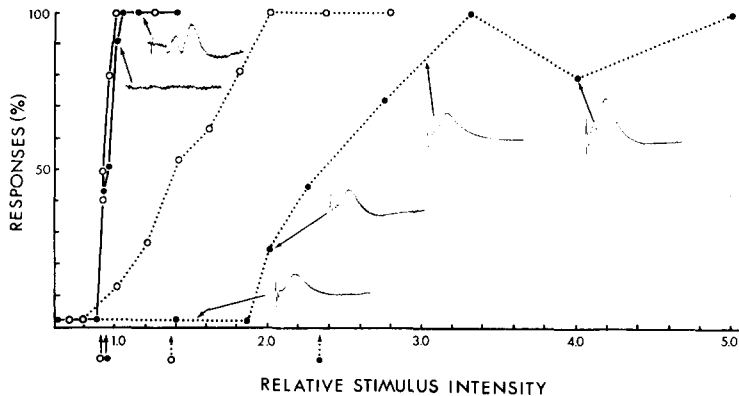


Fig. 1. Comparison of behavioral response curves of the same animal in response to cutaneous nerve (solid lines) and VB stimulation (dotted lines) at low (4 Hz = ●) and high (100 Hz = ○) stimulus rates. Detection thresholds for each stimulus condition are indicated by the small arrows beneath the abscissa. Detection was made in 90% of the trials in the absence of electrocortical activity with low rate stimulation of cutaneous nerve. VB stimulation at low rate did not produce detection until an intensity of 2.35 T, well above values which produced evoked responses. With high-rate stimulation cutaneous detection thresholds were not altered significantly, however, VB stimulation caused a reduction in threshold to 1.38 T. Samples of averaged evoked responses are shown at several relative intensity values. The evoked responses at 1.5 T and 2.0 T for low-rate VB stimulation were unaccompanied by behavioral detection. Calibration: 5 msec, 50 μ V for traces recorded at intensities below 2.0 T; 100 μ V at 2.0 T, 200 μ V at 3.0 T and 4.0 T.

peripheral nerve activity and minimal evoked response activity in primary somatosensory cortex as described in our previous work¹². In the same animals, detection thresholds resulting from VB stimulation occurred always at a stimulus intensity significantly greater than that required to produce a cortical evoked response. In other words, as shown by the evoked responses in Fig. 1, behavioral indication of sensory detection with VB stimulation never occurred unless an evoked cortical response was already clearly evident, whereas with stimulation of primary afferent fibers detection occurred when so few fibers were activated that no electrical event could be observed in cerebral cortex at detection threshold even if averaging methods were employed. During final control procedures no activity could be recorded from peripheral nerves at this same stimulus value.

The evoked responses shown in Fig. 1 were recorded at rates below 4 Hz at the end of behavioral sessions just prior to terminal control procedures and are plotted with arrows on the behavioral response curves to indicate the relative stimulus intensities with which they were produced. The potentials evoked by thalamic stimuli showed characteristic brief latencies of 1–2 msec in SI cortex; the distinct potentials seen at 1.5 T and 2.0 T were not accompanied by any indication of sensory detection at 4 Hz stimulus rates.

A significant difference was revealed in the slopes of the behavioral response curves. A small increase in stimulus intensity to the cutaneous nerve at near-threshold values for detection caused a marked and abrupt improvement in the animal's ability to respond correctly to the stimuli. A comparable increase in stimulus intensity applied

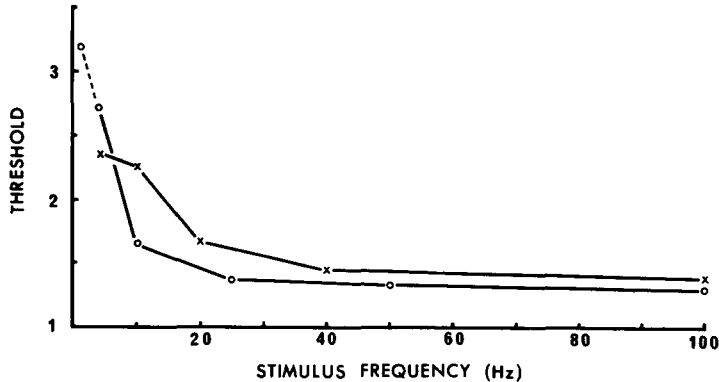


Fig. 2. Influence of stimulus rate on VB behavioral detection thresholds. The ordinate (threshold) is scaled in relative stimulus intensity. Each curve is constructed from data of a different animal. The dashed line on the open-circle curve denotes uncertainty of behavioral responding at 1 Hz. Increase of stimulus rate produced a decrease in behavioral detection threshold until, at rates above 30 Hz, no further decrease in behavioral threshold values occurred.

to VB produced a much smaller influence on the animal's detection performance. These results suggest that the effect of exciting a moderately large number of neurons with VB stimulation is substantially weaker than that produced by exciting a very small population of cutaneous primary afferent fibers.

Another important feature of the data was the effect of stimulus rate on sensory detection threshold. Stimulus rate did not produce any significant change in sensory detection threshold from peripheral nerve. The animal represented in Fig. 1 demonstrated a detection threshold of 0.96 T with 4 Hz stimulation of the superficial radial nerve; with 100 Hz stimulation of the same nerve the detection threshold declined only slightly to 0.92 T. Temporal facilitation, produced from cutaneous primary afferent sources, had little effect on threshold for sensory detection.

Alteration of frequency of VB stimulation produced an entirely different phenomenon. Low-rate stimulation (4 Hz) did not produce detection until the intensity was 2.34 T or greater, a value substantially above threshold for cortical evoked responses. High-rate stimulation (100 Hz), on the other hand, caused the sensory detection threshold to drop sharply to a value of 1.38 T. In no instance, however, did high-rate VB stimulation, even at 300 Hz, cause the sensory detection threshold to decline to values comparable to those produced from primary afferent fibers.

The relationship between the frequency of the VB stimulation and sensory detection threshold for two animals is shown in Fig. 2. At stimulus rates of 1 Hz or less the animals appeared uncertain as to the nature of the sensory cues and often failed to depress the lever even with stimulus intensities above 3.0 T. Only one of the animals responded well enough to allow us to estimate that detection threshold occurred between 3.0 T and 3.5 T. This erratic performance decreased at rates above 4 Hz and the animals' behavior became more predictable. Between stimulus rates of 4 Hz and 40 Hz sensory detection thresholds declined, this decline being most pronounced between 4 Hz and 20 Hz. Rates above 30 Hz did not, as a rule, produce any further change in sensory detection threshold.

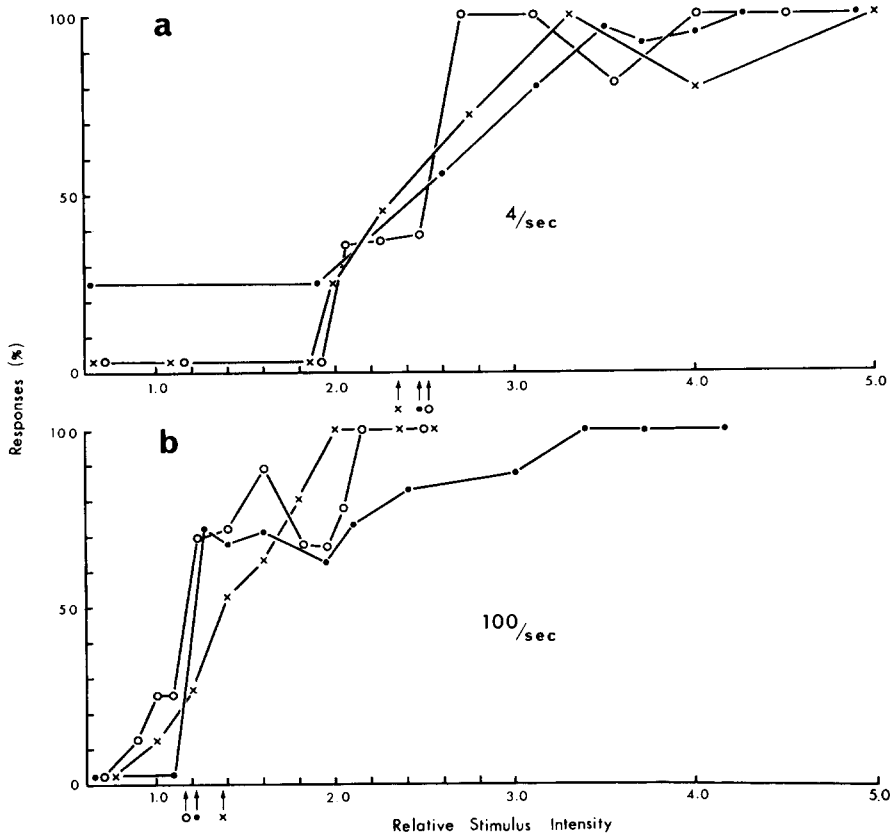


Fig. 3. Consistency of behavioral responding to thalamic stimulation of 3 animals with low- (a) and high-rate (b) stimulation. Sensory detection thresholds for each animal are indicated by the small arrows beneath the abscissae. Even with high-rate stimulation detection thresholds were consistently above electrocortical response threshold, 1.0 T. This comparison illustrates that there was little difference among the animals in the pattern of responding to thalamic stimulation.

The nature of this temporal effect was investigated in more detail using brief trains of high-frequency (100 Hz) pulses delivered once per second. Comparing these conditions to the normal situation in which stimuli were applied to the animal continuously during the duration of a trial, we found continuous rapid stimulation was not essential to produce minimal detection thresholds. More precisely, a stimulus train of 10 pulses at 100 Hz, repeated once per second, produced detection thresholds equivalent to any continuous stimulus rate above 30-40 Hz. A train of 5 pulses at 100 Hz, repeated once per second, produced detection thresholds equivalent to those produced by a continuous 10 Hz stimulus. Thus, minimal sensory detection thresholds resulting from VB stimulation required repetitive stimuli (at 30 Hz or more) for durations between 50 and 100 msec.

Fig. 3. illustrates the advantage of using evoked response threshold as a reference point for normalizing behavioral data. The method gives reliable and consistent results. The behavioral curves plotted in Fig. 3 show the similarity for sensory detection

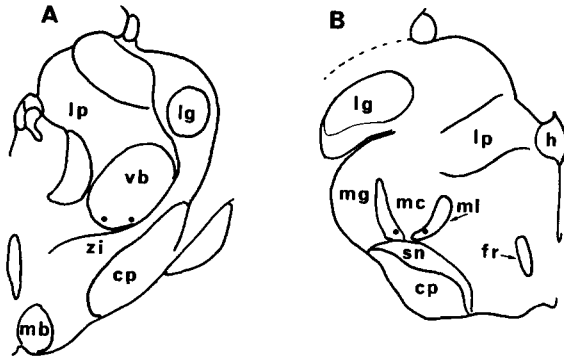


Fig. 4. Localization of stimulus sites from histological reconstruction of electrode tip placements. A: the large dots in ventrocaudal VB indicate the stimulus sites that were nearly identical for 2 animals \times and \circ in Fig. 3. The lateral electrode site was the cathode in both cases. B: electrode tip locations for one animal (\bullet) plotted in Fig. 3. The medial electrode tip, the cathode, was located within the medial lemniscus (ml) and the lateral one was situated in the brachium of the inferior colliculus. Abbreviations: cp, cerebral peduncles; fr, fasciculus retroflexus; h, habenula; lg, lateral geniculate body; lp, nucleus lateralis posterior; mb, mammillary body; mc, magnocellular portion of medial geniculate body; mg, medial geniculate body; ml, medial lemniscus; sn, substantia nigra; vb, ventrobasal complex; zi, zona incerta.

thresholds and behavioral response curves for 3 different animals with both low- and high-rate stimulation parameters. One animal showed a high error rate (Fig. 3a) which seemed not to have influenced behavioral threshold. With 4 Hz stimulation of VB (Fig. 3a) sensory detection thresholds occurred between 2.34 T and 2.55 T. The difference between these two thresholds represents a stimulus intensity range of only 100 mV in absolute stimulus value. The same consistency appears with high-rate stimulation (Fig. 3b), but in this situation the sensory detection thresholds dropped to values between 1.16 T and 1.38 T, a total decline of about 600–700 mV in absolute stimulus intensity.

Initial training of the animals was normally accomplished by beginning first with peripheral nerve stimulation and then transferring the animal to VB stimulus cues. We reasoned that prior training to cutaneous sensory cues might modify, in some unknown manner, behavioral response characteristics or sensory detection thresholds determined by VB stimulation at some later period in the experiment. To test this possibility, one animal was successfully trained to respond exclusively to VB stimulation. The results revealed that detection threshold was 2.72 T at 4 Hz and 1.29 T at 100 Hz, essentially the same as the data shown in Fig. 3. Prior conditioning through primary afferent inputs had no noticeable effect on the ability of a cat to respond predictably to thalamic stimulation.

Stimulation of VB at 100 Hz produced behavioral response latencies similar to, although more variable than, those obtained from cutaneous nerve. At the 4 Hz stimulus rate the variability of the latencies increased greatly. The animals appeared to be uncertain of the sensory cues produced by this low rate stimulation. As seen in Fig. 3, it was not unusual for them to miss making a correct response with stimulus intensities far above sensory detection thresholds, behavior which almost never occurred with peripheral nerve stimulation. Other qualitative differences appeared in the animals'

general responsiveness to peripheral nerve and VB stimuli. Stimulation of the peripheral nerve at 4 Hz with intensities above 2.0–2.5 T caused clear-cut signs of agitation and discomfort from the animal. At 100 Hz the stimulus could not be increased much above 1.3 T without causing similar aversive reactions. VB stimulation, on the other hand, never induced any reaction that suggested discomfort or pain with stimulus intensities as high as 7.0 T at 4 Hz or 5.0 T at 100 Hz. In contrast to reactions to peripheral stimuli, these strong VB stimuli caused widespread electrocortical activity of large amplitude, but the animals, if they showed any overt behavioral reaction, made only a few orienting responses.

The anatomical localization of the VB stimulating electrode placements revealed that two of the three animals reported in this study had the electrode tips within VB proper. Fig. 4a shows a histological reconstruction of two nearly identical electrode placements in two animals described in these experiments. The tips of the electrode pairs lay just rostral to the ventrocaudal boundary of VB and the magnocellular portion of the medial geniculate body. The laterally situated electrodes of the pairs lay within the region of VB most likely to receive input from the contralateral cuneate nucleus^{11,22}. Fig. 4b illustrates the electrode locations in the other animal. The lateral electrode placement was within the brachium of the inferior colliculus whereas the medial electrode was situated within the medial lemniscus. The histological data are in close agreement with the electrophysiological data collected during initial implantation of the electrodes (see Methods) and subsequent evoked potential recordings from cerebral cortex. Thus, the behavioral responses of the animals were nearly identical whether stimulation was applied directly to VB or to the medial lemniscus immediately caudal to the ventroposterior margin of VB.

DISCUSSION

The principal finding of this study is that behavioral detection of VB stimulation occurred only if a significant amount of evoked electrocortical activity existed, whereas detection of cutaneous nerve stimuli, measured in the same animals, invariably occurred at intensities which activated so few cortical units that it was difficult to observe any evidence of an electrocortical response¹². This difference in behavioral threshold is a constant finding and one which has interesting implications, but as stimulus intensity was based on relative values, scaled to a minimum response at the same cortical recording site, it is necessary to resolve whether the difference is real or artifactual.

Waveform, temporal factors, positions of cortical foci, and inherent limitations in resolving small signals all interfere with the accuracy of determining 1.0 T. The only factor which could contribute to an apparent, rather than a real, difference in behavioral thresholds would be preferential influence from the VB evoked response. Conversely, this difference would tend to be reduced if the cortical recording electrode had been overly influenced by the cutaneous response. For these reasons the cortical electrode was first fixed into position over the forelimb focus and then the VB focus was made to be as congruent as possible by adjusting final position and polarity of the VB electrodes. Correct on-focus localization for cutaneous stimuli was confirmed by showing that a

minimal cortical potential occurred at a stimulus intensity necessary for minimal activation of peripheral nerve¹². As a result, it is highly unlikely that VB activation threshold was overestimated; recording conditions, if anything, favored underestimation of behavioral threshold differences relative to evoked response thresholds. We conclude that a real and significant difference exists in the amounts of electrocortical activity present when behavioral detection threshold is attained from both stimulus sites and that estimates of 1.0 T did not contain any significant errors of measurement.

Stimulation of VB in man, as in the cat, produces large-amplitude electrocortical responses without conscious experiences^{28,29}. In both species higher rates of stimulation produce lower detection thresholds. Disagreement exists concerning the lowest frequencies required for minimal detection thresholds in humans; rates as low as 15–20 Hz^{28,29} or as high as 180 Hz have been reported². In our animals minimum detection thresholds occurred at stimulus rates in excess of 30 Hz. At lower stimulus rates evoked potentials became larger, and detection thresholds increased until, at rates below 2 Hz, behavioral responding became uncertain even with stimulus intensities in excess of 7–8 T.

In man, sensations produced by VB stimulation are referenced to contralateral somatic regions^{2,24,28,56}. Judging by the orienting responses that appeared on the first few stimulus presentations, this was also true for the cat. Strong VB stimulation in man does not cause painful sensations^{2,28,29} and our observations in the cat agree with this.

There is disagreement about the total time that stimuli must be applied to produce detection. In cat, isolated pulse trains (10 msec interval between pulses) of less than 100 msec in duration, are as effective in producing minimum detection thresholds as continuous stimulation at the same rate. With train durations less than 50 msec, detection thresholds increased. This differs from reports that stimulation of the human thalamus must be applied for long durations (500–1000 msec) before detection occurs^{28,29}. Albe-Fessard et al.², however, reported effective stimulus durations in man that were similar to our findings. This discrepancy probably reflects differences in threshold testing procedures and test conditions.

Stimulation of VB, compared with stimulation of peripheral nerve, required a large range of stimulus intensities to define the behavioral response curve. The change in electrocortical response amplitude over this range was large and suggests that sensory cues were ill-defined. The decrease in sensory detection thresholds caused by temporal facilitation demonstrates that sensory experience is stronger at a given stimulus value when higher frequencies are employed¹⁷.

We must emphasize that our procedures measure the animal's behavioral responsiveness to the occurrence of a stimulus, i.e. detection, rather than its ability to differentially respond to a change within the stimulus condition, i.e. discrimination. Excitation of 1–2 axons of a cutaneous nerve is all that is required for detection to take place^{12,23,55,58}, but stimulation of VB, in respect to amount of cortical activity produced, is much less effective in both cat and man. How is the wide discrepancy between the ability to detect VB and peripheral nerve stimulation to be explained?

Neither bilateral destruction of the dorsal columns nor, conversely, bilateral destruction of the anterolateral columns, are able to interfere with the ability of the cat

to detect minimal somatosensory stimuli, suggesting that the detection circuits, wherever they may be anatomically, receive convergence actions from the medial lemniscus system and anterolateral pathways^{4,18,35,36,45,46,53,59}.

As VB is a site of convergence for somatosensory activity from the dorsal column nuclei and lateral cervical nuclei^{8,9,11,22}, but possibly not the spinothalamic pathway^{10,25}, it seemed a logical candidate to contain, or have access to, neural elements of the detection system. As already indicated, direct electrical stimulation of VB, in comparison with cutaneous afferents, is relatively ineffective in causing behavioral detection. This ineffectiveness may be a consequence of unnatural patterns of activation of thalamocortical elements⁴⁴. Another possibility is that VB stimulation may elicit a powerful inhibition from the thalamic reticular nucleus which could modify cortical input by inhibiting thalamocortical fibers, but detection was more readily produced at higher VB stimulus frequencies, a condition that should increase the inhibitory influence of these fibers⁶². These possibilities may not adequately explain the difference between VB and peripheral nerve detection thresholds.

Stimulation of VB would by-pass one and possibly two stages of temporal or spatial amplification which are presumed to influence primary afferent signals^{27,31}. Lack of amplification, however, probably does not entirely account for the ineffectiveness of VB stimulation because the amount of electrocortical activity associated with VB detection thresholds is excessively large in comparison with the weak and often unobservable electrocortical events accompanying detection with cutaneous stimuli.

Even if only some neurons in SI and SII were necessary to mediate detection, it would seem reasonable to expect that VB stimulation would influence them in some manner^{21,26,32}. This suggests that VB stimulation does not simply by-pass stages of somatosensory signal amplification; it seems possible that this stimulation recruits neural elements which anatomically by-pass the detection circuits.

Activation of VB, or fibers of the medial lemniscus, produced detection in a consistent manner with comparable multiples of 1.0 T at specific stimulus rates in different animals. If detection had resulted from spread of current to neighboring, non-somesthetic circuits more variation in VB detection thresholds would have been expected. Even if detection was due to stimulus spread it does not adequately explain why VB activation did not result in detection. In a parallel series of yet unpublished observations, stimulation of the thalamic nucleus just rostral to VB (VL) produced consistently higher detection thresholds than those produced from VB. We infer the possible existence of some subcortical structure stimulation of which will produce detection in the absence of electrocortical activity.

It is conceivable that cerebral cortex may not have any, or perhaps only a limited, involvement in detection. Behavioral studies suggest that destruction of either primary (SI) or secondary (SII) cortical somatosensory projection zones, and sometimes both, cause little or no change in sensory detection thresholds although performance on tasks requiring certain kinds of discriminations may be impaired^{3,7,15,20,37,41}. While SI or SII may be able to mediate some functions of somesthesia⁵¹ they seem unessential for detection to occur. The same appears to be true of the primary auditory and visual cortices^{14,52,57}. In addition, studies of single units in VB, and in its cortical projections,

also raise questions about the role of SI in detection. It seems unlikely that neurons receiving convergent actions of cutaneous and muscle afferent inputs^{39,43,49,53,54} are part of the detection circuit because the latter inputs do not produce detection^{19,53}. These data demonstrate that many neurons in VB, as well as its projection zone in cerebral cortex, may have nothing to do with sensory detection.

If cerebral cortex is not directly involved then what structures might mediate detection?

The isolated dorsal column preparation gives rise to normal detection thresholds with minimal cortical involvement³⁵ while stimulation of VB produces detection only when marked cortical activity is present. This suggests that detection may be a consequence of the anatomical connections of the medial lemniscus with subcortical structures other than VB. A related concept was advanced by Liu et al.³⁰ based on spinal and brain stem lesion studies. Fibers of the medial lemniscus are known to project in significant numbers, not only to VB, but also to the zona incerta, medial portion of the medial geniculate body, superior and inferior colliculi and other brain stem and thalamic nuclei^{5,11,42}. Detection of VB stimuli may have resulted from antidromic activation of collaterals of the medial lemniscus. If these collaterals require higher stimulus intensities for activation than the cortically projecting fibers, this may explain why thalamically evoked detection consistently occurred at stimulus intensities well above threshold for evoked cortical responses.

Low rate stimulation of VB probably influenced a spatially and numerically restricted subset of medial lemniscus fibers and their collaterals with the possible consequences that inputs to the detection circuits were insufficient to cause detection as readily as very small inputs through primary afferent channels. High rate stimulation, which was much more effective for detection, may have served to partly restore the temporal facilitation that occurs in discharges of medial lemniscus fibers following a brief afferent volley.

It cannot be excluded that the detection process is influenced by somatosensory cortex. Cerebral cortex certainly appears to be involved in processing complex discriminations, but evidence also suggests that large numbers of cortical neurons are not involved in any direct manner in mediating detection. On the basis of available data it seems to us more likely that detection results from neural activity in subcortical structures, other than VB and its cortical projections, which receive convergent influences from the DC-ML system and the anterolateral pathways.

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