Multiparametric corticofugal modulation of collicular duration-tuned neurons: Modulation in the amplitude domain

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ABSTRACT

The subcortical auditory nuclei contain not only neurons tuned to a specific frequency, but also those tuned to multiple parameters characterizing a sound. All these neurons are potentially subject to modulation by descending fibers from the auditory cortex (corticofugal modulation). In the past, we electrically stimulated cortical duration-tuned neurons of the big brown bat, *Eptesicus fuscus*, and found that its collicular duration-tuned neurons were corticofugally modulated in the frequency and time (duration) domains. In the current paper, we report that they were also corticofugally modulated in the amplitude (intensity) domain. We found the following collicular changes evoked by focal cortical electric stimulation: (1) Corticofugal modulation in the amplitude domain differed depending on whether collicular neurons matched in best frequency (BF) with stimulated cortical neurons. BF-matched neurons decreased their thresholds, whereas BF-unmatched neurons increased their thresholds: the larger the BF difference between recorded collicular and stimulated cortical neurons, the larger the threshold increase. (2) In general, the dynamic range for amplitude coding was larger in the inferior colliculus than in the auditory cortex. BF-matched neurons increased their dynamic ranges and response magnitude, whereas BF-unmatched neurons decreased them. (3) Single duration-tuned neurons were simultaneously modulated by cortical electric stimulation in the amplitude, frequency and time domains. (4) Corticofugal modulation in these three domains indicates that the contrast of the neural representation of repeatedly delivered sound stimuli is increased.
INTRODUCTION

The descending (corticofugal) auditory system is cochleotopically (tonotopically) organized as is the ascending auditory system (Malmierca et al. 1996; Anderson et al. 1980; Herbert et al. 1991). Focal electric stimulation of the auditory cortex (AC) facilitates or inhibits the auditory responses of collicular neurons (Jen et al. 1998; Zhou and Jen 2000) and not only sharpens but also shifts their frequency-tuning curves (Yan and Suga 1998; Zhang and Suga 2000). The best frequency (BF) shifts accompanied with the shifts of the frequency-tuning curves are specific and systematic according to the relationship in BF between the recorded collicular and stimulated cortical neurons. BF shifts, which result in reorganization of the frequency map, occur not only in the inferior colliculus (IC) but also in the medial geniculate body (MGB) (Zhang et al. 1997; Zhang and Suga 2000; He 1997), AC (Chowdhury and Suga 2000; Ma and Suga 2001; Sakai and Suga 2001, 2002) and cochlea (Xiao and Suga 2002).

The central auditory system creates physiologically distinct types of subcortical neurons which are different from peripheral neurons in response properties (e.g., Suga 1984, 1990; Covey and Casseday 1999). The response properties of all these subcortical neurons can presumably be changed by electric stimulation of the AC through nerve fibers descending from the AC. That is, they are subject to corticofugal modulation (Suga and Ma 2003) not only in the frequency (Zhang and Suga 1997; Yan and Suga 1998), but also in the amplitude (Jen and Zhou 2003; Yan and Ehret 2002), time (Yan and Suga 1996; Ma and Suga 2001; Xiao and Suga 2004) and spatial (Zhou and Jen 2005) domains. In the big brown bat, we previously reported that electric stimulation of cortical duration-tuned neurons evoked systematic shifts of the duration- and frequency-tuning curves of collicular duration-tuned neurons (Ma and Suga 2001). However, we did not study corticofugal modulation of collicular duration-tuned neurons in the amplitude domain.

Corticofugal modulation of collicular neurons in the amplitude domain has already been studied in the big brown bat (Jen and Zhou 2003) and house mouse (Yan and Ehret 2002). However, how single neurons corticofugally modulated in the amplitude, frequency and time domains had not been studied. There was a possibility that different
neurons were corticofugally modulated in the amplitude, frequency or time domain. Therefore, the aim of our current study is to demonstrate that corticofugal modulation of single neurons simultaneously occurs in all of these three domains characterizing a sound. We (Ma and Suga 2001) already demonstrated that duration-tuned neurons were simultaneously corticofugally modulated in both the frequency and time (duration) domains. Therefore, we chose the duration-tuned neurons to demonstrate that they were also modulated in the amplitude domain.

If we studied corticofugal modulation of duration-tuned neurons only in the amplitude domain, one might consider that our work was incomplete because simultaneous modulation in the other domains was not demonstrated. Furthermore, the corticofugal modulation of responses to tone bursts in the amplitude domain greatly depends on the modulation in the frequency domain, as shown by our current study. Therefore, we particularly studied corticofugal modulation of duration-tuned neurons in the frequency and amplitude domains. We minimize the description of the modulation in the frequency and time domains in our current paper and focus on our new findings on corticofugal modulation in the amplitude domain.

METHODS

Materials, surgery, acoustic stimulation, cortical electrical stimulation, recording of neural activity and data acquisition and processing were the same as those described in Ma and Suga (2001). Therefore, only the essential portions of these methods are summarized below.

Fourteen adult big brown bats (*Eptesicus fuscus*) were used for the current experiments. Under neuroleptanalgesia (Innovar 4.08 mg/kg b. w.), a 1.5 cm-long metal post was glued on the dorsal surface of the bat’s skull. Physiological experiments were started 3-4 days after the surgery. The awake animal was placed in a polyethylene-foam body-mold which was hung with an elastic band at the center of a soundproof room maintained at 31°C. The metal post glued on the skull was fixed to a metal rod with set screws to immobilize the animal’s head, and the head was adjusted to face directly at a loudspeaker located 74 cm away. Holes (50 - 100 µm in diameter) were made in the skull covering the AC and IC. Through these holes, tungsten-wire electrodes (6 - 8 µm tip diameter, 1 meg-ohm impedance) for recording the
action potentials of cortical and collicular neurons or for electrically stimulating cortical neurons were inserted into the primary AC (AI) or the central nucleus of the IC (ICc). The protocol for this research was approved by the animal studies committee of Washington University in St. Louis.

**Acoustic stimulation**

An acoustic stimulus was a 4.0-ms tone burst with a 0.5-ms rise-decay time, unless otherwise described, which was delivered at a rate of 5/s with a leaf tweeter. Its frequency and amplitude were varied manually or computer-controlled. The amplitude was calibrated with a Bruel & Kjaer microphone placed at the bat’s head and was expressed in decibels in sound pressure level (dB SPL).

The BF and minimum threshold (MT) of collicular or cortical neurons were first measured audiovisually. [A frequency-tuning curve is based on many thresholds measured as a function of frequency. The threshold at the best frequency is called the MT (Suga 1997).] To obtain the frequency-tuning curve of a single collicular neuron or multiple cortical neurons, the frequency and amplitude of the tone burst were varied at random by a computer. This computer-controlled frequency-amplitude scan consisted of 20 different frequencies at 0.5 or 1 kHz steps and 16 different amplitudes at 5 dB steps. An identical frequency-amplitude scan was delivered 10 times. To obtain the frequency-response curve, however, the amplitude of a tone burst was fixed at 10 dB above the MT of a given neuron, and its frequency was randomly varied by a computer across the BF of the neuron in 0.3 or 0.5 kHz steps. This computer-controlled frequency scan consisted of 21 250-ms-long time blocks. In the 21st (last) block, no stimulus was presented in order to count background discharges. An identical frequency scan was delivered 50 times.

The duration-tuning curve of a single collicular or cortical neuron was first audiovisually measured by changing the duration and amplitude of a tone burst set at the BF of a given neuron. The rise-decay time of tone bursts shorter than 5 ms was set at 0.1 ms. Then, the amplitude of a tone burst was fixed where the duration-response curve was sharpest. On the average, this amplitude was 18 ± 4.1 dB (N=58) above the MT of a given neuron. The duration of the tone bursts was randomly varied by a computer across the best duration (BDu) by 0.5 or 1.0 ms steps between 0.0 and 10 ms. This computer-
controlled duration scan consisted of 13 250-ms-long time blocks. In the 13th (last) block, no stimulus was presented in order to count background discharges. An identical duration scan was delivered 50 times.

The amplitude-response curve of a single collicular or cortical neuron was measured by changing the amplitude of a tone burst set at the BF and BDu of a given neuron. The amplitude was randomly changed by a computer in 5 dB steps from 5 to 80 dB SPL. This computer-controlled amplitude scan consisted of 16 blocks. An identical amplitude scan was delivered 50 times.

**Electric stimulation**

To study the effect of electric stimulation of duration-tuned cortical neurons on a duration-tuned collicular neuron, a 6.2-ms-long train of four monophasic electric pulses (100 nA constant current, 0.2 ms duration, 2.0 ms interval) was delivered to the cortical neurons at a rate of 10/s for 30 min through a pair of tungsten-wire electrodes inserted orthogonally into the AC and placed at depths between 400 and 800 µm, i.e., in cortical layers III to VI. The tips of the paired electrodes were 6 - 8 µm in diameter and were separated by ~150 µm, one proximal to the other. It was estimated that such electric stimulation activates cortical neurons within a 60 µm radius in the plane orthogonal to the cortical columns (Yan and Suga 1996). These paired electrodes were first connected with a preamplifier for recording action potentials of multiple neurons at depths between 400 and 800 µm. After the measurement of their BF and MT, the electrodes were connected with a stimulus isolator to electrically stimulate them.

**Data acquisition and processing**

The ICc is huge and the ICd (dorsal division of the IC) is very thin in the big brown bat. In dorsoventral electrode penetrations into the ICc, BFs systematically increased because the ICc is tonotopically organized. The BFs of duration-tuned neurons were recorded at depths between 500 and 1,300 µm and their BFs were between 15 and 48 kHz.

The responses of a single collicular neuron to tone bursts in the identical amplitude, duration, and/or frequency scans repeated 50 times were recorded before and after
cortical electric stimulation, and were displayed as the arrays of the post-stimulus-time (PST) histograms. An action potential was stored on the screen of a digital storage oscilloscope at the beginning of the data acquisition and was used as a template to compare with action potentials discharged during data acquisition. The data acquisition was continued as long as action potentials visually matched the template. Data obtained before and after cortical electric stimulation were stored on a computer hard drive and were used for off-line analysis.

Off-line data processing included plotting amplitude-, frequency- and duration-response curves as well as frequency-tuning curves, with the arrays of PST cumulative histograms displaying the responses of a collicular neuron to an identical scan repeated 50 times. The magnitude of responses to tone bursts was expressed by the number of impulses per 50 stimuli after subtracting background discharges counted in the last block of the scan.

The following criteria were used for a change in the amplitude-, frequency- and duration-response curves (i.e., changes in the MT, BF and BDu) of a collicular neuron evoked by cortical electric stimulation. If the change did not recover by more than 50%, the data were excluded from the analysis. In stable, long recording conditions, the change recovered by more than 80% in 24 of the 26 neurons studied, with the remaining two being excluded. This recovery itself helped prove that the change was significant. The paired t-test was used to test the difference between the responses obtained before and after the electric stimulation.

**RESULTS**

In 14 animals, 10 of the 155 cortical neurons and 48 of the 580 collicular neurons recorded were duration-tuned. The BFs of these cortical and collicular neurons ranged between 18 and 60 (m±sd: 33.2 ± 12.4) kHz and between 15 and 48 (30.1 ± 8.1) kHz, respectively. Their BFs, MTs, DRs (dynamic ranges) and BDus are listed in Table 1. In a single dorsoventral electrode penetration across the ICc, 3-4 single collicular neurons located at different depths were studied without moving the paired stimulating electrodes in the AI. Electric stimulation of the cortical neurons evoked changes in the amplitude-, frequency- and duration-response curves of 25 collicular duration-tuned neurons out of

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**Tab.1**

<table>
<thead>
<tr>
<th>Neuron Type</th>
<th>BF (kHz)</th>
<th>MT (kHz)</th>
<th>DR</th>
<th>BDu</th>
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<tr>
<td>Cortical</td>
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<td>Collicular</td>
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the 48 studied. In the remaining 23 neurons, the changes in the response curve were studied only in two domains out of the three: frequency and amplitude domains in 12 neurons, duration and amplitude domains in two neurons and frequency and duration domains in eight neurons.

**Corticofugal modulation of single duration-tuned neurons in the three domains**

When the stimulated cortical neurons and a recorded collicular neuron were matched in BF and BDu, the frequency- and duration-tuning curves of these collicular neurons (N=6) became sharper after cortical electric stimulation. When they were not matched in BF and BDu, the frequency- and duration-tuning curves became sharper and their BFs and BDus shifted toward the BF and BDu of the stimulated neurons, as reported by Ma and Suga (2001). If their MTs were unmatched in addition to their BFs and BDus, their MTs became higher or did not change.

In Fig.1, the collicular neuron was tuned to 28.0 kHz (A1), 6.0-ms duration (B1) and 65 dB SPL (C1). When cortical neurons tuned to 28.0 kHz, 6.0-ms duration and 55 dB SPL were stimulated, the response of the collicular neuron was augmented at the 28.0 kHz (BF) and 6.0-ms duration (BDu), but suppressed on one or both sides of these (Fig. 1, A2 and B2). Its BF and BDu did not shift, but its amplitude tuning shifted from 65 dB SPL to 55 dB SPL (Fig. 1, C2). All these changes recovered ~45 min after the electric stimulation (Fig.1, A4, B4 and C4).

Fig. 2 shows another example of simultaneous corticofugal modulation of a duration-tuned neuron in the three domains. In Fig. 2, the collicular neuron was tuned to 42.0 kHz (A1), 4.0-ms duration and 60 dB SPL (C1). When the cortical neurons tuned to 38.0 kHz, 2.0-ms duration and 50 dB SPL were electrically stimulated, the collicular neuron shifted its BF from 42.0 kHz to 40.5 kHz (A2), its BDu from 4.0 ms to 3.0 ms (B2), and its best amplitude (BA) from 60 dB SPL to 55 dB SPL (C3). The BF, BDu and BA of the collicular neuron shifted toward those of the stimulated cortical neurons. The response was facilitated at the shifted BF and BDu (A2 and B2), but was suppressed at the shifted BA (C3). All these changes disappeared within 45 min after the cortical electric stimulation (A4, B4 and C4).
Corticofugal modulation of the frequency-tuning curves of duration-tuned neurons

In our previous work (Ma and Suga 2001) on corticofugal modulation of duration-tuned neurons, the modulation in the frequency domain was mainly described in terms of BF shifts, although the changes in response properties other than BF shifts (i.e., changes in MT, dynamic range in amplitude coding, response magnitude and sharpness of frequency-tuning curves) were also associated with the changes in the frequency-tuning curve. Therefore, we first show variations in the corticofugal modulation of frequency-tuning curves and then the changes in the MT etc. (as listed above) that occurred in the 48 neurons.

In Fig. 3A, the collicular neuron matched with stimulated cortical neurons in BF (28.0 kHz) and BDu (3.0 ms), but was different in MT by 5 dB (35 dB SPL for the collicular neuron and 40 dB SPL for the cortical neurons). Electric stimulation of the cortical neurons evoked changes in the collicular frequency-tuning curve: the MT changed from 35 dB SPL (open circle) to 25 dB SPL (filled circle), Q-10 dB changed from 2.8 to 4.6, and Q-30 dB changed from 0.7 to 1.8. The BF at 28.0 kHz did not change. The frequency-tuning curve returned (i.e., recovered) to that in the control condition ~45 min after the electric stimulation (dashed line). In Fig. 3B, the collicular neuron was unmatched with stimulated cortical neurons in BF, BDu and MT: 8.0 kHz higher, 2.0 ms longer and 5 dB lower than the cortical ones. When the cortical neurons were electrically stimulated, the collicular BF, MT and BDu measured with 2.0-ms tone bursts changed from 33.0 kHz to 30.0 kHz, from 30 dB SPL to 35 dB SPL and from 4.0 ms to 2.5 ms. That is, the BF, MT and BDu all changed toward those of the stimulated neurons. The frequency-tuning curve became sharper (filled circles).

In Fig. 3C, the recorded collicular neuron matched with stimulated cortical neurons in MT, but not in BF and BDu. The BF difference between them was large, 10.0 kHz (29.0 kHz for the collicular BF and 19.0 kHz for the cortical BF). When the cortical neurons were electrically stimulated, the collicular neuron shifted its BF from 29.0 kHz to 30.0 kHz, i.e., away from the cortical BF, and its MT from 30 dB SPL to 40 dB SPL, i.e., toward the cortical MT. Fig. 3D shows an additional variation in the change of a frequency-tuning curve evoked by cortical electric stimulation. In Fig. 3D, the collicular neuron was unmatched with stimulated cortical neurons in BF, MT and BDu (See the
table at the bottom). When the cortical neurons were electrically stimulated, the collicular neuron shifted its BF away from the cortical BF and broadened its tuning curve (filled circles).

**Changes in threshold**

When the BFs of delay-tuned neurons shifted after the cortical electric stimulation, the shifted BFs (i.e., the new BFs) were usually associated with the new MTs. The amount of MT shifts (i.e., the differences between the MTs at the control, i.e., original, and shifted BFs) was related to the difference in the control BF between recorded collicular and stimulated cortical neurons (Fig. 4A). Five BF-matched neurons decreased their MTs by 5 – 10 dB and the remaining one did not change its MT (open circles). On the other hand, 16 of the 18 BF-unmatched neurons increased their MTs by 5 – 10 dB and the remaining two decreased their MTs by 5 dB (filled symbols). The increase in MT was larger for the larger BF differences between recorded and stimulated neurons. Out of the 48 neurons, 24 did not show any MT shifts. Their BF differences were mostly larger than 7 kHz (Fig. 4A, x’s).

The differences in MT between the recorded collicular and stimulated cortical neurons were less than 20 dB. The amounts of MT shifts ranged between -10 and +10 dB and were related to the differences in MT between the recorded and stimulated neurons (Fig. 4B). Five out of the six BF-matched collicular neurons had a MT higher (four neurons) or lower (one neuron) than that of the stimulated cortical neurons. Their MTs were decreased by cortical electric stimulation. The remaining one BF-matched neuron had the same MT as that of the stimulated neurons. Its MT was not changed by cortical electric stimulation (Fig. 4B, open circles). In sixteen of the 42 BF-unmatched collicular neurons, their MTs increased after cortical electric stimulation regardless of whether their MTs were lower or higher than the stimulated cortical MT. Two neurons of the 42 lowered their MTs after cortical electric stimulation (Fig. 4B, filled symbols). The remaining 24 BF-unmatched neurons did not show MT shifts. Their MTs were mostly different by more than 7 dB from the stimulated cortical MT (Fig. 4B, x’s), and their BFs were mostly different by more than 7 kHz from the stimulated control BF (Fig. 4A, x’s). The direction of the MT shift was towards the stimulated MT in four BF-matched and 12
BF-unmatched neurons, but away from it in one BF-matched and five BF-unmatched neurons. The tendency was that the larger the MT difference, the larger the MT shift.

When the BF of a BF-unmatched collicular neuron shifted after the cortical electric stimulation, its threshold at the control BF (i.e., at the original BF) usually became higher. Such an increase in the threshold at the control BF was related to the difference in control BF between the recorded and stimulated neurons. The larger the difference between the control BFs of the recorded and stimulated neurons, the larger the threshold increase at the control BF. The increase in the threshold at the control BF caused by the electric stimulation was as large as 50 dB (Fig. 4C, filled symbols).

Fig 4D shows the changes in the threshold at the control BF as a function of the differences between the MTs at the shifted and control BFs. In BF-matched neurons, the larger the MT difference, the larger the threshold decrease (Fig. 4D, open circles). The decrease in threshold was not more than 10 dB. In BF-unmatched neurons, however, the change in the threshold increased up to 50 dB as a function of the differences between the MTs at the shifted and control BFs (Fig. 4D, filled circles).

Changes in the amplitude-response curve and dynamic range in coding stimulus amplitude

The amplitude-response curve was non-monotonic in three collicular neurons and monotonic in the remaining neurons plateauing at 60 – 80 dB SPL. Cortical electric stimulation evoked changes in the threshold and amplitude (dB)-response (number of impulses/stimulus tone) function. The change in threshold at a control BF was small in BF-matched neurons, but it could be very large in BF-unmatched neurons because of their BF shifts. The larger the BF shift, which is related to the BF difference between the recorded and stimulated neurons, the larger the threshold change (Fig. 4C). Therefore, the change in the amplitude-response curve at the control BF was much larger in the BF-unmatched neurons than in the BF-matched neurons.

Fig. 5A shows the amplitude-response curves of a BF-matched neuron at the control BF (open circles) measured before cortical electric stimulation and at the unshifted BF (filled circles). The electric stimulation evoked a 5 dB decrease in the MT and a shift in
the amplitude-response curve toward a smaller amplitude. The response at the plateau and the dynamic range increased by 10% and 4 dB, respectively.

In BF-unmatched neurons, the changes of the amplitude-response curve were just opposite to the above (Fig. 5, B-D). BF-unmatched neurons shifted their frequency-tuning curves along the frequency axis after cortical electric stimulation as shown in Fig. 3. Therefore, the amplitude-response curve of a BF-unmatched neuron was measured at a shifted BF (BFs) and at a control BF (BFc) after the stimulation and was compared with that at the BFc before the electric stimulation. In Fig. 5B, the amplitude-response curve at the BFc before the electric stimulation was monotonic (open circles), but was non-monotonic (filled circles) at the BFs. The MT and DR were 5 and 6 dB smaller than those at the BFc. The amplitude-response curve at BFc after the electric stimulation indicated that the threshold became 30 dB higher than that before the stimulation and the response at the peak became 62% smaller (open triangles). The amplitude-response curves in Fig. 5, C and D, also show that the changes in the DR were associated with changes in the MT.

The DRs in the amplitude-response curves at the control BF’s ranged from 10 to 30 dB (m ± sd: 20 ± 7.1 dB, N=6) for cortical neurons and from 20 to 40 dB (32.5 ± 6.48 dB, N=42) for collicular neurons (Fig. 6A). This difference is statistically significant (t-test, p < 0.05). When cortical neurons were electrically stimulated, the DR increased in three out of the six BF-matched neurons, did not change in two and decreased in the remaining one. Whereas the DR decreased in 16 out of the 18 BF-unmatched neurons and increased in the remaining two. The amount of the DR change was not related to the amount of the difference in any of the DR, BF and MT between the recorded and stimulated neurons (Fig. 6, B-D).

Cortical electric stimulation increased the responses of BF-matched neurons to tone bursts and decreased those of the BF-unmatched neurons (Fig. 7). For example, the response magnitude at 20 dB above the MT of a given neuron increased by 10 - 30% for the six BF-matched neurons and decreased by 0 - 60% for the 42 BF-unmatched neurons (Fig. 7A). At 40 dB and 60 dB above the MT, the response also increased for the BF-matched neurons and decreased for the BF-unmatched neurons (Fig. 7, B and C).
Change in the tuning-curve width

The direction of the BF shift was related to the sharpening or broadening of a frequency-tuning curve. Fig. 8 shows the distributions of quality factors (Q-10 dB, -30 dB and -50 dB). After cortical electric stimulation, for example, the Q-10 dBs of six BF-matched neurons increased whereas the Q-10 dBs of 18 BF-unmatched neurons increased (N = 5), decreased (N =11) or did not change (N = 2). The tendency was that Q-values became larger for the BF-unmatched neurons showing the BF shift toward the BF of stimulated neurons (filled circles), but smaller for those showing the BF shift away from that (filled triangles).

DISCUSSION

There have been only two papers which dealt with corticofugal modulation in the amplitude domain (Yan and Ehret 2002; and Jen and Zhou 2003) and only one paper which dealt with corticofugal modulation of duration-tuned neurons (Ma and Suga 2001). Jen and Zhou (2003) worked on the big brown bat as we did. However, they studied “corticofugally inhibited” collicular neurons, instead of duration-tuned collicular neurons. The cortical electric stimulation was much stronger in their work (5 – 50 µA, 0.1 ms pulses) than in ours (0.1µA, 0.2 ms pulses). Yan and Ehret (2002) studied collicular neurons in the house mouse instead of the bat. Their cortical electric stimulation was 25 times (0.5 µA, 1.0 ms pulses) stronger than ours. Therefore, these three works are different in methods: species, amount of electric stimulation and the types of neurons studied. Accordingly, there are similarities and differences in the results between these three works. In the following, we will discuss (1) MT, (2) DR, (3) response magnitude, (4) BF and (5) the functional significance of corticofugal modulation, comparing the above three works.

(1) Change in the minimum threshold. Yan and Ehret (2002) measured the MTs before and after cortical electric stimulation only at the BF in the control condition, i.e., only at the original BF, and they found that the MT shifts of BF-matched neurons mostly
occurred toward the MTs of stimulated cortical neurons and ranged between -12 and +18 dB. These MT shifts were proportional to the MT differences between the recorded collicular and stimulated cortical neurons. However, the MT shifts of BF-unmatched neurons, which were also measured only at the original BF, always increased (1 - 60 dB) regardless of whether the collicular MTs were lower or higher than those of the stimulated cortical neurons. The tendency was that the larger the MT difference, the larger the MT shift. (These MT shifts of BF-unmatched neurons were not “true” BF shifts, as explained later.)

In our work, the MTs of most BF-matched neurons decreased 5 - 10 dB, whereas the MT shifts of BF-unmatched neurons always increased. The tendency was that the larger the BF difference between the recorded and stimulated neurons, the larger the MT shift. Thus, our data obtained from the bat were similar to those obtained from the mouse. However, the amount of the MT shifts of BF-unmatched neurons in the house mouse (up to 60 dB) was much larger than that in the bat (up to 10 dB).

Yan and Ehret (2002) described an increase in the thresholds of BF-unmatched neurons (up to 60 dB) measured only at the original BF (i.e., the BF in the control condition), as the MT shift (hereafter the “so-called” MT shift). The BF-unmatched neuron usually shifts its BF after cortical electric stimulation (Zhang et al 1997; Ma and Suga 2001; Sakai and Suga 2001, 2002; Yan and Ehret 2001; Xiao and Suga 2002). Then, the threshold at its original BF measured after the electric stimulation is not the MT of the neuron anymore. The threshold at the shifted BF (i.e., the new BF) is the MT. Therefore, we measured the MTs at the shifted BF and at the control BF (i.e., the original BF) to calculate the “true” MT shift, and also measured the thresholds at the control BF before and after the cortical electric stimulation. The true MT shifts of the BF-unmatched neurons were small, not more than 10 dB. However, the threshold shifts (i.e., the so-called MT shifts) of the BF-unmatched neurons measured only at the control BFs were large, up to 50 dB, similar to those measured by Yan and Ehret (2002). The true MT shifts may be not so different between the big brown bat and house mouse.

Jen and Zhou (2003) measured the thresholds at a control BF before and after cortical electric stimulation as did Yan and Ehret (2002), so that the so-called MT shifts calculated by them were not true MT shifts. They did not process the data grouping into
two: BF-matched and -unmatched neurons. In Jen and Zhou’s work the so-called MT shifts (4 to 25 dB) always occurred toward the MTs of stimulated cortical neurons. Therefore, their data were similar to those of the BF-matched neurons in the house mouse, but different from those of BF-unmatched neurons studied by the other two groups.

(2) Change in the dynamic range. In Yan and Ehret’s work (2002), the decrease in the DR was up to 50 dB for BF-matched neurons and up to 80 dB for BF-unmatched neurons. The DRs of BF-unmatched neurons were measured only at the control BF before and after cortical electric stimulation. Jen and Zhou (2003) also measured the DRs only at the control BF before and after cortical electric stimulation.

In our work, BF-matched neurons increased their DRs by up to 5 dB, whereas BF-unmatched neurons decreased their DRs by up to 12 dB when the DRs measured at their shifted and control BFs were compared with each other. Therefore, the changes in DR were much smaller in the bat than in the house mouse.

(3) Change in the response magnitude. According to Yan and Ehret (2002), the responses of BF-matched neurons to the tone bursts at the control BFs increased dramatically in some neurons, but did not change on the average in all matched neurons studied. The responses of BF-unmatched neurons to the tone bursts at the control BFs always decreased. The mean decrease at the control BF was ~80% at a 10 kHz BF difference between the recorded and stimulated neurons and ~50% at an 18 kHz BF difference. The change in response magnitude at the shifted BF (i.e., the new BF) was not measured. In our experiments, the response magnitude of BF-matched neurons increased by 6.2 ± 4.6% (mean ± sd; N=6) and that of BF-unmatched neurons decreased by 10.9 ± 8.8% (N=42) at a shifted BF compared with that at a control BF. Therefore, the change in response magnitude was much smaller in the bat than in the house mouse.

(4) BF shifts. During the current studies, we obtained data which were not reported in our previous paper on corticofugal modulation of duration-tuned neurons in the frequency and time domains (Ma and Suga 2001). That is, we found that the BF shifts were centripetal (i.e., the shifts were towards the BF of stimulated neurons) for BF differences up to 8 kHz and centrifugal (i.e., the shifts were away from the BF of stimulated neurons) for BF differences between 8 and 12 kHz and that the frequency-
tuning curves became narrower in BF-matched neurons, but became broader or narrower, if it they changed at all, in BF-unmatched neurons. It has been found that non-duration-tuned collicular (Ma and Suga 2001) and cortical (Sakai and Suga 2002; Ma and Suga 2004) neurons often shifted their BFs away from the stimulated neurons when the BF difference between the recorded and stimulated neurons was large.

According to Yan and Ehret (2001), the BF shifts of BF-unmatched neurons were predominantly centripetal for BF differences up to 18 kHz, but were mostly centrifugal for BF differences between 18 and 30 kHz. In Jen and Zhou’s work (2003), BF shifts were centripetal for collicular BFs lower than cortical BFs and centrifugal for collicular BFs higher than cortical BFs. The amount of these BF shifts was proportional to the BF differences between the recorded and stimulated neurons. Therefore, our data were qualitatively the same as those obtained from the house mouse by Yan and Ehret (2001, 2002), but were different from those obtained from the bat by Jen and Zhou (2003). In the big brown bat (Ma and Suga, 2004) and the Mongolian gerbil (Sakai and Suga, 2002), the BF shifts of cortical auditory neurons are centripetal in the large area surrounding the electric stimulation site, but are centrifugal in a narrow zone surrounding the area for centripetal BF shifts. Therefore, the BF shifts of cortical and collicular neurons of the big brown bat are basically the same as those of the house mouse and the Mongolian gerbil.

(5) Functional significance of corticofugal modulation. There are three important findings reported in our current and previous (2001) papers: (i) The auditory responses of the BF-matched neurons were corticofugally augmented and their MTs and DRs became lower and wider, respectively. Furthermore, as previously shown, matched neurons were corticofugally augmented and were sharpened in their frequency- and duration-tuning. Therefore, they became more suitable to responding to acoustic signals when the parameter values matched their response properties. (ii) On the other hand, the auditory responses of the BF-unmatched neurons were corticofugally reduced and their MTs and DRs respectively became higher and narrower. Furthermore, as previously shown, their frequency- and duration-tuning curves were shifted toward those of the stimulated cortical neurons. Therefore, they became less suitable to responding to acoustic signals when the parameter values did not match their response properties. (iii) The BF and BDu shifts of the unmatched neurons caused an increase in the population of collicular
neurons which were similar to the electrically stimulated cortical neurons, i.e., similar to the matched collicular neurons. These shifts simultaneously caused a decrease in the population of the BF-unmatched collicular neurons which were different from the electrically stimulated cortical neurons. Therefore, the overall effect of the collicular changes, including the matched and unmatched neurons, improves the neuronal processing of auditory signals which frequently stimulate the auditory system and the contrast in the neural representation of the signals. The improved neural signals ascend from the IC to the AC through the auditory thalamus and contribute to the auditory signal processing in the AC. The behavioral changes related to the changes evoked by the corticofugal system remain to be explored.

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REFERENCES


Table 1. Best frequency (BF), minimum threshold (MT), dynamic range (DR) in amplitude coding and best duration (BDu) of stimulated cortical (AC) and recorded collicular (IC) neurons.

FIGURE LEGENDS

Fig. 1. Simultaneous corticofugal modulation of a duration-tuned collicular neuron in the frequency, time (duration) and amplitude domains. The recorded collicular neuron (ICr) was matched with stimulated cortical neurons (ACs) in best frequency (BF) and best duration (BDu) but was unmatched in best amplitude (BA). The arrays of PSTC histograms displaying the responses of the neuron to tonal stimuli repeated 50 times show the frequency (A)-, duration (B)- and amplitude (C)- response functions. 1: control. 2 – 4: 5, 30 (or 10) and 45 min after cortical electric stimulation. The filled circles and arrows indicate either the BF, BDu or BA of the collicular and cortical neurons, respectively. The BFs, BDus and BAs of the stimulated cortical and recorded collicular neurons are listed at the bottom.

Fig. 2. Simultaneous corticofugal modulation of a duration-tuned collicular neuron (ICr) in the frequency, time and amplitude domains. The recorded collicular neuron (ICr) was unmatched with stimulated cortical neurons (ACs) in best frequency (BF), best duration (BDu) and best amplitude (BA). The arrays of PSTC histograms displaying the responses of the neuron to tonal stimuli show the frequency (A)-, duration (B)- and amplitude (C)- response functions. 1. Control. 2 - 4: 5, 30 (or 10) and 45 min after the electric stimulation. The BFs, BDus and BAs of the stimulated cortical and recorded collicular neurons are listed at the bottom. See Fig. 1. legend for the symbols.

Fig. 3. Corticofugal modulation of the frequency tuning curves of four duration-tuned collicular neurons (A-D). The best frequencies (BF’s), minimum thresholds (MT’s), and
best durations (BDu’s) of electrically stimulated cortical (ACs) and recorded collicular (ICr) neurons for each graph are listed at the bottom. In A, the cortical and collicular neurons were matched in BF and BDu. In B-D, the cortical and collicular neurons were unmatched in BF and BDu. In addition, MT was different in B and D. Open circles: control condition. Filled circles: 5 min after cortical electric stimulation. Dashed lines: 45 min after the electric stimulation. X: BF and MT of cortical neurons electrically stimulated. Cortical electric stimulation evoked changes in the BF and MT of the collicular neurons. BFc and BF’s: BF’s in the control and shifted conditions, respectively. MTc and MT’s: MT in the control and shifted conditions, respectively.

Fig. 4. Shifts in the MT (A and B) or (C and D) threshold as a function of the BF (A and C) or MT (B and D) differences between recorded collicular (ICr) and stimulated cortical (ACs) neurons. MT shifts are the differences between the MTs at the control and shifted BFs, whereas changes in threshold are the differences in threshold at the control BF before and after cortical electric stimulation. Open circles: BF-matched neurons (6 neurons). Filled circles and triangles: BF-unmatched neurons which shifted their BFs toward or away from the stimulated BF, respectively. x’s: neurons showed no threshold shifts (24 neurons). BF: best frequency; MT: minimum threshold; N: total number of neurons studied.

Fig. 5. Corticofugal modulation of the amplitude-response curves and dynamic ranges (DRs) of four duration-tuned collicular neurons. The amplitude-response curves of a BF-matched (A) and BF-unmatched (B-D) collicular neurons are shown at the control BF (open circles) before the cortical electric stimulation and at the shifted BF (filled circles) and control BF (open triangles) after the electric stimulation. The dashed curves with dots are the amplitude-response curves at the control BF obtained 40-50 min after the electric stimulation. A dynamic range (DR) is defined as the difference between the stimulus amplitude at 10% above background discharges and the stimulus amplitude at 10% below the peak or plateau response. As an example, a DR is indicated by the horizontal arrow in (A) for the amplitude-response curve at the control BF (open circles). The change in response magnitude was measured at 20, 40 or 60 dB above the minimum threshold in
the control condition (MTc; See D). In A, the electric stimulation evoked a 5 dB decrease in MT, so the amplitude-response curve was shifted toward a smaller amplitude. The response at the plateau increased by 10% and the dynamic range increased by 4 dB. In B-D, both responses and DRs decreased. BF: best frequency; MT: minimum threshold. The short vertical bars associated with the symbols represent standard errors.

**Fig. 6.** The dynamic ranges (DRs) of the amplitude-response curves at the control BFs of collicular and cortical neurons (A) and the changes in DR as a function of DR (B), BF (C) or MT (D) differences between the recorded collicular (ICt) and stimulated cortical (ACs) neurons. Open and filled columns in A: Cortical and collicular neurons, respectively. Open circles: BF-matched neurons. Filled circles and triangles: BF-unmatched neurons which shifted their BFs toward or away from the stimulated BF, respectively. x’s: neurons which showed no DR changes. BF: best frequency; MT: minimum threshold.

**Fig. 7.** The differences between the response magnitudes at the control and shifted BF (BFc-BFs). The difference is expressed in percent of the response at 20 (A), 40 (B) or 60 (C) dB above MTc of a given neuron. The open and filled bars respectively represent the percent changes of BF-matched and –unmatched neurons. BF: best frequency; MTc: minimum threshold in the control condition.

**Fig. 8.** The relationship between the BF shifts and changes in Q-values (quality factor representing the sharpness of a tuning curve) evoked by cortical electric stimulation. Q-10, -30 and -50 dB are respectively the BF divided by the band widths of a frequency-tuning curve at 10 (A), 30 (B) and 50 (C) dB above the minimum threshold of a given neuron. Open circles: BF-matched neurons. Filled circles and triangles: BF-unmatched neurons which shifted their BFs toward or away from the stimulated BF, respectively. BF: best frequency.
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<thead>
<tr>
<th></th>
<th>AC₂</th>
<th>IC₁</th>
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<tr>
<td></td>
<td>m ± sd (range)</td>
<td>m ± sd (range)</td>
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<tr>
<td>BF (kHz)</td>
<td>33.2 ± 12.44 (18 ~ 60) n=10</td>
<td>30.1 ± 8.07 (15 ~ 48) n=48</td>
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<td>MT (dB SPL)</td>
<td>23.5 ± 10.26 (10 ~ 40) n=10</td>
<td>18.8 ± 6.89 (5 ~ 35) n=48</td>
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<td>DR (dB)</td>
<td>22.1 ± 8.59 (10 ~ 36) n=7</td>
<td>32.2 ± 5.41 (20 ~ 40) n=48</td>
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<tr>
<td>BDU (ms)</td>
<td>3.0 ± 1.78 (1.0 ~ 6.0) n=10</td>
<td>2.5 ± 1.16 (0.5 ~ 5.0) n=48</td>
</tr>
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Table 1  Best frequency (BF), minimum threshold (MT), dynamic range (DR) in amplitude coding and best duration (BDU) of stimulated cortical (AC) and recorded collateral (IC) neurons.
Ma & Suga  Fig. 1
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Ma & Suga  Fig. 2
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Ma & Suga Fig. 3
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Ma & Suga Fig. 4
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Ma & Suga  Fig. 5  
07-02-01
Ma & Suga  Fig. 6
06-08-01

- BF matched neuron;
- BF unmatched neuron showing centrifugal shift;
- BF unmatched neuron showing centripetal shift;
- Neuron unaffected by electric stimulation.
Fig. 8

Ma & Suga
06-08-01