Corticofugal Projection Inhibits the Auditory Thalamus Through the Thalamic Reticular Nucleus

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Corticofugal projection inhibits the auditory thalamus through the thalamic reticular nucleus. J Neurophysiol 99: 2938–2945, 2008. First published April 16, 2008; doi:10.1152/jn.00002.2008. Electrical stimulation of the auditory cortex (AC) causes both facilitatory and inhibitory effects on the medial geniculate body (MGB). The purpose of this study was to identify the corticofugal inhibitory pathway to the MGB. We assessed two potential circuits: 1) the cortico-colliculo-thalamic circuit and 2) cortico-reticulo-thalamic one. We compared intracellular responses of MGB neurons to electrical stimulation of the AC following bilateral ablation of the inferior colliculi (IC) or thalamic reticular nucleus (TRN) in anesthetized guinea pigs. Cortical stimulation with intact TRN could cause strong inhibitory effects on the MGB neurons. The corticofugal inhibition remained effective after bilateral IC ablation, but it was minimized after the TRN was lesioned. Ablation of the MGB neurons. The corticofugal inhibition remained effective, but it was minimized after the TRN was lesioned. Ablation of the IC but it was minimized after the TRN was lesioned. Cortical stimulation with intact TRN could cause strong inhibitory effects on the MGB neurons. The corticofugal inhibition remained effective after bilateral IC ablation, but it was minimized after the TRN was lesioned. Ablation of the MGB neurons. The corticofugal inhibition remained effective, but it was minimized after the TRN was lesioned.

INTRODUCTION

Compared with the ascending thalamocortical projection, the auditory thalamus receives a much stronger reciprocal projection from the cortex (Andersen et al. 1980; Bajo et al. 1995; Montero 1987; Winer and Larue 1987; Winer et al. 2001). Corticothalamic fibers make excitatory synaptic contacts with thalamic relay neurons, local-circuit inhibitory interneurons, and thalamic reticular nucleus (TRN) neurons (Jones 2002; Liu and Jones 1999; Liu et al. 1995a; Ojima 1994; Yen et al. 1985). Corticofugal projection to the thalamus has been suggested to perform a gating or gain control function in the transmission of information from the periphery to the cortex (Crick 1984; Murphy and Sillito 1996; Villa et al. 1991; Yu et al. 2004a). Morphological and physiological results indicate that TRN terminals have a very strong inhibitory effect on the thalamic relay neurons (Bartlett et al. 2000; Cox et al. 1997; Golshani et al. 2001; Montero 1983; Warren et al. 1997). In the auditory system, both corticofugal facilitation and inhibitory effects on medial geniculate body (MGB) neuronal responses to sound stimuli were shown by cooling the primary auditory cortex (AI) (Ryugo and Weinberger 1976; Villa et al. 1991).

Corticofugal feedback could modulate frequency- and time-domain biosonar information (Yan and Suga 1996; Zhang et al. 1997). In bats, the excitatory corticofugal feedback could, on average, amplify collicular auditory responses by 1.5 times and thalamic responses by 2.5 times (Zhang and Suga 1997).

In guinea pigs, the tonotopically organized ventral division (MGl) consists of the pars ovoidea and the pars lateralis, the dorsal (MGd), and medial (MGe) divisions (Andersen et al. 1980; Yu et al. 2004a; Zhang et al. 2008). Recently, we found that activation of the auditory cortex results in a strong and long-lasting inhibition on mainly non-MGv neurons (Xiong et al. 2004; Yu et al. 2004a) in contrast to a strong facilitation and a small inhibitory effect on MGv neurons (He 2003a; He et al. 2002). Such strong centrifugal inhibition to dorsal thalamus could hyperpolarize the membrane potential of the thalamocortical neurons, leading to low-threshold calcium spike burst mode (Llinas and Jahnse 1982; Steriade 2001) in the dorsal thalamus, thereby switching the thalamus from working mode to sleeping mode (Kim et al. 1997; Steriade et al. 1986). However, the pathway of the corticofugal inhibition has not been fully elucidated.

Three candidate pathways by which auditory cortex (AC) induced inhibition in the MGB have been hypothesized: 1) via inferior colliculus (IC) GABAergic neurons, 2) via MGB interneurons, and 3) via TRN neurons (Bartlett et al. 2000; Winer and Larue 1996; Yu et al. 2004a). Option 2 was discarded because very few interneurons exist in the MGB of guinea pigs, although strong centrifugal inhibitions on the thalamus have been observed in this species. In this study, the corticofugal inhibitory pathway was identified by examining the membrane potential of MGB neurons in response to electrical stimulation of the AC following bilateral ablation of the IC or a selective lesion of TRN neurons.

METHODS

Animals

Sixty-four guinea pigs served as subjects in this study. Anesthesia was initially induced with pentobarbital sodium (Nembutal, Abbott, 35 mg/kg, ip) or urethane (Sigma, 1.3 g/kg, 20% solution in 0.9% saline). Supplemental doses of the same anesthetic were administered regularly during the recording session (5–10 mg/kg/h Nembutal or 50 mg/kg/h urethane). Atropine sulfate (0.05 mg/kg initially and 0.01 mg/kg/h urethane). Atropine sulfate (0.05 mg/kg initially and 0.01 mg/kg/h urethane).
mg/kg/h, sc) was administrated 15 min before anesthesia and at regular intervals during the period of electrophysiological recording. The subject was mounted in a stereotaxic device following the induction of anesthesia. A midline incision was made in the scalp, and a craniotomy was performed for vertical access to the right MGB (Yu et al. 2004b). Cerebrospinal fluid was released through the foramen magnum. Artificial respiration was applied to the animal, muscles were relaxed after administration of gallamine triethiodide (Sigma, 50 mg/kg initially 10 mg/kg/h regularly, ip), the animal’s chest was opened bilaterally, and its body was suspended to reduce vibrations to the brain caused by intrathoracic pressure. The end-tidal CO2 was monitored. Throughout the recording, the electrocorticograph was used to assess the level of anesthesia. The procedures were approved by the Animal Subjects Ethics Subcommittee of The Hong Kong Polytechnic University.

Acoustic stimuli

The subjects were placed in a double-walled soundproofed room (NAP, Clayton, Australia). Acoustic stimuli were generated digitally by a MALab system (Kaiser Instruments, Irvine, CA) (He 1997; Semple and Kitzes 1993) or TDT auditory physiology workstation (Tucker-Davis Technologies, Alachua, FL). Bursts of white noise (60 dB, 5-ms rise/full time, 100–200-ms duration, 1200-ms interval) were delivered through a sealed acoustic system, which was a calibrated earphone (TDT EC1) attached to the distal end of a hollow ear bar that positioned directly to the left pinna.

Electrical stimulation

A parallel array of three bipolar low-impedance electrodes was implanted into the auditory cortex (the anterior and dorsocaudal auditory fields) ipsilateral to the thalamus being studied. In most cases, we used electrical stimuli of 0.5 or 1 ms in width, 50–200 μA in amplitude, 50 Hz in frequency, and 1–10 pulses to activate the auditory cortex according to cortical maps obtained in previous research (He 1997; He et al. 2002; Wallace et al. 2000). A sound stimulus was delivered to the ear contralateral to the recording hemisphere 100 ms after the end of the cortical stimulation (He 1997, 2003b).

Recording

A low impedance electrode was implanted in the deep layer of the AC to record the electrocorticogram (ECoG). A glass-pipette filled with 1.0 M KCl or 3.0 M kainic acid (KAc) was used to record the membrane potential of MGB neurons. The impedance of the electrode was between 40 and 90 MΩ. The electrode was advanced vertically from the pial surface of the brain by a stepping motor. After the electrode was lowered to a depth of 4–5 mm, the cortical exposure was sealed using low-melting temperature paraffin. When the electrode was near or in the targeted area, it was slowly advanced at 1- or 2-μm steps. Only those neurons with a resting membrane potential (Vrest) less than −50 mV and spikes that overshot the baseline were analyzed in this study. After physiological recordings, the tracer Neurobiotin (Vector, 1–2% in 1 M KCl or 3 M KAc) was injected into one to two neurons in each subject by delivering rectangular depolarizing current pulses (150 ms, 3.3 Hz, 2 nA for 1–5 min).

IC ablation

The IC was ablated bilaterally in 34 guinea pigs. After we identified the auditory-responsive and corticofugal-inhibitory regions in MGB, another craniotomy (3.0 × 6.0 mm) was made just behind the interaural line. Bilateral ICs were exposed and aspirated with a suction needle, avoiding damage to the transverse sinuses. Absorbable gelatin sponges (Ferrosan) were used to minimize bleeding. Recordings from the right MGB were continued after the suction ablation. In case the MGB neurons were still responsive to noise bursts after surgery, a deeper midbrain aspiration would be made to ensure both ICs were destroyed completely.

TRN lesion

Seven guinea pigs were used in this experiment. Kainic acid (Tocris, 2.5 g/l in 0.9% saline solution), which is excitotoxic to neurons, was delivered to the TRN with a micropipette (tip diam, ~20 μm) attached to a 5-μl syringe mounted on a micromanipulator. Kainic acid was injected in small amounts at three different depths to avoid seizures (usually 0.05 μl over a period of 30–90 min for a total injection of 0.15 μl). At the end of surgery, the bony cavity was packed with absorbable gelatin sponges, and the wound was sutured. The operated animals were returned to single cages. For postoperative care, both lidocaine (Astra) and antibiotic ointment (Furacin, Smith-Kline Beecham Pharmaceuticals) were applied four times daily to the skin wound. Recordings in MGB neurons were performed 2–3 days after the injection, when maximum loss of cell bodies was produced, and the survival period was long enough to verify the extent of lesions histologically (Descheesens and Hu 1990; McGee et al. 1978; Steriade et al. 1985). The extent of thalamic lesions was determined on Nissl-stained coronal sections of 60 μm thickness.

Histology

After physiological recording, the subjects were deeply anesthetized with an overdose of pentobarbital sodium (Nembutal, Abbott, 60 mg/kg, ip) and perfused transcardially with 200 ml 0.9% NaCl, followed by a mixture of cold 4% paraformaldehyde in a 0.1 M phosphate buffer (PB, pH 7.4). The brain was removed from the skull and postfixed for 4 h in the same fixative. After postfixation, the brains were cryoprotected in 30% sucrose in PB (0.1 M, pH 7.4) for 2 days at 4°C. The midbrains were sectioned sagittally across the sites of the lesion. The thalami were sectioned coronally at a thickness of 60 or 90 μm using a freezing microtome. The thalamic sections were collected in 0.01 M potassium PBS (KPBS, pH 7.4) and incubated in 0.1% peroxidase-conjugated avidin-D (Vector) in KPBS with 0.5% Triton X-100 for 4–6 h at room temperature. After the detection of peroxidase activity with 3,3′-diaminobenzidine (DAB), sections were examined under the microscope. Those sections containing labeled neurons were mounted on gelatin-coated slides and counterstained with neutral red or Nissl and examined under the microscope before being photographed.

The subdivision of the MGB was based on the cell packing in Nissl/neuronal red staining (Anderson et al. 2007; Zhang et al. 2008).

Data acquisition and analysis

After amplification, membrane potentials and artifacts of electrical stimulation as well as the auditory stimulus were stored in the computer with the aid of commercial software (AxxoScope, Axon Instruments, Foster City, CA). No manipulations of membrane potentials were made to the data presented in this study. The amplitude of inhibitory postsynaptic potentials (IPSPs) was calculated as the change of the membrane potential caused by cortical stimulation. Numerical results are expressed as mean ± SD. Comparison of corticofugal stimuli effects before and after IC ablation was made using an unpaired t-test. Ninety-five percent confidence were set as the criterion of statistical significance.

RESULTS

In this study, a total of 73 MGB neurons were recorded intracellularly with resting potentials of less than −50 mV. Of 73 neurons, 23 were recorded from intact guinea pigs, 42 were recorded after IC ablations, and 8 were recorded after TRN
lesions. Altogether, 35 neurons were labeled after physiological recording. Among them, 10 were from subjects with intact IC and TRN, 21 from subjects with IC ablation, and 4 from subjects with TRN lesion.

### Corticofugal inhibition on MGB neurons in control animals

Neuronal activities in the AC were synchronized with IPSP activities in the MGB neurons (Fig. 1). As shown in Fig. 1A, slow rhythmic oscillation (<1 Hz) in the AC elicited a small excitatory postsynaptic potential (EPSP) curtailed by a large IPSP in one MGB neuron. The simultaneous recording of the ECoG and intracellular membrane potential was from the deep layer of AC and MGB neurons of a control animal. Without external stimuli, the MGB neuron exhibited IPSPs preceded by a large field potential in the EEG from the AC (Fig. 1). The average amplitude of IPSPs in MGB was 12.7 ± 3.2 mV (8 events; range, 7–17 mV).

To examine such corticofugal inhibitory effects on MGB neurons, 1–10 pulses of electrical shocks were applied to the AC to induce inhibition in MGB neurons in the control group. The neuron shown in Fig. 2 was located in MGd. It responded to a noise-burst stimulus with onset EPSP, which was followed by an IPSP (Fig. 2, left, top trace). The neuron responded to a five-pulse electrical stimulation in the AC with an IPSP, leading to low-threshold spikes (LTSs) as a rebound response. The noise-evoked response only exhibited as some small membrane fluctuation embedded in the long IPSP triggered by electrical pulses (Fig. 2, left, bottom trace). In this study, we calculated the mean and SD of the IPSPs in MGB based on the five-pulse stimulation of the AC. The mean amplitude of IPSP was −10.3 ± 3.2 mV (n = 23; range, 6–15 mV), and the mean duration was 232.8 ± 90.5 ms (n = 23; range, 121–302 ms; Table 1). In this study, neurons that showed EPSPs to cortical stimulation were excluded in the statistics and from further analysis in the control condition. Ten of the 23 neurons were successfully labeled and histologically confirmed to locate on the border region of the MGv or non-MGv.

### Corticofugal inhibition is present after bilateral IC ablation

After complete IC ablation in 34 guinea pigs, responses to electrical AC stimulation were recorded from 42 MGB neurons. Among them, 23 showed an inhibitory effect, 9 showed an excitatory effect, and the remaining 10 showed no effect. Figure 3A shows an example of the extent of IC ablation of the right side in a sagittal section (Fig. 3Ab) in comparison to the intact IC of one normal subject (Fig. 3Aa).

Presence of IPSP in MGB neurons following bilateral IC ablation indicates that the corticofugal effect does not traverse the IC. As shown in one representative MGB neuron after the IC was ablated, the neuron did not respond to noise stimulus (Fig. 3Ba, top trace). Electrical stimulation delivered to the AC caused similar membrane hyperpolarization and longer inhibition, leading to an LTS burst as it did in the IC-intact group (Fig. 3Ba, bottom trace). This neuron was located in the border region between MGd and MGv (Fig. 3Bb). As shown in Table 1, the mean amplitude of IPSPs in the IC-ablated subjects was −11.5 ± 4.3 mV (n = 23; range, 5–20 mV), and the mean duration was 220.4 ± 74.3 ms (n = 23; range, 119–358 ms). No

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### Table 1. IPSPs of MGB neurons caused by electrical stimulation of the auditory cortex

<table>
<thead>
<tr>
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<th>Control Group (IC Intact)</th>
<th>IC-Ablated Group</th>
<th>t-Test</th>
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<tbody>
<tr>
<td>Number of neurons</td>
<td>23</td>
<td>23</td>
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<tr>
<td>Amplitude of corticofugal IPSP, mV</td>
<td>10.3 ± 3.2</td>
<td>11.5 ± 4.3</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Duration of corticofugal IPSP, ms</td>
<td>232.8 ± 90.5</td>
<td>220.4 ± 74.3</td>
<td>P &gt; 0.05</td>
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Values are means ± SD. IPSP, inhibitory postsynaptic potential; MGB, medial geniculate body; IC, inferior colliculus.

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![Fig. 1](image1.png)

**FIG. 1.** Synchronized activities between the auditory cortex (AC) and the medial geniculate body (MGB). Neuronal activities in the AC [electroencephalogram (ECoG)] and MGB (intracellular membrane potentials) under pentobarbital sodium anesthesia. In the bottom 2 expanded traces, spontaneous inhibitory postsynaptic potentials (IPSPs) of the MGB were preceded by the negative wave of ECoG. The resting membrane potential is indicated on the right of the MGB recording traces.

![Fig. 2](image2.png)

**FIG. 2.** Electrical stimulation caused an inhibition in non-lemniscal MGB neurons. **Left:** neuronal responses to auditory stimulus (lower noise-burst stimuli applied to both top traces), and the effects of electrical stimuli with 5 pulses on MGB neurons (triangles indicate onset and offset of electrical pulses). The resting membrane potential is indicated on the left of the recording traces. **Right:** location of the Neurobiotin-labeled neuron (arrow) in a neutral red counterstained section. **Inset:** this neuron in high magnification. d, dorsal division (MGd); v, ventral division (MGv). The conventions here apply to the following figures unless otherwise noted.
In total, 21 neurons were successfully labeled after IC ablation, 14 showed corticofugal inhibition, and the remaining neurons showed either excitation or no effects. Main inhibitory centrifugal effects were recorded in non-MGv. Figure 4 shows corticofugal effects after bilateral IC ablation in four MGB neurons of different subnuclei. Although all showed some IPSPs following electrical stimulation in the cortex, neurons located in the MGd and MGm showed IPSPs immediately after the first electrical shock artifact (Fig. 4A and B, locations of the neurons shown as 1–2 in Fig. 4E), whereas those located in the border region of the MGv showed smaller and slower onset of IPSPs after electrical shock (Fig. 4C and D, locations of the neurons shown as 3–4 in Fig. 4E). The neuron in Fig. 4B showed spontaneous firings before cortical stimulation. The spontaneous firing was depressed after a single electrical shock (Fig. 4B).

Figure 5A shows a simultaneous recording of intracellular MGB and extracellular TRN activities. Inhibitory membrane potentials of MGB neurons were preceded by extracellular discharges of TRN neurons. In both control and IC-ablated animals, many TRN neurons responded to the AC electrical stimulation with oscillatory discharges, as in the example shown in Fig. 5Ba. In separated experiments, oscillation-like IPSPs triggered by cortical stimulation was observed in the MGB neuron. The TRN activity and MGB inhibitory oscillation had similar time courses (Fig. 5B).

**Corticofugal inhibition minimized after TRN lesion**

In seven guinea pigs, kainic acid injections resulted in nearly complete cell loss in the right TRN. Figure 6 shows the extent of the TRN lesion produced by kainic acid in one chronic experiment. In Fig. 6A (b and d), the perikarya of right TRN neurons disappeared compared with the same region on the control side (Fig. 6A, a and c). The total neuronal loss extended from the rostral pole of thalamus to the anterior lateral geniculate nucleus. A marked gliosis was also found in depopulated areas.

Eight MGB neurons were recorded in seven TRN-lesioned animals. Figure 6B shows the noise-evoked responses and cortical modulation effects, and Fig. 6C shows the locations of four Neurobiotin-labeled neurons. The neuron in Fig. 6B1 was located in the caudal pole of MGm (Fig. 6C, I) and responded to noise with a large depolarizing plateau leading to a spike (top trace). Cortical electrical stimulation of one pulse evoked a large EPSP initiated by a spike (middle trace); stimulation by five shocks triggered a ramp-like larger depolarization with repetitive, strongly driven discharges (bottom trace).

Both neurons in Fig. 6B, 2 and 3, were located in the MGv as shown in Fig. 6C (marked with 2 and 3). Both neurons showed EPEP-IPSPs in response to noise stimuli (Fig. 6B, 2 and 3, top traces). Cortical stimulation triggered a transient depolarization and a few spikes in neuron 2, but exerted no effect on the membrane potential of neuron 3. The neuron in Fig. 6B4, located in the dorsal division as marked with 4 in Fig. 6C, responded to noise with a single spike or a strong EPSP. Cortical stimulation triggered a transient depolarization in the MGB neuron. No corticofugal inhibitory effects were observed in any of the eight MGB neurons recorded in TRN-lesioned animals, with respect to all three subnuclei, excitatory, or inhibitory response patterns to noise stimuli. These results suggest that complete connection and intact function of TRN is indispensable for cortical inhibitory modulation of thalamus.

**DISCUSSION**

The purpose of this study was to identify the corticofugal inhibitory pathway to the MGB. By analyzing the responses of MGB neurons to cortical electrical stimuli, this study showed the following: 1) In the control animal group, spontaneous,
noise, and electrical-evoked corticofugal IPSPs were recorded in MGB. 2) After bilateral ICs were ablated, the MGB neurons showed no response to noise but still responded with IPSPs to cortical electrical stimulation. Such inhibition effects were the same as those recorded in control animals. 3) After ipsilateral TRN was lesioned by kainic acid, the MGB neurons no longer exhibited inhibition responses to cortical stimulation, no matter where the neurons located or what auditory response patterns were. These observations are discussed in the following sections.

Patterns of cortical inhibitory effects in the MGB

In a previous study, of 63 neurons that received corticofugal modulation of the membrane potential, 33 were IPSPs and 30 were EPSPs (Yu et al. 2004a). The experiment was similar to our control condition. Of 42 neurons examined in the IC-ablated group in this study, 23 showed corticofugal IPSPs, 9 showed EPSPs, and 10 showed no effect. Corticofugal IPSPs predominated over EPSPs in both conditions.

In intact animals, the electrical stimulation in auditory cortex could trigger similar IPSPs in MGB neurons, as spontaneous ECoG waves and noise burst stimuli did. After the bilateral ICs were ablated, the amplitude and duration of IPSPs of MGB neurons were not statistically different from those in the control group (Figs. 2 and 3). However, after chemical lesion of the TRN, IPSPs were no longer observed in MGB neurons.

Possible corticofugal inhibitory pathways to the MGB

As we have briefly mentioned, the proportion of interneurons in the MGB is species specific. Unlike the cat, monkey,
and human whose MGBs contain >20% interneurons, the guinea pig has only few glutamic acid decarboxylase (GAD) or GABA-immunopositive neurons (~1%) in the dorsal thalamic nuclei (Arcelli et al. 1997). The strong corticofugal inhibition observed in the guinea pig is therefore unlikely to result from this small number of MGB interneurons.

The auditory cortex sends excitatory projection to the IC (Herbert et al. 1991; Ojima 1994). In the cat, ~20–25% of the
neurons in the central nucleus of the IC are GABAergic (Merchán et al. 2005; Oliver et al. 1994). Among the tectothalamic projection IC neurons, GABAergic neurons count for 14–36% in the cat and 20–45% in the rat (Bartlett et al. 2000; Winer et al. 1996). Although previous studies have noted that monosynaptic GABAergic feedforward projections from the IC to MGB might modulate the thalamocortical neurons (Peruzzi et al. 1997), there is little evidence available as to the function of the IC in the corticothalamic inhibitory circuitry. The monosynaptic GABAergic input, which originated from the central nucleus of the IC, was considered as a projection of the main tonotopically organized lemniscal auditory pathway (Peruzzi et al. 1997). In this study, we found similar corticofugal inhibition in both amplitudes and durations of the MGB neurons after the IC was bilaterally ablated (Figs. 3 and 4). This result provided the physiological evidence that the corticocolliculogeniculate pathway was not necessary for corticofugal inhibition in the MGB neurons. Furthermore, the corticofugal inhibition was minimized after selective lesion of the TRN while the corticofugal projections were kept intact leads us to the conclusion that corticofugal inhibition on MGB neurons acted very likely via the TRN. The presence of corticofugal inhibition in MGB neurons following bilateral ablation of the IC strongly suggests that the role of feedforward GABAergic input from the IC might be focused entirely on modulating ascending neural information.

Corticothalamic fibers project only to the ipsilateral MGB and TRN (Huffman and Henson 1990; Ojima 1994) and the neurons of TRN project only to the ipsilateral dorsal thalamus. Thus the ipsilateral AC-TRN-MGB projections compose the inhibitory pathway. Morphologically, GABAergic terminals form synapses on every part of the relay neurons, with a higher portion at the proximal and intermediate parts of the neuron than the distal parts (Liu et al. 1995a). Although the corticothalamic terminals have their main contacts on the distal dendrites, direct corticothalamic excitation could be overcountbalanced by the strong GABAergic inhibition (Golsfani et al. 2001). As shown in Fig. 1, corticofugal inhibition has a much stronger effect than corticofugal excitation on the MGB neuron. The strong and lasting inhibitory effect could be attributed to the proximal contacts of TRN neurons on MGB neurons.

**Functional implications of corticofugal inhibitory pathways**

It is widely accepted that the TRN plays a major role in modulating the transfer of information between thalamus and cortex. The TRN receives excitatory input from collaterals of both thalamic and cortical neurons, whereas in this study, we focused on the corticofugal inhibitory pathways. Our results suggest that the inhibitory corticothalamic pathway is via TRN instead of IC. The majority of the excitatory inputs to the TRN neurons are derived from the cerebral cortex (Liu and Jones 1999), indicating that the corticofugal fibers to TRN neurons modulate the excitability of these neurons (Xu et al. 2007). Although other species might have higher percentages of interneurons in MGB, virtually all TRN neurons in many species (bat, cat, guinea pig, mice, monkey, rabbit, and humans) were GABAergic (Arcelli et al. 1997). TRN neurons extend dendrites within the thin reticular sheet, thus enabling them to receive projections from a wide cortical region and project to widespread areas in the ventroposterior nucleus of the thalamus (Liu et al. 1995b).

The ventral division of the MGB has been established as the recipient of the most direct ascending auditory pathway (Burton and Jones 1976; Jones 1985; Winer and Laure 1987). Previous studies have found that corticofugal axons from the auditory cortex gave rise to small and giant terminals in the thalamus (Ojima 1994; Rouiller and Welker 1991). Giant GABAergic terminals have been found mainly in the MGl and MGm, but not in the central part of MGv in cats (Winer et al. 1999). The mean diameter of GABAergic terminals in the MGd labeled with IC-injected tracer was 0.75 ± 0.41 μm, whereas that without IC-injected tracer was 0.99 ± 0.74 μm (Bartlett et al. 2000), implying that the giant GABAergic terminals in the MGd were likely from the TRN and might be associated with corticofugal inhibition (Xiong et al. 2004). Therefore the corticofugal inhibition through TRN mainly targets not in the core region of the MGv. The selectively inhibition highlights the possible role of TRN in corticofugal gating or even suppression of the ascending information. The central MGv is known as the strictly auditory information conveying subdivision. Thus restricting or interruption of the non-MGv inputs might enable AC rapidly recognize the ongoing acoustic events and dynamically control the influence of nonauditory inputs on the transmission of auditory information even attention shift.

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