Modulation of Responses and Frequency Tuning of Thalamic and Collicular Neurons by Cortical Activation in Mustached Bats

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Zhang, Yunfeng and Nobuo Suga. Modulation of responses and frequency tuning of thalamic and collicular neurons by cortical activation in mustached bats. J Neurophysiol 84: 325–333, 2000. In the Jamaican mustached bat, Pteronotus parnellii parnellii, one of the subdivisions of the primary auditory cortex is disproportionately large and over-represents sound at ~61 kHz. This area, called the Doppler-shifted constant frequency (DSCF) processing area, consists of neurons extremely sharply tuned to a sound at ~61 kHz. We found that a focal activation of the DSCF area evokes highly specific corticofugal modulation in the inferior colliculus and medial geniculate body. Namely a focal activation of cortical DSCF neurons tuned to, say, 61.2 kHz with 0.2-ms-long, 100-nA electric pulses drastically increases the excitatory responses of thalamic and collicular neurons tuned to 6.12 kHz without shifting their best frequencies (BFs). However, it decreases the excitatory responses of subcortical neurons tuned to frequencies slightly higher or lower than 61.2 kHz and shifts their BFs away from 61.2 kHz. The BF shifts are symmetrical and centrifugal around 61.2 kHz. These corticofugal effects are larger on thalamic neurons than on collicular neurons. The cortical electrical stimulation sharpens the frequency-tuning curves of subcortical neurons. These corticofugal effects named “ecocentric selection” last ≤2.5 h after the cessation of a 7-min-long cortical electrical stimulation. In the mustached bat, corticofugal modulation serves to increase the contrast in neural representation of sound at ~61 kHz, which is an important component of an echo bearing velocity information. It is also most likely that the corticofugal system plays an important role in the plasticity of the central auditory system. Another subdivision of the auditory cortex of the mustached bat is called the FM-FM area. This area consists of delay-tuned combination-sensitive neurons, called FM-FM neurons, and has the echo-delay axis for the systematic representation of target distances. A focal electric stimulation of the FM-FM area evokes changes in the responses of collicular and thalamic FM-FM neurons. These changes are basically the same as those described in the present paper. Therefore corticofugal modulation takes place for frequency domain analysis in exactly the same way as it does in time domain analysis.

INTRODUCTION

In the motor (Nudo et al. 1996), somatosensory (Recanzone et al. 1993; Spengler and Dinse 1994), and auditory cortices (Maldonado and Gerstein 1996), an electrical stimulation of a part of the cortex evokes an expansion in the cortical or subcortical representation of that part. In the big brown bat, Eptesicus fuscus, a focal electrical stimulation of the auditory cortex evokes asymmetrical and centripetal shifts in best frequencies (BFs) accompanied with the shifts of frequency-tuning curves (hereafter, “BF shifts” for simplicity) of neurons in the inferior colliculus (Yan and Suga 1998) and the auditory cortex (Chowdhury and Suga 2000). That is, the BF shifts predominantly occur for the BFs slightly higher than the BF of electrically stimulated cortical neurons (hereafter, cortical BF), and the direction of the shifts is downward toward the cortical BF. Basically the same BF shifts can also be evoked in the inferior colliculus (Gao and Suga 1998) and the auditory cortex (Gao and Suga 2000) by an acoustic stimulus alone or paired with an electric leg-stimulation as in a conditioning paradigm. The auditory cortex and the somatosensory cortex both are necessary for the BF shifts in the inferior colliculus evoked by auditory conditioning (Gao and Suga 1998). The data obtained from the big brown bat strongly suggest that the corticofugal system plays an important role in the plasticity of the central auditory system.

In the Jamaican mustached bat, Pteronotus parnellii parnellii, the auditory cortex consists of several subdivisions which are physiologically distinct from each other (Suga 1990). The FM-FM area consists of delay-tuned combination-sensitive neurons, called FM-FM neurons, and has the echo-delay axis for the systematic representation of target distances (O’Neill and Suga 1979, 1982; Suga and O’Neill 1979; Suga et al. 1978; 1983). A focal inactivation of cortical FM-FM neurons tuned to, say, a 5-ms echo-delay with a local anesthetic drastically reduces the facilitative responses of thalamic and collicular FM-FM neurons tuned to a 5- ms echo-delay without shifting their best (echo) delays for facilitative responses. However, subcortical FM-FM neurons tuned to echo delays other than 5-ms increase their facilitative responses and shift their best delays toward 5 ms. A focal activation of the FM-FM area with electric pulses evokes changes in subcortical FM-FM neurons that are opposite to those evoked by focal inactivation. These data clearly indicate that cortical FM-FM neurons mediate, via corticofugal projection, a highly focused positive feedback to subcortical neurons “matched” in tuning to a particular echo delay, and a widespread lateral inhibition to “unmatched” subcortical neurons (Suga et al. 1995; Yan and Suga 1996). The corticofugal system modulates the subcortical delay maps, augments auditory responses, and sharpens neuronal tuning curves so as to enhance the neural representation of frequently occurring signals in the central auditory system. In other
words, the corticofugal functions, named “egocentric selection,” adjust and improve the cortical neurons’ own input and, consequently, cortical signal processing, perhaps according to auditory experience (Yan and Suga 1996).

The Doppler-shifted constant frequency (DSCF) area of the primary auditory cortex of the mustached bat is large and consists of neurons extremely sharply tuned to ~61 kHz. The disproportionately large DSCF area and the sharp tuning of DSCF neurons can be easily correlated with fine frequency analysis of the DSCF component of an echo for processing velocity information (Suga and Jen 1976). A focal inactivation of cortical DSCF neurons tuned to, say, 61.2 kHz with a local anesthetic drastically reduces the excitatory responses of thalamic and collicular DSCF neurons tuned to 61.2 kHz (“matched” subcortical neurons) without shifting their BFs. However, subcortical neurons tuned to frequencies slightly higher or lower than 61.2 kHz (“unmatched” subcortical neurons) increase their excitatory responses and shift their BFs toward 61.2 kHz. These corticofugal effects are almost two times larger on thalamic neurons than on collicular neurons (Zhang et al. 1997). Therefore egocentric selection works for the adjustment and improvement of auditory signal processing not only in the time domain but also in the frequency domain. A focal activation of the cortical DSCF area with electric pulses is expected to produce the changes in subcortical DSCF neurons that are opposite to those evoked by the focal inactivation of the cortical DSCF area. The aim of the present paper is to report our findings resulting from cortical activation experiments that are complementary to the cortical inactivation experiments.

METHODS

Materials, surgery, recording of neural activity, and acoustic stimulation were basically the same as those described in Suga et al. (1983). Cortical electrical stimulation, data acquisition, and data processing were basically the same as those described in Yan and Suga (1996). The essential portions of the methods are summarized in the following text.

Nine adult mustached bats were used for the present experiments. The “resting” frequency of the second harmonic CF component (CF2) of biosonar signals emitted by each bat was measured before surgery. The CF2 resting frequency was used to normalize the BFs of individual neurons to those in the mustached bat, which emitted biosonar pulses at a 61.00 kHz CF2 resting frequency (Suga and Suzuki 1985). Under neuroleptanalgesia (Innovar 4.08 mg/kg body wt), the dorsal surface of the bat’s head was exposed and a 1.8 cm-long metal post was glued onto the skull. Four days after the surgery, the unanesthetized bat was placed in a styrofoam restraint suspended by an elastic band at the center of a soundproof, echo-attenuated room maintained at 30–32°C. The head was immobilized by fixing the post on the skull to a metal rod with set-screws and adjusted to face directly at a condenser loudspeaker located 74 cm away. DSCF neurons of the bat emitting biosonar pulses of a 61.00 kHz CF2 resting frequency are tuned to 60.6–62.3 kHz sounds (Suga et al. 1987) and are clustered in the DSCF area of the auditory cortex (AC), the ventral division of the medial geniculate body (MGB), and the dorsoposterior division of the inferior colliculus (IC). To record their auditory responses, a tungsten-wire microelectrode was inserted into one of these structures through holes of ~50 μm in diameter made in the skull. DSCF neurons were identified by their BFs and locations in the AC, MGB, and IC. A BAK amplitude window discriminator was used to isolate action potentials of single neurons.

Electrical stimulation

The best frequencies of cortical neurons were first measured at four to five loci in the DSCF area representing 60.47–62.30 kHz, as in our previous experiments (Zhang et al. 1997). To activate one of these cortical loci, a tungsten wire electrode (negative pole) was placed at a depth of ~700 μm from the cortical surface and another (positive pole) was placed at a depth of ~150 μm. (The AC of the mustached bat is ~900-μm thick.) A 100-nA, 0.2-ms electrical pulse was delivered to the cortical locus at a rate of 5/s for 7 min through these electrodes. Each electric pulse was synchronized with the onset of each acoustic stimulus.

Acoustic stimulation

The acoustic stimuli were 23-ms-long tone bursts with a 0.5-ms rise-decay time. These were generated by a voltage-controlled oscillator and an electronic switch, and were delivered at a rate of 5/s. The frequency of a tone burst was varied manually or by a computer. Collicular, thalamic and cortical DSCF neurons were tuned to particular frequencies (BFs), and particular amplitudes (best amplitudes). To obtain a “frequency-response” curve of a single neuron, the amplitudes of the tone bursts of a computer-controlled frequency scan were set at the best amplitude of a given neuron, which was usually ~30 dB above minimum threshold. When the best amplitude of a neuron could not be determined because of a monotonic or plateau amplitude-response curve, the amplitudes of the tone bursts were set at 30 dB above minimum threshold of the neuron. The frequency scan consisted of 21 time blocks. In the first 20 blocks, frequency was changed in 0.10-kHz steps, and in the 21st (last) block, no stimulus was presented to count background discharges. The duration of each block was 200 ms so that the duration of the frequency scan was 4,200 ms. An identical frequency scan was repeated 50 times, and the responses of a single neuron to them were displayed as an array of peri-stimulus time (PST) histograms or PST cumulative (PSTC) histograms (Figs. 1 and 2).

To obtain a “frequency-tuning” curve of a single neuron, both the frequency and amplitude of a tone burst were computer controlled. In this frequency-amplitude scan, an identical frequency scan consisting of 33 time blocks was delivered five times. Every five scans, the amplitude of the tone bursts was changed in a 5-dB step from 0 to 100 dB SPL. Action potentials discharged by a single neuron were displayed as a raster (Fig. 6A) or the arrays of PST or PSTC histograms. A frequency-tuning curve was obtained with a criterion of threshold at 20% increase in background discharges.

Data acquisition and processing

To study the effects of cortical activation on the auditory responses of neurons in the MGB and the IC (hereafter, subcortical neurons), the responses of single subcortical neurons to tone bursts in the frequency or frequency-amplitude scan were recorded with a computer before, during, and after the focal cortical activation with electric pulses. The waveform of an action potential was stored on a digital storage oscilloscope at the beginning of the data acquisition. This waveform was used to compare with incoming action potentials. Action potentials were continuously monitored on the screen of the digital storage oscilloscope before, during, and after the cortical activation. Data acquisition was continued as far as incoming action potentials visually matched the template. Data were stored on a computer hard drive and were used for off-line analysis.

Off-line data processing included plotting PST or PSTC histograms displaying responses to 50 identical acoustic stimuli and frequency-response curves based on frequency scans or frequency-tuning curves based on frequency-amplitude scans obtained before, during, and after cortical activation. The magnitude of auditory responses was expressed by a number of impulses per 50 identical stimuli after sub-
tracting background discharges counted in the last block of the frequency or frequency-amplitude scan. A \( t \)-test was used to test the difference between the auditory responses obtained before and after the focal cortical stimulation and to test the difference between the responses of thalamic and collicular neurons.

The following criteria were used for a shift in the frequency-response or -tuning curve (or BF) of a subcortical neuron evoked by a focal cortical activation. If a shifted frequency-response or -tuning curve did not recover by 50\%, the data were excluded from the analysis. In stable, long recording conditions, all curves shifted by the cortical activation recovered by more than 50\%. This recovery itself helped prove that the shift was significant. When a BF shift was small and its significance was not obvious, a weighted average frequency (i.e., BF) was calculated for the summed responses to five consecutive frequency scans (Blaisdell 1993). Then the mean and standard deviation of these weighted averages were computed, and a two-tailed paired \( t \)-test was used to determine whether or not the weighted-average frequencies obtained for control and stimulus conditions were significantly different for \( P < 0.05 \). The criterion for an increase or decrease in response magnitude (number of impulses per stimulus) was a change of 20\% from a control value.

**RESULTS**

All neurons studied and reported in the present paper were sharply tuned to a sound between 60.47 and 62.30 kHz. For simplicity, they are called DSCF neurons. The number of DSCF neurons studied was 62 in the AC, 32 in the MGB, and 30 in the IC. The cortical neurons were first recorded to measure their BFs and then electrically stimulated. On the other hand, the subcortical neurons were recorded and were studied to examine the effects of the electrical stimulation of the cortical neurons on their responses.

When cortical DSCF neurons were electrically stimulated, subcortical neurons showed either augmentation of the auditory responses at their BFs and BF shift (i.e., shift in frequency-tuning curve). Subcortical neurons that showed no BF shift had a BF different by more than 0.2 kHz from the cortical BF. These two groups of neurons are called “matched” and “unmatched” neurons, respectively. The effects of focal cortical activation on subcortical neurons were opposite to those of focal cortical inactivation on them reported by Zhang et al. (1997).

In our sample, eight thalamic and six collicular neurons were matched in BF to electrically stimulated cortical neurons. Figure 1A shows the PST histograms displaying the responses to tone bursts (a) and the arrays of PSTC histograms displaying frequency-response curves (b) of a thalamic neuron which was tuned to 61.40 kHz (Fig. 1ab1; ●). When cortical neurons tuned to 61.50 kHz (b2, ▼) were electrically stimulated, the responses to tone bursts of 61.3–61.5 kHz increased but the BF stayed the same, 61.4 kHz (x in b2). The increase in response was 75.9\% of the control at 61.40 kHz. This increase was due to an overall increase in response and was not due to an increase in the later portion of the response, nor to an addition of a long latency response (a2). Therefore the envelope of the PST histogram of the augmented response (a2) was the same as that in the control condition (a1). The increase in response was not accompanied by an increase in background discharges (the last PST histogram in b2). This was also true in 11 neurons of the 14. The augmented response reduced toward the response in the control condition (hereafter, recovered) by 71.6\% 39 min after the cessation of the cortical electrical stimulation (b3). Complete recovery was observed 69 min after the electrical stimulation.

Figure 1B shows the responses to tone bursts (a) and frequency-response curves (b) of a collicular neuron which was tuned to 60.91 kHz (b1, ●). When cortical neurons tuned to 61.00 kHz (b2, ▼) were electrically stimulated, the responses to tone bursts of 60.3–61.5 kHz increased but the BF stayed the
same, 60.9 kHz (b2, x). The increase in response was 53.9% of the control at 60.9 kHz. This was due to an overall increase in response (a2), which was not accompanied by an increase in background discharges (the last PSTC histogram in b2). The augmented response recovered by 84.6% 42 min after the cessation of the cortical electrical stimulation (b3). Complete recovery was observed 108 min after the electrical stimulation.

In our sample, 24 thalamic and 24 collicular neurons were unmatched in BF to electrically stimulated cortical neurons. Figure 2A shows the PST histograms displaying responses to tone bursts (a) and the arrays of PSTC histograms displaying frequency-response curves (b) of a thalamic neuron tuned to 60.70 kHz. When cortical neurons tuned to 61.50 kHz were electrically stimulated (b2, ↓), all the responses to tone bursts shown in b1 reduced. The amount of the reduction was 80.8% at 60.7 kHz. Percent reduction was smaller at frequencies below 60.7 and was only 42.4% at 60.5 kHz. As a result of these frequency-dependent percent reductions, the BF shifted from 60.7 kHz to 60.5 kHz (b2, x), together with the frequency-response curve (b2). That is, the BF and the frequency-response curve shifted away from the cortical BF. The decrease in response was due to an overall decrease in response (a2), including a decrease in background discharges (the last PSTC histogram in b2). This was also true in 19 neurons out of the 48. The suppressed responses recovered by 89.4% 35 min after the cessation of the cortical electrical stimulation (b3).

Figure 2B shows the responses to tone bursts (a) and the frequency-response curves (b) of a collicular neuron tuned to 61.22 kHz (b1, ◦). Electrical stimulation of the cortical neurons tuned to 60.70 kHz (b2, ↓) reduced all the responses of the collicular neuron to tone bursts from 60.9 to 61.8 kHz (b2). Percent reduction was large for 61.2 kHz (77.6%) and frequencies below it, but was small for frequencies higher than 61.2 kHz (e.g., 27.4% at 61.3 kHz). As a result of these frequency-dependent reductions, the BF shifted from 61.2 to 61.3 kHz (b2, x) together with the frequency-response curve. That is, it shifted away from the cortical BF. The reduction in response was due to an overall decrease in response. However, the long-latency component of the response (a1, right of ↓) was more reduced than the short latency component (a2). The decrease in response was not accompanied by a decrease in background discharges (the last PSTC histogram in b2). This was also observed in 29 neurons of the 48. The responses and the frequency-response curve of the neuron recovered to those in the control condition ~26 min after the cessation of the cortical electrical stimulation.

To substantiate the corticofugal modulation of the frequency-response curves of subcortical neurons described in the preceding text, Fig. 3 shows the frequency-response curves of three thalamic (A–C) and three collicular neurons (D–F) measured prior to, during, and after focal electrical stimulation of the AC. The responses of matched subcortical neurons (A and D) were augmented, and their frequency-response curves and BFs were not shifted at all by cortical electric stimulation. On the other hand, the response of the unmatched neurons (B, C, E, and F) were reduced, and their frequency-response curves and BFs were shifted by cortical electric stimulation. The direction of the shifts in the curves and BFs of subcortical neurons depended on the relationship in BF between the stimulated cortical neurons and recorded subcortical neurons studied in a pair. When the cortical BF was higher than the subcortical BF, the shift was downward toward the cortical BF. When the cortical BF was lower than the subcortical BF, the shift was upward toward high frequencies (C and F). In other words, the directions of BF shifts and shifts in tuning curves were always away from the BF of electrically stimulated cortical neurons.

A percent change in response magnitude and a BF shift were measured for each of the 32 thalamic and the 30 collicular neurons studied (Fig. 4). The percent increase in the responses of matched neurons at their BFs was 54.2 ± 29.2% (21.6–109%) for the eight thalamic neurons and 37.3 ± 18.2% (10.1–66.0%) for the six collicular neurons (Fig. 4, A and C, △). The thalamic increase appeared to be 1.5 times larger than the collicular increase. However, the difference in percent increase is statistically insignificant (P = 0.11) due to a large variation and a small sample. The percent change in the re-
The percent decrease is significant ($P < 0.05$). All the frequency-response curves in the present paper were measured with tone bursts fixed at the best amplitude or 30 dB above minimum threshold of a given neuron. The shifts in a frequency-response curve and BF were always associated with an overall shift in a frequency-tuning curve along the frequency axis. Figure 5 shows the frequency-tuning curves of matched (A and C) and unmatched subcortical neurons (B and D) to electrically stimulated cortical neurons. The thalamic neuron in A tuned to 61.61 kHz showed augmented responses to tone bursts by 10.2 dB for the electrical stimulation of the cortical neurons also tuned to 60.80 kHz. Its augmented responses returned to the responses in the control condition 106 min after the electrical stimulation. The thalamic neuron in C tuned to 60.80 kHz did not change its tuning curve at all, but increased its responses to tone bursts for the electrical stimulation of the cortical neurons also tuned to 60.80 kHz. Its augmented responses returned to the responses in the control condition 64 min after the cortical electrical stimulation. The thalamic neuron in B was tuned to 60.64 kHz. Its tuning curve shifted to 60.94 kHz for the electrical stimulation of the cortical neurons tuned to 60.04 kHz. The thalamic neuron in D was tuned to 61.53 kHz. Its tuning curve shifted down to 61.43 kHz for the electrical stimulation of the cortical neurons tuned to 62.03 kHz. The “shifted” tuning curves in both B and D were matched subcortical neurons. The change was 23.2 ± 16.9% (−10.9–47.7%) for the 24 thalamic neurons and 7.59 ± 14.5% (−12.9–39.0%) for the 24 collicular neurons (Fig. 4, A and C, ○). The thalamic decrease was 1.4 times larger than the collicular decrease. This difference in percent decrease is significant ($P < 0.01$). The percent changes in the responses of the unmatched neurons were also calculated at BFs in the shifted condition by cortical electrical stimulation. The change was 23.2 ± 16.9% (−10.9–47.7%) for the 24 thalamic neurons and 7.59 ± 14.5% (−12.9–39.0%) for the 24 collicular neurons (Fig. 4, A and C, ○). The thalamic decrease was 3.1 times larger than the collicular decrease. This difference is also significant ($P < 0.01$). Therefore corticofugal effects on the thalamic neurons are larger than those on the collicular neurons. A change in BF was zero for both the eight matched thalamic and the six matched collicular neurons (Fig. 4, B and D, △). However, it linearly decreased with an increase in BF difference between recorded subcortical neurons and electrically stimulated cortical neurons. The direction of BF shifts was centrifugal (Fig. 4, B and D, △). The slope of a regression line ($a$) and the correlation coefficient ($r$) were, respectively, 0.30 and 0.89 for the thalamic neurons and 0.20 and 0.82 for the collicular neurons. The slope of the regression line was 1.5 times steeper for the thalamic neurons than for the collicular neurons. This difference in slope is significant ($P < 0.05$). The dashed lines in Fig. 4, B and D, obtained by Zhang et al. (1997), are respectively the regression lines for the BF shifts of thalamic and collicular neurons evoked by focal inactivation of cortical neurons. The direction of the BF shifts is centripetal and the slope of the regression line is 0.33 for the thalamic neurons and 0.18 for the collicular neurons. The effect of cortical inactivation was 1.8 times larger on the thalamic neurons than on the collicular neurons. This difference in slope is also significant ($P < 0.05$).

The percent changes at BFs in the control condition (BFc) and at the shifted condition by cortical electrical stimulation. The abscissae represent the difference in BF between the recorded thalamic (MGB) or collicular neurons (IC) and the electrically stimulated cortical neurons (AC) paired for the experiments. The ordinates represent percent changes in response magnitude (number of impulses per tone burst) in A and C or changes in BF in B and D. ○ and ●, the data obtained from matched and unmatched subcortical neurons, respectively. ○ and ● in A and C, respectively, represent the changes in response magnitude at the BFs in the control condition (BFc) and at the shifted condition (BFs) evoked by cortical activation. The regression lines, slopes ($a$), and correlation coefficients ($r$) are shown in B and D. - - - −, the regression lines for BF shifts evoked by focal cortical inactivation with lidocaine (Zhang et al. 1997).
The difference between the BFs of recorded subcortical and stim-
corticical electric stimulation is plotted as a function of the
with cortical electrical stimulation. A change in width due to
measured at 10, 30, 50, and 70 dB above the minimum thresh-
ons are electrically stimulated. A width of a tuning curve was
some subcortical neurons became narrower when cortical neu-
110 min after the cortical stimulation (\(P < 0.01\)). These curves returned to the curves in the control condition 138 min after the electrical stimulation.

As described in the preceding text, the frequency-tuning curves of unmatched collicular neurons tuned to sounds between 60.5 and 62.3 kHz shifted away from the BF of electrically stimulated cortical neurons. The amount of the shift could be very small, only 0.1 kHz, but was significant. To substantiate this further, an additional example of a shift in frequency-tuning curve is shown in Fig. 6. The rasters in Fig. 6A show action potentials discharged by a thalamic neuron with a 61.32 kHz BF during the frequency-amplitude scan (see METHODS). In the control condition, the neuron responded to a sound between 61.22 and 61.42 kHz. It was very sharply tuned to 61.32 kHz. Its response to the 61.32 kHz tone burst appeared between 22 and 72 dB SPL, which were the minimum and upper thresholds of the neuron, respectively (A1). When 61.03 kHz tuned cortical neurons (\(\uparrow\)) were electrically stimulated, the response of this thalamic neuron decreased to 61.32 kHz, dramatically increased to 61.42 kHz and appeared for 61.52 kHz. As a result, the frequency-tuning curve of the neuron shifted higher by 0.1 kHz (A2) \(P < 0.01\). The shifted frequency-tuning curve returned to that in the control condition 110 min after the cortical electrical stimulation (A3). In Fig. 6B, all action potentials discharged over 12–72 dB SPL shown in Fig. 6A are summed up as a function of the frequency scan. It is clear that the peak response at 61.32 kHz shifted to 61.42 kHz for the cortical electrical stimulation and then returned to 61.32 kHz 110 min after the cortical stimulation \(P < 0.01\). Background discharges of this collicular neuron were not affected by the cortical electrical stimulation.

As shown in Fig. 5, A, B, and D, frequency-tuning curves of some subcortical neurons became narrower when cortical neurons are electrically stimulated. A width of a tuning curve was measured at 10, 30, 50, and 70 dB above the minimum threshold of each of the 32 thalamic and 30 collicular neurons studied with cortical electrical stimulation. A change in width due to cortical electric stimulation is plotted as a function of the difference between the BFs of recorded subcortical and stim-
ulated cortical neurons (Fig. 7). Ten thalamic and 8 collicular neurons showed changes larger than 0.1 kHz at 50 dB above minimum threshold. However, neither thalamic nor collicular neurons, except one thalamic neuron, showed a change larger than 0.1 kHz at 10 dB above minimum threshold.

**DISCUSSION**

*Corticofugal modulation of matched and unmatched subcortical neurons*

As shown in our present paper, focal cortical activation with electric pulses evoked the changes in subcortical neurons that were opposite to those evoked by cortical inactivation. Namely matched subcortical neurons, with BFs within ±0.2 kHz of the BF of the activated cortical neurons, were augmented, without shifting their BFs, by a focal cortical activation. Unmatched subcortical neurons, with BFs different by more than ±0.2 kHz from the BF of the activated cortical neurons, were inhibited at their BFs and were shifted in BF by a focal cortical activation. The BF shifts, always accompanied with the shifts in frequency-tuning curves, were based on frequency-dependent inhibition and facilitation. The frequency-tuning curves of most matched and unmatched subcortical neurons were sharpened by a focal cortical activation. [It has been known that the width of a frequency-tuning curve sharpened by lateral inhibition generally does not change at 10 dB above minimum threshold but changes noticeably at higher stimulus levels (e.g., Suga et al. 1997). This is also true for our data shown in Fig. 7.] These corticofugal functions, called “egocentric selection,” were first found in an auditory subsystem specialized for processing echo delays, bearing target-distance information (Suga et al. 1995; Yan and Suga 1996). Our present and previous experiments (Zhang et al. 1997) indicate that exactly the same mechanisms operate for the processing of auditory information not only in the time domain but also in the frequency domain and that the subcortical frequency map and response properties of subcortical neurons are adjusted and improved by the corticofugal system according to cortical excitation.
Difference in egocentric selection between two species of bats

The recent data obtained from the big brown bat (Chowdhury and Suga 2000; Gao and Suga 1998; Yan and Suga 1998) and the mustached bat (Zhang et al. 1997; the present paper) indicate that the effects of egocentric selection on subcortical neurons are different between these two species of bats. This difference, described in the following text in detail, indicates that when the ascending auditory system is specialized for fine frequency analysis, the corticofugal system is also specialized for fine frequency analysis.

In the big brown bat (Yan and Suga 1998), a focal cortical activation augments the auditory responses of collicular neurons whose BFs are within ±0.5 kHz of the BF of the electrically stimulated cortical neurons (not within ±0.2 kHz as in the mustached bat). The BFs of these matched collicular neurons are not shifted by the focal cortical activation. The difference in the range of BFs of matched neurons between the two species appears to be related to the difference in the sharpness of frequency-tuning curves: wider in the big brown bat than in the DSCF neurons of the mustached bat. The effect of the focal cortical activation on unmatched collicular neurons is inhibitory on the responses at the BFs of collicular neurons in both the species. However, the direction of BF shifts is centripetal and asymmetrical in the big brown bat and centrifugal and symmetrical in the mustached bat. The centripetal BF shifts evoke overrepresentation of the frequencies adjacent to the frequency to which activated cortical neurons are tuned, while the centrifugal BF shifts evoke underrepresentation of frequencies adjacent to the frequency to which the activated cortical neurons are tuned.

Yan and Suga (1998) speculated that the difference in BF shift between the big brown bat and the mustached bat is related to the difference in shape and sharpness of the frequency-tuning curves between these two species of bats. As in the little brown bat, Myotis lucifugus (Suga 1964), guinea pig (Evans 1975), cat (Liberman 1978), and monkey (Katsuki et al. 1962), the high-frequency slope of frequency-tuning curves of peripheral neurons in the big brown bat is presumably much steeper than the low-frequency slope. Thus a stimulus tone at a given frequency co-activates many more neurons tuned to higher frequencies than neurons tuned to lower frequencies. The corticofugal projection perhaps reflects this, and co-excitation of subcortical neurons by the corticofugal system is presumably related to BF shifts toward the BF of neurons optimally excited. On the other hand, at the auditory periphery of the mustached bat, frequency-tuning curves tuned to ~61 kHz are extremely sharp and symmetrical in shape (Suga and Jen 1977). A stimulation with a ~61-kHz tone burst excites only neurons tuned to ~61 kHz. In the central auditory system, such focal excitation is associated with strong lateral inhibition (Suga 1995; Suga and Manabe 1982). The corticofugal projection of the mustached bat perhaps reflects these and evokes centrifugal BF shifts. The mechanisms for centripetal and
directly excited cortical neurons within a delivered at a rate of 5/s for 7 min. Each electric pulse perhaps evoked by a stimulus of 100-nA, 0.2-ms-long electric pulses of subcortical signal processing. Suga 1997). Therefore subcortical auditory responses to tone colliculus and by 60% in the medial geniculate body (Zhang and system. A nonfocal inactivation of the cortical DSCF area with necessary but to describe what is going on in the central auditory system. It has been demonstrated that cortical over-representation can be evoked by electrical stimulation of a particular portion of the cortex (Chowdhury and Suga 2000; Maldonado and Gerstein 1996; Nudo et al. 1996; Recanzone et al. 1993; Spengler and Dinse 1994; Yan and Suga 1998). In the big brown bat, Yan and Suga (1998) studied “short-term” corticofugal modulation, which lasted ≤180 min. They stimulated the auditory cortex with a train of four electric pulses (100 nA, 0.2-ms long each) and found facilitation of responses of matched collicular neurons and suppression of responses at BF frequencies (asymmetrical BF shifts) in the mustached bat (Chowdhury and Suga 2000; Gao and Suga 1998; Yan and Suga 1998) and ±1.6 kHz (symmetrical BF shifts) in the mustached bat (Zhang et al. 1997; the present paper). This large difference in the affected ranges is apparently related to the difference in sharpness of the frequency-tuning curve; generally wide in the big brown bat (Haplea et al. 1994) and very sharp without exception in the mustached bat at the DSCF area of the cortex (Suga 1995; Suga and Manabe 1982) and at the periphery (Suga and Jen 1977; Suga et al. 1975).

Possible functions of egocentric selection

Focal cortical inactivation evokes suppression of auditory responses of matched subcortical neurons, augmentation of the responses of unmatched subcortical neurons, BF shift of the unmatched subcortical neurons toward the BF of inactivated cortical neurons, and broadening of frequency-tuning curves of both matched and unmatched subcortical neurons (Zhang et al. 1997). Focal cortical activation evokes the phenomena opposite to the preceding ones, as described in our present paper. These observations indicate that the corticofugal system improves and adjusts subcortical auditory signal processing, in other words, cortical neurons improve and adjust their own input through the corticofugal system and that auditory signal processing would become poor without the corticofugal system.

Since neurons with a BF at ~61 kHz are very sensitive and sharply tuned to ~61 kHz in the mustached bat, one may consider that no improvement in their response properties is necessary. We are not in a position to discuss whether it is necessary or unnecessary but to describe what is going on in the central auditory system. A nonfocal inactivation of the cortical DSCF area with muscimol reduces single-tone responses by 34% in the inferior colliculus and by 60% in the medial geniculate body (Zhang and Suga 1997). Therefore subcortical auditory responses to tone bursts would be noticeably small without the corticofugal system. It is clear that the corticofugal system plays an important role in subcortical signal processing.

In our present experiments, focal cortical activation was evoked by a stimulus of 100-nA, 0.2-ms-long electric pulses delivered at a rate of 5/s for 7 min. Each electric pulse perhaps directly excited cortical neurons within a ~60-µm radius around a stimulating electrode (Yan and Suga 1996). The mustached bat emits biosonar pulses at a rate of 5–10/s during the search or cruising phase of echolocation so that its auditory system is self-stimulated at this rate. The cortical electrical stimulation is of course unnatural but is somewhat comparable to the self-stimulation by the emitted pulses.

Corticofugal modulation of collicular neurons described in our present paper occurs in a slow time course. Therefore BF shifts, for example, do not occur every time when the bat emits a biosonar pulse. Instead corticofugal modulation (egocentric selection) occurs to maintain the auditory system in a state appropriate for signal processing in a given auditory environment. In the big brown bat, Jen et al. (1998) found short-latency “rapid” modulation of collicular responses following each cortical electric stimulation with a train of four electric pulses (1.25–85 µA, 0.1-ms long each). This rapid modulation was either facilitation of responses accompanied with broadening of frequency tuning or inhibition of neurons accompanied with sharpening of frequency tuning. These two types of modulation were found for both matched and unmatched collicular neurons. Corticofugal inhibition and facilitation were found for 74 and 26% of collicular neurons studied, respectively. Therefore they suggested that the function of corticofugal modulation is to improve the processing of subsequent biosonar signals for echolocation.

The auditory, visual, and somatosensory systems, respectively, have cochleotopic, retinotopic, and somatosensory maps in their central neural pathways. These sensory epithelial maps are modified by deprivation, injury, and experience in young (Hubel et al. 1977) and adult animals (Clark et al. 1988; Irvine and Rajan 1996; Jenkins et al. 1990; Kaas et al. 1990; Merzenich et al. 1984; Pettet and Gilbert 1992; Recanzone et al. 1993; Snyder et al. 1990, 1991; Weinberger et al. 1993). Such plasticity has been explained by changes in divergent and convergent projections of neurons in the ascending sensory system. It has been demonstrated that cortical over-representation can be evoked by electrical stimulation of a particular portion of the cortex (Chowdhury and Suga 2000; Maldonado and Gerstein 1996; Nudo et al. 1996; Recanzone et al. 1993; Spengler and Dinse 1994; Yan and Suga 1998). In the big brown bat, Yan and Suga (1998) studied “short-term” corticofugal modulation, which lasted ≤180 min. They stimulated the auditory cortex with a train of four electric pulses (100 nA, 0.2-ms long each) and found facilitation of responses of matched collicular neurons and suppression of responses at BF frequencies of unmatched neurons. Gao and Suga (1998, 2000) obtained the data indicating that the short-term corticofugal modulation is directly involved in long-term plasticity of the auditory cortex evoked by auditory conditioning. The data we have reported in our present paper is different from these. The strong augmentation of the responses of matched subcortical DSCF neurons and the centrifugal BF shifts of unmatched subcortical DSCF neurons are related to the specialization of the auditory system of the mustached bat for extremely fine frequency analysis of the frequency-modulated echoes from flying insects. Regardless of the difference in corticofugal effect between the mustached bat and the big brown bat, the corticofugal system of the mustached bat is most likely to be directly involved in long-term plasticity of the auditory cortex as that of the big brown bat is.

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REFERENCES

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