Corticofugal Amplification of Facilitative Auditory Responses of Subcortical Combination-Sensitive Neurons in the Mustached Bat

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INTRODUCTION

Neurons in the deep layers of the auditory cortex (AC) project to the medial geniculate body (MGB) or the inferior colliculus (IC) (Huffman and Henson 1990; Saldana et al. 1996). The corticofugal projections are organized tonotopically (Andersen et al. 1980; Herbert et al. 1991). Physiological data of corticofugal effects on MGB and IC neurons have been controversial: inhibitory (Amato et al. 1969; Massopust and Ordy 1962; Sun et al. 1996; Watanabe et al. 1966); excitatory (Andersen et al. 1972; Villa et al. 1991), or both (Ryugo and Weinerberger 1976; Sun et al. 1989; Syka and Popelar 1984).

In the mustached bat, Pteronotus pamelai pamelai, it first was found that cortical “FM-FM” neurons, which are combination-sensitive and are tuned to particular echo delays, mediate a highly focused positive feedback incorporated with widespread lateral inhibition via the corticofugal system and that the corticofugal system adjusts and improves auditory information processing in the subcortical auditory nuclei (Suga et al. 1995; Yan and Suga 1996a). These cortical functions, named egocentric selection, (Suga et al. 1997; Yan and Suga 1996a) work not only for the processing of echo delays but also for the processing of frequency information in the mustached bat (Zhang et al. 1997), big brown bat (Yan and Suga 1998), and cat (He 1997), so that it may be a general function of the corticofugal system. As a matter of fact, corticofugal positive feedback associated with inhibition also has been found in the visual system (Tsumoto et al. 1978). These findings, indicating that an inhibitory or excitatory corticofugal effect depends on a topographic relationship between cortical and subcortical neurons, and the study by Zhang and Suga (1997) have solved the long-lived controversy.

Musclem decades ago, the long-lived controversy. It is the agonist to γ-aminobutyric acid-A receptors, which mediate synaptic inhibition (de Feudis 1978; Lester and Pesk 1979). Zhang and Suga (1997) applied muscle to a particular subdivision of the primary auditory cortex, called the Doppler-shifted constant-frequency (DSCF) processing area, and inactivated the corticofugal fibers originating from this area. They found that such an inactivation, including cortical neurons retained in frequency tuning with a given subcortical DSCF neuron, evoked a prominent decrease in excitatory responses (number of impulses/stimulus) of subcortical DSCF neurons to single tones: 34% in the IC and 60% in the MGB on the average. Gao and Suga (1998) repeated the same experiments as above with the big brown bat (Eptesicus fuscus) and found that the decrease in collateral responses to single tones was 38% on the average.

FM-FM neurons tuned to specific time delays (echo delays) of echo FM components from the FM components of an emitted biosonar pulse (Kawasaki et al. 1988) have been found in the IC (Mittmann and Wenstrup 1995; Yan and Suga 1996b), MGB (Olsen and Suga 1991; Wenstrup and Grose 1995), and AC (O’Neill and Suga 1979; Suga et al. 1978, 1983). In the AC, they are clustered in the FM-FM (O’Neill and Suga 1979; Suga and O’Neill 1979), dorsal fringe (DF) (Suga and Horikawa 1986), and ventral fringe (VF) areas (Edamatsu et al. 1989). These combination-sensitive neurons are more complex in response properties than neurons primarily responding to single tones because they show strong facilitative responses to paired sounds with specific relationships in the frequency, amplitude, and time domains.

The aim of our present paper is to report our finding that muscle inactivation of the entire FM-FM area of the cortex, containing neurons both matched and unmatched in delay tuning with thalamic and collicular FM-FM neurons, reduces...
the facilitative responses of these subcortical neurons to paired FM sounds by a surprisingly large amount, that combination sensitivity of some subcortical neurons almost entirely depends on corticofugal feedback, and that the processing of complex sounds by combination-sensitive neurons depends more heavily on the corticofugal system than that by noncombination-sensitive neurons.

**METHODS**

Materials, surgery, recording of neural activity, acoustic stimulation, and data acquisition were basically the same as those described elsewhere (Suga et al. 1983; Zhang and Suga 1997). The essential portions of these are summarized below. Five adult mustached bats, *P. pardinelli pardinelli*, from Jamaica were used for the present experiments. Under neuroleptanalgesia (Innovar 4.08 mg/kg body wt), a 1.8-cm-long metal post was glued onto the exposed dorsal surface of the bat’s skull. Four days after the surgery, the unanesthetized and untrianquilized bat was placed in a polyethylene form 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 to a metal rod with set-screws and was adjusted to face directly at a condenser loudspeaker located 74 cm away.

To record the auditory responses of FM-FM neurons, a tungsten-wire microelectrode with a tip diameter of 6–8 μm was inserted into the AC, MGB, or IC through holes of ~50 μm in diameter made in the skull. FM-FM neurons were identified by their combination sensitivity, delay tuning, best delays, and locations in the AC, MGB, and IC. A window discriminator was used to isolate action potentials of single neurons.

To excite FM-FM neurons, the parameters of a pair of FM sounds were set to be similar to those of the FM components of species-specific biosonar signals. Each FM sound was 3.0-ms long and had a 0.5-ms rise-decay time. There were four types of FM sounds (FM1, FM2, FM3, and FM4), which were harmonically related to each other. In FM1, the frequency swept downward by either 6, 12, 18, or 24 kHz from the frequency at ~30, 61, 92, or 122 kHz, respectively. These FM sounds were generated by a voltage-controlled oscillator, an electronic switch, and a voltage-ramp generator. Sound amplitude was adjusted by an analog or digital attenuator. A pair of these instruments was used to mimic the bat’s biosonar pulse and its echo. The paired FM sounds were delivered at a rate of 5/s. Because the FM-FM neurons are tuned to particular time delays (hereafter, echo delays) of FM1, only frequency and amplitude of paired sounds, but also echo delay, was varied manually or with a computer. A “delay scan” program was used to control echo delay. The delay scan created 13 time blocks. The duration of each block was 150 ms and was repeated at a rate of 6.7/s. A 3.0-ms-long FM1 (pulse stimulus: P) was delivered alone in the first block. A 3.0-ms-long FMn (echo stimulus: E) was delivered alone in the 12th block. A P-E pair was delivered in each of the 2nd to 11th blocks, for which an echo delay was varied from 0 to 9Δτ. Δτ was set at between 0.25 and 4.0 ms, depending on the best delay of E from P to excite a given FM-FM neuron. No acoustic stimulus (N) was delivered in the 13th block so that background discharges could be counted. An identical delay scan was delivered 100 times at a rate of 5/s. The auditory responses to these stimuli were displayed as perstimulus time (PST) or PST cumulative (PSTC) histograms.

After the electrophysiological mapping of the FM-FM area of the AC, a ~1.0 mm³ triangular hole was made in the skull over the FM-FM area with forceps, and a ~1.0-mm-long piece of vinyl tubing (~1.5 mm ID hereafter a well) was placed over the hole. The well was filled with antibiotic (Furacin) ointment. Three to 6 days later, single thalamic or collicular FM-FM neurons, ipsilateral to the mapped FM-FM area, were recorded, and 0.20 μg muscimol (5-aminomethyl-3-hydroxyisoxazole, Sigma) in 0.2 μl saline solution was applied to the mapped FM-FM area with a 1.0-μl Hamilton microsyringe to inactivate the entire FM-FM area. Gelfoam was placed in the well to prevent leakage of muscimol and to increase the contact time with the cortical surface. To study the effect of cortical inactivation on the auditory responses of subcortical FM-FM neurons, the responses of the single subcortical neurons to FM sounds in the delay scan were recorded before, during, and after cortical inactivation.

Off-line data processing included plotting PST or PSTC histograms displaying these responses. Delay-response curves were based on the responses to 100 identical delay scans. The magnitude of auditory responses was expressed by the number of impulses per 100 identical stimuli after subtracting the background discharges counted in the last block of the 100 delay scans. A t-test was used to test the significance (P < 0.05) of the difference between the facilitative responses obtained before and after a muscimol application and between the facilitative responses of thalamic and collicular neurons.

**RESULTS**

As previously reported (O’Neill and Suga 1979, 1982; Suga et al. 1978, 1983), FM-FM neurons commonly showed poor or no excitatory response to pulse FM1 (P) or echo FMn (E) delivered at the amplitude necessary to evoke the best facilitative response, but a strong facilitative response to a P-E pair with a specific E delay. Inactivation of the FM-FM area in the AC with muscimol evoked a prominent reduction in the facilitative responses of all 9 thalamic and 10 collicular FM-FM neurons studied, and evoked no change in their best delays (BDs). (The sample size was small because of a difficulty in long-term recording of single-unit activity. Nevertheless, the results were consistent.)

Figure 1 shows such a reduction in the auditory responses of two thalamic (A and B) and one collicular neuron (C). They are selected for the figure because they responded to P alone and E alone. In A, the responses of a single thalamic FM-FM neuron to P alone and E alone were reduced by 47.2 and 24.0% by cortical inactivation, respectively. The response to a P-E pair with a 10.3-ms E delay was 302% larger than the sum of the responses to P alone and E alone. This facilitative response was reduced by 73.1% by cortical inactivation. In Fig. 1B, the responses of another thalamic FM-FM neuron to P alone and E alone were reduced by 90.6 and 88.0% by cortical inactivation, respectively. Its response to a P-E pair with 4.0-ms E delay was 254% larger than the sum of the responses to P alone and E alone and was reduced by 97.7% by cortical inactivation. The reduction of facilitative response by >90% was observed in four thalamic neurons and one collicular neuron. In Fig. 1C, the change in the responses of a collicular FM-FM neuron to P alone and E alone evoked by cortical inactivation was insignificant, but the reduction (67.2%) in the facilitative response to a P-E pair was significant.

The amount of reduction in facilitative response ranged from 65.5 to 99.9% (mean ± SD: 82.1 ± 14.0%) for the nine thalamic FM-FM neurons and from 30.0 to 92.9% (65.5 ± 19.5%) for the 10 collicular FM-FM neurons. The difference in reduction between the thalamic and collicular neurons is significant (P < 0.05). The responses to P alone and E alone were so small that percentage reduction in these responses was influenced greatly by background discharges as well as by cortical inactivation. The changes in the responses to P alone and E alone during the cortical inactivation were respectively 4.9 ± 81.6% and −34.8 ± 52.7% for the thalamic neurons,
and $-21 \pm 70\%$ and $-28.8 \pm 27.0\%$ for the collicular neurons. The difference between these mean values was insignificant.

These data indicate the following: 1) The corticofugal system amplifies thalamic facilitative responses by 5.6 times (100/18) and collicular facilitative responses by 2.9 times (100/34) on the average. 2) Normal auditory responses would be very weak without these two-step amplifications by the corticocollicular and corticothalamic projections. 3) In nearly half of the thalamic FM-FM neurons, almost all responses to single and paired sounds depend on the corticofugal system, i.e., on the feedback loop consisting of the ascending and descending systems.

The amount of reduction by muscimol was largest for the response to the P-E stimulus at the best delay of a given subcortical FM-FM neuron, so that its delay-tuning curve tended to be less tuned during cortical inactivation. No significant shift in best delay was observed. Figure 2 shows the delay-response curves of four subcortical FM-FM neurons that were affected somewhat differently from each other by cortical inactivation. In five of the nine thalamic neurons, a delay-response curve in a partially recovered condition was noticed to be broader than that in the control condition (Fig. 2, A–C). The data shown in Fig. 2D is exceptional in that the delay-response curve was inverted by cortical inactivation. The response to E alone was not reduced by cortical inactivation, but the response to a P-E pair was.

The effect of cortical inactivation was generally much less on collicular neurons than on thalamic neurons. The delay-response curve of the collicular neuron in Fig. 2C became rather flat after cortical inactivation. In thalamic and collicular neurons, a delay-response curve in a partially recovered condition was noticed to be broader than that in the control condition (Fig. 2, A–C). The data shown in Fig. 2D is exceptional in that the delay-response curve was inverted by cortical inactivation. The response to E alone was not reduced by cortical inactivation, but the response to a P-E pair was.

Rates of background discharges ranged between 1.9 and 9.4/s (5.1 $\pm$ 3.4/s) for the 9 thalamic neurons and between 10.6 and 11.1/s (4.3 $\pm$ 3.5/s) for the 10 collicular neurons. Cortical inactivation reduced the background discharges of most subcortical neurons, but not in the others: $-30.8 \pm 32.9\%$ for the 9 thalamic neurons and $-18.8 \pm 61.0\%$ for the 10 collicular neurons.
Figure 3 shows the time courses of muscimol’s effect on auditory responses and background discharges of a single thalamic (A) and a single collicular neuron (C), and the average time courses for the 9 thalamic (B) and 10 collicular neurons (D). The reduction in facilitative response started to appear in the thalamic and collicular neurons within 5.3 or 7.8 min after muscimol application, respectively. The amount of reduction increased rapidly. The maximum reductions based on the av-
eraged time courses in Fig. 3, B and D (75.0% for thalamic neurons and 54.3% for collicular neurons) were smaller than the means of maximum reductions in the individual neurons (82.1 ± 14.0% for thalamic neurons and 65.5 ± 19.5% for collicular neurons), because the latency for a maximum reduction differed from neuron to neuron, ranging between 54 and 190 min for the thalamic neurons and between 28 and 110 min for the collicular neurons. The mean latencies of 50% recovery were 218 ± 78.0 and 177 ± 82.6 min for the thalamic and collicular neurons, respectively. This difference is statistically insignificant (P > 0.05).

**Discussion**

*Inactivation of the corticofugal system by muscimol*

One may consider the possibility that the reduction in subcortical auditory response by muscimol is not due to the inactivation of corticofugal fibers from the FM-FM area in the AC but the inactivation of subcortical neurons due to diffusion of muscimol from the AC to the MGB and IC. Muscimol (0.20 μg) applied to the FM-FM area did not in any way reduce the responses of thalamic DSCF neurons located immediately ventrolateral to thalamic FM-FM neurons but did reduce the responses of thalamic FM-FM neurons. Muscimol applied to the DSCF area locating immediately posterolateral to the FM-FM area did not in any way reduce the responses of thalamic FM-FM neurons but did reduce the responses of thalamic DSCF neurons (Zhang and Suga 1997). The effect of muscimol specifically depended on the relationship in response properties between the inactivated cortical and the studied subcortical neurons. These control experiments indicate that the effect of muscimol described in the present paper was not due to diffusion of muscimol to the MGB and IC but to the inactivation of the corticofugal fibers originating from the FM-FM area.

Muscimol of 0.20 μg applied to the FM-FM area evoked a prominent temporary deficit in time-interval (echo-delay) discrimination but no deficit in frequency discrimination. On the other hand, the same dose of muscimol applied to the DSCF area evoked a temporary deficit in frequency discrimination but no deficit in time-interval discrimination (Riquimaroux et al. 1991). The effect of muscimol specifically depended on the relationship in function between the inactivated cortical subdivision and the tested behavioral task. The distance between the FM-FM and DSCF areas in the AC is shorter than that between the FM-FM area and the MGB. Therefore the lack of effect of muscimol applied to the FM-FM area on both thalamic DSCF neurons and frequency discrimination indicates that muscimol did not diffuse to the DSCF area and accordingly also not to the MGB.

Our conclusion is supported or favored by the data obtained by Villa et al. (1991) from the cat that showed that inactivation of the entire AC by cooling reduced the auditory responses of thalamic auditory neurons. The observation that the reduction in response of thalamic and collicular neurons began simultaneously (Fig. 3) also favors our conclusion.

Focal electrical activation and focal lidocaine inactivation of the FM-FM area of the AC, respectively, increased and decreased the facilitative responses of “physiologically matched” collicular (Yan and Suga 1996a) and thalamic FM-FM neurons (Suga et al. 1995). In the IC, the amount of reduction due to focal cortical inactivation was ~62% (Yan and Suga 1996a), which is not significantly different from the present data, 65.5 ± 19.5%. The reduction of facilitative responses in the IC and MGB is apparently due to the inactivation of the corticofugal system evoked by muscimol applied to the cortical FM-FM area.

**Did muscimol evoke general suppression of the brain?**

An inactivation of the cortical FM-FM area with muscimol dramatically reduced the facilitative responses of subcortical FM-FM neurons. Therefore in spite of the preceding control experiments, one still may consider the possibility that the reduction was due to the inactivation of cortical areas adjacent to the FM-FM area, a vegetalized animal, and/or general suppression (i.e., suppression of the reticular activation system). However, this possibility is nonexistent, as explained in the following text.

In the AC, the DSCF area is located immediately ventrolateral to the FM-FM area and shows an extremely fine representation of frequencies between 60.6 and 62.3 kHz. The DSCF area apparently is related to fine frequency analysis (Suga and Manabe 1982; Suga et al. 1987). As already described, 0.2 μg muscimol applied to the FM-FM area reduces neither the responses of subcortical DSCF neurons (Zhang and Suga 1997) nor the frequency discrimination ability (Riquimaroux et al. 1991). Therefore the inactivation of cortical areas adjacent to the FM-FM area is very limited.

Cortical focal inactivation by microinjection of lidocaine and cortical focal activation by electrical microstimulation indicate that the corticofugal positive feedback from the FM-FM area is extremely specific to physiologically matched subcortical FM-FM neurons and that the inactivation or activation of adjacent cortical areas has no effect on the responses of subcortical FM-FM neurons (Suga et al. 1995; Yan and Suga 1996a). Therefore it is extremely unlikely that the reduction in the facilitative responses reported in our present paper was due to the inactivation of cortical areas adjacent to the FM-FM area.

The cortical FM-FM area was inactivated with 0.20 μg muscimol in exactly the same way for the previous behavioral (Riquimaroux et al. 1991) and the present electrophysiological experiments. In the behavioral experiment, mustached bats treated with muscimol performed a frequency-discrimination task just as well as untreated mustached bats did. In our present electrophysiological experiments, the bats treated with muscimol moved occasionally during single-unit recording, just as untreated mustached bats did, and caused single-unit responses to disappear. The bats treated with 0.2 μg muscimol were not vegetables. An application of 0.2 μg muscimol to the cortical FM-FM area did not reduce the responses of subcortical DSCF neurons (Zhang and Suga 1997). Therefore, the reduction of facilitative responses reported in our present paper is not due to general suppression of the AC.

**Places where the responses of FM-FM neurons are modulated by the corticofugal system**

The mustached bat emits orientation sounds (biosonar “pulses”). Each pulse consists of constant frequency (CF) and
FM components. Distance information is carried by a delay of the echo FM components from the pulse FM components (that is, the echo delay). FM-FM neurons, tuned to particular echo delays, have been found in the IC (Mittmann and Wenstrup 1995; Yan and Suga 1996b), the MGB (Olsen and Suga 1991; Wenstrup and Grose 1995), and the AC (O’Neill and Suga 1979, 1982; Suga et al. 1978, 1983). The responses of these to an echo FM in (n = 2, 3, or 4) are facilitated by the pulse FM, emitted by the bat when the echo FM returns from the target at a particular distance, that is, with a particular time delay (Kawasaki et al. 1988). The neural mechanisms for creating the response properties of FM-FM neurons have not yet been completely explored. However, it is clear that the essential components involved in the mechanisms are delay lines and coincidence detectors. Delay lines neurally shift the response to the pulse FM. Long delay lines are created by different durations of inhibition that evokes a rebound off-response. Coincidence detectors detect the coincidence in time between the off-response and the excitatory response to an acoustically delayed echo FM (Suga 1990). When antagonists to inhibitory synaptic transmitters are iontophoretically injected into the IC, the delay tuning of collicular as well as cortical FM-FM neurons is shortened or eliminated (Leroy and Wenstrup 1998; Saitoh and Suga 1995). Therefore, the response properties of FM-FM neurons are most likely to be first created in the IC and are further shaped in the MGB and the AC (Suga and Yan 1996b; Suga et al. 1995). Accordingly, the corticofugal influences on collicular FM-FM neurons reported here would not likely be due to changes in the subcollicular nuclei but rather to changes in the IC.

Corticofugal signals may potentially influence the activity of cochlear hair cells through the olivocochlear bundle (Huffman and Henson 1990; Saldana et al. 1996; Warr 1992). Therefore it is impossible to deny completely the possibility that the reduction in the facilitative responses of collicular FM-FM neurons reported in our present paper was at least partially due to changes in the responses of subcollicular neurons, including peripheral ones, even if FM-FM neurons indeed are created first in the IC, not in the subcollicular auditory nuclei. The functional significance of the corticofugal system in signal processing in the subcollicular nuclei and the cochlea remains unknown.

Unilateral versus bilateral inactivation of the corticofugal system

Corticocollicular fibers bilaterally project to the IC in cats (Andersen et al. 1980; Rouiller et al. 1989), rats (Herrera et al. 1994; Saldana et al. 1996), and guinea pigs (Feliciano and Potashner 1995). The ipsilateral projection is much heavier in density, much more extensive in area, and much more topographically organized than the contralateral projection. Corticothalamic fibers project only ipsilaterally to the MGB and the reticular nucleus (Bajo et al. 1995; Ojima 1994; Rouiller and de Ribauipierre 1990). These anatomic data clearly indicate that ipsilateral corticofugal modulation would be much larger than contralateral corticofugal modulation in the IC and MGB.

The directional sensitivity curves of cortical FM-FM neurons suggest that they are excited binaurally by the pulse FM but are excited monaurally (contralaterally) by an echo FM (Suga et al. 1990). In other words, the processing of target distance information by FM-FM neurons in the IC, MGB, and AC appears to be mostly performed homolaterally.

As a matter of fact, a unilateral inactivation of the cortical FM-FM area evoked a large decrease in the facilitative responses of FM-FM neurons in the ipsilateral IC and MGB as reported in our present paper. We don’t know yet whether bilateral inactivation of the cortical FM-FM areas evokes a further reduction in facilitative responses. Our finding of a larger reduction in the MGB than in the IC (82% in the MGB vs. 66% in the IC on the average) indicates that the facilitative responses of FM-FM neurons are amplified not only by the corticocollicular projection but also by the corticothalamic projection. If the bilateral inactivation evokes a larger reduction in the IC than the unilateral inactivation does, it will evoke an extremely large reduction in thalamic facilitative responses.

Corticofugal amplification for FM-FM and DSCF neurons

In the AC, FM-FM neurons are clustered in three separate areas: the FM-FM (O’Neill and Suga 1979; Suga and O’Neill 1979), dorsal fringe (Suga and Horikawa 1986), and ventral fringe areas (Edamatsu et al. 1989). We applied muscimol only to the FM-FM area, the largest among the three, because inactivation of all these areas would require a large amount of muscimol, which could spread to other brain tissue. The reduction of facilitative response due to inactivation of the FM-FM area was 92.3–99.9% in four out of the nine thalamic neurons but was 65.5–79.1% in the remaining five. If all corticofugal fibers from these three cortical areas were inactivated with muscimol, the mean reduction in facilitative response might become larger than 82.1%. H. Teng and N. Suga (unpublished data) injected 66–132 nl of 1% lidocaine into the FM-FM area of the cortex and frequently observed that the responses of thalamic FM-FM neurons to a P-E pair or E alone nearly were abolished. It appears that combination sensitivity of some subcortical neurons almost entirely depends on the corticofugal feedback. The neural mechanisms to produce the response properties of FM-FM neurons are not so simple as previously described, although the basic mechanisms must include delay lines and coincidence detectors as previously described (Olsen and Suga 1991; Suga 1990; Suga et al. 1995).

FM-FM neurons are tuned to specific echo delays, i.e., target distances (O’Neill and Suga 1979, 1982; Suga et al. 1978, 1983), whereas DSCF neurons are sharply tuned to specific frequencies (Suga and Manabe 1982). Although DSCF neurons show facilitative response to paired sounds (Fitzpatrick et al. 1993), FM-FM neurons have more complex response properties than DSCF neurons. The effect of cortical inactivation with muscimol was significantly larger on subcortical FM-FM neurons than on subcortical DSCF neurons (Zhang and Suga 1997): 82.1 ± 14.0 (n = 9) versus 59.8 ± 15.8 (n = 5) for the MGB (P < 0.001) and 65.5 ± 19.5 (n = 10) versus 33.5 ± 7.8 (n = 6) for the IC (P < 0.001).

Response properties of combination-sensitive neurons such as FM-FM neurons greatly depend on facilitation, i.e., nonlinear amplification, which mostly is mediated by the corticofugal feedback (Yan and Suga 1996; present paper). Therefore, it is
quite reasonable that cortical inactivation affects facilitative responses of FM-FM neurons much more than it does single tone responses of DSCF neurons. A possible general principle in auditory information processing that emerged from our data are that the processing of complex sounds by combination-sensitive neurons more heavily depends on the corticofugal system than does sound processing by noncombination sensitive neurons.

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