Associative Retuning in the Thalamic Source of Input to the Amygdala and Auditory Cortex: Receptive Field Plasticity in the Medial Division of the Medial Geniculate Body

Jean-Marc Edeline
Center for the Neurobiology of Learning and Memory
University of California, Irvine

Norman M. Weinberger
Center for the Neurobiology of Learning and Memory
and Department of Psychobiology
University of California, Irvine

The medial division of the medial geniculate body (MGM) projects to the lateral amygdala and the upper layer of auditory cortex and develops physiological plasticity rapidly during classical conditioning. The effects of learning on frequency receptive fields (RFs) in the MGM of the guinea pig have been determined. Classical conditioning (tone-footshock), as indexed by rapid development of conditioned bradycardia, produced conditioned stimulus (CS)-frequency specific RF plasticity: increased response at the CS frequency with decreased responses at other frequencies, both immediately and after a 1-hr retention period. Sensitization training produced only general changes in RFs. These findings are considered with reference to both the elicitation of amygdala-mediated, fear-conditioned responses and the mechanism of retrieval of information stored in the auditory cortex during acquisition.

The two fields of the neurobiology of learning and sensory physiology have traditionally remained quite separate, although they share an important common goal: to understand information processing in the brain. Of interest, these two fields generally use complementary nonoverlapping experimental paradigms (Weinberger & Diamond, 1988). In learning, the physical parameters of stimuli are held constant while their significance is changed (e.g., by establishing a relationship between a stimulus and a reinforcer, as in Pavlovian conditioning). On the other hand, in sensory physiology, the physical parameters of stimuli are varied so that the sensory receptive fields (RFs) of neurons can be determined while their behavioral significance is held constant (e.g., by anesthetizing the subjects). However, both fields share a dominant belief that sensory systems are not actively involved in learning and memory.

This view is based in part on the assumption that veridical information about the environment requires a nonplastic sensory substructure. Yet, it has long been recognized that an adequate account of perception must go beyond a physical analysis of stimuli to include psychological factors (e.g., Gregory, 1974). Another reason for discounting sensory systems in learning is that neurophysiological studies of conditioning have emphasized the convergence of input from the conditioned (CS) and unconditioned (UCS) stimuli, and such polymodal convergence is incompatible with the assumption that sensory systems are unimodal (e.g., Fuster, 1984; Miller, Pfingst, & Ryan, 1982; Thompson, Berger, & Madden, 1983).

These views ignore the extensive literature that physiological plasticity develops in sensory systems during learning. In the case of the auditory cortex, which is probably the sensory structure most extensively studied in the neurophysiology of learning, the dominant effect is an increased response to acoustic CSs during Pavlovian conditioning. These findings have been replicated and extended for more than 40 years and have been shown to be due to associative processes (for a review see Weinberger & Diamond, 1987).

In light of these findings, at least two basic questions arise. (a) Does this functional plasticity in sensory systems during learning reflect a general increase in neuronal excitability or does it index an actual modification of the processing and representation of information about the CS? (b) Can the well-established paradigms and findings of the fields of learning and sensory physiology be mutually supportive in attempts to understand how the brain acquires, represents, and stores information?

Both questions can be investigated simultaneously by combining the paradigms of learning and sensory physiology within the same experiment. This can be accomplished by obtaining sensory RFs before and after behavioral training, thus determining the effects of learning on RFs. If Pavlovian conditioning increases responses to the CS because it increases excitability in general, then responses to other (non-CS) stimuli within the RF of a cell will also be increased. In contrast, if learning specifically modifies the processing of information about the
CS, then responses to this stimulus will be facilitated, whereas responses to other stimuli within the RF will be less affected, perhaps even reduced.

Recent studies in both the primary and nonprimary auditory cortical fields, using non–best frequency (non-BF), pure-tone stimuli as CSs, have found that Pavlovian conditioning does modify information processing. Responses to the CS are increased, whereas responses to other frequencies are altered less or are actually decreased. Moreover, these effects can be sufficiently strong to “retune” cells such that the frequency of the CS becomes the new BF (Bakin & Weinberger, 1990a; Diamond & Weinberger, 1986, 1989). Sensitization training does not produce CS-specific RF plasticity but rather produces general increases in responsivity. That is, associative processes alter information processing, whereas sensitization only increases excitability.

Combined conditioning and RF experiments have also been accomplished for two of the three major subdivisions of the medial geniculate body (MGB), which is the obligatory thalamic relay to the auditory cortex. Neurons in the dorsal division (MGd), which is part of a lemniscal-adjunct auditory pathway (Graybiel, 1972), project to nonprimary cortical auditory fields and also develop CS-specific RF plasticity during conditioning and general increased responses during sensitization (Edeline & Weinberger, 1991a). The lemniscal, tonotopically organized ventral division (MGv), which projects to layer IV of primary auditory cortex, develops CS-specific RF plasticity but only if the CS frequency is very close (within 0.125 octave) to the pretraining BF. Moreover, unlike the auditory cortex and the MGd, such plasticity in the MGv is transient, being present immediately after but not 1 hr postconditioning (Edeline & Weinberger, 1991b).

This article reports the results for the third major subdivision of the MGB, the medial (“magnocellular,” MGm) compartment. This nucleus of the auditory thalamus is particularly interesting for several reasons. First, it is probably the most intensively studied thalamic nucleus for which neuronal responses have been recorded during learning trials. Neurons in the MGm rapidly develop response plasticity during habituation (Edeline, 1990; Weinberger, 1982) and conditioning (Birt & Olds, 1981; Edeline, 1990; Edeline, Dutrieux, & Neuen Schwarzer-El Massiou, 1988; Edeline, Neuen Schwazer-El Massiou, & Dutrieux, 1990a, 1990b; Gabriel, Miller, & Saltwick, 1976; Ryugo & Weinberger, 1978; Weinberger, 1982).

Of course, as just emphasized, such studies in which neuronal responses are recorded to the CS only during training trials cannot distinguish between general changes in excitability versus specific modification of the representation of information, either of which could be induced by associative processes. Moreover, long-term potentiation can be induced in this nucleus by brief stimulation of its ascending input, the brachium of the inferior colliculus (Gerren & Weinberger, 1983).

Second, both anatomical and physiological evidence suggest that this division is the first locus of convergence between auditory and nonauditory information in the auditory system because it receives spinothalamic and also trigeminal somatosensory input (Calford & Aitkin, 1983; LeDoux, Ruggiero, Forest, Stornetta, & Reis, 1987; Love & Scott, 1969; Wepsic, 1966; Winer & Morest, 1983). This characteristic of bimodality is a clear case of a sensory system structure that is not unimodal. In addition, lesions of the medial region of the MGB, which apparently includes at least some of the MGm, prevent fear conditioning to acoustic stimuli (LeDoux, Iwata, Pearl, & Reis, 1986). Also, the MGm is the only part of the auditory thalamus that projects to the upper layer (layer 1) of the cortex, and it also projects to all cortical auditory fields (Mitani, Itoh, & Mizuno, 1987; Niimi, Ono, & Kusunose, 1984; Ryugo & Killackey, 1974; for review see Winer, 1985). Thus, the learning-induced plasticity that develops in the MGm can potentially influence all areas of the auditory cortex.

Third, the MGm is a pivotal component in a preliminary model proposed to explain RF plasticity at the level of the auditory cortex (Weinberger, Ashe, Metherate, McKenna, Diamond, & Bakin, 1990; Weinberger, Ashe, Metherate, McKenna, Diamond, Bakin, et al., 1990). This is considered in the Discussion section.

Materials and Method

We will only summarize major features of the procedures because they were identical to those described previously (Edeline & Weinberger, 1991a, 1991b).

Subjects and Surgical Preparation

Adult male Hartley guinea pigs (n = 34, 350–420 g) were implanted bilaterally in the MGB with bundles of 3–6 Teflon-coated tungsten microelectrodes while under pentobarbital–neuroleptic anaesthesia (Evans, 1979). Two cylindrical threaded tubes, included in the pedes tal of dental acrylic, provided foratraumatic fixation of the animal’s head during subsequent training sessions.

General Procedure and Experimental Protocol

Twenty-four hours after surgery, the animals were adapted for 3–7 days in a hammock within an acoustic chamber. Stabilization of the head, while in a resting posture, ensured a constant distance between the ear canal and a calibrated speaker. Special care was taken to avoid discomfort, which could induce heart rate instability and prevent observation of cardiac conditioned responses (CRs).

On the training day, RFs were determined before (Pre), immediately after (Post), and 1 hr after training (1 hr Post) by presenting sequences of 8–15 frequencies in a pseudorandom order proportional to the recording site.

Tones were presented at one to four intensities between threshold and the CS intensity in 10-dB steps. Each tone (50 ms) was repeated 10 times, and the interstimulus interval was approximately 1 s.

The conditioning session (n = 25) began immediately after the pretraining RF by the sensitization phase (10 CS and 10 UCS presentations given in a pseudorandom order), which was followed by the conditioning phase (30 CS–UCS presentations, intertrial interval [ITI] average = 2 min, range = 1–3 min during both sensitization and conditioning). The CS was one of the frequencies used to determine the RF and was chosen to never elicit the strongest cellular response; that is, it was not the BF. The CS duration was 6 s (70–80 dB), and the UCS, which was provided by a Grass stimulator (Quincy, MA, No. S88) and isolation unit (60 Hz, 5.0 ms, 250-ms train), was delivered to both hind paws at the CS offset. In addition to conditioning, a sensitization-only control group (n = 9) was run: 40 CS and 40 UCS trials were given in a pseudorandom order (explicitly unpaired presentations, mean ITI = 2 min).
Table 1

<table>
<thead>
<tr>
<th>Type of training</th>
<th>Subjects</th>
<th>Recording sites</th>
<th>RF difference functions*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditioning</td>
<td>25</td>
<td>29</td>
<td>93</td>
</tr>
<tr>
<td>Sensitization</td>
<td>9</td>
<td>13</td>
<td>48</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>42*</td>
<td>141*</td>
</tr>
</tbody>
</table>

*Refers to the immediately postconditioning RF minus the preconditioning RF.
*In eight cases (conditioning = 4, sensitization = 4), the data from two electrodes were recorded simultaneously.
*For each recording site, the RF was determined at several intensities.

After the last recording session, the animals were given an overdose of Nembutal (sodium pentobarbital; 100 mg/kg), and small electrolytic lesions were made at recording sites. Anatomical determination of electrode locations was achieved using the nomenclature described by Winer (1985).

Data Analysis

Heart rate was measured during the 5-s pretone, during the last 5 s of tone, and for 5 s after UCS offset for each trial. The difference between the number of beats observed during the tone and the pretone periods, as well as the difference between the number of beats observed post-UCS and pretone, were computed for each trial to obtain the cardiac CR and the cardiac unconditioned response (UCRs).

Single-unit or cluster discharges, (minimal signal-to-noise ratio = 3:1) were stored in a microcomputer to build on-line rasters and histograms for each frequency at each intensity. Two channels of activity were occasionally recorded simultaneously (n = 8 sessions, Table 1). For each neuronal recording, a temporal window for the tone-evoked responses was selected (either 0–25 ms in the case of "on" responses or all 50 ms of the tone presentation in cases of a sustained response) and maintained to analyze the Pre, Post, and 1-hr Post RFs. To rule out spurious changes in response to tones caused simply by changes in spontaneous activity, evoked discharge was calculated by subtracting background firing during the 200 ms immediately preceding each tone from the number of spikes during that tone, for each selected temporal window. The RF was quantified as the average evoked discharge for each frequency across the frequency range studied. The effects of training were determined by subtracting the pretraining RF from the immediate postconditioning RF (Post RF – Pre RF) and from the 1-hr postconditioning RF (1-hr Post RF – Pre RF). The resultant data are hereafter called RF difference functions.

To compare cells, each RF difference function was normalized by dividing each difference score by the absolute value of the difference score of the tone that exhibited the greater change from pretraining and multiplying by 100. Examination of the difference functions in previous studies led us to classify the neuronal recordings into three categories—CS–frequency specific (CS–FS), general (Gen), and random (Rand) changes (see the Results section)—by using previously described criteria (Edelstein & Weinberger, 1991a, 1991b).

To provide group RF difference functions that illustrate maximum effects, the largest effect across intensities was selected for each recording site, and these were averaged separately across sessions for the CS–FS, Gen, and Rand groups. For each recording, the CS frequency was taken as the reference, and the distance between the CS frequency and all other frequencies were expressed in fractions of an octave. Statistical analyses were based on all the data obtained from each recording site for all the intensities studied.

Results

The findings presented in this article were obtained from 34 subjects (conditioning = 25; sensitization = 9) and are based on data from 42 recording sites (conditioning = 29; sensitization = 13) and a total of 141 RF difference functions immediately postconditioning (Table 1).

Behavioral Data

For the conditioned animals, tone presentation initially elicited heart rate decreases during the first 5-trial block of CS–UCS unpaired presentations, which habituated (Figure 1). During the subsequent CS–UCS pairing trials, conditioned bradycardia developed rapidly. The first CRs were usually observed as early as the first 5-trial block (Figure 1). Compared with the last block of sensitization trials, conditioned bradycardia was significant at the second block of pairing, $F(1, 24) = 3.61, p < .05$, reached asymptote in 15–20 trials, and maintained this level until the completion of training, $F(1, 24) = 13.55, p < .05$, for the last block of conditioning.

For the sensitization control animals, the tone presentation also induced heart rate decreases during the first five trials, which habituated by the second block of trials (Figure 1). No bradycardia CR developed during continued unpaired presentation of the CS and UCS (Figure 1). There was no statistical difference between the second block of sensitization trials and the following blocks ($F < 1$ in all cases).

Figure 1. Behavioral group data for the animals undergoing classical conditioning (Condit.) and sensitization (Sens.) training. (Each point is the mean ± SE] heart rate changes [beats per minute, BPM] during the last 5 s of tone compared with the last 5 s before tone onset. The first two 5-trial blocks were sensitization trials for all animals [conditioned stimulus, CS, and unconditioned stimulus, UCS, explicitly unpaired]. The following trials were CS–UCS pairing trials for the Condit. group, but still CS–UCS unpaired presentations for the Sens. group. Heart rate decelerations were observed in both groups during the first 5-trial block [orienting responses]. Conditioned bradycardia began to develop as early as the first 5-trial block of pairing [Block 3], reached asymptotic level in 15 trials [Block 5], and maintained this level until the end of the training. No such effects were observed for the Sens. group.)
In an analysis of variance, the interaction between the trial block and group variables was significant, \( F(1, 7) = 8.90, p < .0001 \), which corroborates the differential evolution of heart rate changes in the two groups of animals. Thus, as we previously reported, a conditioning paradigm rapidly induces conditioned bradycardia, whereas a sensitization paradigm does not.

As mentioned in our previous articles using the same experimental design (Edeline & Weinberger, 1991a, 1991b), careful examination of the heart rate recordings failed to reveal any tonic or phasic arousal during the RF determinations. Probably by virtue of the many contextual differences between the RF determination and the training situation perse (e.g., tones of 50 ms vs. 6 s, intertone interval of 1 s vs. 2 min, different frequencies presented vs. the CS frequency only), the animals did not show any type of behavioral responses during RF determination, including during presentations of the CS frequency, whatever the intensity (for details see also Diamond & Weinberger, 1989).

**Neuronal Data**

As noted in numerous studies, the frequency RF of neurons in the medial part of the MGB can be quite broad (Aitkin, 1973; Calford, 1983; Morel, Rouiller, DeRibaupierre, & DeRibaupierre, 1987; Rouiller et al., 1989). Using the square-root transformation (\( \sqrt{2} \sqrt{1} \), where \( \sqrt{2} \) is the highest frequency and \( \sqrt{1} \) is the lowest frequency eliciting discharges at 20 dB above threshold; Calford, Webster, & Semple, 1983; Whitfield, 1968), we obtained a mean (±SE) breadth of tuning of 1.54 ± 0.12 octaves (range = 0.26–3.58), which is not very far from the value reported by Calford (1983) for the anesthetized cat (1.39 ± 1.02 octaves). The value reported here is much broader than that observed in the MGv (M = 0.56 octave; Edeline & Weinberger, 1991b). However, as mentioned in previous studies (Aitkin, 1973; Calford, 1983; Morel et al., 1987), some cells in the MGm can be as narrowly tuned as those in the MGv. Our analysis of the effects of classical conditioning on RFs took into account the initial breadth of the RF. Many investigators have also reported a heterogeneity in tone-evoked latencies and also the fact that cells in the MGm can be polymodal (i.e., can respond to stimuli other than auditory). The use of a 50-ms tone to determine the RF obliged us to record cells that responded in less than 50 ms. We report here data from cells that had a latency from 10 to 30 ms at the highest intensity used. We did not check systematically the responses to nonauditory stimuli, even when we observed for some cells a broad contralateral somatosensory RF.

**Effects Induced by the Conditioning Paradigm**

The data obtained during conditioning were derived from 29 recording sites (cluster = 22, single unit = 7) from 25 animals. Because the RF was determined at several intensities for each recording, 93 RF difference functions were obtained immediately postconditioning (Table 1).

The criteria used to classify the effects of training into categories were exactly the same as described previously (Edeline & Weinberger, 1991a). A change was classified as CS–FS when three criteria were met: (a) the largest change in the RF had to be at the CS frequency, (b) the change centered on the CS frequency had to be selective (i.e., could not extend more than ±0.25 octave around the CS frequency), and (c) the change at the CS frequency had to be at least 50% greater than the change at the pretrained BF. Gen changes were consistent increases or decreases of the evoked responses across the RF; and Rand changes were small increased or decreased responses at adjacent frequencies across the RF.

In the present study, CS–FS effects were observed in 14/29 (48%) of the recordings, Gen changes were observed in 12/29 (42%), and RAND effects were observed in 3/29 (10%) cases (Table 2). The data reported here are the effects of training on the frequency RF; the data collected during the conditioning and sensitization trials will be reported separately.

**CS–FS Effects on RFs**

In 14/29 cases, conditioning produced a CS–FS increase; there were no FS decreases. In 10 of these cases, the changes were large enough to retrain the neuron such that the CS frequency became the new BF. Figure 2 shows records for a cluster exhibiting such a retuning. For Pre, the BF was 2.5 kHz, and the responses ranged from 1.5 kHz to 5.0 kHz (\( \sqrt{2} \) – ...

*Note. CS–FS = conditioned stimulus–frequency specific changes; Gen = general changes; Rand = random changes. Numbers in parentheses are percentages of the total.*

<table>
<thead>
<tr>
<th>Type of training/ modification</th>
<th>CS–FS</th>
<th>Gen</th>
<th>Rand</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditioning</td>
<td>14 (48%)</td>
<td>12 (42%)</td>
<td>3 (10%)</td>
<td>29</td>
</tr>
<tr>
<td>Increase</td>
<td>14</td>
<td>7</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>Decrease</td>
<td>0</td>
<td>5</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Sensitization</td>
<td>0 (0%)</td>
<td>13 (100%)</td>
<td>0 (0%)</td>
<td>13</td>
</tr>
<tr>
<td>Increase</td>
<td>0</td>
<td>8</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Decrease</td>
<td>0</td>
<td>5</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>20</td>
<td>3</td>
<td>37</td>
</tr>
</tbody>
</table>

1 The breadth of tuning for single units and unit clusters was not significantly different: For conditioning, the square-root transform values were 1.34 ± 0.29 octaves and 1.58 ± 0.19 octaves, respectively, \( t(7, 22) = -0.63, p > .05. \)

2 The conditioned heart rate decreases observed in animals from which non-CS–FS changes were observed were not significantly different from those that developed CS–FS plasticity (analysis of variance [ANOVA], \( p = .73 \)); also, there was no interaction between conditioned heart rate decreases observed across blocks of trials and FS versus non-FS (Gen and Rand) effects (ANOVA, \( p = .16 \)).

3 The proportions of FS effects for single units and unit clusters were not significantly different: single units = 3/7; clusters = 11/22. No differences were observed between single-unit and cluster recording for any measures in this experiment. Data from both are presented in various figures without separate consideration.
After conditioning, during which the CS frequency was 4.5 kHz, there were increased responses at 4.0 and 4.5 kHz, whereas the pretraining BF was unaffected. One hour later, responses at 4.0 and 4.5 kHz were still increased, whereas responses at the pretraining BF had decreased, so that the CS became the new BF. The quantified RF functions (Figure 3) confirmed these observations. For Post, the largest increase was at 4.5 kHz, the CS frequency (Figures 3A and 3C), with no change at the pretraining BF, whereas the 1-hr Post decreased responses at the pretraining BF allowed the CS to become the new BF (Figures 3B and 3D).

Figure 4 shows another example of a shift of tuning; in this case, it occurred immediately postconditioning and was maintained for 1 hr Post. The BF of this single neuron was 24.0 kHz before conditioning, and the CS frequency was selected to be 25.0 kHz. For Post, the CS frequency became the new BF (Figure 4A), and the RF difference function (Figure 4C) shows that this was due to increase responses at the CS frequency, whereas all the other frequencies showed decreased responses. For 1 hr Post, increased responses to frequencies higher than the CS led to a less selective effect, but the BF was still the CS frequency.

CS–FS increases without complete retuning of the BF to the CS frequency were observed in 4/14 cases, including very broadly tuned multipeaked RFs, even when the CS was far from the BF. Figure 5 shows rasters and histograms for such a case. There were pretraining responses from 5.0 (BF) to 32.0 kHz ($\sqrt{f_2} - \sqrt{f_1} = 3.24$). For Post, there were increased responses at the CS frequency (15.0 kHz); the BF was not much affected, and several frequencies higher than the CS exhibited decreased responses. For 1 hr Post, the maximal increased response was maintained at the CS frequency, and decreased responses at some higher frequencies were still observed. The quantified RF functions (Figure 6) confirmed these observations: For both Post and 1 hr Post, the responses at the CS frequency were selectively increased, whereas the BF remained unaffected, and responses to frequencies immediately higher than the CS were decreased.

The average maximal increase of the 14 CS–FS increases was 78% at the CS frequency, and the responses at the pretraining BF decreased an average of 58%, which resulted in an average CS–BF difference of 136% (Table 3). The average of the normalized difference function (Figure 7A) shows the selectivity of the increase centered on the CS frequency, with side-band decreases at higher and lower frequencies.

In 12 of the 14 CS–FS increases, recordings were also obtained 1 hr later. For these 12 cases, the mean increase at the CS frequency for the maximal effect was 73%, and the CS–BF difference averaged 108%. The average of the normalized difference curves from these 12 cases (Figure 7B) shows that the selective increase at the CS frequency was still present, even though less selective than for immediately postconditioning (0.31 octaves vs. 0.19 octaves, respectively, Table 3).

Across intensity, 48 RF difference functions were obtained immediately Post, and 45 were obtained 1 hr Post. For immediately Post, the mean increase at the CS frequency was 63%, the mean bandwidth of the CS-centered increase aver-
Figure 3. Quantified receptive fields (RFs; window analysis = 0–50 ms after tone onset) and RF difference functions for the recording presented in Figure 2. (Before conditioning [Pre], responses were from 1.5 kHz to 5.0 kHz ($\chi^2 = 1.01$), and the best frequency [BF] was 2.5 kHz. For immediately postconditioning [Post; conditioned stimulus, CS = 4.5 kHz], there were increased responses at 4.0 and 4.5 kHz [A]. One hour later [1 Hour Post; B], the evoked responses at these two frequencies were still enhanced, whereas decreased responses at the pretraining BF allowed the CS to become the new BF. The RF difference functions [C and D] show that the largest increases for both immediately post- and 1-hr post-conditioning were at the CS frequency and that the evoked responses at the initial BF were clearly decreased at 1 hr postconditioning.}

aged 0.44 octave, and the mean CS–BF difference was 122% (Table 3). For 1 hr Post, the values for the increase at the CS frequency (40%), the mean bandwidth (0.63 octave), and the CS–BF difference (93%) indicated a clear tendency for reduction of the effects. This was validated statistically; these values were all significantly different from those obtained immediately postconditioning (Table 3).

**Effect of stimulus intensity.** On average, the RF was determined at 3.4 intensities per recording. We previously found that the CS–FS effects were a function (increasing in the MGd, decreasing in the MGv) of the intensity used to determine the RFs. Therefore, we analyzed, as before, (a) the probability, (b) the magnitude, and (c) the selectivity of the CS–FS effects as a function of stimulus intensity.

**Probability.** Across intensity, 28 RF difference functions, of the 48 (58%) obtained immediately postconditioning for the CS–FS increases, met the three criteria to be classified as CS–FS. The probability of the CS–FS effects (Figure 8A) was not a function of the intensity used: 14/24 (58%) RF difference functions met the criteria at 80 dB and 70 dB, and 14/24 also met the criteria at 60, 50, and 40 dB ($\chi^2 = 0.08, df = 1, ns$). The same outcome was observed for 1 hr Post; 9/22 functions met the criteria at 80 and 70 dB, whereas 10/23 met the criteria at 60, 50, and 40 dB ($\chi^2 = 0.16, df = 1, ns$).

**Magnitude.** The magnitude of the increase at the CS frequency did not depend on the intensity that was used to determine the RF for either Post or 1 hr Post, (Figure 8B; Kruskal-Wallis test: $H = 4.07, df = 4, ns$, for Post; and $H = 3.96, df = 4, ns$, for 1 hr Post).

**Frequency selectivity.** Selectivity (Figure 8C), of the CS-centered increase was not related to intensity for either Post or 1 hr Post ($H = 1.98, df = 4, ns$, and $H = 0.042, df = 4, ns$, respectively).

**General Increases in RFs**

In 7/29 recordings, Gen increases were observed immediately postconditioning (Table 2). Figure 9 shows data for a
cluster that responded from 9.0 to 25.0 kHz ($\sqrt{2} - \sqrt{1} = 2.0$) pretraining. For immediately postconditioning, responses at the CS frequency (15.0 kHz) were increased, but this was not the largest increase, and there were increases at almost all other frequencies (Figures 9A and 9C). The same effect was observed for 1 hr Post (Figures 9B and 9D).

The average of the maximum normalized RF difference functions for the Gen increases showed (a) that the CS frequency was not favored compared with the other frequencies and (b) that the extent of the increases across the RFs was more than one octave. One hour later, these broad increases were maintained without any favored increase at the CS frequency (Figure 10A). The three parameters used to quantify the RF changes were very similar for Post and 1 hr Post (Table 3). Seventeen RF difference functions were obtained for both Post and 1 hr Post, and their analyses confirmed that the Gen increases were still present 1 hr later. There were no statistical differences for the two time periods: increase at the CS frequency, 22% versus 24%, $t(32) = 0.21$, ns; mean bandwidth, 1.54 octaves versus 1.57 octaves, $t(32) = 0.13$, ns; CS–BF difference, 1% versus −10%, $t(32) = 0.89$, ns (Table 3). The Gen increases differed significantly from the CS–FS increases for all three parameters for both time periods (Figure 3).

There were no effects of stimulus intensity (Figure 11) for either Post or 1 hr Post on probability, $\chi^2$s = 0.12 and 0.13, respectively, $df = 1$ for both, ns; magnitude, $H$s = 4.16 and 7.02, respectively, $df = 4$ for both, $ns$; or bandwidth, $H$s = 5.32 and 6.47, respectively, $df = 4$ for both, $ns$.

**General Decreases in RFs**

In 5/29 recordings, Gen decreased responses were observed for Post, and all were maintained for 1 hr Post (Table 3). Figure 12 gives an example of a Gen decrease. Across intensities, maintenance of Gen decreases was evident in the absence of statistically significant differences for Post versus 1 hr Post: 21% versus −32% for the decrease at the CS frequency, $t(32) = 1.15$, ns; 1.35 octaves versus 1.32 octaves for the bandwidth of the effect, $t(32) = 0.12$, ns; and 37% versus 25% for the CS–BF difference, $t(32) = 0.814$, ns.
There were no relationships between stimulus intensity and the RF changes probability, Post $\chi^2 = 0.23$, df = 1, ns, and 1 hr Post $\chi^2 = 0.29$, df = 1, ns; magnitude of decrease at the CS frequency, Post $H = 3.52$, df = 3, ns, and 1 hr Post $H = 0.17$, df = 3, ns; bandwidth, Post $H = 3.96$, df = 3, ns, and 1 hr Post $H = 3.78$, df = 3, ns.

**Random Changes in RFs**

Three recordings were classified as Rand because they neither reached criteria for CS–FS effects nor exhibited Gen changes. The average of the normalized difference functions did not reveal any type of systematic effect for either Post or 1 hr Post (Figure 10C).

**Effects Induced by the Sensitization Paradigm**

Recordings were obtained from 13 sites for subjects that were trained in the sensitization paradigm. None of the RF difference curves obtained from these recordings met the CS–FS criteria. However, all of them developed Gen changes in their RF (increases = 8, decreases = 5) for both Post and 1 hr Post (Table 2).

**General Increases in RFs**

An example of Gen increased responses is given in Figures 13A and 13B, and the group function is presented in Figure 14A. Across intensities, Gen increases revealed significant differences compared with the CS–FS increases induced by the conditioning paradigm. Increase at the CS frequency was smaller, bandwidth was larger, and the CS–BF difference was smaller. In contrast, none of the three parameters differed between Gen increases during sensitization and Gen increases induced by the conditioning paradigm (Table 3). For 1 hr Post, the same relationships were found (Table 3).

Thus, as previously reported (Bakin & Weinberger, 1990a; Edeline & Weinberger, 1991a, 1991b), the Gen effects that develop in sensitization were indistinguishable from those that developed in conditioning, but they differed in all aspects from the CS–FS effects observed for conditioning.

There were no relationships to stimulus intensity; probability, Post $\chi^2 = 0.27$, df = 1, ns, and 1 hr Post $\chi^2 = 0.12$, df = 1, ns; magnitude, Post $H = 1.87$, df = 5, ns, and 1 hr Post $H = 3.79$, df = 5, ns; bandwidth, Post $H = 3.79$, df = 5, ns, and 1 hr Post $H = 4.33$, df = 5, ns.

**General Decreases in RFs**

In five cases, the sensitization paradigm induced Gen decreased responses (Figures 13C and 13D). The average of the normalized RF difference functions for the maximal effects (Figure 14B) shows that these effects were maintained for 1 hr Post and were very similar to the Gen decreases induced by the conditioning paradigm (compare with Figure 10B). Both conclusions were corroborated by analysis of the 21 RF difference curves obtained from these placements. First, maintenance was evident by the absence of statistically significant
Figure 6. Quantified receptive fields (RFs; window analysis = 0–50 ms after tone onset at 70 dB) and RF difference functions for the recording presented in Figure 5. (Before conditioning [Pre], the RF was multipeaked and extended from 5.0 kHz to 30.0 kHz \( \sqrt{2} \times \sqrt{1} = 3.24 \); BF = 5.0 kHz; CS = 15.0 kHz. For immediately Post [A] and 1 hr later [1 Hour Post; B], there were increased responses at 15.0 kHz, whereas the BF remained unaffected, and the frequencies higher than the BF were decreased. The RF difference functions [C and D] show that the largest increases for both immediately post- and 1 hr postconditioning were at the CS frequency, with decreased responses for 17.0–32.0 kHz.)

Differences between the values obtained for Post and 1 hr Post: decrease at the CS frequency, -19 versus -24%, \( t(40) = 0.84, ns \); bandwidth of the decrease, 1.69 octaves versus 1.79 octaves, \( t(40) = 0.45, ns \); CS–BF difference, 31% versus 23%, \( t(40) = 0.7, ns \). Second, there was no difference between these values and those obtained for the corresponding Gen decreases induced by conditioning for either Post or 1 hr Post (Table 3).

RF changes were unrelated to intensity probability, Post \( \chi^2 = 0.45, df = 1, ns \), and 1 hr Post \( \chi^2 = 0.31, df = 1, ns \); magnitude, Post \( H = 2.85, df = 5, ns \), and 1 hr Post \( H = 5.65, df = 5, ns \); bandwidth, Post \( H = 5.30, df = 5, ns \), and 1 hr Post \( H = 7.18, df = 5, ns \).

CS–FS Plasticity: Pretraining Characteristics Related to Occurrence and Retention

We previously reported that the probability of occurrence and the degree of retention of CS–FS plasticity in the MGv were related to pretraining parameters. CS–FS plasticity was obtained only when the distance between the CS frequency and the pretraining BF were very close—equal to or less than 0.125 octaves. Retention of FS plasticity 1 hr Post for these narrowly tuned cells was essentially nonexistent (Edeline & Weinberger, 1991b), in contrast to retention for broadly tuned cells in the MGd, which was excellent (Edeline & Weinberger, 1991a). Given that FS plasticity develops in the MGm, it was of interest to determine whether FS effects were related to pretraining parameters. We analyzed both (a) the probability of obtaining FS plasticity versus non-FS effects and (b) the degree of retention of FS plasticity for CS–BF distance, amount of excitatory response to the CS frequency, breadth of tuning, and the locus of recording within the MGm.

Probability of Obtaining FS Plasticity

The probability of obtaining FS plasticity with respect to pretraining parameters was analyzed in two ways: for all recordings and for narrowly versus broadly tuned cells.

All recordings. There was no significant relationship between CS–BF distance and the occurrence of FS plasticity.
A Immediately Post-Conditioning

B One Hour Post-Conditioning

Figure 7. Group data for the conditioned stimulus–frequency specific (CS–FS) increases observed immediately post- and 1-hr postconditioning. (These functions are the means [±SE] of the normalized receptive field [RF] difference functions for the maximal effect [based on the greatest CS–best frequency, BF, difference] for the 14 recordings that met the CS–FS criteria immediately postconditioning. For each recording, the percentage of change at each frequency was expressed as a function of the distance from the CS, the mean. For immediately postconditioning, there was a 78% increase at the CS frequency, and decreased responses were 0.125 octave away. B: One hour postconditioning, there was still a 73% increase at the CS frequency, the bandwidth of the effects was 0.25 octave, and side-band suppression was still present.)

However, the absence of a relationship might have been related to differences in the shapes of RFs in the MGv versus the MgM. In the MGv, pretraining RFs generally have single peaks (inverted-V shapes) so that the frequency distance between the BF and CS tends to be proportional to the relative strength of response to these frequencies before training; the smaller the distance, the greater the response to the CS in relation to the BF. Therefore, the significant CS–BF distance relationship found in the MGv might actually reflect the amount of pretraining excitatory response to the CS frequency in relation to the BF: the greater the CS response, the greater the probability of developing FS plasticity. MgM cells generally do not have such simple RFs but have usually complex RFs with multiple peaks. In these cases, CS–BF frequency distance would not be a good indication of CS response strength in relation to BF response. Therefore, we directly measured the responses to the CS and BF before training and calculated the percentage of CS response in relation to the BF response using the following formula: (CS/BF spikes-s) × 100. Response values were taken from the intensity that showed the maximal FS effect. However, this analysis also failed to find a significant relationship between the relative amount of CS excitatory drive and the occurrence of FS plasticity: The values were 42% for the FS effects versus 41% for the non-FS effects (Table 4).

Also, pretraining breadth of tuning was not related to the probability of obtaining FS effects. Using the square-root transformation (see the Method section), the mean breadth of tuning was 1.38 octaves for the FS effects versus 1.64 octaves for the non-FS (Gen and Rand) changes (Table 4). A comparison of FS versus only Gen effects was not significant: Gen = 1.71, t(24) = 0.21.

Figure 15 gives a histological summary of the electrode placements in the MgM and the types of effect. It reveals that the CS–FS effects were found throughout the rostrocaudal axis of the nucleus, but the probability of observing an FS effect varied along this axis. In the rostral part of the nucleus (the upper sections), 10/15 (66%) placements developed FS plasticity; whereas in the caudal part (the lower sections), only 4/14 (28%) sites developed this plasticity. This difference was statistically significant (Table 4). There were no significant differences as a function of rostral versus caudal locus for (a) magnitude of increase at the CS frequency, (b) bandwidth of the increase, or (c) CS–BF difference, either for maximal or across-intensities measures for either the Post or 1-hr Post periods (Table 5).

A summary to this point is that only one pretraining characteristic was related to the development of CS–FS plasticity, the locus of recording: FS plasticity was more likely in the rostral half than in the caudal half of the MgM. However, when FS plasticity developed, its parameters were not significantly different regardless of its locus in nucleus.

Narrowly versus broadly tuned cells. The RFs of MgM cells were broader than are those of MGv cells; nonetheless, some cells in the MgM were as narrowly tuned as those in the MGv (Aitkin, 1973; Calford, 1983; Morel et al., 1987; Rouiller et al., 1989). Therefore, we divided cells into two categories based on their pretraining breadth of the tuning: narrowly tuned ($\sqrt{f_2} - \sqrt{f_1} < 1.0$) and broadly tuned ($\sqrt{f_2} - \sqrt{f_1} \geq 1.0$). This revealed two different populations of neurons: The mean breadth of tuning for the narrowly tuned cells ($n = 8$) was 0.60 octave, whereas the mean breadth of the broadly tuned cells ($n = 21$) was 1.99 octaves, unpaired $t$ test: $t(27) = 6.74, p < .0001$. For Post, 5/8 (62%) of the narrowly tuned cells showed FS plasticity, but only 9/21 (43%) broadly tuned cells exhibited such effects; however, this difference was not significant, $X^2 = 0.86, df = 1, n.s.$ As was the case for the entire population of recordings, pretraining breadth of tuning was not the critical factor for the occurrence of FS plasticity.

Separate comparisons within the two groups of narrowly and broadly tuned cells were performed for the same pretraining parameters as for all the cells (as described earlier). CS–BF distance, breadth of tuning, and magnitude of excitatory drive to the CS frequency were not significantly different between FS and non-FS recordings, for either the narrowly or broadly.
### Table 3

**Summary of the Effects Induced by Conditioning and Sensitization on the Percentage of Change (M ± SE) at the Conditioned Stimulus (CS), the Bandwidth of the Changes (in Octaves), and the Difference Between the Percentage of Change at the CS and at the Best Frequency (BF; CS–BF Difference)**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Percentage change at CS</th>
<th>Bandwidth of effects</th>
<th>CS–BF difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Post 1 Hr Post</td>
<td>Post 1 Hr Post</td>
<td>Post 1 Hr Post</td>
</tr>
<tr>
<td>CS-FS</td>
<td></td>
<td>Maximal Effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increases</td>
<td>14</td>
<td>78 ± 6 73 ± 15</td>
<td>0.19 ± 0.05 0.31 ± 0.12</td>
<td>136 ± 11 108 ± 15</td>
</tr>
<tr>
<td>Decreases</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>12</td>
<td>42 ± 8 27 ± 11</td>
<td>1.6 ± 0.84 1.72 ± 0.75</td>
<td>-14 ± 33 -5 ± 25</td>
</tr>
<tr>
<td>Increases</td>
<td>7</td>
<td>-36 ± 10 -37 ± 09</td>
<td>1.76 ± 0.42 1.56 ± 0.53</td>
<td>79 ± 28 63 ± 29</td>
</tr>
<tr>
<td>Decreases</td>
<td>5</td>
<td>9 ± 36 20 ± 25</td>
<td>- -</td>
<td>35 ± 16 43 ± 22</td>
</tr>
<tr>
<td>Random</td>
<td>3</td>
<td>26 ± 23 40 ± 23</td>
<td>0.18 ± 0.6 0.812 ± 0.23</td>
<td>-47 ± 15 -35 ± 10</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>36 ± 5 33 ± 15</td>
<td>0.6 ± 0.11 0.875 ± 0.12</td>
<td>34.5 ± 14 61 ± 25</td>
</tr>
<tr>
<td>Sensitization</td>
<td>13</td>
<td>Increases</td>
<td>8</td>
<td>26 ± 23 40 ± 23</td>
</tr>
<tr>
<td>Decreases</td>
<td>5</td>
<td>-36 ± 5 -33 ± 15</td>
<td>0.6 ± 0.11 0.875 ± 0.12</td>
<td>34.5 ± 14 61 ± 25</td>
</tr>
<tr>
<td>Grand total</td>
<td>42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effects Observed Across All RF Difference Curvesb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CS-FS</td>
<td>48</td>
<td>Increases</td>
<td>48</td>
<td>63 ± 5 40 ± 4</td>
</tr>
<tr>
<td>Decreases</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>34</td>
<td>Increases</td>
<td>17</td>
<td>24 ± 7 22 ± 5</td>
</tr>
<tr>
<td>Decreases</td>
<td>17</td>
<td>-21 ± 4 -32 ± 17</td>
<td>1.35 ± 0.16 1.32 ± 0.22</td>
<td>37 ± 26 25 ± 10</td>
</tr>
<tr>
<td>Random</td>
<td>11</td>
<td>-7 ± 13 -7 ± 12</td>
<td>0.70 ± 0.13 0.55 ± 0.06</td>
<td>65 ± 17 74 ± 14</td>
</tr>
<tr>
<td>Total</td>
<td>93</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitization</td>
<td>48</td>
<td>Increases</td>
<td>27</td>
<td>22 ± 6 22 ± 4</td>
</tr>
<tr>
<td>Decreases</td>
<td>21</td>
<td>-19 ± 5 -24 ± 6</td>
<td>1.68 ± 0.21 1.79 ± 0.20</td>
<td>31 ± 7 23 ± 9</td>
</tr>
<tr>
<td>Grand total</td>
<td>141</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Comparisons

<table>
<thead>
<tr>
<th>FS post vs. 1 hr post</th>
<th>p &lt; .002</th>
<th>p &lt; .005</th>
<th>p &lt; .001</th>
<th>p &lt; .001</th>
<th>p &lt; .001</th>
<th>p &lt; .001</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS inc vs. gen inc</td>
<td>p &lt; .001</td>
<td>p &lt; .03</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
</tr>
<tr>
<td>FS inc vs. sens inc</td>
<td>p &lt; .001</td>
<td>p &lt; .01</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
</tr>
<tr>
<td>Sens inc vs. gen inc</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Sens dec vs. gen dec</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

*Note.*  
FS = frequency specific; RF = receptive field; inc = increase; gen = general; sens = sensitization; dec = decrease.

*Effects are for immediately postconditioning data. *When a recording site was classified as CS-FS, all RF difference functions obtained from it were incorporated in the CS-FS group. *t* tests: These comparisons refer to effects across all RF difference functions.

### Discussion

Tuned cells (Table 4). However, locus of recording was highly significant for narrowly tuned cells: FS plasticity was more likely in the rostral part than in the caudal part of the MGm, \( \chi^2 = 4.30, p < .04 \). No such relationship was found for broadly tuned cells (Table 4).

In summary, the occurrence of FS plasticity was related only to the locus of cells within the MGm. CS–FS plasticity was more likely in the rostral part of the nucleus for all recordings, and this effect appeared to be due to the fact that narrowly tuned cells in the rostral part developed FS plasticity but that narrowly tuned cells in the caudal part did not develop RF plasticity.

**Retention of CS–FS Plasticity**

The preceding analyses indicated, among other findings, that narrowly and broadly tuned cells did not differ in the probability of occurrence of FS plasticity. However, as noted earlier, narrowly tuned cells in the MGv that developed FS plasticity for immediately Post conditioning did not retain this effect for 1 hr Post (Edeline & Weinberger, 1991b), whereas broadly tuned cells in the MGd did retain FS plasticity (Edeline & Weinberger, 1991a). Therefore, we asked whether these same relationships held for narrowly and broadly tuned cells within the MGm.

Examples of RFs presented previously in this article do indeed suggest that retention was poor for narrowly tuned cells but better for broadly tuned cells. Thus, Figures 3 and 6 show good retention for cells with broad tuning, the square-root breadth of tuning values were 1.01 octaves and 3.24 octaves, respectively. In contrast, Figure 4 shows RFs for a more narrowly tuned cell (\( \sqrt{f_2} - \sqrt{f_1} = 0.79 \)) for which FS plasticity appears to be reduced for 1 hr Post versus Post; the bandwidth of increase that was centered on the CS frequency was broader. Figure 16 presents data for a very narrowly tuned cluster (\( \sqrt{f_2} - \sqrt{f_1} = 0.28 \)) located in the rostral MGm. Its pretraining BF was 1.0 kHz. After conditioning, in which the
Group RF difference functions for FS plasticity were computed separately for narrowly and broadly tuned cells, for both Post and 1-hr Post conditioning (Figure 17). For Post, both groups exhibited FS plasticity that was centered on the CS frequency (Figures 17A and 17C). However, the retention data for 1 hr Post indicated that the broadly tuned cells continued to develop FS plasticity, whereas the narrowly tuned cells exhibited a loss of FS plasticity (Figures 17B and 17D). Thus, although broadly tuned cells showed larger increases at the CS frequency, narrower bandwidth of increase, and even slightly greater CS–BF magnitude differences, narrowly tuned cells exhibited the opposite trend (Table 6). Analysis of the data across intensities confirmed this differential evolution. The three parameters used to quantify the effects of conditioning were very similar for immediately Post: 62.8% versus 62.9% for increase at the CS frequency, 0.438 octaves versus 0.439 octaves for the bandwidth; 114% versus 127% for the CS–BF difference, respectively, for narrowly and broadly tuned cells. However, these measures were significantly different for 1 hr Post: Increase at the CS frequency was smaller, 29% versus 49%, \( t(43) = 2.36, p < .03 \); bandwidth was larger, 0.84 octave versus 0.48 octave, \( t(43) = 3.49, p < .002 \), and the CS–BF difference was smaller, 74% versus 107%, \( t(43) = 2.33, p < .03 \), for narrow versus broad, respectively.

To further elucidate the differences in retention, we calculated a retention index by subtracting the values for these three parameters obtained for Post from their corresponding values for 1 hr Post. Regression analyses were then done for pretraining breadth of tuning versus each of the three parameters. These revealed that the pretraining breadth of tuning was directly related both to (a) retention of the CS–BF difference, \( r = .627, df = 11, F(1) = 6.49, p < .05 \), and (b) bandwidth of the CS-centered increase, \( r = .591, df = 11, F(1) = 5.36, p < .05 \). There was also a nonsignificant tendency for retention of the increase at the CS frequency to be linked with the pretraining breadth of the tuning, \( r = .452, df = 11, F(1) = 2.57, p = .13 \).

In summary, retention of FS plasticity differed for narrowly and broadly tuned cells. Narrowly tuned cells tended to lose FS plasticity, whereas broadly tuned cells maintained, perhaps even increased, FS plasticity. *4*

Discussion

Overview of the Findings

The main finding of this study is that classical conditioning produces RF plasticity in the MGrm that is specific to the frequency of the CS. Immediately after training, responses to the CS increased, whereas responses to most other frequencies, including the pretraining BF, decreased or changed little. Specificity to the CS frequency was characterized by maximal

---

*4 The CS–BF frequency distance was smaller for narrowly tuned cells than for broadly tuned cells, 0.244 octave versus 0.851 octave, \( t(27) = 3.05, p < .01 \), so that retention might be thought to be predicted by this parameter rather than by the pretraining breadth of tuning. However, retention indices (magnitude of change at CS, bandwidth centered on CS frequency, and CS–BF magnitude difference) were not significantly correlated with CS–BF distance, *p* = .09–.23, *t* tests).
increase at the CS frequency, narrow bandwidth of change centered on the CS frequency, and even an actual shift of tuning such that the CS became the new BF after conditioning in 10/14 (71%) of the FS cases.

Immediately postconditioning CS–FS increases were observed in both broadly and narrowly tuned cells. However, although CS–FS plasticity developed for broadly tuned cells (becoming even stronger 1 hr later), it was weaker or absent 1 hr after training for the narrowly tuned cells. The expression of CS–FS plasticity was independent of intensity in the MGm, which may reflect a lack of well-defined rate-level functions for individual frequencies in awake animals under nonlearning circumstances (Aitkin & Prain, 1974). This contrasts with the intensity relationships found in both the MGd and the MGv (Edeline & Weinberger, 1991a, 1991b).

CS–FS effects were found along the entire rostrocaudal axis of the MGm, but their probability of occurrence was higher in the rostral half than in the caudal half of the MGm. This finding might be related to anatomical and physiological evidence that spinothalamic tract input from the UCS is more heavily distributed to the rostral region than the caudal region of this nucleus (LecDoux et al., 1987; Poggio & Mountcastle, 1960; Winer & Moster, 1983; see also Jones, 1985). Thus, the higher percentage of CS–FS effects in the rostral part of the MGm may be the consequence of a higher percentage of cells that received convergent input from both the CS and the UCS. (We were unable to quantify neuronal responses to the UCS due to artifacts.)

As already noted, FS plasticity was maintained after the 1-hr retention interval. This experiment did not include longer retention intervals so that the maximal duration of retention remains to be determined. Neither did it permit determination of the minimal amount of CS–UCS pairing that is sufficient to induce FS plasticity. Only 30 training trials were used, and behavioral CRs (cardiac bradycardia) were evident within the first 5 trials of pairing, even after 10 trials of sensitization training that would tend to retard the rate of acquisition. The rapid establishment of FS plasticity in this study, as well as previous findings for the auditory cortex (Diamond & Weinberger, 1986, 1989) and other divisions of the MGB (Edeline & Weinberger, 1991a, 1991b), are impressive compared with the much slower rates of development of discharge plasticity that
narrowly tuned cells versus the broadly tuned cells is noteworthy in view of our previous observations in the MGv, the cells of which are narrowly tuned. MGv cells that developed CS–FS increases exhibited no retention 1 hr later (Edeline & Weinberger, 1991b). The fact that narrowly tuned neurons located

Figure 10. Group data for the general increases, general decreases, and random effects induced by the conditioning paradigm. (Each of these functions is the average of the normalized receptive field [RF] difference curve for the maximal effect within its category. Seven recordings classified as general increases developed marked increased responses of more than 1.0 octave around the conditioned stimulus [CS] frequency that were maintained 1 hr postconditioning. Five recordings classified as general decreases developed decreased responses of more than 1.0 octave around the CS frequency, and they were still observed 1 hr postconditioning. Three recordings were categorized as random effects, and they did not exhibit any particular effects 1 hr later. Note the absence of selectivity of these three types of RF modifications compared with the CS-frequency specific increases presented in Figures 7A and 7B.)

occur in circuitry that is apparently responsible for specific somatic CRs (Thompson et al., 1983; Tsukahara, Oda, & Notsu, 1981; Woody, 1982).

The differential retention of the CS–FS increases for the

Figure 11. Relation of the intensity to the parameters describing the general increases observed immediately post- (IPC; open bars) and 1 hr postconditioning (1HPo; hatched bars). (The probability of obtaining a general increase was not related to the intensity used to determine the receptive field [RF]. The magnitude of the increase at the conditioned stimulus [CS] frequency was not related to the intensity. The selectivity of the effects observed was not related to the intensity. For these three measures, the number of RF difference functions used was, from 80 dB to 40 dB, respectively, 4, 4, 5, 3, and 1 both immediately post- and 1 hr postconditioning.)
in the MGm also failed to retain FS plasticity suggests that the lemniscal property of high-fidelity representation of the physical parameters of stimuli is incompatible with retention of frequency selective effects, regardless of their location within the auditory thalamus. Several nonexclusive hypotheses can be proposed to explain this characteristic: (a) strong lateral inhibition (Müller & Scheich, 1988) mediated by the actions of γ-aminobutyric acid, which are known to prevent the development of long-term synaptic plasticity (Artola & Singer 1987, 1990); (b) weak effects of neuromodulator actions compared with their effects on sensory cortical cells (e.g., norepinephrine: Rogawski & Aghajanian, 1980; Waterhouse et al., 1988; Waterhouse & Woodward, 1980; acetylcholine: Ashe, McKenna, & Weinberger, 1989; McKenna, Ashe, Hui, & Weinberger, 1988; McKenna, Ashe, Weinberger, 1989; Metherate, Tremblay, & Dykes, 1988; Sillito & Kemp, 1983); (c) different morphology of broadly versus narrowly tuned cells (Most, 1964; Winer, 1985; Winer & Most, 1983), which have differential membrane properties that could be linked to differential retention of FS plasticity. In any event, it seems that cells in the MGB that provide detailed frequency information serve to reflect mainly the physical parameters of sound rather than the acquired significance of sound, except for a brief period after the learning experience. In short, the subcortical lemniscal pathway appears to be “protected” from long-term plasticity, perhaps to provide accurate representation of the acoustic environment.

CS-FS Plasticity Is Associative

CS-FS plasticity is produced by associative processes for the following reasons. First, it developed only in animals that were trained with CS-UCS pairings. Second, it was not produced by chance, perhaps due to the large number of RFs that were obtained across intensities. All FS plasticity was an increased response at the CS frequency, although there was no instance of an FS decreased response at the CS frequency; chance would have produced apparent FS decreases as well as increases. Moreover, none of the 48 RF difference curves that were obtained in the sensitization group met the criteria for FS
plasticity; rather, all sensitization recordings developed general changes in RFs (Tables 2 and 3).

Third, CS–FS plasticity was not due to the state of arousal during posttraining RF determinations. We have previously considered in detail why putative phasic arousal could not have accurately "tracked" the rapid presentation of various frequencies. Briefly, even if elicited by the CS, arousal could not have been active to facilitate the short-latency (10–35 ms) discharges reported here and then have been terminated before the presentation of the next tone; nor could the opposite have been accomplished (i.e., BF-evoked reduced arousal) to account for decreased responses to the BF (Diamond & Weinberger, 1989). Moreover, arousal would be expected to have some effect on spontaneous discharges, but FS plasticity develops in both the auditory thalamus and the auditory cortex and in the absence of changes in the background rate of discharge (see Figures 2 and 5 of this article; see also Bakin & Weinberger, 1990a; Edeline & Weinberger, 1991a). Finally, direct measurements of pupil diameter (Diamond & Weinberger, 1989) and heart rate in this and previous studies (Edeline & Weinberger, 1991a, 1991b) revealed no change in arousal level. Diamond and Weinberger (1989) have considered in detail the many differences in context between training trials and periods of RF determinations that may explain why subjects do not respond to the CS frequency and other tones presented during RF determination.

Characteristics of RF Plasticity in the MGm, MGv, and Auditory Cortex

This study completes an initial survey of the effects of associative learning on frequency RFs in the thalamocortical auditory system of the guinea pig during classical conditioning and sensitization. In this section, we consider the key characteristics of CS–FS plasticity in the MGm, MGv, and primary auditory cortex and distinguish between common and different features. In the next section, we discuss the possible functional role of CS–FS plasticity in the MGm, MGv, and primary
RECEPTIVE FIELD PLASTICITY IN MEDIAL MGB

Figure 14. Group data for the general increases and decreases induced by the sensitization paradigm. (Each function is the average of the normalized receptive field [RF] difference curve for the maximal effect of each recording. Eight recordings developed increased responses of more than 1.0 octave around the training frequency that were maintained 1 hr postconditioning. Five recordings developed marked decreased responses of more than 1.0 octave around the training frequency that were still observed 1 hr postconditioning. Note the absence of selectivity of these RF modifications compared with the CS–frequency specific increases presented in Figures 7A and 7B and the similarities with the general increases and decreases presented in Figures 10A and 10B.)

<table>
<thead>
<tr>
<th>Parameters/statistic</th>
<th>All recordings</th>
<th>Narrowly tuned cells</th>
<th>Broadly tuned cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS–BF distance</td>
<td>0.62 (ns)</td>
<td>0.26 (ns)</td>
<td>0.83 (ns)</td>
</tr>
<tr>
<td>t test</td>
<td>0.23 (ns)</td>
<td>0.64 (ns)</td>
<td>1.80 (ns)</td>
</tr>
<tr>
<td>Breadth of tuning</td>
<td>1.38 (ns)</td>
<td>1.14 (ns)</td>
<td>0.31 (ns)</td>
</tr>
<tr>
<td>t test</td>
<td>0.81 (ns)</td>
<td>41</td>
<td>41</td>
</tr>
<tr>
<td>Excitatory drive (%)</td>
<td>42</td>
<td>0.49 (ns)</td>
<td>1.25 (ns)</td>
</tr>
<tr>
<td>t test</td>
<td>0.04 (ns)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Rostral (%)</td>
<td>66</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>Caudal (%)</td>
<td>28</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>Chi-square</td>
<td>4.06 (p &lt; .05)</td>
<td>4.30 (p &lt; .04)</td>
<td>0.35 (ns)</td>
</tr>
</tbody>
</table>

Table 4
Pretraining Parameters for Conditioned Stimulus–Frequency Specific (CS–FS) Increases Versus Non-CS–FS Effects


Common Characteristics of CS–FS RF Plasticity

The common features of CS–FS RF plasticity in the MGm, MGV, and primary auditory cortex are (a) rapid development (i.e., present after only 30 CS–US trials) that follows 10 sensitization trials, (b) a high degree of specificity (i.e., narrow bandwidth of change centered on the CS frequency), (c) decreased responses at the pretraining BF and other frequencies in addition to increased responses at the CS frequency, (d) returning to the CS frequency (i.e., in many cases the CS becomes the new BF), and (e) associative dependence (i.e., CS–UCS pairing is necessary for the development of CS–FS plasticity).

Also, although non-FS-maintained general increases in response have been found in the MGm, MGV, and primary auditory cortex in some conditioning sessions, these same effects are produced in sensitization sessions. However, these general changes in frequency RFs in the MGm and MGV are probably not caused by the presence of an acoustic stimulus during sensitization training because the same effect is produced in the auditory cortex when subjects undergo sensitization training with a visual stimulus that is presented unpaired with shock (Bakin & Weinberger, 1990b). Of interest, general increases in the RFs found in some conditioned subjects are indistinguishable from those induced by sensitization training. Therefore, it seems quite possible that general increases across the RF reflect fear that is conditioned not to the CS but to the background cues of the training context.

Different Characteristics of CS–FS Plasticity

The major differences of plasticity among the MGm, MGV, and primary auditory cortex are (a) CS–BF proximity (i.e., the MGV requires that the CS be within 0.125 (5th) octave, whereas the MGm and auditory cortex do not have such a narrow restriction), (b) retention (i.e., the MGV shows no retention 1 hr after conditioning, whereas the MGm and
auditory cortex exhibit retention of CS–FS plasticity at the longest intervals tested, 1 hr and 24 hr, respectively), (c) intensity (i.e., the MGv exhibits FS plasticity only at the lowest intensity levels, whereas the FS plasticity in the MGm and auditory cortex are observed across intensities), and (d) frequency tuning and expression. Although FS plasticity in the MGv, MGm, and auditory cortex all indicate that processing of the CS frequency is facilitated in relation to other frequencies, the expression of this plasticity is very different given the marked variations in frequency tuning. The MGv has very
Table 5
Comparison of the Parameters Obtained for the Conditioned Stimulus–Frequency Specific (CS-FS) Increases in the Rostral and Caudal Parts of the Medial Medial Geniculate Body

<table>
<thead>
<tr>
<th>Structure</th>
<th>CS increase (%)</th>
<th>Bandwidth (in octaves)</th>
<th>CS–BF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudal</td>
<td>92</td>
<td>0.386</td>
<td>147</td>
</tr>
<tr>
<td>Rostral</td>
<td>78</td>
<td>0.338</td>
<td>124</td>
</tr>
<tr>
<td>Comparison</td>
<td>( t(12) = 0.28 )</td>
<td>( t(12) = 0.55 )</td>
<td>( t(12) = 0.20 )</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data across intensities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudal</td>
</tr>
<tr>
<td>Rostral</td>
</tr>
<tr>
<td>Comparison</td>
</tr>
</tbody>
</table>

Note. BF = best frequency.

sharply tuned cells with single peak RFs so that FS plasticity is expressed as a relatively simply shift of the peak (Figures 2–5, Edeline & Weinberger, 1991b). In the auditory cortex, there are both single- and multipeaked RFs. FS plasticity is expressed in many ways, which include producing a response to a previously ineffectual frequency, filling in a “notch” between two peaks, creating a second peak on a previously single-peaked RF, and even maintaining response at the CS fre-

Figure 16. Transient shift of tuning for a narrowly tuned cluster recorded in the rostral part of the medial geniculate body. (The quantified receptive fields [RFs; window analysis = 0–50 ms] show that this cluster responded between 0.7 kHz and 1.2 kHz at 70 dB [\( \sqrt{2} - \sqrt{1} = 0.28 \)] with its BF at 1.0 kHz. The conditioned stimulus [CS] was selected to be 0.7 kHz. Immediately postconditioning [A] marked increased response at the CS frequency and decreased response at the initial best frequency [BF] allowed a complete shift of tuning; the CS frequency became the new BF. However, for 1 hr postconditioning, the BF shifted back to 1.0 kHz [B]. The RF difference functions show the selectivity of the increase immediately postraining [C] and the decreased responses at the pretraining BF. For 1 hr postconditioning, the responses at the pretraining BF came back to the pretraining level, the increased responses at the CS frequency were weaker, and there were increased responses at the frequency higher than the BF.)
Broadly Tuned Cells

A Immediately Post-Conditioning

Percent Changes

-100 -50 0 50 100

-0.6 -0.4 -0.2 0.0 0.2 0.4 0.6 Distance from CS (octave)

B 1 Hour Post-Conditioning

Percent Changes

-100 -50 0 50 100

-0.6 -0.4 -0.2 0.0 0.2 0.4 0.6 Distance from CS (octave)

Narrowly Tuned Cells

C Immediately Post-Conditioning

Percent Changes

-100 -50 0 50 100

-0.6 -0.4 -0.2 0.0 0.2 0.4 0.6 Distance from CS (octave)

D 1 Hour Post-Conditioning

Percent Changes

-100 -50 0 50 100

-0.6 -0.4 -0.2 0.0 0.2 0.4 0.6 Distance from CS (octave)

Figure 17. Average of the normalized receptive field (RF) difference curves immediately post- and 1 hr postconditioning for broadly tuned cells (A) and narrowly tuned cells showing conditioned stimulus–frequency specific (CS–FS) increase after the conditioning paradigm. (A: The average of the nine broadly tuned recordings exhibiting CS–FS increases shows that from immediately postconditioning to 1 hr postconditioning, the increase at the CS frequency became bigger, whereas the bandwidth of the effect became sharper. B: In contrast, the average of the five narrowly tuned recordings shows that from immediately postconditioning to 1 hr postconditioning, the increase at the CS frequency became smaller, whereas the bandwidth of the effect became broader.)

frequency when all other frequencies develop decreased responses (Figures 2–5, Bakin & Weinberger, 1990a). In the MGm, pretraining RFs are generally extremely complex and broad so that CS–FS effects, although clear, can’t be related in a simple manner to the shape of the RF (e.g., Figures 3A, 4A, and 6A). In short, the common increases at the CS frequency and decreases at the other frequencies in all three structures should not obscure the marked differences in how this FS plasticity is expressed.

Thalamic and Cortical Plasticity

A common assumption is that if a subcortical structure has any physiological characteristics in common with its cortical projection area, then it probably projects these characteristics to that area. For example, if discharge plasticity is observed in both the thalamus and the cortex, particularly if the latency is shorter in the thalamus than in the cortex, then it may be concluded that the cortex plays a passive role. However, because corticothalamic projections reciprocate thalamocortical projections, it could also be argued that the thalamic plasticity is “projected” from the cortex. A shorter latency of evoked discharge plasticity in the thalamus would not rule this out because tonic influences from the cortex could “gate” the thalamic short-latency plasticity on succeeding trials or tests (Disterhoft, 1977; Gabriel, 1976).

CS–FS plasticity in the MGv could account completely for only an extremely limited aspect of cortical FS plasticity, that is, for CS frequencies within 0.125 octave of the BF, but only for the period immediately after conditioning and only for test stimuli given at the lowest intensities. Similar considerations hold for the relationship between the MGm and the auditory cortex. For this nucleus, the issues of CS-BF proximity and maintenance of FS plasticity do not hold. Some of the effects reported here in the MGm have not been observed in any cortical field: General decreased responses were found in the MGm during both conditioning and sensitization but were not observed in either the primary auditory cortex (Bakin & Weinberger, 1990a) or the nonprimary cortical fields (Dia-
Table 6
Temporal Evolution of the Parameters That Describe the Maximal Effects of the Conditioned Stimulus–Frequency Specific (CS–FS) Increase Developed by Broaddly Tuned Cells and Narrowly Tuned Cells in the Medial Medial Geniculate Body

<table>
<thead>
<tr>
<th>Parameter/cell type</th>
<th>Immediately</th>
<th>Post</th>
<th>1 Hr Post</th>
<th>Retention (1 Hr Post – Post)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narrowly tuned</td>
<td>89</td>
<td>52</td>
<td>–32</td>
<td></td>
</tr>
<tr>
<td>Broaddly tuned</td>
<td>69</td>
<td>84</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Bandwidth (in octaves)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narrowly tuned</td>
<td>0.312</td>
<td>0.375</td>
<td>0.063</td>
<td></td>
</tr>
<tr>
<td>Broaddly tuned</td>
<td>0.327</td>
<td>0.250</td>
<td>–0.075</td>
<td></td>
</tr>
<tr>
<td>CS-BF (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narrowly tuned</td>
<td>114</td>
<td>56</td>
<td>–58</td>
<td></td>
</tr>
<tr>
<td>Broaddly tuned</td>
<td>146</td>
<td>151</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

Note. BF = best frequency.

Receptivity of the Bässalid: Some of the effects described at the cortical level were not found in the MGm. For example, CS-specific relative decreased responses involving general increased responses to all frequencies except that of the CS were reported in the secondary auditory cortex (see Diamond & Weinberger, 1989, Figures 9 and 11) but were not observed in the MGm. Finally, if the RF plasticity that occurs in the MGm completely accounts for CS–FS plasticity in the cortex, then only the broadly tuned cells should be able to maintain long-term RF plasticity at the cortical level. In fact, narrowly tuned cells are able to maintain FS RF plasticity at the cortical level (e.g., see Bakin & Weinberger, 1990a, Figure 3).

As discussed later, our working hypothesis was that the MGv, MGm, and auditory cortex operate in an integrated manner rather than in a “serial chain” manner. Each contributes something unique; and plasticity in the thalamus, although not being simply projected to a passive cortex, plays a key role in cortical FS plasticity.

Functional Implications of FS Plasticity

In this section, we consider the relationship of the present and previous findings to our preliminary model of associatively induced plasticity of representation and storage of information in the auditory cortex. First, it is necessary to provide a brief recapitulation of the model; supporting findings have been previously presented in detail (Ashe & Weinberger, 1991; Weinberger, Ashe, Metherate, McKenna, Diamond, & Bakin, 1990; Weinberger, Ashe, Metherate, McKenna, Diamond, Bakin, et al., 1990).

The Preliminary Model

During CS–UCS pairing trials, the MGv provides essentially unaltered, detailed frequency input to layer IV of the auditory cortex. In contrast, the MGm, which receives both CS and UCS input, is the first site of associative plasticity. However, its broad tuning and complex response properties provide little if any detailed frequency information to the auditory cortex. Rather, it projects an increased response to the CS to layer I of the auditory cortex. The MGm also provides information on the CS–UCS association to the amygdala, which initiates autonomic and somatic CRs and also initiates an increased release of acetylcholine via its projections to the nucleus basalis of Meynert. The release of acetylcholine amplifies the input from the MGm on the apical dendrites of pyramidal cells and produces a widespread enhancement of postsynaptic activation during training trials. Via modified Hebbian rules, MGv effects on pyramidal cells are strengthened for the CS frequency (the only frequency active during CS presentation), but synaptic strengths are reduced for inputs from non-CS frequencies, which are not active during trials. The result is seen in posttraining cortical RFs as increased responses to the CS frequency and decreased responses to many other frequencies. In summary, synapses are first changed in the MGm and then changed in the link between FS input from the MGv to cortical pyramidal cells.

Findings subsequent to the original formulation of this model are that RF plasticity develops in the auditory thalamus: short-term, frequency- and intensity-constrained FS plasticity in the MGv (Edeline & Weinberger, 1991b) and more enduring, less-constrained FS plasticity in the MGm, as reported here. The MGv effects, which operate only in reduced circumstances and are transient, have been considered as a short-term information store that directly promotes long-term synaptic change in the auditory cortex (Edeline & Weinberger, 1991b). Here we consider the functional roles of CS–FS RF plasticity in the MGm. Because the MGm projects subcortically to both the amygdala and the auditory cortex, we will consider its two functions separately.

MGm Plasticity, Fear Conditioning, and the Amygdala

We emphasize once again (Weinberger, Ashe, Metherate, McKenna, Diamond, & Bakin, 1990; Weinberger, Ashe, Metherate, McKenna, Diamond, Bakin, et al. 1990; Weinberger & Diamond, 1987, 1988) that FS plasticity indexes a rapidly developing association between the CS and the UCS, not the afferent link in an immediately expressed specific, somatic CR (see also Rescorla, 1985, 1988). If a behavioral state is to be attached to the RF plasticity reported here, then a state of “conditioned fear” or a “conditioned emotional response” (CER) is far more appropriate (LeDoux, 1990; Weinberger & Diamond, 1987). Considerable evidence has implicated the amygdala in fear conditioning (Gallagher, Kapp, Pascoe, & Rapp, 1981; Kapp, Pascoe, & Bidler, 1984). The cardiac decelerative CR is one behavioral component of this state. Others include pupillary dilation (Ashe, Cooper, & Weinberger, 1978; Gerall & Obrist, 1962; Oleson, Westenberg, & Weinberger, 1972), interruption of ongoing behavior (Estes & Skinner, 1941), freezing, and a sustained increase in blood pressure (Iwata, Chida, & LeDoux, 1987; Iwata, Ledoux, Meley, Arneric, & Reis, 1986; Iwata, LeDoux, & Reis, 1986). FS plasticity in the MGm could account for how rapidly acquired behavioral CRs are expressed after initial learning. Several lines of evidence support the view that the learning-induced CS–FS plasticity in the MGm is involved in amygdala-mediated emotional aspects of defensive conditioning.

First, cells located in the medial aspect of the MGB that
receive projections from the inferior colliculus (including the MGm and the posterior intralaminar nucleus), project to the lateral amygdala as well as to the auditory cortex (LeDoux, Ruggiero, & Reis, 1985; LeDoux et al., 1987). These connections were also demonstrated physiologically (Clugnet & LeDoux, 1990; Clugnet, LeDoux, & Morrison, 1990). Second, lesions of the MGB prevent acquisition of conditioned fear responses to sound (LeDoux, Sakaguchi, & Reis, 1984; LeDoux, Sakaguchi, Iwata, & Reis, 1986), and the connections between the MGm (and adjacent medial regions of the acoustic thalamus) and the lateral nucleus of the amygdala must be intact for fear conditioning (LeDoux, Iwata, Pearl, & Reis, 1986). Third, both the amygdala (Applegate, Frysinger, Kapp, & Gallagher, 1982; Pascoe & Kapp, 1985) and the MGm develop discharge plasticity during classical conditioning. More specifically, the MGm develops discharge plasticity in both simple conditioning and discrimination in rabbit (Miller et al., 1982), cat (Ryugo & Weinberger, 1978; Weinberger, 1982), and rat (Birt & Olds, 1981; Edeline, 1990b; Edeline et al., 1988, 1990a, 1990b). Also, artificially induced long-term potentiation can be induced in the MGm (Gerren & Weinberger, 1983; Weinberger, 1982) and in the connection from this nucleus to the amygdala (Clugnet & LeDoux, 1990).

Unknown is whether the region of the MGm simply relays acoustic input to the amygdala or is a site of CS–UCS convergence that accounts for or contributes to discharge plasticity that develops in the amygdala during acoustic conditioning (LeDoux, 1990). However, recent studies have shown that electrical microstimulation of the medial aspect of the MGB, including the posterior intralaminar nucleus (PIN), produces cardiac UCRs and is sufficient for the development of cardiac CRs when paired with a preceding tone (Cruikshank, Edeline, & Weinberger, 1991, in press). This supports the view that the MGm–PIN region is an active site of CS–UCS plasticity and thus provides information about CS–UCS relationship to the amygdala.

It is not known whether the neurons that project to the amygdala are the same neurons that develop discharge plasticity to the CS during training trials or develop CS–FS RF plasticity, as reported here. Whatever the case, because most of the MGm cells are broadly tuned, the MGm may provide before training little or no FS information to the amygdala (see also LeDoux, 1990). The fact that the few narrowly tuned cells present in the MGm do not retain CS–FS plasticity suggests that the MGm probably could not provide sustained retuned FS information to the amygdala after learning. In short, because the CS–FS effects are maintained only for the broadly tuned neurons, the activation provided by the MGm to the subcortical areas responsible for the fear emotional responses should not be very selective in term of frequency range. One of the more direct consequences could be that these emotional responses exhibit a large amount of generalization. Several studies have shown in the past that the CER, like conditioned suppression, shows generalization of greater than 2 octaves around the CS frequency (Desiderato, 1964; Hoffman & Fleshler, 1961; for reviews see Mackintosh 1974, Sutherland & Mackintosh, 1971). We suggest that if CS–FS plasticity in the MGm is a way to trigger a cascade of fear emotional response to the CS presentation, then this may explain why these CERS showed quite a large amount of generalization along the CS frequency dimension.

**MGm Plasticity as a Retrieval Mechanism for the Auditory Cortex**

We believe that the role of the MGm in cortical function is not to promote the immediate elicitation of behavioral CRs to CS presentation. Rather, we hypothesize that the auditory cortex is an important site where information about both the physical features of environmental sounds (i.e., "physical parameters") and their adaptive behavioral significance (i.e., "psychological parameters") are integrated and stored. We assume that information stored in the cerebral cortex may be used for many situations, at any time period after acquisition. We hypothesize that one role of the MGm after training is to enable retrieval of the meaning of the CS, including the context within which the original learning occurred.

The MGm has several features that might be particularly useful for retrieval: (a) retention, (b) rapid development, (c) specificity for information to be retrieved, and (d) a diffuse projection pattern that is specific to layer I.

Retention of CS–FS plasticity would appear to be a sine qua non for a retrieval mechanism. The rapid development of CS–FS plasticity would enable retrieval at any time after acquisition of the CS–UCS relationship. A retrieval mechanism should be accurate, a criterion met by the CS specific RF plasticity in the MGm. In addition, the retrieval substrate should be able to access the stored information. Here, the unusual projections of the MGm to the auditory cortex are of special interest.

As emphasized in the introduction of the article, the MGm is of particular importance because it is the only part of the thalamic auditory system that (a) projects diffusely to all auditory cortical fields, primary tonotopic and secondary nontonotopic alike, and (b) projects to layer I, in contrast to lemniscal projections from the MGs to layer IV. These highly structured anatomical and connectional features are undoubtedly highly relevant to the processing, representation, and storage of information. Of particular note, the same architecture of lemniscal projections to layer IV of primary sensory cortex and nonlemniscal diffuse projections to layer I of sensory cortex has been described for both the visual and somatosensory systems (for review see Herkenham, 1986). Therefore, although RF plasticity during behavioral learning has been studied only in the auditory system to date, the results of the present study may be relevant to the visual and somatosensory systems as well.

We suggest that, after training, the MGm serves an "adaptive filter" that projects facilitated excitation from the CS throughout the auditory cortex (Diamond & Weinberger, 1989). Although the functions of nonprimary auditory cortical fields are unknown, the fact that the MGm alone projects to layer I of all fields strongly suggests that it binds diverse components of a memory. It is well documented from behavioral studies that a memory trace is multidimensional (Spear, 1978) or can be viewed as a collection of attributes (Underwood, 1969). We have already discussed how the emotional or affective components of a memory for the acquired meaning of
an auditory CS could be activated by the link from the MGl to
the amygdala. With reference to the auditory cortex, the MGl
could serve to retrieve the detailed CS frequency information
within the context of the total acoustic environment present
during training trials in the following way. Assume that all of
the cells excited by the MGl during training constitute the
network that represents the storage of acoustic information
during training, including that of the CS frequency and all
background “contextual” sounds. Then posttraining, facil-
itated responses to the CS frequency could access and reacti-
vate the entire network via the diffuse projections of the MGl
to layer I of all cortical auditory fields. The activation of such
a network might constitute a major aspect of retrieval.

Interestingly, and perhaps paradoxically, highly specific
limniscal information seems insufficient for retrieval. Thus,
presentation of the CS posttraining would produce a facilitat-
ted response in the limniscal (MGn) input to the primary
auditory cortex because those synapses were strengthened
during conditioning trials. The MGn itself, having returned to
a pretraining state, would contribute nothing special to re-
trieval after training. The facilitated limniscal responses to the
CS in the primary auditory cortex would increase the probability
of discharge of cells with CS input synapses that were
strengthened during training. However, this would not neces-
sarily activate the network because of the extremely specific
and limited region of auditory cortex engaged by the CS
limniscal pathway. Instead, we hypothesize that this narrow
beam of CS input from the MGn together with the CS-specific
but broad beam input from the MGl would reactivate the
network that had been established during training trials. The
MGn–layer IV message is a highly specific frequency informa-
tional input that provides raw sensory detail without learning-
based content or context. The MGl message is essentially an
auditory-coded representation of the CS–UCS association, a
conditioned reactivation message that provides for the con-
tent. Both aspects of the memory trace must be integrated to
provide an accurate and complete representation of the
acquired meaning of a particular stimulus frequency. Each
alone could provide different and incomplete fragments of the
learned experience.

Thus, contrary to what might be expected, recall of the CS
and its acquired behavioral significance and associative link-
ages would be accomplished not merely by the detailed
physical parameters of the CS but by a nonlimniscal, diffusely
projecting system the frequency resolution of which is quite
poor. Although these hypotheses are admittedly highly specu-
lative, they are subject to empirical test.

References

tonal stimuli of neurons in medial division. Journal of Neurophysiol-
ology, 36, 275–283.


Applegate, C. D., Frysinger, R. C., Kapp, B. S., & Gallagher, M.
(1982). Multiple unit activity recorded from amygdala central
nucleus during Pavlovian heart rate conditioning in rabbit. Brain
Research, 238, 457–462.


Artola, A., & Singer, W. (1990). The involvement of N-methyl-D-
aspartate receptors in induction and maintenance of long-term
potentiation in rat visual cortex. European Journal of Neuroscience,
2, 254–269.

Ashe, J. H., Cooper, C. L., & Weinberger, N. M. (1978). Mesence-
phalic multiple-unit activity during acquisition of conditioned pupi-

Ashe, J. H., McKenna, T. M., & Weinberger, N. M. (1989). Cholin-
ergic modulation of frequency receptive fields in auditory cortex: II.
Frequency-specific effects of anticholinesterases provide evidence
for a modulatory action of endogenous ACh. Synapse, 4, 44–54.

of cellular excitability via muscarinic receptors: Functional plasticity
in auditory cortex. In R. T. Richardson (Ed.), Activation to acquisition:
Functional aspects of the basal forebrain cholinergic system (pp.

induces CS-specific receptive field plasticity in the auditory cortex

non-specific increased responses of receptive fields in guinea pig

medial tegmentum and medial geniculate during differential

Calfford, M. B. (1983). The parcelation of the medial geniculate body
of the cat defined by the auditory response properties of single units.
Journal of Neuroscience, 3, 2350–2364.

medial geniculate body of the cat: Evidence for multiple parallel
auditory pathways through thalamus. Journal of Neuroscience, 11,
2365–2380.

ment of frequency selectivity of single neurons in the central

conditioning circuits: Induction of LTP in the lateral nucleus of the
amygdala by stimulation of the medial geniculate body. Journal of
Neuroscience, 10, 2818–2824.

responses evoked in the amygdala and striatum by electrical
stimulation of the medial geniculate body. Journal of Neuroscience,
10, 1055–1061.

Microstimulation of a specific region of the medial geniculate (MG)
serves as an unconditioned stimulus (US) for autonemic fear

Stimulation at a site of auditory–somatosenory convergence in the
medial geniculate nucleus is an effective unconditioned stimulus for
fear conditioning. Behavioral Neuroscience.

Journal of Comparative & Physiological Psychology, 57, 434–437.

rapidly induces specific changes in frequency receptive fields of
single neurons in secondary and ventral esotobian auditory cortical

expression of learning-induced plasticity of single neurons in audi-

way to search for the engram. Physiological Psychology, 5, 275–280.


LeDouX, J. E., Sakaguchi, A., Iwata, J., & Reis, D. J. (1986). Interruption of projections from the medial geniculate body to an archi-neostriatal field disrupts the classical conditioning of emotional responses to acoustic stimuli. Neuroscience, 17, 615–627.


inhibition to the response characteristics of auditory units in the avian forebrain. Journal of Neurophysiology, 59, 1673–1689.
Niimi, K., Ono, K., & Kusunose, M. (1984). Projection of the medul- 
late nucleus to layer I of the auditory cortex in the cat traced 
with horseradish peroxidase. Neuroscience Letters, 45, 222–228.
Characteristics of the pupillary dilation response during Pavlovian 
Pascoe, J. P., & Kapp, B. S. (1985). Electrophysiological characteristics of 
amygdaloid central nucleus neurons during Pavlovian fear condi-
tioning in the rabbit. Behavioral Brain Research, 16, 117–133.
contributions of the lemniscal and spinothalamic systems to somatic 
contiguity. In N. M. Weinberger, J. L. McGaugh, & G. L. Lynch 
(Eds.), Memory systems of the brain: Animal and human cognitive 
processes (pp. 211–230). New York: Guilford Press.
Rogawski, M. A., & Aghajanian, G. K. (1980). Norepinephrine and 
serotonin: Opposite effects on the activity of lateral genulate 
neurons evoked by optic pathway stimulation. Experimental Neuro-
logy, 69, 678–694.
Rouiller, E., Rodrigues-Dagaeff, C., Simm, G., DeRibaupierre, Y., 
medial geniculate division of the medial geniculate body of the 
cat: Tunotopic organization, spatial distribution of response proper-
projection of the medial and ventral divisions of the medial 
geniculate body of the rat. Brain Research, 82, 173–177.
Ryugo, D. K., & Weinberger, N. M. (1978). Differential plasticity of 
morphologically distinct neuron populations in the medial genicu-
late body of the cat during classical conditioning. Behavioral Biology, 
22, 275–301.
functional organization of the cat visual cortex. Brain Research, 289, 
143–155.
Spear, N. E. (1978). The processing of memories: Forgetting and 
processes of learning and memory in the mammalian CNS. Annual 
Review of Neuroscience, 6, 447–491.
mediated by the red nucleus in the cat. Journal of Neuroscience, 1, 
72–79.
559–573.
Waterhouse, B. D., Sessler, F. M., Cheng, J. T., Woodward, D. J., 
action of norepinephrine in central neuronal circuits of mammalian 
Waterhouse, B. D., & Woodward, D. J. (1980). Interaction of 
norepinephrine with cerebrocortical activity evoked by stimulation 
of somatosensory afferent pathways in the rat. Experimental Neuro-
logy, 67, 11–34.
Weinberger, N. M. (1982). Sensory plasticity and learning: The 
magnocellular medial geniculate nucleus of the auditory system. In 
C. D. Woody (Eds.), Conditioning: Representation of involved neural 
function (pp. 697–710). New York: Plenum Publishing.
Weinberger, N. M., Ashe, J. H., Metherate, R., McKenna, T. M., 
by learning: A preliminary model of receptive field plasticity. Concepts 
in Neuroscience, 7, 91–131.
Weinberger, N. M., Ashe, J. H., Metherate, R., McKenna, T. M., 
Diamond, D. M., Bakin, J. S., Lennartz, R. C., & Cassady, J. M. 
model of receptive field plasticity in auditory cortex during Pavlov-
ian conditioning. In M. Gabriel & J. Moore (Eds.), Neurocompu-
tation and learning: Foundations of adaptive networks (pp. 91–138). 
in auditory cortex: Rapid induction by learning. Progress in Neurobi-
ology, 29, 1–55.
the auditory system by associative learning. In G. M. Edelman, W. E. 
Gall, & W. M. Cowan (Eds.), Auditory function: The neurobiologi-
Wepsic, J. G. (1966). Multimodal sensory activation of cells in the 
magnocellular medial geniculate nucleus. Experimental Neurology, 
15, 299–318.
dorsal division of the medial geniculate body of the cat: A study with the 
rapid Golgi method. Journal of Comparative Neurology, 221, 
1–30.

Received June 24, 1991
Revision received August 7, 1991
Accepted August 16, 1991

105