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Frequency selectivity is related to temporal processing in parallel thalamocortical auditory pathways

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Lemniscal and non-lemniscal parallel thalamocortical auditory pathways have been identified with the ventral medial geniculate body (MGB) vs. the dorsal and medial MGB, respectively. Lemniscal neurons have narrow frequency tuning and provide highly specific frequency information to the auditory cortex whereas non-lemniscal neurons generally have broader tuning and greater response lability, including plasticity of frequency receptive fields during learning. To determine if frequency selectivity is related to temporal fidelity of response, we measured both the breadth of tuning and neuronal excitability in a paired tone paradigm for single neurons throughout the MGB. Excitability to the second tone of a pair was directly correlated with frequency selectivity: the narrower the frequency tuning, the greater the excitability. Cells with broad tuning based on multiple-peak response areas also were less excitable than cells with single-peak RAs. Cells in the ventral MGB showed greater temporal fidelity of response (greater excitability) than cells in the dorsal and medial MGB. These findings show that high degrees of both frequency selectivity and temporal response fidelity are characteristic of the lemniscal, but not the non-lemniscal, thalamocortical auditory system.

INTRODUCTION

The medial geniculate body (MGB) is an obligatory thalamic synaptic link in the processing of acoustic stimulation from the periphery to the auditory cortex. The MGB is anatomically and physiologically heterogeneous. It is comprised of three major divisions: ventral (MGv), dorsal (MGd) and medial (MGm)[33,34]. These parallel auditory paths have been classified into the 'lemniscal' and 'lemniscal adjunct' components of the thalamocortical auditory system[30], with the MGv representing the former and the MGd and MGm comprising the latter. Other more detailed parcellations have been suggested[11,16], but all recognize the basic distinction between lemniscal and non-lemniscal paths.

Physiologically, the lemniscal MGv is tonotopically organized, projects topographically to auditory cortical fields that have organized representation of frequency (including 'primary' auditory cortex), has cells that are highly frequency selective (narrowly tuned), with shortest latency onset responses, and less lability of response than the MGd and MGm. The non-lemniscal MGd projects to secondary, non-tonotopic fields and has broadly tuned cells that have long latency responses. The non-lemniscal MGm projects to all cortical auditory fields (but to layer I rather than to layer IV as for the MGv and MGd), has cells with a wide range of morphologies and response properties, including onset latencies and frequency tuning that are generally intermediate to the values found in the MGv and MGd[7,16,17,35,45–47,49,50] (for review see ref. 3).

A major implication of these findings is that the parallel lemniscal and non-lemniscal systems have different functions in the processing of acoustic stimulation, with the MGv responsible for highly accurate representation of physical parameters such as frequency[3,43].

Given the existence and characteristics of these parallel inputs to the auditory cortex, the temporal aspects of acoustic processing become of particular interest. Temporal aspects of processing have been studied by presenting pairs of clicks at various interstimulus inter-

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vals (ISI) to determine the response of the second stimulus as a function of time of delivery after the first stimulus[4,5,8,25–27]. To summarize their findings, the response to the second click, when measured as an evoked field potential, passes through a period of inhibition, recovers (at approx. 100–150 ms) and then passes through a second phase of inhibition (approx. 150–250 ms). When measured in terms of neuronal discharge rate, more variety is observed in the responses, such as a facilitatory period preceding the 2nd inhibition[4,25].

The present investigation is concerned with two aspects of temporal processing: (1) a comparison of excitability functions among the three major subdivisions of the MGB; (2) a comparison of excitability functions with frequency selectivity within the same neuron. We used tones at the characteristic frequency (CF) rather than clicks, to avoid widespread frequency activation of the auditory system. This permitted a further inquiry into the extent to which any relationship between excitability and frequency selectivity is related to frequency. Preliminary findings have been reported in abstract[31].

MATERIALS AND METHODS

Subjects and preparation

The subjects were 38 adult male Hartley guinea pigs (*Cavia procellus*) (350–500 g). The organization and connectivity of the guinea pig MGB are similar to those of other mammals[36] (J. Winer, personal communication). They were housed in groups of 2–3 in standard guinea pig group cages on a 12 h light–dark cycle with food and water continually available. Surgery and recording were conducted during the light phase of the cycle with the animals under pentobarbitol-neuroleptic anesthesia (0.05 mg/kg atropine i.p., 35 mg/kg sodium pentobarbitol i.p. (Nembutal, Abbott Labs.), supplemented to maintain a state of areflexia with fentanyl and droperiodol (10 mg/kg i.p.; Innovar-Vet, Pitman-Moore). During surgery and anesthesia, body temperature was maintained with a heating pad. A dental acrylic pedestal, including two threaded spacers, was constructed on the calvarium of the animal, allowing the head to be held securely without the use of earbars. The animal recovered in an incubator until mobile and was returned to its home cage. Recording from one MGB was done at the time of surgery ($n = 3$) or 2–6 days later at which time the animals were anesthetized in the same manner as for initial surgery ($n = 35$). Recording at a later date reduced the length of time that subjects were anesthetized during one day. This reduced morbidity in the subjects which are sensitive to prolonged periods of anesthesia. In most cases ($n = 29$), recordings were obtained from the other MGB in a second recording session held 2–10 days after the first session. None of the findings appeared to be related to whether they were obtained in the first or second session. All procedures adhered to the Guidelines for the Use of Animals in Neuroscience Research and the Guidelines of the American Physiological Society.

Acoustic stimulation and recording

The acoustic stimulation and recording systems have been described previously[44]. Briefly, tones were generated by a Wavetek 5100 digital synthesizer and passed through an acoustic gate (rise/fall times = 5.0 ms) and digital attenuators which were controlled by a PDP 11/73 minicomputer. The speaker (AIWA) was connected to a 15 mm plastic tube that was set at the entrance to the ear canal contralateral to the recording site. The speaker was calibrated at the entrance to the ear canal with a B&K 4134 condenser microphone and a Hewlett-Packard wave analyzer. This method was employed, rather than a closed system with calibration at the tympanic membrane, to permit direct comparison with previous and subsequent experiments using waking animals, in which closed system calibration is not feasible. This type of calibration has been used previously to determine the response characteristics of single units in the auditory system in both anesthetized[6] and unanesthetized[41] animals.

Immediately before recording, a burr hole was placed overlying the MGB while head stabilization was maintained by attaching the pedestal to a heavy frame. A tungsten microelectrode (3–6 MΩ at 1 kHz) was lowered into the MGB while click search stimuli were delivered. Discharges were amplified (Dagan 2400) and continuously monitored on a storage oscilloscope. Only stable waveforms of at least 4:1 s/n ratio were accepted; these were passed through a voltage window which provided a pulse to the computer for each spike. Once a single unit was clearly isolated, the response to tones (50 ms duration, 5 ms rise-fall) was assessed. If the tone response was consistent enough to allow estimation of the threshold at CF (lowest intensity yielding responses on 50% of presentations) and had a latency of < 50 ms, then tuning was determined by presenting ascending frequency sequences of tones (50 ms) at ascending intensities (5 dB steps), yielding the response area (RA).

Next, the excitability function of the cell to acoustic stimulation was determined in a paired-tone paradigm. The tone was the CF at 20 dB above threshold. Two tones (50 ms each) were delivered at the following ISI: 15, 25, 50, 75, 100, 150, 200, 250, 500, 1,000 and 2,000 ms. There were 20 repetitions at each ISI with a 2,000 ms inter-pair interval. All data were collected on a PDP 11/73 computer for construction of poststimulus histograms (PSTHs) and quantitative analyses.

Data analysis

In order to quantify the breadth of tuning, the square-root transform[18] was calculated. The formula is:

$$\sqrt{F_2} - \sqrt{F_1} = \text{square root transform}$$

where F_2 is the upper frequency limit and F_1 is the lower frequency limit of the bandwidth measured at 20 dB above threshold. This transform is advantageous because, unlike Q measures, it is not affected by the absolute CF.

To quantify the excitability of a cell, the prestimulus activity (50 ms) was first subtracted from the response during the tone to give the evoked activity. Then the excitability score was calculated:

$$\frac{\bar{s}_2 - \bar{s}_1}{\bar{s}_1} \cdot 100 = \text{excitability score}$$

where

$\bar{s}_2$ = the mean evoked response (20 trials) to the 2nd tone, and
$\bar{s}_1$ = the mean evoked response (20 trials) to the 1st tone.

The s_1 value serves as the control. The excitability score is the response to the second tone expressed as a percent change from control response. Thus, if the excitability score were 0, the response to s_2 would be the same as when there were no preceding tone (complete recovery); a positive value indicates a facilitation of the response to the second tone in the pair, compared to the control value; a negative value indicates relative suppression of response to the second tone. Recovery function plots were constructed by graphing these values as a function of ISI.

Marking lesions were made at the end of each recording. After the final recording, the animal was sacrificed (100 mg/kg sodium pentobarbitol, i.p.) and perfused (saline and 10% formalin), and the brain sectioned and stained (Nissl) to determine the recording site. The three major divisions of the MGB were defined as by Morest[33,34] as the ventral (MGv), medial (MGm) and dorsal (MGd).

RESULTS

Frequency tuning

The complete protocol was conducted on 77 units. Forty-two yielded V-shaped frequency-intensity plots (in two cells the upper limit of frequency response was beyond the limit of the equipment). An example of a plot for frequency–intensity plot for such a single peak unit is depicted in Fig. 1A. This unit had a threshold of 55 dB and a CF of 3.75 kHz. This particular unit was located in the ventral division; such tuning curves with clear definable CFs and thresholds are typical of this part of the MGB[15].

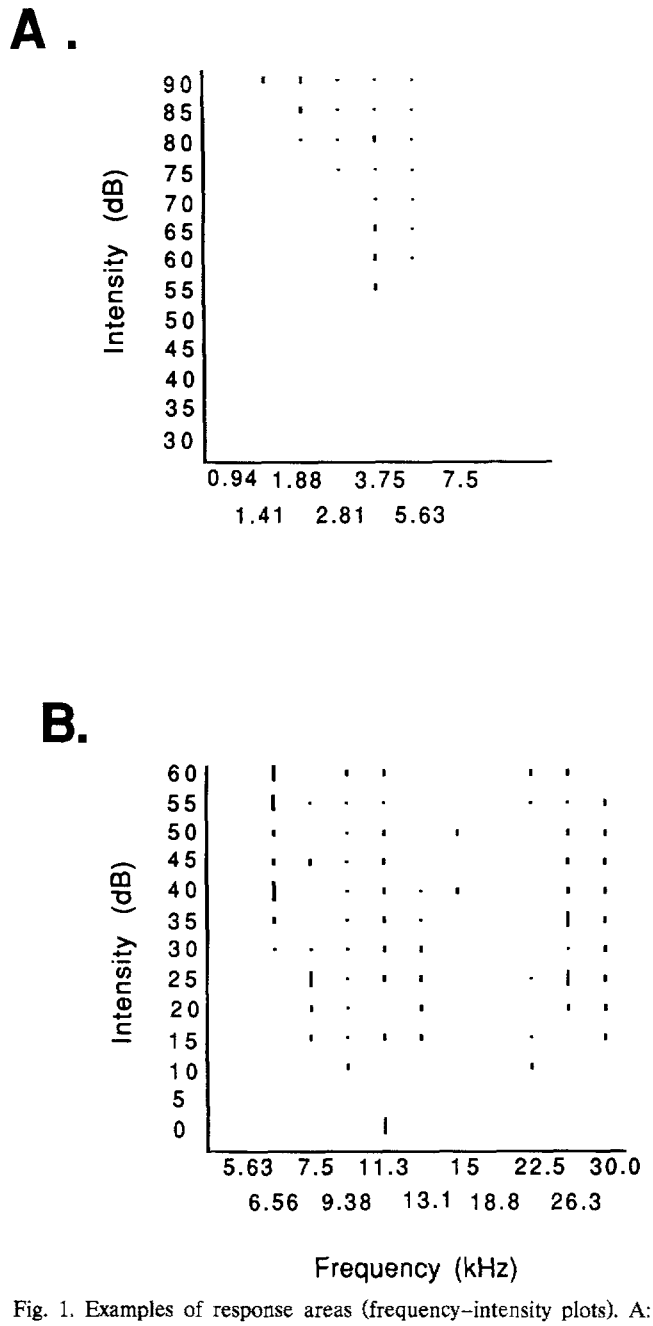

Fig. 1. Examples of response areas (frequency–intensity plots). A: single-peaked tuning curve. The CF of this unit was 3.75 kHz and the threshold was at 55 dB. B: multiple-peaked tuning curve. This unit showed two response areas; the CF in these cases was chosen at the lowest threshold. In this case, the CF was 9.38 kHz and the threshold 10 dB. Length of vertical bars is proportional to number of spikes for each frequency–intensity combination.

Twenty of the RAs were multiple-peaked, as illustrated in Fig. 1B. For units such as these, the CF and threshold were judged from the lowest threshold response. In this example, it was 9.38 kHz at 10 dB (there was also a response seen at 10 dB at 22.5 kHz, but, the 9.38 kHz response was more consistent). Often several RAs had to be obtained to ascertain the CFs and thresholds of such units. Breadth of tuning was not calculated for multiple-peak units.

Seven cells had very broad tuning (square root transforms of at least 2.0); threshold and CF determinations were very difficult and often required the generation of several RAs to make these determinations. Finally, 8 of the units were judged unclassifiable; the RAs were inconsistent. As with the multiple-peaked cells, breadth of tuning calculations were not possible for units in these last two groups.

Excitability functions

Cells displayed a variety of excitability functions including combinations of suppression (negative excitability scores), recovery (0 or near 0 scores) and facilitation (positive excitability scores). Fig. 2 illustrates an excitability function and sample PSTHs from a unit exhibiting considerable suppression. There was no recovery to control (1st tone response) values until the 500 ms intertone interval. Fig. 3 presents data from a unit showing initial suppression followed by a pronounced facilitation lasting from 100 to 500 ms. Thus, this cell displayed both extremes of excitability before reaching control level at 2,000 ms. The data in Fig. 4 are from a cell which displayed a prolonged facilitatory period. The period started at 15 ms, returning almost to the control value at 75 ms before once again passing through a facilitatory period until 2,000 ms.

These data demonstrate the variety of excitability patterns observed in the MGB. Although a classification scheme could be developed to provide a framework for analyses, this would not fully incorporate the variety. Thus, the actual excitability scores served as the basis for all analyses.

Relation between frequency selectivity and excitability

Breadth of tuning data were available for 39 of the 42 single peaked units with V-shaped RAs. Given that both the square root transform and excitability scores are continuous variables, correlational analyses were performed to determine their relation (Table I). The data are provided separately for all cells ('All CF') and

broken down into CF less than and greater than 2.0 kHz, as explained later.

The correlations across all CF are significant at the 75 through 500 ms ISIs. The correlations are all negative: the more selective (narrower) is the tuning, the greater is the excitability score. Thus, cells with broader tuning tend to exhibit more suppression (or less facilitation) than do more narrowly tuned cells. The tuning–excitability correlation is strongest at the 200 ms ISI ($r = -0.525$). The relationship at this interval is presented in Fig. 5A.

Further analysis revealed that this correlation was not present across the full range of CFs. The population of 39 units was separated into two approximately equal-sized groups, with CFs < 2.0 kHz and CFs > 2.0 kHz, and tuning-excitability correlations calculated on each subpopulation. These correlations are also presented in Table I. The cells with CF < 2.0 kHz exhibited no significant correlation at any ISI, although most values are negative. For the units with CF > 2.0 kHz, the first significant correlation was at 50 ms (it was at 75 ms for the whole population). Unlike the results from the whole population of CFs, there was no significance at 150 and 250 ms. However, the strongest correlation was at 200 ms for the CF > 2.0 group just as it was across CFs. The correlations at 200 ms for the CF < 2.0 kHz and CF > 2.0 kHz data are illustrated in Fig. 5B, C, respectively.

To illustrate the correlations between breadth of tuning and excitability, Fig. 6 depicts tuning and excitability data from two neurons. Fig. 6A presents data from a unit with narrow tuning and high excitability. The square root transform is 0.18. There was suppression at 25 ms ISI, but at all other points there was either facilitation or recovery. The unit in Fig. 6B is more broadly tuned (square root transform = 0.90),

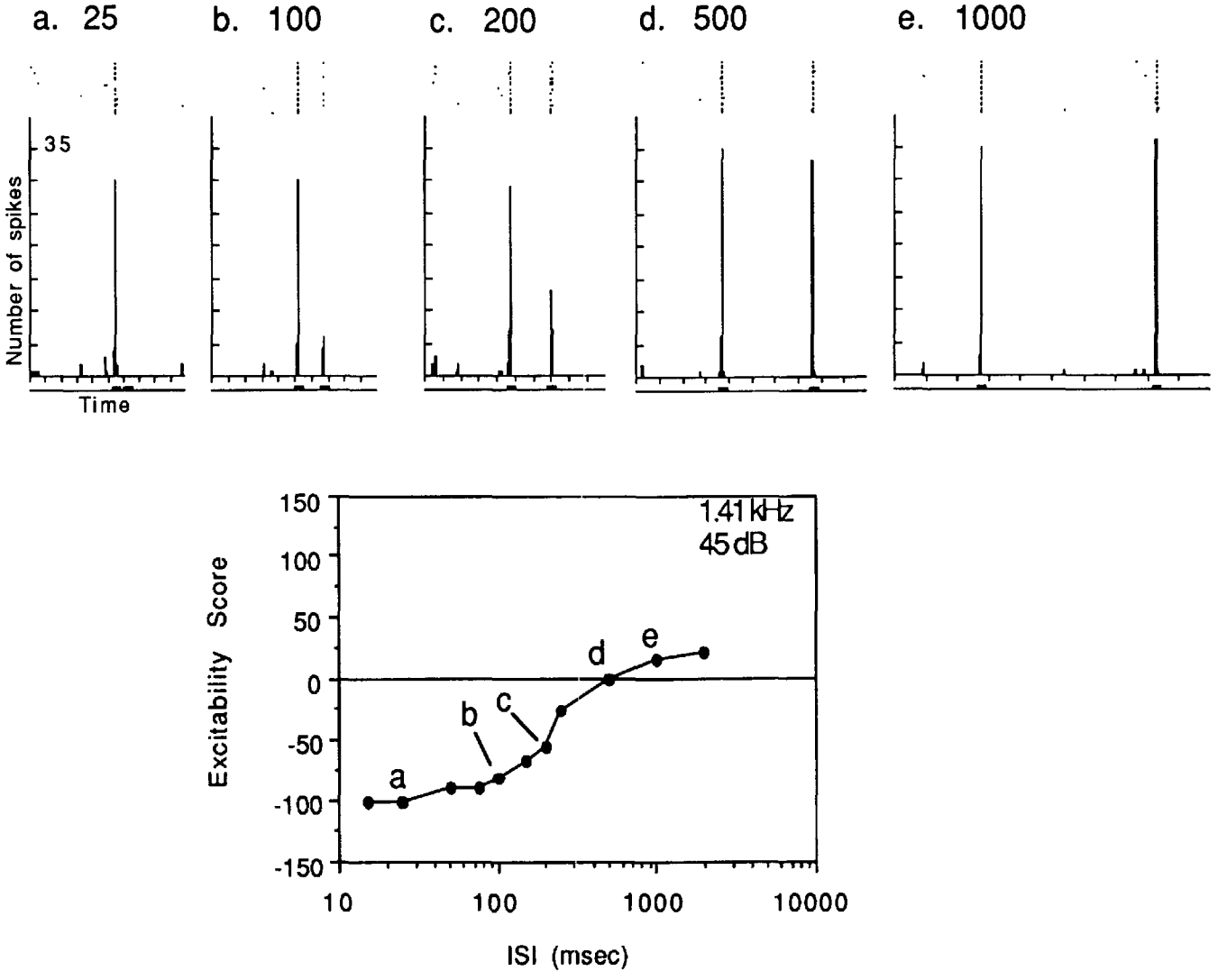

Fig. 2. Example of a unit exhibiting prolonged suppression. In this case, the response to the second tone remains suppressed, relative to the first response, up to the 500 ms ISI. In this and Figs. 3 and 4—top: PSTHs for selected ISIs; bottom: the complete excitability function for the cell; the lower case letters refer to the PSTHs shown above. '0' excitability score (horizontal line) indicates no facilitation or suppression.

and exhibited suppression up to 200 ms. Thus, the overall excitability is greater for the more narrowly tuned cell. The group data indicated that excitability at the 200 ms ISI is an especially strong correlate of bandwidth, and these examples illustrate this relationship. The excitability at 200 ms for the narrowly tuned cell in Fig. 6A is almost at 100%, while for the broadly tuned cell in Fig. 6B it is near 0.

Excitability of multiple-peak units

Although breadth of tuning could not be determined for multiple-peak units and they could not be included in the correlational analysis, they were compared to the single peak units in order to determine if their excitability functions were different.

Five of the 39 single peak cells had no initial suppression and even had initial facilitation; they were dropped to avoid bias by a small group of unusual cells. To insure that any excitability differences between the two groups were not confounded by differences in CF (which is related to excitability), the two groups were matched on mean CF ($n = 11$ each): single peak = 9.9 (± 5.6) kHz, multiple-peak = 10.2 (± 5) kHz, $P > 0.05$, Mann–Whitney test. This also resulted in no significant difference for threshold: single = 26.8 (± 17.1) dB, multiple-peak = 25.9 (± 17.7) dB, $P > 0.05$. Fig. 7 shows group excitability functions for the single peak and multiple-peak units. It is clear that, while both groups show an initial suppression, the multiple-peaked cells take longer to recover than do the single-peaked cells: approximately 100 ms vs. 50 ms. The difference at 50 ms is statistically significant (two-tailed Mann–Whitney, $P \leq 0.05$).

General observations on recording locus and responses to tones

Forty of the recording sites were definitely localized anatomically; 14 of the units were located in the ven-

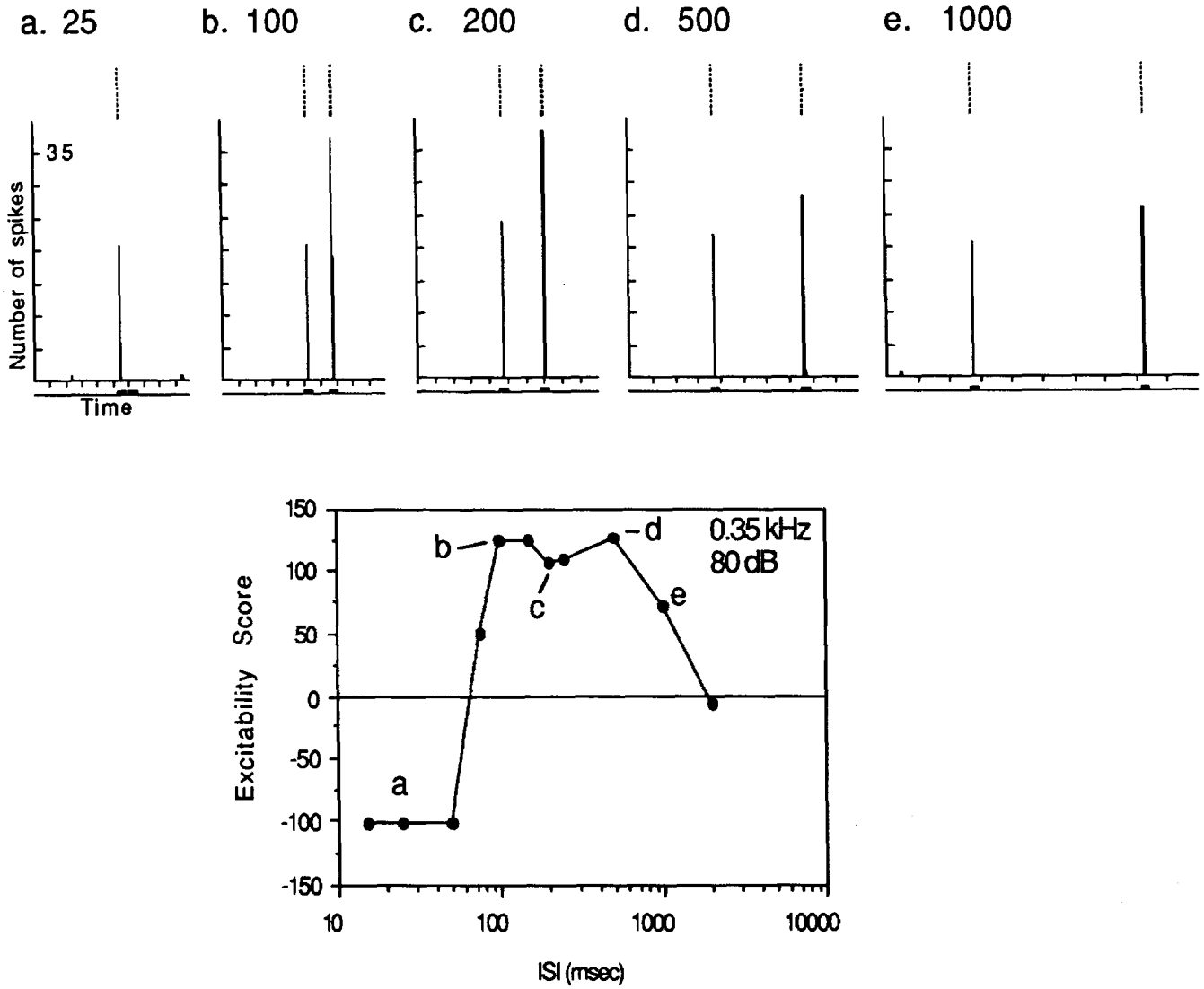

Fig. 3. Example of a unit exhibiting mixed suppression and facilitation. The response to the second tone remains suppressed, relative to the first response, at the 15 through 50 ms ISIs; there is then a strong facilitation (representing an increase of 100% or more) for 100 through 500 ms. The excitability returns to control values at 2,000 ms.

TABLE I

Correlations between excitability scores and breadth of tuning

ITI (ms)	*Correlation coefficients*		
	All CFs	*CF < 2.0 kHz*	*CF > 2.0 kHz*
15	−0.016	0.134	−0.172
25	−0.088	0.075	−0.224
50	−0.272	−0.009	−0.524 *
75	−0.412 **	−0.237	−0.572 *
100	−0.446 **	−0.36	−0.543 *
150	−0.384 *	−0.347	−0.416
200	−0.525 **	−0.195	−0.726 **
250	−0.345 *	−0.272	−0.418
500	−0.366 *	−0.011	−0.642 **
1,000	−0.133	0.100	−0.234
2,000	0.232	0.005	0.415

* $P \leq 0.05$; ** $P \leq 0.01$.

tral division, 17 in the dorsal division and 9 in the medial division. Table II summarizes the subdivisions on the basis of type of RA (single-peak, multiple-peak, broad, or unclassifiable) and latency of onset response. The observation that 78.6% of the ventral division cells are single-peaked and 92.9% have onset latencies of 11–15 ms is in agreement with previous reports that MGv cells have short latencies and clear and consistent tone responses[7,15]. A binomial test comparing the number of single-peak cells in the MGv vs. the number of multiple-peak and broadly tuned cells together (the unclassifiable cells were omitted from this analysis) showed significantly more single peak cells in the MGv (two-tailed, $P \leq 0.022$). Likewise, the number of cells in the MGv with very short latencies (11–15 ms) was significantly higher than the number of longer (16–25 ms) latency cells (two-tailed binomial test, $P \leq 0.002$). These same analyses did not yield statistically significant results for the MGm and MGd. Thus, the units in these divisions show more heterogeneity, as previously reported[15].

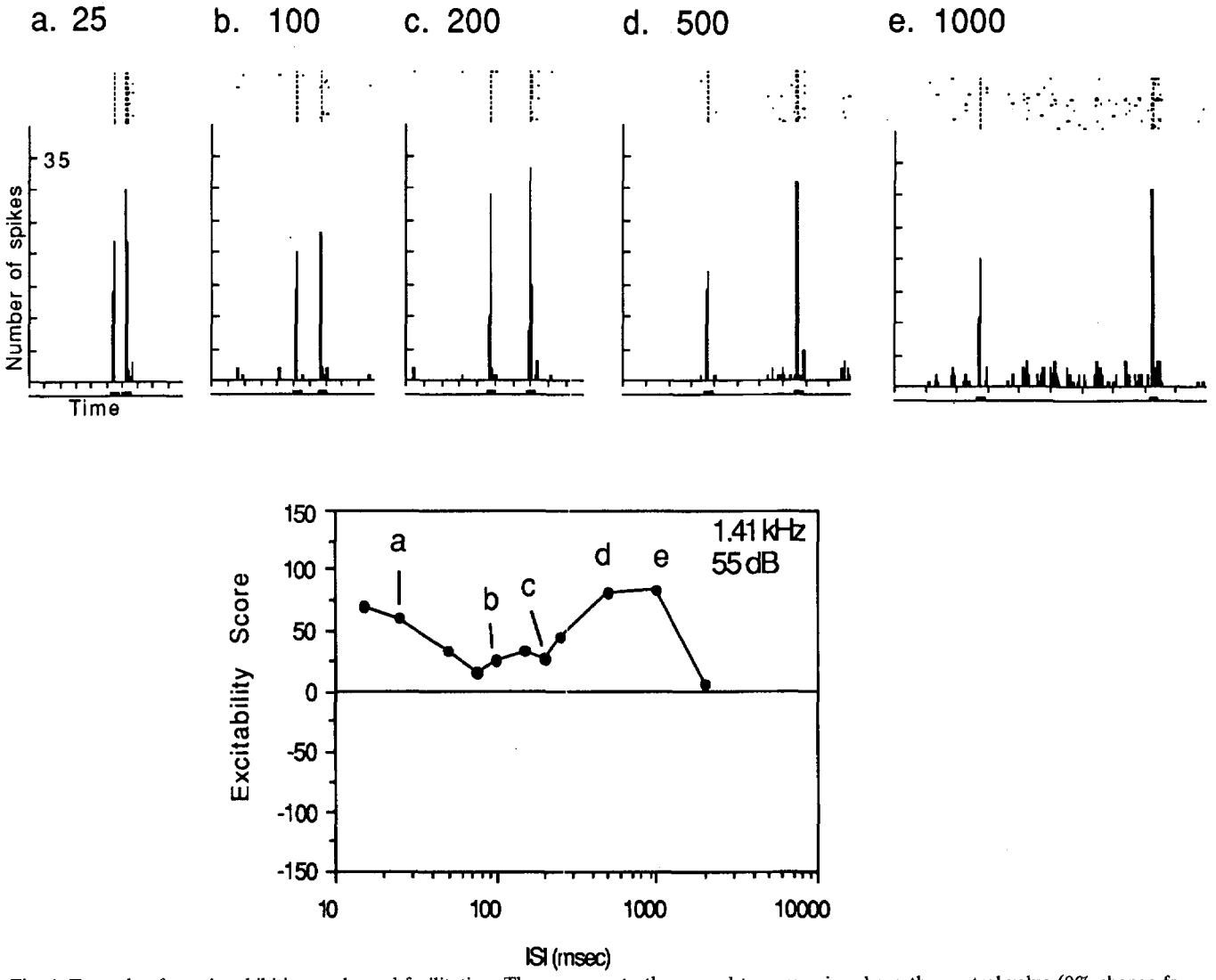

Fig. 4. Example of a unit exhibiting prolonged facilitation. The response to the second tone remains above the control value (0% change from first tone response) until 2,000 ms.

Breadth of tuning comparisons among divisions could not be done due to the small number of single peak cells in the MGd and MGm. However, whereas only 14.3% of the MGv cells are in the 'broad' or 'multiple-peak' class, the percentage is 64.7% in the MGd and 55.5% in the MGm. Multiple-peak cells are in a sense broadly tuned units; thus, these data show a higher percentage of broadly tuned cells in the MGm and MGd than in the MGv. This is in agreement with other reports[2,15,17]. Overall, the MGB units in this investigation are similar in response to tone as those reported by other investigators.

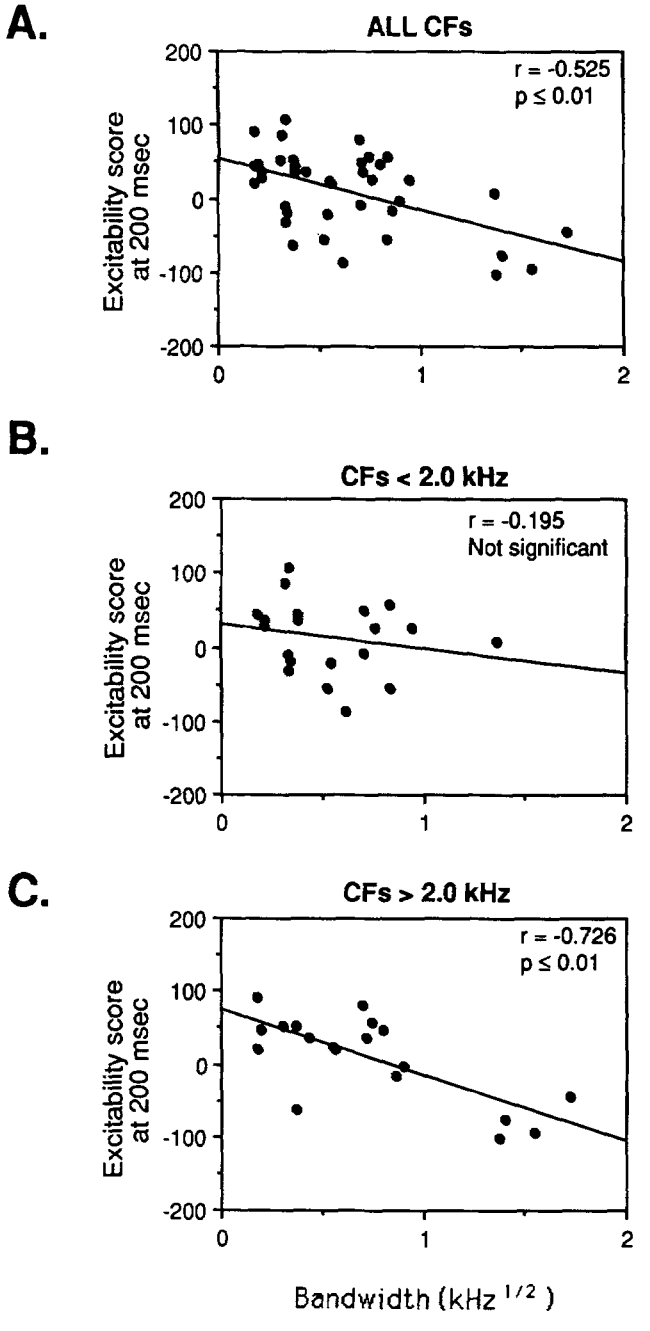

Fig. 5. Correlations between bandwidth and excitability at the 200 ms ISI. A: across all characteristic frequencies, there is a significant negative correlation between the bandwidth (measured as the square root transform) and excitability (measured as excitability score). B: for cells with CFs < 2.0 kHz, the correlation between the two measures is insignificant. C: for cells with CFs > 2.0 kHz, the correlation is significant and is even larger than it is across the entire CF range.

Divisions of the MGB and temporal processing

To determine if temporal processing differs among the divisions of the MGB, group excitability functions were calculated for each division. (Two of the 14 MGv cells had initial facilitation rather than suppression and were not included in this analysis.) Fig. 8A compares excitability of the MGv and MGd. The data are from two samples of cells which were matched both for mean CF and threshold—CF: MGv = 6.14 (±3.8) kHz, MGd = 10.8 (±10.9) kHz, $P > 0.05$; threshold: MGv = 31.9 (±18.5) dB, MGd = 31.3 (±14.3) dB, $P > 0.05$. The ventral division cells showed rapid recovery, even facilitation at 50 ms and 500 ms. The dorsal division reached recovery at 75 ms. The two divisions are significantly different at 15–50 ms and at 500 ms.

Fig. 8B compares excitability of matched cells in the ventral and medial divisions—CF: MGv = 6.04 (±4.5) kHz, MGm = 12.7 (±11.2) kHz, $P > 0.05$; threshold: MGv = 33.3 (±22.9) dB, MGm = 30.8, (±24.8) dB, $P > 0.05$. Both divisions reached at least recovery at 50 ms, although the medial division reached this point at a slower rate; the functions are statistically different at the 25 ms point. Beyond this, the two functions are quite similar until the facilitatory period of the MGv function at 500 ms, although the difference at this point was not statistically significant.

Fig. 8C compares the excitability functions for cells of the dorsal and medial divisions (MGd, CF = 13.6 (±10.8) kHz, MGm, CF = 15.8 (±10.5) kHz; MGd threshold = 25.6 (±13) dB, MGm threshold = 22.2 (±23.5) dB, $P > 0.05$ for each parameter). The medial division cells recovered at 50 ms and the dorsal division cells at 75 ms, but this difference failed to meet statistical significance ($P > 0.05$). There were no statistically significant differences at any ISI.

In summary, the MGv has the highest degree of temporal fidelity. It shows much faster recovery than the MGd and shows greater excitability even at 500 ms. (Moreover, it alone contained cells ($n = 2$) which showed only facilitation, no suppression, at the shorted ISI; as indicated above, these 'pure facilitation' tones were not included in the group data.) The MGv also recovered faster than the MGm. The excitability of the dorsal and medial divisions was not statistically different for the matched sub-groups in the MGd and MGm cells available in this study.

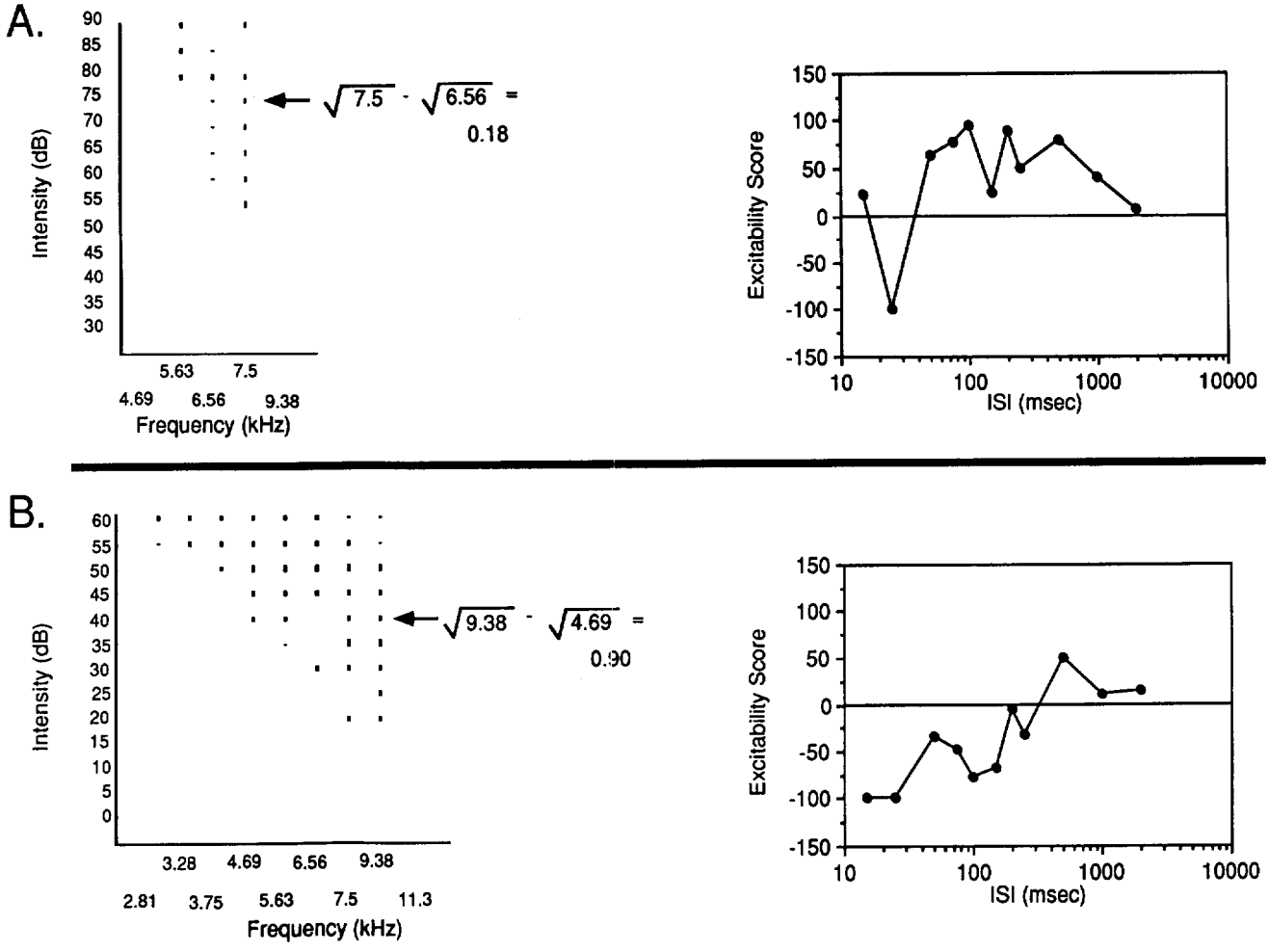

Fig. 6. Two examples illustrating the bandwidth–excitability relationship. A: data from a unit with narrow tuning (RA, left) and a large amount of facilitation (graph, right). B: data from a unit with relatively broad tuning (left) and prolonged suppression (graph, right).

TABLE II

Response areas and onset latencies in divisions of the MGB

Note: percents are based on total N for each division.

	Response area type				*Onset latency*		
	Single peak	*Multiple peak*	*Broad*	*Other*	*11–15 ms*	*16–20 ms*	*21–25 ms*
Ventral	11/14	2/14	0/14	1/14	13/14	1/14	0/14
	78.6%	14.3%	0%	7.1%	92.9%	7.1%	0%
Dorsal	4/17	8/17	3/17	2/17	10/17	6/17	1/17
	23.5%	47.1%	17.6%	11.8%	58.8%	35.3%	5.9%
Medial	3/9	3/9	2/9	1/9	5/9	2/9	2/9
	33.3%	33.3%	22.2%	11.1%	55.6%	22.2%	22.2%

DISCUSSION

Overview of the major findings

The present experiment employed a two-tone paradigm to elucidate the excitability patterns of single MGB units. Three correlates were found: frequency selectivity, type of tuning (single-peak vs. multiple-peak), and subdivision of the MGB.

First, a positive correlation was found between the excitability scores and frequency selectivity. The greater the frequency selectivity (narrower tuning), the greater the excitability (including less suppression) following a CF stimulus. The correlation was highest at 200 ms. It was higher if restricted to cells with CFs above 2.0 kHz and was not significant if restricted to units with CFs below 2.0 kHz. The basis for the lack of relationship

below 2.0 kHz is unclear, but it might be related to phase-locking[19].

Second, the excitability functions were significantly different for units with multiple-peaked tuning as opposed to units with single-peaked tuning; the multiple-peaked cells were less excitable, i.e., exhibited more suppression. As multiple-peaked response areas indicate broad tuning, these findings also support the conclusion that excitability is lower for broadly tuned vs. narrowly tuned neurons.

Third, differences in excitability were observed among the three major divisions of the MGB. Ventral division units exhibited significantly less suppression than did dorsal division cells at 15 through 50 ms and significantly more facilitation at 500 ms. These differences were observed although the two groups were matched on threshold and CF. Medial division cells displayed significantly more suppression relative to the ventral division for sub-populations matched on threshold and CF only at 25 ms. Although there was no statistical difference at any ISI between the dorsal and medial divisions for matched cells, the findings suggest that medial cells recover before dorsal cells. Thus, while the dorsal division units are considerably less excitable than are the ventral division cells, the difference between the medial and ventral division units is not as great. These findings are in general agreement with previous findings that the medial division cells have characteristics that are intermediate to the ventral, lemniscal cells and the dorsal division neurons (see Introduction).

Relation to previous findings

It is difficult to directly relate these findings to previous investigations of the excitation patterns of the MGB because of the use of clicks, the lack of comparison of the major divisions of this nucleus and the absence of information on frequency tuning. Aitkin and Dunlop[4] identified the placements on some of their figures, but drew no conclusions on excitability relative to locus of recording. The general pattern of relative suppression at the shortest ISIs and facilitation at longer ISIs was confirmed but facilitation was confined largely to cells within the MGv.

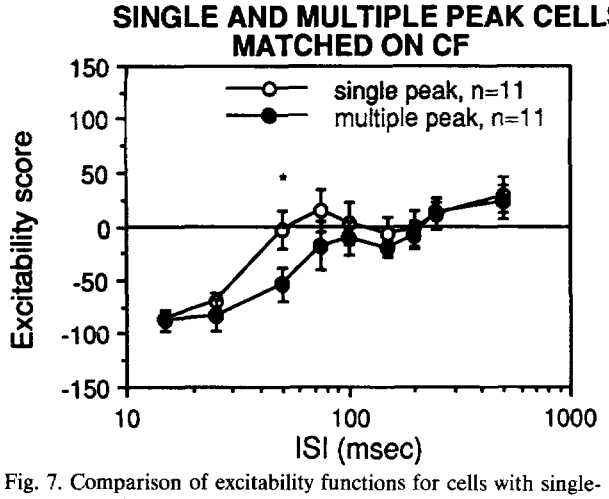

Fig. 7. Comparison of excitability functions for cells with single- and multiple-peak tuning curves. The cells were matched on CF. The multiple-peaked cells show more suppression, which was statistically different at the 50 ms ISI (* $P \leq 0.05$).

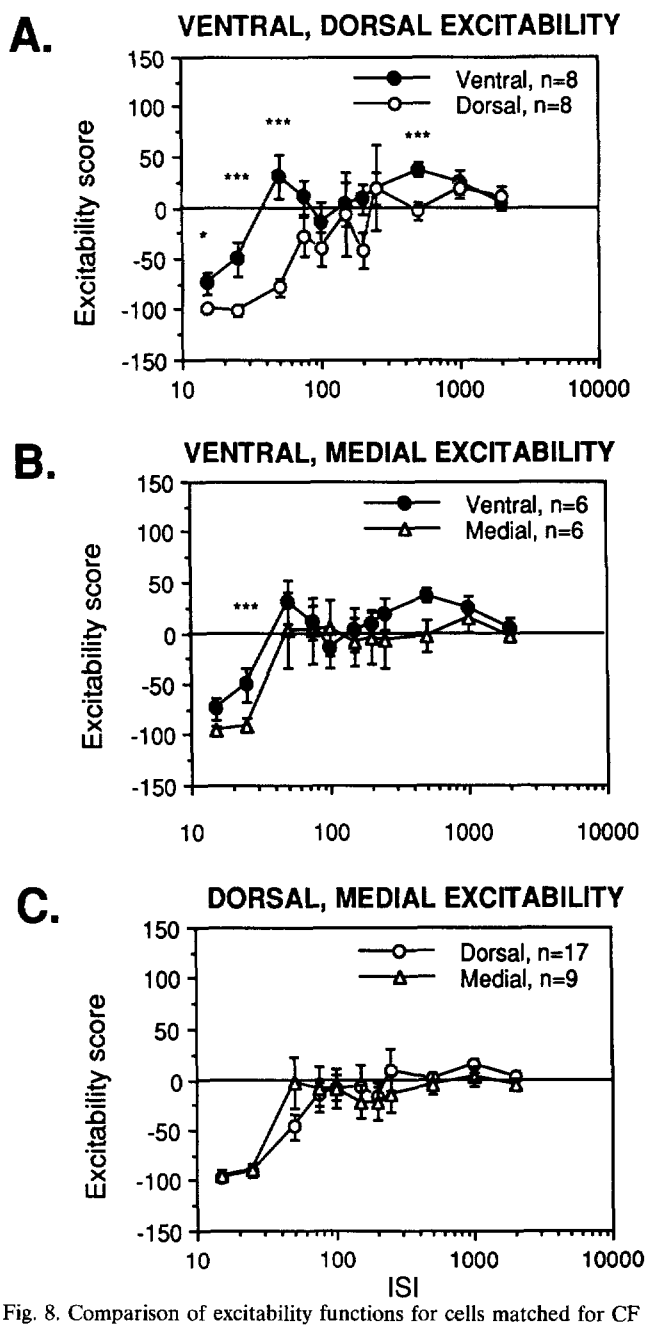

Fig. 8. Comparison of excitability functions for cells matched for CF and threshold in the MGv, MGd and MGm. A: comparison of the ventral and dorsal division cells shows that the dorsal cells were more suppressed than were the ventral cells, significant at 15, 25, 50 and 500 ms ISI. B: comparison of ventral and medial cells shows that the medial cells had more suppression at 25 ms ISI. C: comparison of the dorsal and medial cells indicates that the medial cells recovered more quickly at 50 ms ISI, but neither this nor any other ISI were statistically significant. * $P \leq 0.05$; *** $P \leq 0.01$.

Calford[15] studied the ability of cells to respond to a tone repetition rate of 1 Hz or less ('habituation'). He found that MGv cells showed more consistent responses at higher repetition rates than cells in either the dorsal or medial divisions. The longest intervals used in this study (1,000 and 2,000 ms) included some of the intervals used by Calford. Strict comparison is difficult because the length of time over which the effects of repetition rate were tested were not reported; in this experiment, measures were taken only over brief periods, i.e., for only 20 repetitions at each ISI (e.g. 20 s for ISI = 1,000 ms) and 'habituation' effects might have developed only after longer stimulation. With this caveat in mind, we found no statistically significant differences at 1.0 and 2.0 s among the MGB divisions for cells that were matched for threshold and CF (Fig. 8). Thus, differences in the ability to respond consistently to tones presented continuously may not simply be a function of subdivision within the MGB but may be more closely related to certain other physiological characteristics, many of which are correlated with cell locus within these subdivisions.

Multiple-peaked units have been previously reported in the MGm[2]. Almost half of the MGd units in the present study were multiple-peaked. Previous reports have noted broadly tuned units in this division[15,17], but did not specifically note multiple-peaked units. These studies may have observed such units, but classified them as broadly tuned. Suppression following a response of a multiple-peaked cell has been reported in the auditory cortex in a paradigm similar to this one[1]. Suppression for 20–100 ms was observed if the first and second tones were from the same range of a multirange cell; if the two tones were from different ranges, there was less suppression. Whether or not the cortical effect is 'passed on' from the thalamus can only be speculated on at present.

Possible mechanisms of excitability patterns

Measuring evoked potentials in both the inferior colliculus and MGB reveals that in a paired click paradigm, the IC exhibits less suppression and no cyclicity of excitability[5,25]. This suggests that excitability patterns in the MGB are influenced by a mechanism(s) operating above the level of the IC. Ablating auditory cortex does not affect the MGB excitability patterns elicited by paired stimulation of the brachium of the inferior colliculus[5]; this indicates that a centrifugal influence from cortex is unlikely.

Excitability using paired stimuli—in most cases electrical stimulation of the peripheral or central nervous system—has been studied in the ventrobasal thalamus[9,10,12] of the somatosensory system and the lateral geniculate[13,14] of the visual system. A mechanism that was often suggested for the thalamic inhibition—and could explain the cyclic recovery—was a recurrent collateral, where collaterals of the thalamocortical units projected to an inhibitory interneuron, which then projected postsynaptically to the thalamocortical cells. This would explain effects such as why replacing the 1st click with cortical stimulation yields the same results as two clicks[5].

Other work has implicated the thalamic reticular nucleus in the sensory thalamus inhibition[39,40,42]. In the medial geniculate body, paired pulses delivered to the IC yield the same suppression observed as when the first pulse is replaced with thalamic reticular nucleus stimulation[39]. This is also observed in the lateral geniculate body: stimulation of the visual portion of the thalamic reticular nucleus inhibits the response to a subsequent optic track stimulation[42]. In addition, lesioning the nucleus reticularis dramatically reduces the inhibition normally observed with paired optic tract stimulation.

If, indeed, the reticular nucleus is the source of the post-stimulus suppression patterns observed here, this would suggest that the three MGB divisions may differ in their input from this nucleus. Projections from the reticular nucleus to the dorsal and ventral divisions have been reported[32,37] but it is not clear from these investigations if the two divisions differ in the density of projections. Assuming that the response suppression involves actual neural inhibition, then the role of GABA must be considered. The ventral division does contain a greater density of GABA terminals than does the dorsal division[48], which would would seem to be opposite from what one would predict from the finding of more suppression in the dorsal division.

The point should be emphasized that a number of units displayed facilitation at certain time intervals; the discussion here has been focused on the suppression. The two phenomena are not unrelated: the facilitation could be due to a state of 'post-anodal exaltation' following an inhibitory period[9]. It has been suggested that units with the largest inhibitory postsynaptic potentials are the most likely to be hyperexcitable after such a strong potential[9], so perhaps the facilitatory responses in the MGv (Fig. 8) are consistent with the data on GABA. More anatomical and physiological data are needed to elucidate the mechanisms behind the excitability of MGB neurons.

Some functional implications

That neurons with greater frequency selectivity also exhibit faster recovery following a tone indicate that these cells provide a high degree of response fidelity to

the physical parameters of sound, at least for the type of stimuli used in this study. The addition of data on excitability to the previously known characteristics of narrow frequency tuning for cells in the ventral MGB extends the functional specification of the lemniscal pathway to the temporal domain.

That more broadly tuned in the MGd and MGm also show slower recovery than do lemniscal cells provides another parameter which distinguishes the lemniscal from the lemniscal-adjunct pathways. This does not delineate the functions of this pathway, and in some sense merely extends their definition in negative terms, e.g., 'less frequency selective and less excitable than the lemniscal pathway'. The lemniscal adjunct path might be selective for acoustic stimulus parameters which are more complex than those for isolated pure tones. Alternatively or additionally, this pathway may be involved in other aspects of auditory function. For example, this pathway shows greater physiological plasticity than does the lemniscal pathway during associative conditioning; this has been found consistently both for responses to an acoustic conditioned stimulus during training and for frequency receptive field plasticity, determined before and after training: the lemniscal MGv is less plastic than the non-lemniscal MGm and MGd[20–25,28,29,38]. However, the specific sensory roles of the lemniscal-adjunct divisions of the MGB remain to be determined.

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