Reorganization of the Frequency Map of the Auditory Cortex Evoked by Cortical Electrical Stimulation in the Big Brown Bat

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Chowdhury, Syed A. and Nobuo Suga. Reorganization of the frequency map of the auditory cortex evoked by cortical electrical stimulation in the big brown bat. *J. Neurophysiol.* 83: 1856–1863, 2000. In a search phase of echolocation, big brown bats, *Eptesicus fuscus*, emit biosonar pulses at a rate of 10/s and listen to echoes. When a short acoustic stimulus was repetitively delivered at this rate, the reorganization of the frequency map of the primary auditory cortex took place at and around the neurons tuned to the frequency of the acoustic stimulus. Such reorganization became larger when the acoustic stimulus was paired with electrical stimulation of the cortical neurons tuned to the frequency of the acoustic stimulus. This reorganization was mainly due to the decrease in the best frequencies of the neurons that had best frequencies slightly higher than those of the electrically stimulated cortical neurons or the frequency of the acoustic stimulus. Neurons with best frequencies slightly lower than those of the acoustically and/or electrically stimulated neurons slightly increased their best frequencies. These changes resulted in the over-representation of repetitively delivered acoustic stimulus. Because the over-representation resulted in under-representation of other frequencies, the changes increased the contrast of the neural representation of the acoustic stimulus. Best frequency shifts for over-representation were associated with sharpening of frequency-tuning curves of 25% of the neurons studied. Because of the increases in both the contrast of neural representation and the sharpness of tuning, the over-representation of the acoustic stimulus is accompanied with an improvement of analysis of the acoustic stimulus.

INTRODUCTION

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. However, recent findings, briefly reviewed below, indicate that the cerebral cortex and the descending (corticofugal) system play an important role in modifying these maps.

In the motor (Nudo et al. 1996), somatosensory (Recanzone et al. 1993; Spengler and Dinse 1994), and auditory cortices (Maldonado and Gerstein 1996; Yan and Suga 1998), electrical stimulation of particular parts of the cortex evokes an expansion in the cortical or subcortical representation of those parts. In the big brown bat, an acoustic stimulus paired with electric leg-stimulation as in a classical conditioning paradigm evokes an expansion in the representation of the acoustic stimulus in the inferior colliculus. The auditory cortex is necessary for this expansion (Gao and Suga 1998).

In the mustached bat (*Pteronotus parnellii*), cortical auditory neurons mediate, via corticofugal projection, a highly focused positive feedback to subcortical neurons "matched" in tuning to a particular acoustic parameter in the frequency or time domain, and a widespread lateral inhibition to "unmatched" subcortical neurons. This cortical feedback changes subcortical maps, augments excitatory neural responses, and sharpens neural tuning curves so as to enhance the neural representation of frequently occurring signals in the central auditory system. This function, named "egocentric selection," adjusts and improves the cortical neurons' own input, and, consequently, cortical signal processing (Yan and Suga 1996; Zhang et al. 1997). In the big brown bat (*Eptesicus fuscus*), egocentric selection shifts the best frequencies (BFs) of collicular neurons not only toward the BF of electrically stimulated cortical neurons but also toward the frequency of a repetitively delivered acoustic stimulus (tone burst), resulting in local reorganization of the frequency map in the inferior colliculus (Yan and Suga 1998). Egocentric selection also evokes BF shifts according to auditory experience based on associative learning (Gao and Suga 1998).

It appears that the cerebral cortex has mechanisms to adjust and improve sensory epithelial (frequency) and computational (echo delay) maps not only in the cortex, but also in subcortical nuclei via corticofugal feedback. In the above experiments on bats, however, changes evoked by acoustic stimuli and/or focal cortical electrical stimulation were studied only in the subcortical auditory nuclei. The aim of our present paper is to report our finding that the changes in the frequency map of the primary auditory cortex are similar to, but slightly larger than, those in the inferior colliculus.

METHODS

Sixteen adult big brown bats, *Eptesicus fuscus*, were used in the present experiment. Under neuroleptanalgesia (Innovar 4.08 mg/kg body weight), a 1.5-cm-long metal post was glued on the dorsal surface of the bat's skull. The physiological experiment was started 3–4 days after the surgery. The animal was placed in a polyethylene-foam body mold and hung at the center of a soundproof room which was maintained at 31°C. The metal post mounted on the skull was fixed on a metal rod with set screws to immobilize the animal's head and adjusted to face directly at a loudspeaker located 74 cm away. (The protocol of our research was approved by the animal studies committee of Washington University.) To record action potentials of

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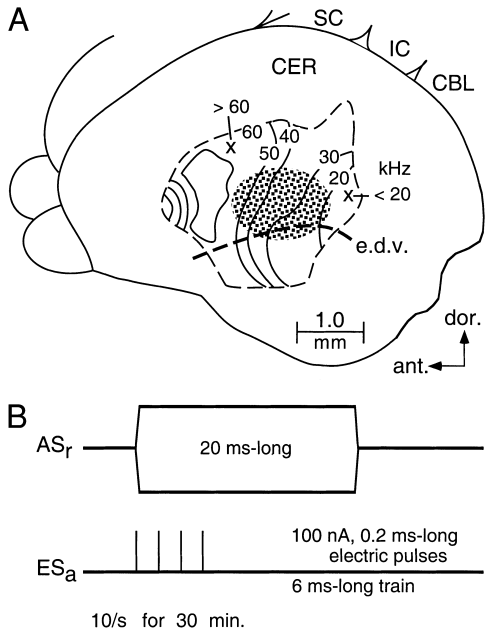

FIG. 1. Cochleotopic map in the primary auditory cortex (*A*) and stimulus configurations (*B*). *A*: numbers and lines on the left auditory cortex indicate isobest frequency contour lines. Our recordings of auditory responses were made within the dotted area. (The map is based on Dear et al. 1993.) *B*: tone burst used for repetitive acoustic stimulation (AS_r) and a train of electric pulses used for cortical stimulation (ES_a). These stimuli were delivered at a rate of 10/s for 30 min. CBL, cerebellum; CER, cerebral cortex; e.d.v., epidural vessel; IC, inferior colliculus; SC, superior colliculus.

cortical auditory neurons, a tungsten-wire electrode (6–8 μm tip diam) was orthogonally inserted into the auditory cortex (AC), which is tonotopically organized and ~900-μm thick (Fig. 1*A*). All recordings were made at the depth of 200–800 μm. A BAK window discriminator was used to select action potentials from a single neuron. When the selection was difficult and action potentials originating from 2–3 neurons were recorded, the recording was classified as a multiunit recording. The BF and minimum threshold of a single neuron or multiple neurons were first measured audiovisually. Then, the computer-controlled frequency scan was delivered, which consisted of 22 time blocks, each 200-ms long. A single tone burst was delivered at the beginning of each block. The frequency of the tone burst was shifted from block to block in 0.5-kHz steps across the BF of the neuron(s). The amplitude of tone bursts in the scan was set at 20 dB above the minimum threshold of the neuron or varied every 10 scans in 5 dB steps from 80 to 0 dB sound pressure level. Neural responses to tone bursts were displayed as peristimulus-time (PST) or PST cumulative (PSTC) histograms. (In a PSTC histogram, impulse counts in the bins of a PST histogram are successively added.) The responses to the frequency scans were displayed on a computer monitor as an array or arrays of PST or PSTC histograms, stored on a computer hard drive, and used to construct a frequency-response or frequency-tuning curve. Such a curve was obtained before and after repetitive acoustic stimuli (AS_r) or focal cortical electric stimulation (ES_a) paired with AS_r, delivered at a rate of 10/s for 30 min.

AS_r consisted of 300 tone bursts, each of which was 20-ms long with a 0.5-ms rise-delay time (Fig. 1*B*). Its amplitude and frequency were set at 50 dB SPL and at a frequency the same as or lower or higher than the BF of a recorded cortical neuron, respectively. ES_a was delivered through a pair of tungsten-wire electrodes glued side by side. The tips of these electrodes were 6–8 μm in diameter and were separated by ~150 μm along the electrode shaft. These stimulating electrodes were placed at a 500–700 μm depth of the AC. In the paired acoustic-electrical stimulation ($AS_r + ES_a$), the AS_r frequency was always the same as the BF of cortical neurons electrically stimulated. ES_a was a train of four monophasic electric pulses (100 nA, 0.2-ms duration, 2.0-ms interval). The first pulse of ES_a and the onset of each tone burst were in register in time (Fig. 1*B*). AS_r or $AS_r + ES_a$ was delivered at a rate of 10/s for 30 min.

To measure a BF shift as a function of distance between the recorded and electrically stimulated cortical neurons, the BFs of cortical neurons were first measured at 12–14 locations. These locations were ~100 μm apart and rostral or caudal to the location of ES_a along the frequency axis in the AC. Then, $AS_r + ES_a$ were delivered for 30 min. Within 60 min thereafter, BFs of neurons at these 12–14 locations were remeasured.

The following criteria were used for a shift in the frequency-response or -tuning curve (or BF) of a neuron by AS_r or $AS_r + ES_a$: if a shifted frequency-response or -tuning curve did not shift back by more than 50%, the data were excluded from the analysis. In stable, long recording conditions, all curves shifted by the stimulation 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 response to five consecutive frequency scans. 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 (BFs) obtained for control and stimulus conditions were significantly different for $P < 0.01$.

RESULTS

Shifts in best frequencies

In the AC of the big brown bat, the low-to-high-frequency axis was parallel to the caudorostral axis of the brain, as previously reported (Fig. 1*A*; Dear et al. 1993; Jen et al. 1989). We recorded 71 single and 45 multiple neurons in the AC and found shifts in BFs that were the same as those found in the inferior colliculus (Yan and Suga 1998). That is, AS_r or ES_a paired with the AS_r mainly evoked downward shifts in the BFs of cortical neurons which had a BF slightly higher than the frequency of the AS_r. These cortical neurons were located within ~600 μm rostral to the neurons activated with the ES_a. The BF shifts were larger and longer-lasting for the $AS_r + ES_a$ than for the AS_r alone.

In Fig. 2, the frequency-response curves of two single cortical neurons (*A* and *B*) are shown by the arrays of PSTC histograms displaying their responses to tone bursts obtained before, immediately after, and 90 min after AS_r (*Aa*) or $AS_r + ES_a$ (*Ba*). The amplitude of the tone bursts was 10 dB above the minimum threshold of a given neuron. In *Aa*, the neuron was tuned to 43.5 kHz in the control condition. When AS_r at 41.0 kHz was delivered for 30 min, its BF shifted down to 43.0 kHz. The BF returned to 43.5 kHz 90 min after the AS_r. In *Ba*, the neuron was tuned to 58.5 kHz in the control condition. When AS_r at 53.0 kHz was paired with ES_a to stimulate 53.0 kHz tuned cortical neurons, the 58.5-kHz BF shifted down to 55.5 kHz. The BF returned to 58.5 kHz 90 min after $AS_r + ES_a$. These shifts in the BFs were due to a decrease in the response at the BF in the control condition and an increase in the response at the shifted BF. Neither decrease nor increase in response was associated with a change in response pattern, as shown by the PST histograms in Fig. 2.

The time course of a BF shift evoked by AS_r alone or $AS_r + ES_a$ was measured in 19 and 42 neurons, respectively. The BF shift was always largest and stayed nearly the same in a period of 30–60 min after the cessation of AS_r or $AS_r + ES_a$. Then,

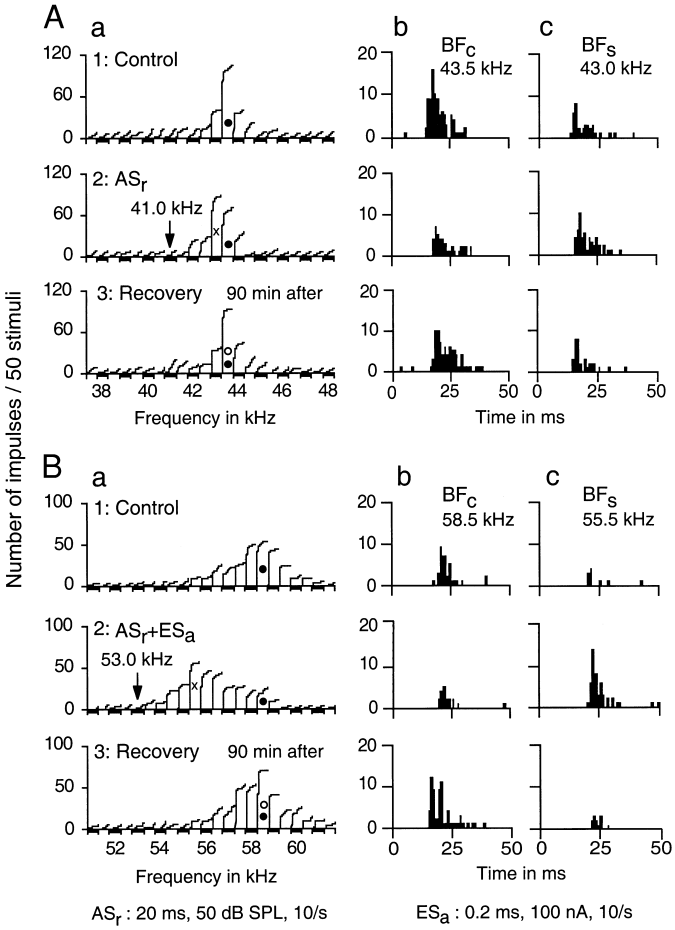

FIG. 2. Changes in the responses of 2 cortical neurons (*A* and *B*) evoked by AS_r (*A*) or (ES_a) paired with AS_r (*B*). *a*: arrays of poststimulus-time cumulative (PSTC) histograms displaying the responses to tone bursts at different frequencies. *b* and *c*: poststimulus-time (PST) histograms displaying the responses to the tone bursts at the best frequencies in the control (43.5 or 58.5 kHz) or the shifted condition (43.0 or 55.5 kHz). *1*, *2*, and *3*, respectively, show the responses in the control, shifted (AS_r or AS_r + ES_a), and recovery conditions. The frequency of AS_r is indicated by the arrow. ES_a was delivered to cortical neurons tuned to the AS_r frequency. *a*: filled circles, ×s, and open circles indicate the best frequencies (BF) in the control, shifted, and recovery conditions, respectively. Changes in response evoked by AS_r + ES_a were larger than those evoked by AS_r alone. The parameters of AS_r and ES_a are listed at the bottom.

BFs gradually returned to those in the control condition over 2–3 h after the cessation (Fig. 3). A 75% recovery occurred at 55.0 ± 21.2 min (n = 19) after AS_r or at 100.2 ± 28.3 min (n = 42) after AS_r + ES_a.

The data obtained from 154 neurons indicate that the amount of the maximum BF shift of each neuron was different depending on the difference between its BF and the frequency of AS_r (Figs. 4, *A* and *B*, and 5). (Note that in AS_r + ES_a the BF of neurons electrically stimulated was the same as the frequency of AS_r.) We considered that the higher the AS_r and/or the BF of cortical neurons electrically stimulated, the larger the range of BFs affected by the AS_r and/or ES_a. That is, we considered that if the AS_r was one octave higher, the amount of a BF shift was one octave larger. The AS_r frequency in AS_r + ES_a was between 22.6 and 54.0 kHz (34.6 ± 11.2 kHz; n = 83). The maximum BF shift and the largest BF difference between recorded and stimulated cortical neurons for a just-noticeable BF shift were, respectively, −2.6 and 11 kHz for 23–27 kHz AS_r frequencies (n = 9), and −2.4 and 14 kHz for 46–54 kHz AS_r frequencies (n = 7). The maximum BF shift and the largest BF difference for a just-noticeable BF shift did not differ between the above two ranges of AS_r frequencies. Therefore in the following text, the BF shifts and the differences between BF and AS_r are expressed in kilohertz, not in octave.

The relationship between a BF shift and a difference between the BF of a recorded neuron and a AS_r frequency or a BF difference between recorded and stimulated cortical neurons is shown in Fig. 4. Figure 4*A* shows that AS_r alone evoked the downward shifts of the BFs of neurons which had a BF within 8 kHz above the AS_r frequency. The maximum BF shift observed was 1.0 kHz, which occurred at ~3 kHz above the AS_r frequency. Figure 4*B* shows that AS_r + ES_a evoked the downward shifts of the BFs of neurons which had a BF within 12 kHz above the BFs of electrically stimulated cortical neurons. The maximum BF shift observed was 3.0 kHz, which occurred at 5 kHz above the BFs of electrically stimulated neurons. Small but significant BF shifts were also noticed for neurons in which BFs were more than 12 kHz higher or lower than the BFs of neurons electrically stimulated. Therefore the BF shifts between −1.0 and +0.5 kHz shown in Fig. 4*B* are replotted on the expanded ordinate in Fig. 4*C*. The following are indicated by Fig. 4*C*. *1*) AS_r + ES_a also evoked the decrease in the BFs of some neurons with a BF within a range of 6–8 kHz lower (4 open circles on the *left*) or ~19 kHz higher (3 triangles on the *far right*) than the BF of electrically stimulated neurons. *2*) It also evoked an increase in the BFs of some neurons with a BF within a range of 1–6 kHz lower (7 triangles on the *left*) or 12–15 kHz higher (7 open circles on the *right*) than the BF of electrically stimulated neurons. *3*) BF shifts between −3 and +8 kHz (triangle) tended to evoke over-representation of the AS_r frequency or the BF of electri-

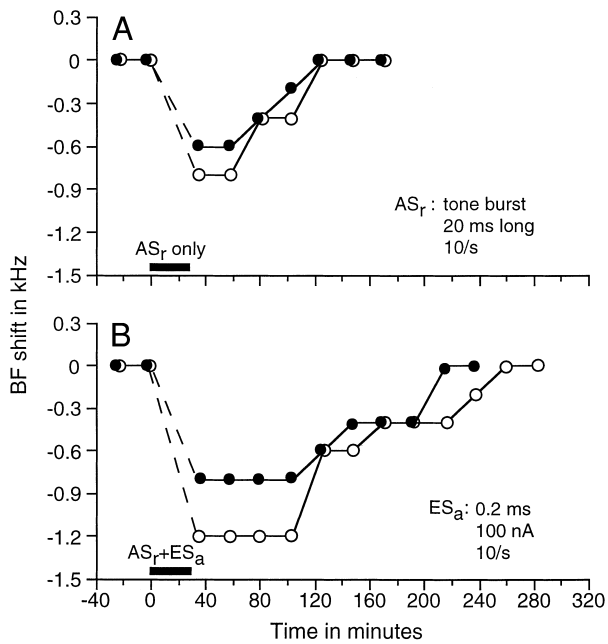

FIG. 3. Recovery curves of BF shifts in 4 cortical neurons evoked by AS_r (*A*) or (ES_a) paired with AS_r (*B*). ES_a was delivered to cortical neurons tuned to the AS_r frequency. *A*: AS_r was 2.8 (●) or 3.6 kHz (○) lower than the BFs (43.4 or 25.2 kHz) of 2 neurons. *B*: AS_r was 2.4 (●) or 3.6 kHz (○) lower than the BFs (31.4 and 37.8 kHz) of 2 neurons.

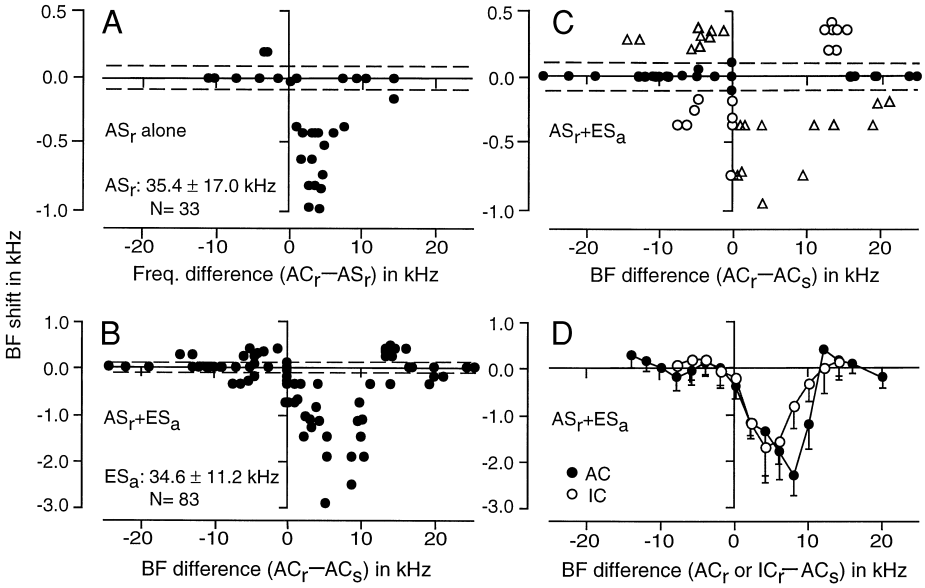

FIG. 4. Shifts in the BFs of cortical neurons evoked by AS_r (*A*) or by ES_a paired with AS_r (*B*) as a function of difference between the BF of a neuron and the AS_r frequency. ES_a was delivered to cortical neurons tuned to the AS_r frequency, which was 34.6 ± 11.2 kHz (n = 83). *C*: BF shifts between −1.0 and +0.5 kHz in *B* are replotted on the expanded BF shift axis. Triangles and open circles, respectively, indicate BF shifts toward and away from the AS_r frequency. *D*: mean BF shifts with a bar for one standard deviation are plotted for cortical (●) and collicular neurons (○). *A–C*: horizontal dashed lines indicate ±SD. AC_r: cortical neurons recorded. AC_s: cortical neurons stimulated. IC_r: collicular neurons recorded. (The collicular data were obtained by Yan and Suga 1998.)

cally stimulated cortical neurons, but those between −3 and −8 kHz and between +8 and +15 kHz (open circles) tended to evoke under-representation of these frequencies. In other words, the BF shifts occurred to increase the contrast of neural representation of AS_r or the BF of electrically stimulated cortical neurons.

As shown in Fig. 4, the most noticeable BF shifts were downward toward the BF of electrically stimulated cortical neurons and occurred on the high-frequency side of the BF of electrically stimulated cortical neurons or the frequency of AS_r. Therefore the BF shifts (i.e., frequency map adjustment) is asymmetrical and centripetal. The comparison of the present cortical data with the collicular data obtained by Yan and Suga (1998) indicate that BF shifts evoked by AS_r + ES_a were slightly larger for cortical neurons than for collicular neurons ($P < 0.005$ at 6 and 9 kHz above the BF of cortical neurons electrically stimulated) (Fig. 4*D*).

The BF shifts at a given BF difference between recorded and stimulated cortical neurons are different from neuron to neuron. For example, a BF shift occurred in some neurons, but did not occur in some others at the BF difference of −5 kHz. If a shift did occur, the direction of BF shift could be different between neurons. Such variation might be due to pooling the data obtained for AS_r + ES_a in which ES_a was delivered to different locations of cortical iso-BF lines tuned to a frequency between 22.6 and 54.0 kHz (34.9 ± 11.2 kHz, n = 83). Therefore a pair of electrodes for ES_a was implanted at a 500–700 μm depth at a 30.2 ± 0.6 kHz tuned location and single or multiple neurons were recorded from different locations rostral or caudal to the stimulation electrodes along the frequency axis of the AC. The data obtained from three animals (Fig. 5) indicate that cortical neurons located rostrally <600 μm (corresponding to ~47 kHz) to the stimulation electrodes decreased their best frequencies and that those located caudally <400 μm (corresponding to ~22 kHz) to the stimulation electrodes increased their best frequencies. The decrease in BF was much larger than the increase in BF. The BF shifts were thus asymmetrical and centripetal. The largest downward BF shift observed was 1.8 kHz, which occurred at 0.2 mm rostral (corresponding to ~35 kHz) to the electrically stimulated neurons. The largest upward BF shift was 0.4 kHz, which occurred at 0.1 mm caudal (corresponding to ~24 kHz) to the electrically stimulated neurons. The BF shifts toward the BF of the electrically stimulated neurons tended to evoke an over-representation of the BF of the electrically stimulated neurons. The over-representation is, however, associated with the under-representation of BFs at 0.2–0.6 mm rostral and −0.1 to −0.4 mm caudal portions to the electrically stimulated neurons, because the amount of BF shift became less at the portion more rostral to the 0.2 mm rostral place or more caudal to the 0.1 mm caudal place to the electrically stimulated neurons.

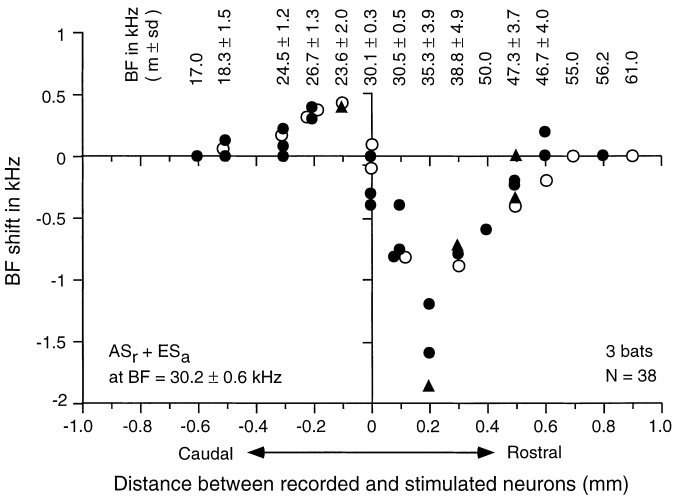

FIG. 5. Shifts in the BFs of cortical neurons as a function of the distance between recorded and stimulated cortical neurons. The data obtained from 3 different bats are indicated by the 3 different symbols. The best frequency of cortical neurons stimulated was 30.2 ± 0.6 kHz. The BFs of neurons recorded at different locations are shown at the top.

Sharpening of frequency tuning curves

A shift in BF of a neuron was always accompanied by a similar shift of the whole frequency-tuning curve. The shift in a tuning curve was mostly parallel to the frequency axis

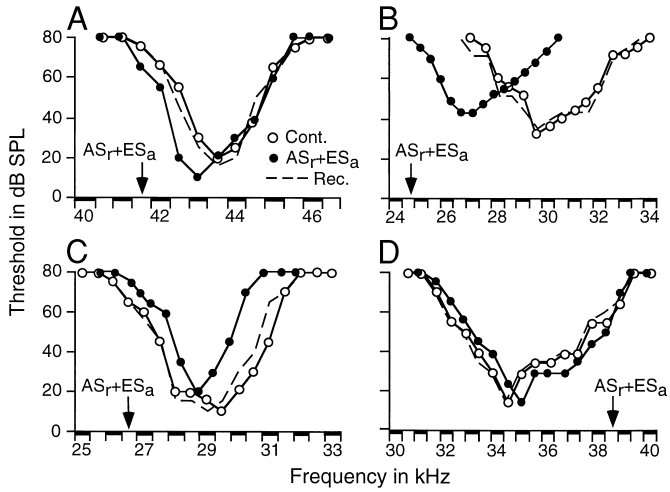

FIG. 6. Changes in the frequency-tuning curves of four cortical neurons (*A–D*) evoked by paired acoustic and electric stimuli (AS_r + ES_a). *A–C*: BFs of the recorded neurons were higher than the BFs of the electrically stimulated cortical neurons (arrows). *D*: BF of the recorded neuron was lower than that of the electrically stimulated neuron (arrow). The frequency of AS_r was the same as the BFs of neurons electrically stimulated. The open and filled circles and dashed lines indicate the frequency-tuning curves measured in the control, shifted, and recovered conditions, respectively. *A–D*: tuning curves shifted toward the BFs of electrically stimulated cortical neurons (arrows).

(Fig. 6). For AS_r alone, the minimum threshold and the shape of a frequency-tuning curve did not change in all 33 neurons studied, perhaps because a change was too small to be detected in our measurement. However, for AS_r + ES_a, change in minimum threshold was observed, which was ±5 dB in 61 neurons out of the 83 neurons showing a BF shift and was ±10 dB in the remaining 22 neurons. The overall shape of a tuning curve did not change in 70 neurons out of the 83 (Fig. 6, *A*, *B*, and *D*), but changed in the remaining 13 neurons (Fig. 6*C*).

Twenty-one neurons out of the 83 had a BF within a range of −6 and +20 kHz of the AS_r frequency and shifted the BF by −3.2 to +1 kHz (Fig. 4*B*). They showed a decrease in the width of the tuning curve, i.e., sharpening in the tuning curve. Sharpening at 30 dB above minimum threshold was small, 0.4–1.0 kHz, in 16 neurons (Fig. 6*B*), but large, 1.2–1.6 kHz, in the remaining three neurons (Fig. 6*C*).

It has been known that the width of a frequency-tuning curve sharpened by lateral inhibition generally does not change or changes only a little at 10 dB above the minimum threshold, but changes noticeably at higher stimulus levels (e.g., Suga et al. 1997). Therefore a width of a tuning curve was measured at 10, 30, and 50 dB above the minimum threshold of each of the 83 neurons studied with AS_r + ES_a. Sixty-two out of 83 neurons showed no change at all in the bandwidth of their tuning curves, regardless of stimulus levels because the amount of change was not more that 0.1 kHz ($P > 0.05$). However, the remaining 21 neurons showed changes larger than 0.1 kHz, so that the changes at different stimulus levels were plotted against the difference in BF between the recorded and stimulated cortical neurons (Fig. 7, *A–C*). Out of the 21, 19 neurons showed 0.3–1.6 kHz narrower widths of a tuning curve at 30 dB above minimum threshold than those in the control condition (Fig. 7*B*), and 1 neuron showed 1.0 kHz wider width than that in the control condition. Such changes (sharpening) were significant at all three stimulus levels: values of *P* are 0.0330, 0.0002, and 0.0049 for 10, 30, and 50 dB above minimum threshold, respectively (Fig. 7, *A–C*).

There was a tendency that sharpening was somewhat larger for the neurons with BFs within ±2 kHz of the AS_r frequency, which was the same as the BF of electrically stimulated cortical neurons (Fig. 7*B*). However, cross-correlation analysis indicates that there is no correlation between BF shift and change in bandwidth: r = 0.17, 0.24, and 0.10 at 10, 30, and 50 dB above minimum threshold, respectively (Fig. 7, *D–F*).

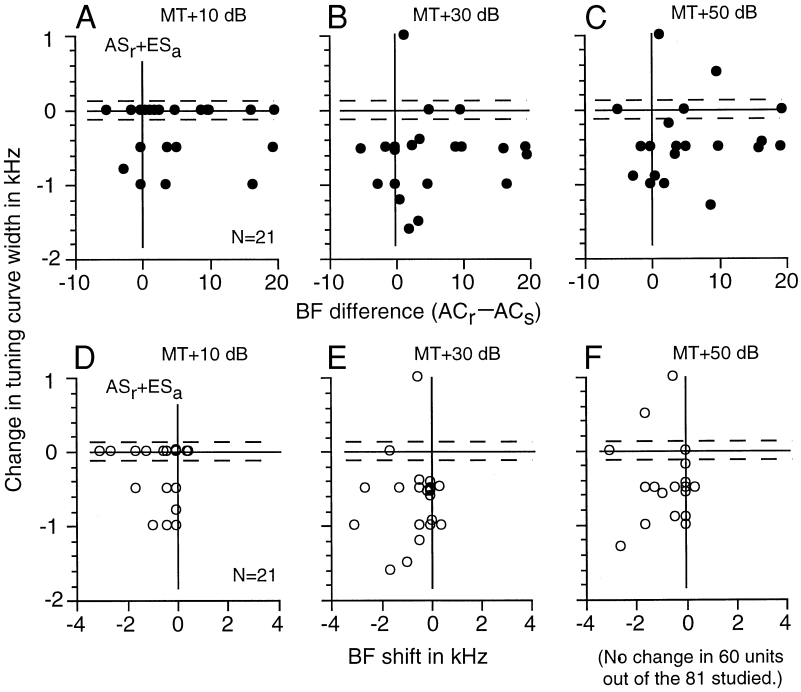

FIG. 7. Changes in the widths of frequency-tuning curves of cortical neurons evoked by ES_a paired with AS_r. *A–C*: changes in widths at 10, 30, and 50 dB above minimum threshold, as the function of difference in BF between recorded and electrically stimulated cortical neurons. *D–F*: changes in widths at 10, 30, and 50 dB above minimum threshold as a function of the BF shift.

DISCUSSION

Adjustment of frequency representation in the AC and inferior colliculus

The adjustment of frequency representation in the AC evoked by AS_r alone or $AS_r + ES_a$ is similar to that in the inferior colliculus (Yan and Suga 1998), although the former is slightly larger than the latter. Classical conditioning with tone bursts and electric leg-stimulation also evokes the adjustment of frequency representation in the inferior colliculus which is the same as that evoked in the inferior colliculus by $AS_r + ES_a$. This adjustment evoked by conditioning does not occur when the AC or the somatosensory cortex is inactivated during conditioning. These findings indicate that the corticofugal system plays an important role in the plasticity of the central auditory system (Gao and Suga 1998).

Recent studies indicate that the cholinergic basal forebrain plays an important role in cortical reorganization. Electrical stimulation of the basal forebrain paired with tone bursts evokes massive cortical reorganization for the over-representation of the frequency of the tone bursts (Bakin and Weinberger 1995; Bjordahl et al. 1998; Kilgard and Merzenich 1998).

Weinberger (1995) proposed a model to explain cortical frequency-tuning plasticity in the learning of a classical conditioning paradigm. An auditory signal (tone burst, conditioning stimulus) is sent to the AC through the ventral division of the medial geniculate body (MGB_v), which is nonplastic, and is also sent to the magnocellular division of the medial geniculate body (MGB_m), which is plastic, and the posterior intralaminar complex, both in the thalamus. A somatosensory signal (electric foot-shock, unconditioned stimulus) is also sent to the MGB_m and posterior intralaminar complex, where the somatosensory and auditory signals are first associated with each other for associative learning. The associated signal is sent up to the AC to strengthen the effect of MGB_v neurons, excited by the conditioning stimulus, on cortical neurons. This associated signal is also sent to the amygdala, which in turn projects to the nucleus basalis. Then, the nucleus basalis increases cortical acetylcholine levels and amplifies the effect of the MGB_m neurons on the cortical neurons which are excited by the conditioning stimulus.

The MGB_v shows "short-term" frequency-specific plasticity for fear conditioning (Edeline and Weinberger 1991), although it is assumed to be nonplastic in the above model. Because the inferior colliculus also shows plastic changes according to associative learning (Gao and Suga 1998), as does the AC (Gao and Suga 2000), the plastic changes of the MGB_m may be at least partially due to those in the inferior colliculus. MGB_m neurons often have a broad or multipeaked frequency-tuning curve and habituate after several stimulus presentations (Aitkin 1973; Calford 1983). If so, MGB_m may not be suited for the fine adjustment and improvement of the central auditory system for signal processing. These must be performed within the auditory system, where the fine analysis of auditory signals takes place. It has been demonstrated that egocentric selection mediated by the corticofugal system evokes subcortical changes which are highly specific to acoustic stimuli (Yan and Suga 1996, 1998; Zhang et al. 1997). Therefore the corticofugal system is expected to play an important role in stimulus-specific cortical plasticity.

Gao and Suga (1998) therefore proposed a model which is somewhat different from Weinberger's model. A train of sounds combined with an electric leg-stimulation excite the AC and the somatosensory cortex, respectively. These sensory cortices send signals to the amygdala through the association cortex (Amaral et al. 1992; Romanski and LeDoux 1993). The train of acoustic stimuli evokes changes in the AC, which are highly specific to acoustic stimuli, and are based on egocentric selection mediated by the corticofugal system. When associative learning takes place in the amygdala, that is, when an animal is conditioned for the train of acoustic stimuli paired with electric leg stimulation, the cholinergic basal forebrain is excited by these stimuli through the amygdala and increases the acetylcholine level in the cortex. As a result, the train of acoustic stimuli-related changes in the AC are augmented in magnitude and duration. In other words, the processing of behaviorally relevant acoustic stimuli is adjusted and improved. Our present data favor the hypothesis that the AC has the basic neural circuit which works together with the corticofugal system for the adjustment and improvement of auditory signal processing.

In the AC, the duration of plastic changes is 2–3 h for a behaviorally irrelevant acoustic stimulus or direct cortical electrical stimulation, but many hours for a behaviorally relevant acoustic stimulus (Gao and Suga 2000). In the inferior colliculus, however, it is 2–3 h for both conditions (Gao and Suga 1998; Yan and Suga 1998). These data indicate that Gao and Suga's model is a useful working hypothesis and that multiple mechanisms are involved in the plastic changes of the auditory system.

Difference in the adjustment of frequency representation between the big brown and mustached bats

The data obtained from the big brown bat (Gao and Suga 1998; Yan and Suga 1998) and the mustached bat (Zhang et al. 1997; Y. Zhang and N. Suga, unpublished data) indicate the following. *1*) By action of the corticofugal system, the neural responses of subcortical neurons tuned to frequencies the same as or close to the BF of activated cortical neurons (i.e., so-called matched subcortical neurons) are augmented, but those of unmatched subcortical neurons are suppressed. *2*) The BFs of unmatched neurons are shifted away from the BF of activated cortical neurons in the mustached bat, but are shifted toward the BF of activated cortical neurons in the big brown bat. *3*) The change in frequency representation due to BF shifts is symmetrical in the DSCF neurons of the mustached bat, but is asymmetrical in the big brown bat. *2*) and *3*) are also true in the AC of the big brown bat (present study) and are expected to be true in the AC of the mustached bat. [In the mustached bat, corticofugal effects on subcortical neurons tuned in echo-delay are the same as those on subcortical DSCF neurons sharply tuned in frequency. That is, the best delays for the facilitative responses of unmatched subcortical delay-tuned neurons are symmetrically shifted away from the best delay of activated cortical delay-tuned neurons (Yan and Suga 1996).]

Focused augmentation and widespread lateral inhibition of the auditory responses are respectively evoked for matched and unmatched neurons in both species of bats, but BF shifts are

different between these two species. Possible interpretations of this difference are described below.

As in the little brown bat, *Myotis lucifugus* (Suga 1964), guinea pig (Evans 1975), cat (Liberman 1978), and monkey (Katsuki et al. 1962), the frequency-tuning curves of peripheral neurons of the big brown bat are presumably asymmetrical: their high-frequency slope is much steeper than their low-frequency slope. Therefore a stimulus tone at a given frequency activates more neurons tuned to higher frequencies than neurons tuned to lower frequencies, and the effect of egocentric selection on auditory neurons is asymmetrical. In the mustached bat, however, frequency-tuning curves of peripheral neurons tuned to about 61 kHz are roughly symmetrical (Suga and Jen 1977), so that the effect of egocentric selection on collicular neurons is also symmetrical (Zhang et al. 1997).

In the big brown (Haplea et al. 1994) and little brown bats (Suga 1964), frequency-tuning curves of neurons at the periphery and/or cochlear nucleus are generally much wider ($Q_{10dB} < 20$) than those (Q_{10dB} up to 320) of 61-kHz tuned neurons of the mustached bat (Suga and Jen 1977; Suga et al. 1975), so that any single tone can excite many cortical and subcortical neurons tuned to different frequencies in a much wider range in the big brown bat than in the mustached bat. BF shifts indicate that each cortical or subcortical neuron has multiple inputs tuned to different frequencies, and that the BF of an unmatched neuron shifts toward the BF of the input maximally excited, because the excitation transmission is augmented for the maximally excited input and is suppressed for other inputs, including the input for its original BF (Fig. 2). In the big brown bat, augmentation of cortical and subcortical responses by corticofugal feedback may be stronger and more widespread in the frequency domain than the suppression of their responses. In the mustached bat, however, suppression may be stronger and more widespread than augmentation. The direction of the BF shifts appears to depend on the interaction of augmentation and suppression.

Because focal cortical electrical stimulation alone evokes the asymmetric BF shift as repetitive acoustic stimulation does (Yan and Suga 1998), anatomic differences in the AC and/or corticofugal projections may exist between the DSCF area of the mustached bat and the AC of the big brown bat and may be partly responsible for the differences observed between the two species of bats. Regardless of this unsolved problem, it is clear that the DSCF area and its corticofugal modulation in the mustached bat are much more specialized for fine frequency representation than the AC and its corticofugal modulation in the big brown bat.

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