Heterosynaptic Long-Term Facilitation of Sensory-Evoked Responses in the Auditory Cortex by Stimulation of the Magnocellular Medial Geniculate Body in Guinea Pigs

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The magnocellular nucleus of the medial geniculate body (MGM) develops physiological plasticity during classical conditioning and may be involved in learning-induced receptive field plasticity in the auditory cortex. To determine the ability of the MGM to produce long-term modification of evoked activity in the auditory cortex, the experimenters paired electrical stimulation of the MGM with preceding clicks in adult guinea pigs under barbiturate anesthesia. The amplitudes of average click-evoked potentials were significantly facilitated in all subjects. Facilitation endured for 2 hr, the maximum duration of recording. Sham-stimulated control guinea pigs did not develop facilitation. Thus, a nonlemniscal thalamic sensory nucleus can produce enduring facilitation of sensory-evoked activity in primary sensory cortex, suggesting that long-term physiological plasticity in the sensory cortex during learning may involve nonlemniscal thalamic mechanisms.

Classical conditioning produces highly specific receptive field (RF) plasticity in the primary auditory cortex. Neuronal responses to the frequency of the conditioned stimulus (CS) are increased, whereas responses to the preconditioning best frequency (peak of the tuning curve) and many other frequencies are decreased. These changes produce a shift of frequency tuning toward or to the frequency of the CS. This type of RF plasticity is associative (Bakin, Lepan, & Weinberger 1992; Bakin & Weinberger, 1990) and discriminative (Edeline & Weinberger, 1993), develops rapidly (in as few as five trials; Edeline, Pham, & Weinberger, 1993), and lasts indefinitely (tested to 8 weeks; Weinberger, Javid, & Lepan, 1993).

The substrates of this RF plasticity are currently unknown. One possibility is that it develops subcortically and is projected to the auditory cortex. However, this is extremely unlikely. Two auditory thalamic nuclei project to primary auditory cortex and neither exhibits the RF plasticity that is observed in the auditory cortex. The lemniscal ventral nucleus of the medial geniculate body (MGr) exhibits only very weak and transient RF plasticity (Edeline & Weinberger, 1991). The nonlemniscal magnocellular nucleus of the medial geniculate body (MGM) does develop CS-specific RF plasticity after conditioning. However, the tuning of its cells is extremely broad and highly complex, differing markedly from tuning in the auditory cortex (Edeline & Weinberger, 1992).

Another possibility is that thalamic structures contribute in other ways to cortical RF plasticity. The lemniscal MGr does not develop neuronal plasticity during classical conditioning trials. Therefore, its contribution appears to be the provision of unmodified highly specific frequency information to the auditory cortex. In contrast, the MGM develops rapid and enduring increased responses to acoustic CSs (Edeline, Duflieux, & Neuenschwander-El Massioui, 1988; Gabrielli, Miller, & Saltwick, 1976; Ryugo & Weinberger, 1978). It has been hypothesized that the MGM promotes RF plasticity in the auditory cortex via its synapses in Layer I on the apical dendrites of pyramid cells (Weinberger et al., 1990).

One way to test the involvement of the MGM is to determine whether it can induce long-term modification of acoustic responses in the auditory cortex. We investigated this possibility by determining the effects of electrical stimulation of the MGM on click-evoked potentials (EPs).

Method

Subjects and Preparations

The subjects were 11 adult male Hartley guinea pigs (Cavia porcellus; Hilltop Farms, Scottsdale, PA) weighing 503-808 g. They were housed 3 per group in standard guinea pig cages (46 × 61 × 38 cm), in a temperature-controlled vivarium on a 12-hr light–dark cycle (lights on at 6 a.m.) and with food and water freely available. Acute experiments were performed with the subjects under general anesthesia (initially, sodium pentobarbital, 40.0 mg/kg ip) and atropine methyl nitrate, which acts peripherally to reduce secretions (0.02 mg/kg ip). Subjects were maintained under general anesthesia for the duration of the experiment (3-5 h) by means of an infusion pump (Model 351, Sage Instruments, Orion Research, Cambridge, MA), that delivered sodium pentobarbital (2.5 mg/ml) to the peritoneal cavity at a rate of approximately 1.92 ml/hr. Two threaded cylinders, which were embedded within a pedestal of dental acrylic anchored to the subject's skull by stainless steel screws, allowed the head to be fixed in a stereotactic

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frame during the experiment. One of the stainless steel screws served as the reference electrode for recording.

The stimulating electrodes were composed of three twisted Teflon-coated tungsten wires (two stimulating electrodes and one central support wire), each 50 μm in diameter, with an impedance of 0.5 MΩ at 1 kHz. The electrodes were lowered stereotaxically into the MGM: (ML = +3.6 mm; AP = -5.6 mm from bregma, DV = -8.0 to 8.5 mm from pia). The recording electrodes were tungsten wires (0.127 mm in diameter), etched to about 1 μm at the tip, and coated with Epoxylite 6001-S insulating varnish, Epoxylite Corp., Columbus, OH). On the day of the experiment, the impedance was lowered to 0.5-1.0 MΩ at 1.0 kHz. The electrodes were lowered 200 μm (Layer 1) into the auditory cortex ipsilateral to the stimulating electrode and perpendicular to the surface of the brain. The auditory cortex was determined by the characteristic cerebral vasculature immediately posterior to the sylvian fissure and confirmed by monitoring the evoked responses to clicks delivered to the contralateral ear (described below).

**Stimulation and Recording**

Acoustic stimulation was delivered to the ear contralateral to the recording and stimulation sites via a speaker assembly composed of an earphone (Realistic) placed in a damped metal housing. The speaker was calibrated with a calibrated 1.27 cm condenser microphone, a sound level meter (Brue! and Kaer, Marlborough, MA), and a wave analyzer (Hewlett-Packard, Palo Alto, CA). The clicks were produced by an S48 stimulator (Grass Instruments, Quincy, MA). Intensity was controlled by a Hewlett-Packard 350D attenuator.

Electrical stimulation of the MGM consisted of a train (50 ms) of biphasic (±) pulses (0.2- ms duration, 200 Hz, and 0.25 ms apart) provided by a constant current stimulator and stimulus isolation unit (Grass S88, Quincy, MA). Recordings were made in a sound attenuating chamber (LAC, Bronx, NY), amplified (Model 2400 preamplifier Dagan, Minneapolis, MN) and filtered (30-300 Hz). The click EPs, the click stimulus, and the electrical stimuli were recorded on a four-channel instrumentation recorder.

**Experimental Design**

Two groups of subjects were used: MGM stimulation (n = 9) and sham stimulation (n = 3). One subject in the MGM stimulation group was studied in a second experiment several hours after its first experiment, but on the contralateral side of the brain. Therefore, there were a total of nine sessions for this group. A session consisted of the presentation of clicks to establish a baseline followed by paired stimulation of clicks and MGM stimulation (or sham stimulation) followed by continued presentation of clicks for up to 2 hr. At the start of a session, clicks were delivered at 0.2 Hz, at a submaximal intensity (usually at 55 dB). This slow rate ensured full recovery of the response before the presentation of the next click. After a steady baseline of evoked responses was obtained (about 15-30 min), a series of click and electrical train pairings was then administered. Thirty trials were presented at the rate of 1.0 Hz. Each trial consisted of a click followed 100 ms later by a brief train of stimulation (50 ms). The first three sessions used a current level of 600 μA to determine if stimulation could be effective. When this was found to be the case, stimulus intensity was halved to 300 μA for the remaining six sessions. Further reductions of stimulus intensity were not investigated in this initial study. Immediately after the last stimulation trial, we presented clicks again using parameters identical to the baseline period (i.e., 0.2 Hz). The MGM stimulation group continued to receive clicks for up to 2 hr poststimulation; the sham stimulation group continued to receive clicks following the time of sham stimulation for approximately 90 min, at which time recording was discontinued because no facilitation had developed.

**Data Analysis**

The click EPs were analyzed off-line and averaged into groups of 16 consecutive responses on a Hitachi VC 6024 digital storage oscilloscope (Leeds, UK). As clicks were presented at the rate of 0.2 Hz, each average EP was obtained over a period of 80 s (~1.3 min). Each average EP was recorded by a plotter (Hewlett-Packard 7475A, San Diego, CA) on graph paper. The amplitude of each EP was measured by hand from its preclick baseline to the peak of each of its three components (see below). These measurements had a resolution of ±0.5 μm, corresponding to an accuracy of approximately ±10-20 μV. For small EP components, this method of measurement yielded a relatively small number of discrete amplitude measurements. All EPs were quantified for the first hour after pairing, and every fourth EP (approximately every 5 min) was quantified thereafter.

EPs consisted of three components, a sequence of positive, negative, and positive waves. Their average latencies (L) to peak were P1, ~12 ms; N1, ~21 ms; P2, ~37 ms. The magnitude of the peak of each component was measured from the baseline activity preceding each click (peak values). To characterize the effects of stimulation, we determined the magnitude of change and the latency of this change for each component. Four criteria and the latencies to achieve these criteria were calculated for each component as follows:

1. Onset of initial change: first of five consecutive EPs (spanning 6.7 min) larger or smaller than the baseline mean (grand average of all values). This criterion provided the shortest latency of consistent change regardless of its magnitude; five consecutive values of the same sign have a probability of 0.031 (binomial test, Siegal & Castellan, 1988).
2. Maintenance of initial change: first of five consecutive EPs, all of which were larger or smaller than the baseline average for the duration of the recording.
3. Onset of 3 SD change: first EP that was at least 3 SD above or below the baseline mean (Z score ≥ 3.0; p = .001). This criterion provided the latency to the first large magnitude of change.
4. 3 SD maintenance: first of at least three consecutive EPs at least 3 SD above or below the baseline mean. The probability for this measure was 1 × 10⁻¹⁰.

Z scores were determined as follows:

\[
\frac{\text{Value of each EP} - \text{Grand mean of baseline}}{\text{standard deviation of baseline}}
\]

![Graphs showing Z scores for P1, N1, and P2 EPs.](image)

**Figure 2.** Example of facilitation of click-evoked potential (EP) for the lower stimulation intensity (300 µA). Magnitudes of the average EPs are shown in Z scores for each component for 20 min preceding pairing and approximately 80 min after pairing. Insets show average EP waveforms for 6.7 min preceding pairing and 25.3 and 68.0 min after pairing. Thick vertical bars denote period of click-magnocellular nucleus of the medial geniculate stimulus pairing; dashed horizontal line indicates a positive Z score of 3.0; closed arrowhead = criterion for onset of initial change; open arrowhead = criterion for magnitude change during the 1st hr after pairing. Calibrations = 10 ms and 250 µV.

**Figure 3.** Example of facilitation of click-evoked potentials (EP) for the higher stimulation intensity (600 µA). Magnitudes of the average EPs are shown in Z scores for each component for 20 min preceding pairing and approximately 120 min after pairing. Insets show average EP waveforms for 13.3 min preceding pairing and 22.7 and 84.0 min after pairing. Calibrations = 20 ms and 500 µV. Thick vertical bars denote period of click-magnocellular nucleus of the medial geniculate body stimulation pairing; dashed horizontal line indicates a positive Z score of 3.0; closed arrowhead = criterion for onset of initial change; open arrowhead = criterion for maximum magnitude of 3 SD change during the 1st hr after pairing.

All latency criteria were determined for the first hour following stimulation. Any component that did not attain a criterion was assigned a value of 60 min. In addition to the latency criteria, the magnitude of change was determined for the maximum percentage change as follows:

\[
\frac{\text{Maximum postpairing value} - \text{Prepairing baseline}}{\text{Prepairing baseline} \times 100}
\]

The maximum percentage change and the latency to this measure were obtained for the entire 2-hr postpairing period.
Table 1

| EP component | Latency to criteria (min) | Maximum magnitude(%) | | | |
|--------------|--------------------------|----------------------|---|---|
|              | Onset | Maintenance | Onset | Maintenance | Maximum | Hour 1 | Hour 2 | Maximum | Hour 1 | Hour 2 |
| P1           | 7.88 (8/8) | 37.00 (2/8) | 23.75 (6/8) | 42.63 (1/8) | 24.00 (8) | 66.43 (7) | 27.40 (8) | 39.71 (7) |
| N1           | 4.67 (9/9) | 6.78 (9/9) | 13.45 (8/9) | 20.11 (7/9) | 33.22 (9) | 76.50 (8) | 58.11 (9) | 94.22 (8) |
| P2           | 4.11 (9/9) | 8.22 (9/9) | 9.78 (9/9) | 18.89 (8/9) | 30.33 (9) | 64.75 (9) | 80.25 (9) | 123.53 (8) |

Summary of p values

<table>
<thead>
<tr>
<th></th>
<th>P1 vs. N1</th>
<th>P1 vs. P2</th>
<th>N1 vs. P2</th>
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<tbody>
<tr>
<td>Onset</td>
<td>ns</td>
<td>.02</td>
<td>ns</td>
</tr>
<tr>
<td>Maintenance</td>
<td>ns</td>
<td>.02</td>
<td>ns</td>
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</tbody>
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Note. For values presented as fractions within parentheses, the numerator denotes the number of cases in which the criterion was attained and the denominator denotes the total number of cases. Values presented alone within parentheses indicate the total number of cases. Mgm = magnocellular nucleus of the medial geniculate body.

Histology

At the conclusion of the experiment, an electrolytic lesion (10 μA, 5 s) was made at the tip of the stimulating electrode, and the brain was perfused with saline and 10% formalin. Frozen sections were taken at 50 μm and stained with cresyl violet. Relevant sections were traced (x20) and examined microscopically.

Results

Mgm Stimulation Group

Data were obtained from nine sessions in the Mgm stimulation group. Of these, eight had verified placement of the stimulating electrode within the Mgm (see Figure 1). Histology could not be obtained for 1 subject, but its data were within the range of values of the other subjects. In all nine cases, stimulation produced long-term facilitation of click EPs. Facilitation could occur as early as the first postaverage (1.3 min), more often during the second average (2.6 min), and was maintained while recordings were obtained. Typically, the amount of facilitation continued to increase during the second hour. There were no significant differences on any measure as a function of the level of stimulating current (300 μA, n = 6; 600 μA, n = 3), so the data were pooled.

An example of facilitation using the lower stimulus intensity is presented in Figure 2. Following a baseline period of 20 min, stimulation produced facilitation of P1, N1, and P2. All three components attained the latency criteria for both the onset and the maintenance of initial facilitation and 3 SD facilitation, except for P1, which failed to maintain facilitation greater than 3 SD above baseline. The magnitude of facilitation increased throughout the observation period: maximum percentage increase, Hr 1 versus Hr 2—P1, 33% versus 67%; N1, 48% versus 167%; and P2, 44% versus 170%.

Figure 3 presents an example of facilitation for the higher stimulus intensity. As was the case for the previous example, P1, N1, and P2 developed increased responses that met the latency criteria for both the onset and the maintenance of initial and 3 SD facilitation, except for P1, which did not maintain facilitation for 3 SD above baseline. Facilitation endured throughout the approximately 2-hr period following stimulation. Also, as for the previous example, the maximum magnitude of facilitation was greater during the second hour than during the first hour: P1, 39% vs. 48%; N1, 64% vs. 73%; and P2, 92% vs. 156%.

Summaries of group data are presented in Table 1. The average latencies to the onset of initial facilitation for the three components ranged from about 4 to 8 min, and latencies to the onset of 3 SD facilitation were approximately 10 to 24 min. Latencies to the onset of both initial and 3 SD facilitation were longer for P1 than for N1 and P2. Statistical significance was marginal for the latency to initial facilitation of P1 versus N1 (Mann Whitney test; p < .06) and latency to 3 SD facilitation of P1 versus P2 (p < .06) but reached significance for P1 versus N1 for onset to 3 SD facilitation (p < .03); N1 versus P2 were not statistically different for either latency measure. The latencies to the criteria for the maintenance of both initial and 3 SD facilitation were significantly longer for P1 than for either N1 or P2; the latter were not significantly different from each other. Moreover, far fewer subjects met these criteria for P1 (2/8 and 1/8) than for N1 (9/9 and 7/9) and P2 (9/9 and 8/9), respectively. The latencies to the times at which maximum facilitation was attained were not statistically different among P1, N1, and P2 during either the first or second hr.

The average percentage magnitudes of maximum facilitation ranged from about 27% to 80% for the first hour and from about 40% to 124% for the second hour across EP components. These were significantly greater for each EP component during the second hour than during the first hour (Wilcoxon paired tests: P1, p < .04; N1, p < .01; P1, p < .028). The magnitudes of maximum facilitation were greater the longer the latency of the EP components (i.e., P2 > N1 > P1); all paired comparisons were statistically significant except for the P2 vs. N1 components during the second hour, which was marginal (p < .07); (see Table 1). Across the three components, the relationship of greater maximum facilitation for longer latency of evoked component was significant for both the first and second hours (nonparametric test for trend (Siegel & Castellan, 1988): Hour 1, L = 111 ± 8, p < .001; Hour 2, L = 97 ± 7, p < .001. However, the average facilitation across the entire 2-hr period after stimulation was significantly greater for N1 than P2, paired t test, t(57) = 4.872,
MGM Stimulation

A.

Figure 4. Average group means (+SE) for the magnocellular nucleus of the medial geniculate nucleus (MGM) stimulation group for each of the three evoked potential components, A: P1, B: N1, C: P2. Vertical line denotes time of stimulation.

p < .0001; both N1 and P2 were significantly greater than P1, t(57) = 16.233, p < .0001; t(57) = 14.861, p < .0001, respectively. A comparison of the means for each of the periods showed significant differences, Hour 2 > Hour 1 > Pre for each of the three components. The average group functions for each EP component are presented in Figure 4.

The possibility that the effects of stimulation were mediated by the spread of current from the MGM to the adjacent MGv, which also projects directly to the primary auditory cortex, was assessed by determining the relationship between the magnitude of facilitation and the distance from each site of stimulation to the nearest border of the MGv. Not one of the six correlation coefficients (i.e., maximum percentage increase for P1, N1, and P2 for both Hour 1 and Hour 2) was negative, as would be expected if loci close to the MGv yielded greater magnitudes of facilitation.

Sham Stimulation Group

Subjects that did not receive MGM stimulation did not exhibit facilitation of EPs. Instead, they developed reductions in amplitude of all three components. Table 2 presents a summary of the results. The average latency of onset of initial reduction for the three components ranged from more than 6 to about 22 min and latencies to the onset of 3 SD reduction were approximately 21 to 32 min following the time of sham stimulation. The only significant differences in criteria were significantly shorter latencies to maintenance of initial reduction for N1 vs. both P1 and P2, and there were no significant differences in the magnitude of maximum reduction for either the first hour or the succeeding 30 min period. However, the average reduction across the entire 1.5 hr period after sham stimulation was greatest for N1, which was marginally greater than P1, paired t test, t(50) = 1.19, p < .06, and significantly greater than P2, t(50) = 9.724, p < .0001; the reduction for P1 also was significantly greater than P2, t(50) = 7.245, p < .0001. A comparison of the means for each of the periods showed significant differences in the amount of reduction (Hour 2 > Hour 1 > Pre; see Table 3). The average group functions for the sham stimulation group are presented in Figure 5 (left).

Comparison of the MGM Stimulation and Sham Stimulation Groups

Because the sham group developed a reduction in click EPs, the facilitation that developed in the MGM stimulation group appears to have occurred on a decreasing baseline. To obtain a graphic summary of the difference between the groups, we subtracted the Z score functions of the sham group from the corresponding functions of the stimulation group. These difference functions are shown in Figure 5 (right) and indicate larger Z score changes than observed for the stimulation group considered alone, as expected (see Figure 4). The maximum differences were approximately 7 SD for P1, 13 SD for N1, and 10 SD for P2. Statistical comparisons between the two groups revealed no significant differences during the prestimulation period and significant differences during the poststimulation periods for each of the EP components (see Table 3).

Discussion

The findings show that electrical stimulation of the MGM can produce long-term facilitation of sensory EPs in the auditory cortex. Facilitation developed within a few minutes, continued to increase during both the first and second hours following pairing, and was maintained for the duration of the recording period of 2 hr. Subjects that received sham stimulation did not develop facilitation but rather their EPs became smaller over time. These changes may reflect an uncontrolled
Table 2
Sham Stimulation Group: Latencies to Criteria and Maximum Magnitude of Reduction of Click-Evoked Potentials (EPs)

<table>
<thead>
<tr>
<th>EP components</th>
<th>Latency to criteria (min)</th>
<th>Maximum magnitude (%)</th>
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<tbody>
<tr>
<td></td>
<td>Initial reduction</td>
<td>3 SD reduction</td>
<td>Maximum reduction</td>
</tr>
<tr>
<td></td>
<td>Onset Maintenance</td>
<td>Onset Maintenance</td>
<td>Hour 1</td>
</tr>
<tr>
<td>P1</td>
<td>21.78 (3/3) 38.67 (2/3)</td>
<td>31.56 (3/3) 42.11 (3/3)</td>
<td>49.33 (3) 65.33 (3)</td>
</tr>
<tr>
<td>N1</td>
<td>6.22 (3/3) 6.22 (3/3)</td>
<td>21.33 (3/3) 36.89 (2/3)</td>
<td>35.10 (3) 72.67 (3)</td>
</tr>
<tr>
<td>P2</td>
<td>12.89 (3/3) 34.22 (2/3)</td>
<td>29.78 (3/3) 43.56 (1/3)</td>
<td>40.89 (3) 73.33 (3)</td>
</tr>
</tbody>
</table>

Summary of p values*

| P1 vs N1      | ns  | .05 | ns  | ns  | ns  | ns  | ns  | ns  |
| P1 vs P2      | ns  | .05 | ns  | ns  | ns  | ns  | ns  | ns  |
| N1 vs P2      | ns  | ns  | ns  | ns  | ns  | ns  | ns  | ns  |

Note. For values presented as fractions within parentheses, the numerator denotes the number of cases in which the criterion was attained and the denominator denotes the total number of cases. Values presented alone within parentheses indicate the total number of cases.
*Derived by Mann–Whitney U test.

The reduction in the state of anesthesia across the period of the experiment because it is known that click EPs in the auditory cortex are reduced in amplitude as sleeping guinea pigs change toward a state of increasing arousal (Molnar, Karmos, & Csere, 1986; Murphy & Starr, 1971; Wickelgren, 1968; Winter, 1964). Thus, facilitation was produced by stimulation of the MGm rather than by general changes in state.

The effects for the longer latency components were stronger than for P1; latencies to the onset and maintenance of facilitation were longer and the magnitude of facilitation was smaller for the P1 than for N1 and P2. The magnitude of maximum facilitation was a direct function of the latency of each component (i.e., P2 > N1 > P1), and the average amount of facilitation was greater for N1 and P2 than P1. The shortest latency P1 component is generally believed to represent part afferent lemniscal thalamocortical activity, whereas the later components are believed to reflect a larger contribution of intracortical activity and possibly longer latency thalamocortical inputs (Creutzfeldt, 1974). However, at present there is no unequivocal interpretation of the processes that generate each of the components of the click EP in the auditory cortex (Molnar et al., 1986). Facilitation was greater during the second hour than during the first hour. This might be a function of stimulus parameters. The complete time course of the effect needs to be determined in parametric studies.

Although the sources of each of the components remain uncertain, it is well established that the MGm projects mainly to Layer I of the auditory cortex and does not terminate in Layers III and IV, which are the major target of projections from the lemniscal MGv (Winer, 1992). Thus, stimulation of the MGm is likely to have modified the cortical responses to click stimulation rather than having altered the auditory lemniscal input to the cortex itself. Regarding this point, it is possible that stimulation of the MGm actually affected other thalamic nuclei, which in turn modified the click EP. Although this alternative cannot be ruled out, it seems unlikely for the following reasons. First, the MGm itself does not project to other thalamic nuclei, including the ventral medial geniculate,

Table 3
Comparison of Changes of Average Evoked Potential Within and Between Groups

<table>
<thead>
<tr>
<th></th>
<th>P1</th>
<th>N1</th>
<th>P2</th>
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<tr>
<td>Comparison</td>
<td>Difference</td>
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<td>Within groups</td>
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<td>Sham stimulation</td>
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<tr>
<td>Pre vs. Hr 1</td>
<td>1.892</td>
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<tr>
<td>Pre</td>
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</table>

Note. Difference indicates mean difference between grand mean of Z scores (i.e., Hour 1 − Pre), and for between-groups calculations are for stimulation group minus sham group. Hour 2 denotes the poststimulation period of 61–90 min for sham group. Unpaired t tests were used for within-groups results, and paired t tests were used for between-groups results. MGm = magnocellular nucleus of the medial geniculate body; pre = prestimulation; hr = hour.
which is the only other nucleus that has a major projection to the primary auditory cortex. Second, current spread to the MGv is unlikely, given the use of bipolar stimulation (Ranck, 1975) and the fact that the magnitude of facilitation was not larger for stimulating sites closer to the MGv. Alternatively, stimulation of the MGm may have altered cortical click EPs via the subcortical projections in the MGm. Thus, electrical stimulation of the MGm elicits responses in the amygdala and the striatum (Cherkes, Kolomiets, Lukhanina, & Litvinova, 1985; Clugnet, LeDoux, & Morrison, 1990; Lukhanina, Cherkes, & Litvinova, 1983), and long-term potentiation can be induced in the lateral nucleus of the amygdala by stimulation of the MGm (Clugnet & LeDoux, 1990). Little is known about the effects of striatal or amygdaloid influences on the auditory cortex. Stimulation of the caudate nucleus actually suppresses, rather than facilitates, click EPs in the auditory cortex (La Grutta, Giammanco, & Amato, 1969).

Although a motivation for this study was the associative effects of learning on receptive fields in the auditory cortex, the present experiment does not address the issue of associativity. Although clicks were paired with subsequent stimulation of the MGm, nonassociative controls were not used, and no claims of associative effects are warranted or claimed. The possible associativity of the findings is one of a number of questions that are raised by this initial study.

The current experiment complements previous studies of long-lasting facilitation of responses to sensory stimulation in primary sensory cortex. Those findings consist of homosynaptic long-term potentiation (LTP) in the visual and somatosensory cortices induced by stimulation of thalamocortical afferents (Tsumoto, 1992; see also Lee & Ebner, 1992). These studies do not themselves show how such stimulation would affect cortical responses to sensory stimuli. The present experiment promotes links among studies of LTP, sensory physiology, and learning.

The present findings are consonant with a model of frequency specific RF plasticity that postulates a facilitative role for the MGm (Weinberger, Ashe & Edeline, 1994; Weinberger et al., 1990). However, the current findings do not address the issues of the specificity of the modulatory effects of MGm stimulation, the site(s) of interaction between MGm stimula-
tion and cortical responses to auditory stimuli, or the cellular mechanisms of this long-term facilitation. These issues may be addressed more incisively in the future by determining the effects of MGm stimulation on the receptive fields of neurons in the MGv and in various layers of the auditory cortex, plus reductionistic studies of relevant synaptic events.

The present findings may have relevance for the visual and somatosensory systems, both of which also have nonlemniscal thalamic nuclei that project to supragranular layers of their primary cortices (Herkenham, 1986). Therefore, nonlemniscal thalamic nuclei in these systems may have the capacity to induce facilitation of visual and somatosensory stimuli, respectively. The possibility that a common substrate of long-term cortical plasticity involves nonlemniscal thalamic sensory nuclei seems worth pursuing.

References


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