

Brief and Short-Term Corticofugal Modulation of Subcortical Auditory Responses in the Big Brown Bat, *Eptesicus fuscus*

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Zhou, Xiaoming and Philip H.-S. Jen. Brief and short-term corticofugal modulation of subcortical auditory responses in the big brown bat, *Eptesicus fuscus*. *J Neurophysiol* 84: 3083–3087, 2000. Recent studies show that the auditory corticofugal system modulates and improves ongoing signal processing and reorganizes frequency map according to auditory experience in the central nucleus of bat inferior colliculus. However, whether all corticofugally affected collicular neurons are involved in both types of modulation has not been determined. In this study, we demonstrate that one group (51%) of collicular neurons participates only in corticofugal modulation of ongoing signal processing, while a second group (49%) of collicular neurons participates in both modulation of ongoing signal processing and in reorganization of the auditory system.

another group of collicular neurons additionally participates in corticofugal reorganization of the auditory system.

METHODS

One or two days before the recording session, a 1.8-cm nail was glued onto the exposed skull of each of nine pentobarbital sodium (Nembutal)-anesthetized (45–50 mg/kg body wt) bats (body wt 20–24 g). During recording, each bat was administered the neurolept-analgesic Innovar (0.08 mg/kg body wt of fentanyl, 4 mg/kg body wt of droperidol) and was strapped to an aluminum plate with transparent plastic sheeting inside a double-wall, sound-proof room (temperature 28–30°C). The bat's head was immobilized by fixing the shank of the nail into a metal rod with a set screw (Suga and Schlegel 1972). Small holes were then bored in the skull above the primary auditory cortex (AC) and the IC.

Acoustic stimuli (4 ms with 0.5 ms rise-decay times at 2 pps) were generated with an oscillator (KH model 1200) and a homemade electronic switch. These stimuli were then amplified after passing through a decade attenuator (HP 350D) before they were fed to a small condenser loudspeaker (AKG model CK 50, 1.5 cm diam, 1.2 g) that was placed 23.5 cm away from the bat and at 40° contralateral to the recording site. The loudspeaker was calibrated with a Brüel and Kjaer ¼-in. (4135) microphone placed at the bat's head. The output was expressed in dB SPL in reference to 20 μ Pa root mean square.

During experiments, custom-made, two tungsten-in-glass electrodes, described previously (Jen et al. 1998) (tip: <10 μ m, inter-tip distance: 30–50 μ m), were inserted into the AC at depths of 500–700 μ m (the 5th layer of the AC) (Jen et al. 1997). When a single neuron was isolated, the frequency and intensity of the sound were systematically varied to determine the best excitatory frequency (BF_{AC}) at which the neuron had the lowest threshold to sound stimulus (i.e., the minimum threshold or MT_{AC}). At the MT_{AC}, the neuron responded to each of two consecutive presentations of BF_{AC} pulses. The neuron's latency_{AC} to a BF_{AC} sound at 10 dB above the MT_{AC} was determined. A 3 M KCl glass micropipette electrode (diameter 1 μ m, impedance 5–10 M Ω) was then used to record auditory response of neurons in the central nucleus of the IC ipsilateral to the AC. After determining the BF_{IC}, the MT_{IC}, and the latency_{IC} of each isolated collicular neuron, a BF_{IC} sound at 10 dB above the MT_{IC} (abbreviated as AS_{IC}), was used to obtain the neuron's response (i.e., the control response). Then the same BF_{IC} sound was delivered together with an electrical stimulation (4-ms train stimulus consisting of 4 monophasic pulses of 0.1 ms at 2 trains/s) in the AC (abbreviated as ES_{AC}) to obtain the collicular neuron's responses (referred to as AS_{IC} + ES_{AC} stimulation conditions). When the neuron's response was affected by ES_{AC}, the interval between ES_{AC} and AS_{IC} was adjusted (1–6 ms, usually 1–3

INTRODUCTION

The processing of auditory information carried by complex sounds has been explained by neural interactions based on divergent and convergent projections within the ascending auditory system, but without considering the contribution of the descending (corticofugal) auditory system (Suga 1997). However, recent studies have shown that the massive corticofugal system, which is topographically as well-organized as the ascending system (Games and Winer 1988; Herbert et al. 1991; Huffman and Henson 1990; Saldaña et al. 1996), extensively adjusts and improves subcortical auditory signal processing in the frequency, time, and spatial domains (He 1997; Jen and Zhang 1999; Jen et al. 1998; Suga et al. 1997; Sun et al. 1989, 1996; Villa et al. 1991; Yan and Suga 1996, 1998; Zhang and Suga 1997; Zhang et al. 1997). These corticofugal modulations are based on highly focused positive feedback to subcortical neurons "matched" in tuning to a particular acoustic parameter and widespread negative feedback (lateral inhibition) to "unmatched" subcortical neurons. The corticofugal system also contributes to the reorganization (plasticity) of subcortical sensory maps, according to sensory experience including associative learning (Gao and Suga 1998; Yan and Suga 1998). However, these studies did not explore whether these two types of corticofugal modulation were mediated through the same or different groups of subcortical auditory neurons.

Using the big brown bat, *Eptesicus fuscus*, as a mammalian model, we report here that one group of neurons in the central nucleus of the inferior colliculus (IC) participates only in corticofugal modulation of ongoing signal processing while

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ms) such that the neuron's response was either decreased or increased at least 20%. The electrical current (5–50 μ A, usually 5–25 μ A) that produced a 30–50% change in response relative to the control response was then chosen for subsequent experiments.

To determine whether corticofugal modulation of the response of a collicular neuron had different time courses, the neuron's response was monitored under two stimulation conditions. First, the responses of each corticofugally affected collicular neuron to AS_{IC} alone and to $AS_{IC} + ES_{AC}$ were monitored when the ES_{AC} was delivered at 2 trains/s. The neuron's response to AS_{IC} was also monitored on cessation of ES_{AC} and at 5-min intervals for 35 min thereafter. Second, an ES_{AC} at 10 trains/s and a BF_{AC} sound at 10 dB above the MT_{AC} was delivered for 30 min (referred to as $AS_{AC} + ES_{AC}$ stimulation conditions). The neuron's response to AS_{IC} was then monitored on cessation of $AS_{AC} + ES_{AC}$ and at 5-min intervals for 35 min thereafter. This $AS_{AC} + ES_{AC}$ stimulation condition was comparable to the one used in previous studies that produced short-term corticofugal modulation (Gao and Suga 1998; Yan and Suga 1998).

Recorded action potentials were amplified with conventional techniques and sent to a computer (Gateway 2000, 486) for acquisition of peristimulus time histograms (binwidth: 500 μ s, sampling period: 100 ms) of the neuron's responses to 32 stimuli. The total number of impulses in each histogram was used to quantify the neuron's response under each stimulation condition.

RESULTS

In this study, 30 corticofugally inhibited and 9 corticofugally facilitated collicular neurons were isolated. The effect of corticofugal modulation in 20 (51%, 16 corticofugally inhibited and 4 facilitated) collicular neurons vanished within 5–10 s following cessation of either $AS_{IC} + ES_{AC}$ or $AS_{AC} + ES_{AC}$.

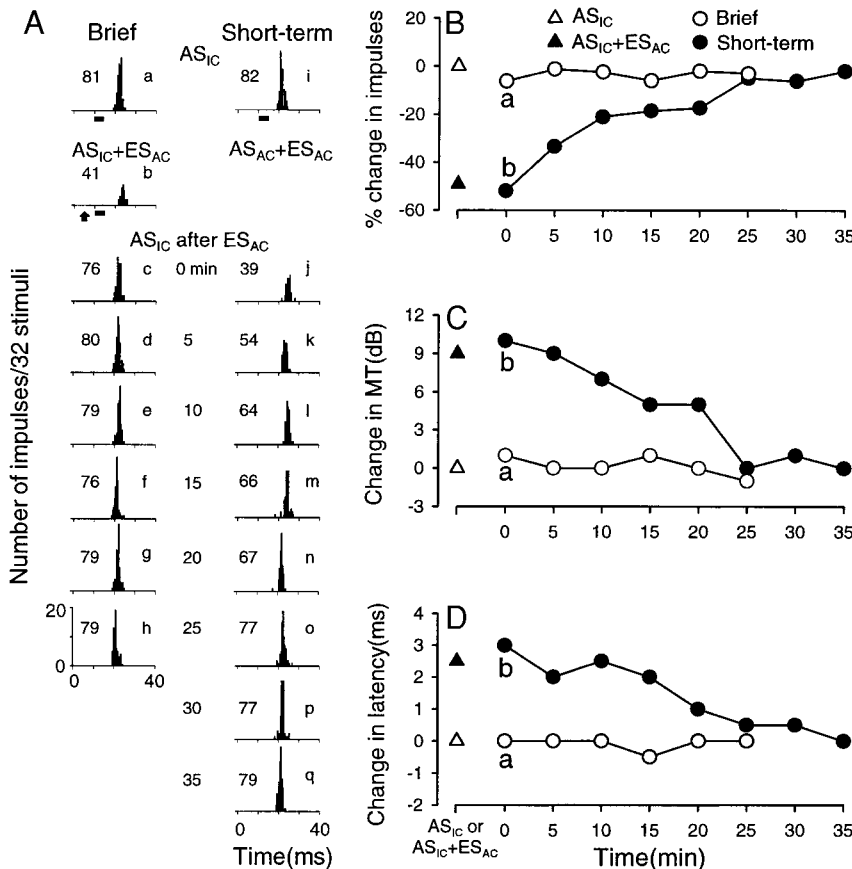


FIG. 1. Brief and short-term corticofugal inhibition on auditory responses of an inferior collicular (IC) neuron. A: the neuron's discharge pattern in peristimulus time histograms (PST) obtained with a best frequency sound delivered at 10 dB above the minimum threshold (MT ; AS_{IC} , shown in short horizontal bar) before (Aa, Ai), during (Ab) and after ($A, c-h$ and $j-q$) cortical electrical stimulation (ES_{AC}). This neuron discharged a total of 81 (Aa) or 82 (Ai) impulses to AS_{IC} . Sound stimulation plus cortical electrical stimulation ($AS_{IC} + ES_{AC}$, 4-ms train of 4 pulses of 0.1 ms, at 33 μ A and 2 trains/s, shown in arrow) produced only 41 impulses (Ab). After $AS_{IC} + ES_{AC}$, the number of impulses in response to AS_{IC} increased to 76 (Ac), which varied between 76 and 80 when monitored over a period of 25 min at 5-min intervals ($A, d-h$). This fast recovery from ES_{AC} is called brief corticofugal modulation. However, after 30-min sound stimulation (delivered at the BF_{AC} and 10 dB above the MT_{AC} of the AC neuron) plus cortical electrical stimulation ($AS_{AC} + ES_{AC}$ at 10 trains/s), the neuron's number of impulses elicited by AS_{IC} gradually returned to within 5% of its control values (Ai) over a period of 35 min ($A, j-q$). This slow recovery from ES_{AC} is called short-term corticofugal modulation. B–D: time course for variation in the number of impulses (B), MT (C), and latency (D) of the collicular neuron during brief (open circles, Ba, Ca , and Da) and short-term (filled circles, Bb, Bc , and Db) corticofugal inhibition. The neuron's number of impulses, MT, and latency determined under AS_{IC} and $AS_{IC} + ES_{AC}$ stimulation conditions are shown in open and filled triangles. The BF (kHz), MT (dB SPL), and latency (ms) of the IC and AC neurons were 29.8, 61, 9 (IC); 29.9, 54, 12 (AC).

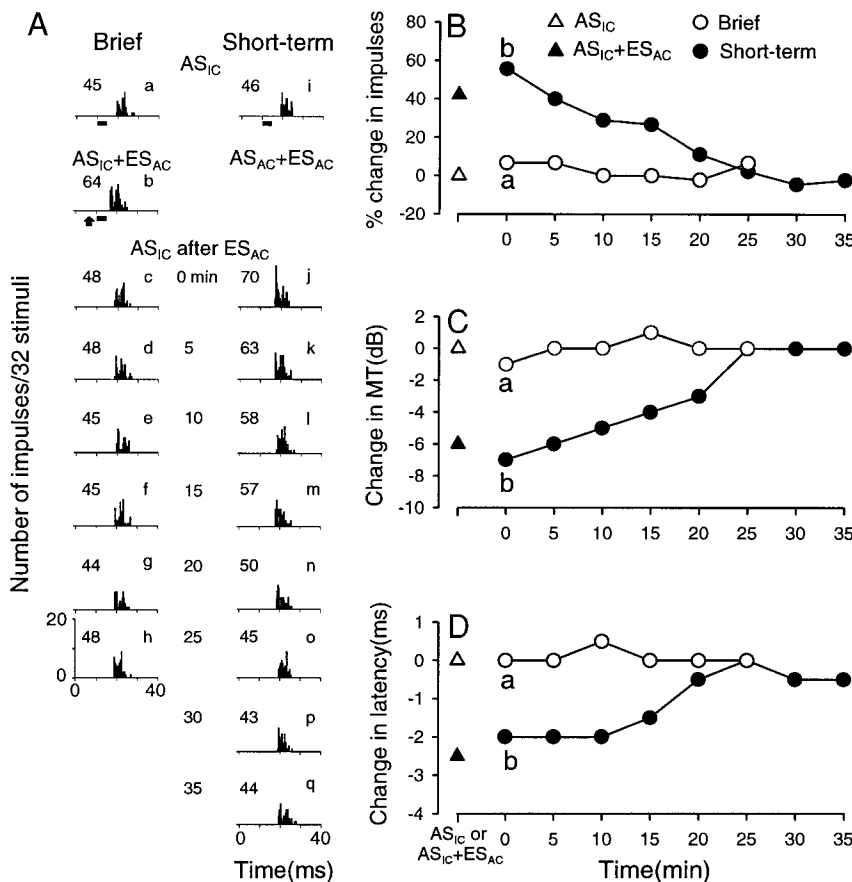


FIG. 2. Brief and short-term corticofugal facilitation on auditory responses of a collicular neuron. A: the neuron's PST histograms obtained with an AS_{IC} before (A, a and i), during (Ab) and after (A, c–h and j–q) the ES_{AC}. This neuron discharged 45 (Aa) or 46 (Ai) impulses to AS_{IC} (shown in short horizontal bar). During AS_{IC} + ES_{AC}, this neuron discharged a total of 64 (Ab) impulses. On cessation of AS_{IC} + ES_{AC}, the neuron's number of impulses in response to AS_{IC} decreased to 48 (Ac), which varied between 44 and 48 when monitored over a period of 25 min (A, d–h). However, on cessation of AS_{AC} + ES_{AC}, the number of impulses was increased to 70, which gradually returned to within 2% of the control value (Ai) over a period of 25 min (A, j–q). B–D: time course for variation in the number of impulses (B), MT (C), and latency (D) during brief (open circles, Ba, Ca, and Da) and short-term (filled circles, Bb, Cb, and Db) corticofugal facilitation. The neuron's number of impulses, MT, and latency determined under AS_{IC} and AS_{IC} + ES_{AC} stimulation conditions are shown in open and filled triangles. The BF (kHz), MT (dB SPL), and latency (ms) of the IC and AC neurons were 38.1, 51, 9 (IC); 36.4, 56, 15 (AC; see Fig. 1 for legends).

period of 35 min after AS_{AC} + ES_{AC} (Fig. 1, B–D, filled circles).

Figure 2 shows both brief and short-term corticofugal modulation in the auditory response of a representative corticofugally facilitated collicular neuron. This neuron discharged a total of 45 or 46 impulses to AS_{IC}. During AS_{IC} + ES_{AC}, the neuron's number of impulses increased from 45 (Fig. 2Aa) to 64 (Fig. 2Ab). The number of impulses decreased to 48 on cessation of AS_{IC} + ES_{AC} (Fig. 2Ac) and was between 44 and 48 within the subsequent 25 min (Fig. 2A, d–h). In contrast, the number of impulses increased from 46 to 70 (Fig. 2Aj) and did not return to within 2% of the control level until 25 min after AS_{AC} + ES_{AC} (Fig. 2Ao). Variation in the number of impulses, the MT, and the latency during AS_{IC} + ES_{AC} (Fig. 2, B–D; filled vs. open triangles) returned to within 5% of the control level after AS_{IC} + ES_{AC} and remained at the same level when monitored for 25 min thereafter (Fig. 2, B–D, open circles). However, the neuron's varied responses only gradually returned to within 5% of the control level over a period of 25 min after AS_{AC} + ES_{AC} (Fig. 2, B–D, filled circles).

Figure 3 shows responses of corticofugally inhibited (Fig. 3, A1–A3) and corticofugally facilitated (Fig. 3, B1–B3) collicular neurons that were involved only in brief corticofugal modulation. Their responses returned to within 5% of the control level (Fig. 3, filled vs. open triangles) after both AS_{IC} + ES_{AC} and AS_{AC} + ES_{AC}. These two neurons had similar recovery time course for both stimulation conditions (Fig. 3, open vs. filled circles).

Previous studies (Gao and Suga 1998; Yan and Suga 1998) reported that AS_{AC} + ES_{AC} produced an asymmetrical BF_{IC}

shift toward BF_{AC} when BF_{IC} was within 10 kHz above the BF_{AC} and the maximal BF_{IC} shift occurred when the BF_{AC-IC} difference between cortical and collicular neurons was ~5 kHz. Among 19 neurons that were involved in both brief and short-term corticofugal modulation, the BF_{IC}s of four corticofugally inhibited and three corticofugally facilitated collicular neurons were above the BF_{AC} by 0.23–2.91 kHz. AS_{AC} + ES_{AC} produced a BF_{IC} shift toward BF_{AC} in two neurons with BF_{IC} above the corresponding BF_{AC} by 1.91 and 2.91 kHz. However, the BF_{IC} shifts due to AS_{AC} + ES_{AC} in five other neurons were too small to determine confidently.

We examined the BF_{AC-IC} difference in relation to brief and short-term corticofugal modulation. As shown in Table 1, BF_{AC-IC} difference was significantly larger in collicular neurons that were only involved in brief corticofugal modulation (e.g., Fig. 3) than in collicular neurons that were involved in both types of corticofugal modulation (e.g., Figs. 1 and 2; *t*-test, *P* < 0.001). Although not significant, BF_{AC-IC} difference within each group of collicular neurons was smaller for corticofugal facilitation than for corticofugal inhibition (*t*-test, *P* > 0.05).

DISCUSSION

Our finding of brief corticofugal modulation confirms that the corticofugal system can actively modulate collicular responses through inhibition (Fig. 1A, b–h, and B–D, open circles) and facilitation (Fig. 2A, b–h, and B–D, open circles) to improve ongoing signal processing. We found that short-term modulation of collicular responses (e.g., Figs. 1 and 2, Aj–Aq, and B–D, filled circles) persisted for 5–35 (average

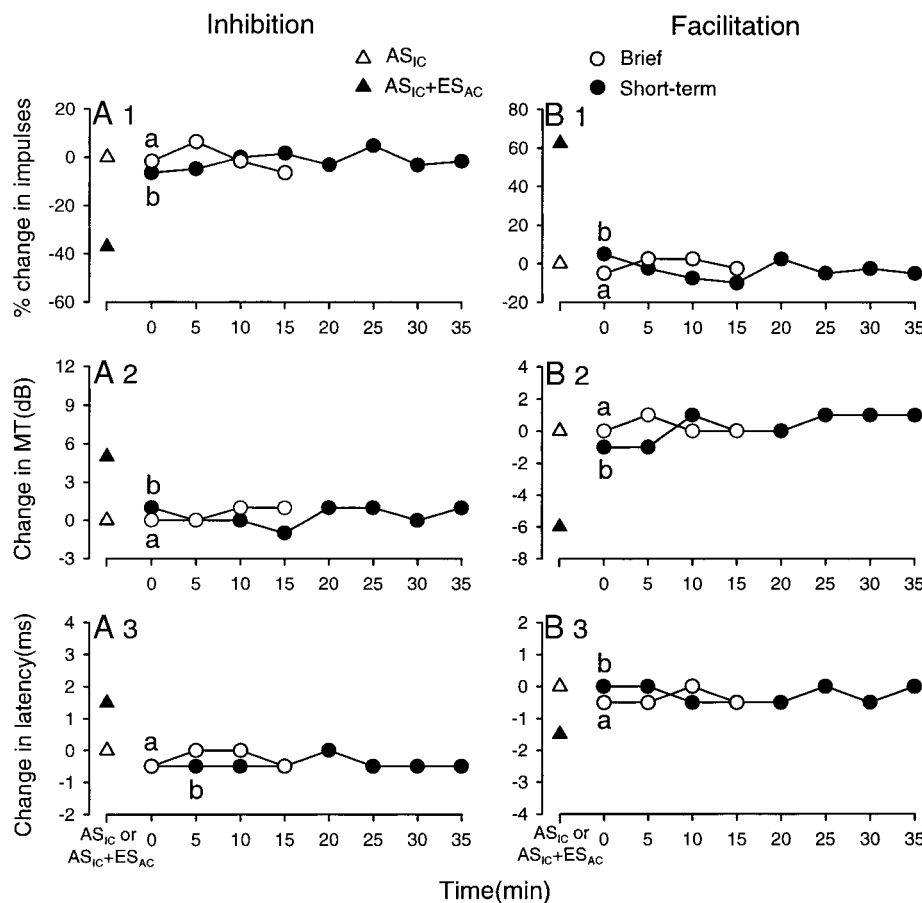


FIG. 3. The time course for variation in the number of impulses (*A1* and *B1*), MT (*A2* and *B2*), and latency (*A3* and *B3*) during brief (open circles) and short-term (filled circles) corticofugal inhibition (*A1*–*A3*) and facilitation (*B1*–*B3*) of auditory responses of 2 collicular neurons. The number of impulses, MT, and latency determined under AS_{IC} and $AS_{IC} + ES_{AC}$ stimulation conditions are shown in open and filled triangles. Note that the number of impulses, MT, and latency of these 2 neurons returned to within 5% of the control level (open triangles) on cessation of both $AS_{IC} + ES_{AC}$ and $AS_{AC} + ES_{AC}$ stimulation conditions. The BF (kHz), MT (dB SPL), and latency (ms) of the IC and AC neurons were 27.6, 52, 12.5 (IC) and 21.5, 68, 18 (AC) for neuron A; 35.9, 67, 10 (IC) and 32.0, 78, 16 (AC) for neuron B.

20 \pm 9.0) min after $AS_{AC} + ES_{AC}$. Variation in the number of impulses, the MT, and the latency during this time period suggests a plastic change in collicular auditory sensitivity. This finding supports earlier studies (Gao and Suga 1998; Yan and Suga 1998) that the corticofugal system contributes to neuroplasticity in the sensory system.

We have shown that one group of collicular neurons participated in both brief and short-term modulation (Figs. 1 and 2) and the other group participated only in brief corticofugal modulation of collicular signal processing (Fig. 3). The BF_{AC-IC} difference in these two groups of collicular neurons was significantly different (Table 1). Future work is needed to determine whether these two groups of collicular neurons have different neural pathways for corticofugal modulation.

TABLE 1. The range and average difference in best frequency between cortical and collicular neurons based on the type and time course of corticofugal modulation

Type	BF_{AC-IC} Difference, kHz		<i>t</i> -Test, <i>P</i>
	Brief	Brief and short	
Inhibition	8.3 \pm 4.7 (16) [1.1–15.9]	2.1 \pm 1.9 (14) [0.1–5.3]	<0.0001*
Facilitation	4.0 \pm 1.4 (4) [2.5–5.7]	1.6 \pm 1.0 (5) [0.1–2.9]	<0.001*
<i>t</i> -Test, <i>P</i>	0.045	0.26	

Values are means \pm SD; numbers in parentheses indicate number of neurons, and numbers in brackets are ranges. * Significant difference 1-tailed *t*-test, *P* < 0.001.

As described earlier, many recent studies (He 1997; Jen and Zhang 1999; Jen et al. 1998; Suga et al. 1997; Sun et al. 1989, 1996; Yan and Suga 1996, 1998; Zhang and Suga 1997; Zhang et al. 1997) have shown that the effect of corticofugal modulation can either be very brief or last for more than 3 h on cessation of ES_{AC} . Furthermore, corticofugal modulation of sensory maps due to classical conditioning may last for periods ranging from 3 h to 8 wk (Weinberger et al. 1993). In this study, we used brief and short-term modulation to respectively describe a corticofugal modulation that vanished within 5–10 s or persisted up to 5–35 min following cessation of ES_{AC} (Figs. 1 and 2, *Aa*–*Ah*, and *Ba*, *Ca*, and *Da*; and Fig. 3). To avoid confusion when comparing studies of auditory corticofugal modulation in the future, we propose that short-term modulation includes corticofugal modulation that lasts up to 3 h. We also propose that long-term modulation be used to describe corticofugal modulation associated with classical conditioning experiments, which lasts for more than 3 h.

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