GABA-Mediated Modulation of the Discharge Pattern and Rate-Level Function of Two Simultaneously Recorded Neurons in the Inferior Colliculus of the Big Brown Bat, *Eptesicus Fuscus*

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Abstract

Neurons in the central nucleus of the inferior colliculus (IC) receive excitatory and inhibitory inputs from both lower and higher auditory nuclei. Interaction of these two opposing inputs shapes response properties of IC neurons. In this study, we examine the interaction of excitation and inhibition on the responses of two simultaneously recorded IC neurons using a probe and a masker under forward masking paradigm. We specifically study whether a sound that serves as a probe to elicit responses of one neuron might serve as a masker to suppress or facilitate the responses of the other neuron. For each pair of IC neurons, we deliver the probe at the best frequency (BF) of one neuron and the masker at the BF of the other neuron and vice versa. Among 33 pairs of IC neurons recorded, this forward masking produces response suppression in 29 pairs of IC neurons and response facilitation in 4 pairs of IC neurons. The degree of suppression decreases with recording depth, sound level and BF difference between each pair of IC neurons. During bicuculline application, the degree of response suppression decreases in the bicuculline-applied neuron but increases in the paired neuron. Our data indicate that the forward masking of responses of IC neurons observed in this study is mostly mediated through GABAergic inhibition which also shapes the discharge pattern of these neurons. These data suggest that interaction among individual IC neurons improves auditory sensitivity during auditory signal processing.

Key Words: bat, bicuculline, discharge pattern, facilitation, inferior colliculus, masker, probe, rate-level function, suppression

Introduction

In the auditory pathway, the central nucleus of the inferior colliculus (IC) receives and integrates excitatory and inhibitory inputs from many lower auditory nuclei as well as from the auditory cortex (1, 2, 15, 16, 44, 45, 48). The predominant inhibitory inputs to the IC are either GABAergic, which originates extrinsically and intrinsically, or glycinergic, which originates extrinsically (12, 39, 43). Many studies have shown that the interplay between excitation and GABAergic and/or glycinergic inhibition shapes auditory response properties and multi-parametric selectivity of IC neurons (*e.g.*, duration, frequency,

amplitude, direction, *etc*)(6, 7, 13, 18, 20, 22, 23, 27, 28, 29-31, 32, 49, 50, 52, 55). In these studies, the role of GABA- or glycine-mediated inhibition in shaping the discharge patterns and multi-parametric selectivity of IC neurons has been examined before and during iontophoretic application of bicuculline and strychnine which are antagonists for $GABA_A$ and glycine receptors, respectively (3, 8).

Alternatively, many studies have examined the interaction of excitation and inhibition on auditory temporal processing in the IC using a probe (excitatory tone) and a masker (inhibitory tone) under forward masking paradigm. In the frequency domain, these studies show that IC neurons typically have inhibitory areas on one or both flanks of the excitatory frequency tuning curves (FTC) (11, 13, 19, 32, 46, 47, 54, 55). Inhibition of auditory responses only occurs when both excitatory and inhibitory tones are presented within a certain temporal window. Inhibitory tone decreases the number of impulses, lengthens the response latency, and sharpens the excitatory FTCs of IC neurons. Furthermore, the degree of inhibition increases with increasing inhibitory tone duration and intensity but decreases with increasing excitatory tone intensity (13, 33, 34).

We recently studied the effect of excitation-inhibition interaction on the responses of two simul-taneously recorded IC neurons of the big brown bat, *Eptesicus fuscus* (25). We specifically examined whether a sound that served as a probe to elicit response of one neuron might serve as a masker to suppress the responses of the other neuron. We observed that when a masker was delivered within the excitatory FTC of one IC neuron, the response of the other neuron was either suppressed or facilitated. We also observed that the area of suppression and facilitation of a neuron was always within the excitatory FTC of the other neuron. However, the neural mechanism underlying the suppression or facilitation of response of these IC neurons was not determined.

As an extension of this study, we determined the effect of interaction of excitation and GABAergic inhibition on the responses of two simultaneously recorded IC neurons in amplitude domain using the same forward masking paradigm. Specifically, we studied the discharge rate, discharge pattern and rate-level function (RLF) of each neuron before and during application of bicuculline to one of the paired neurons.

Materials and Methods

As in previous studies (26), the flat head of a 1.8 cm nail was glued onto the exposed skull of each of the 7 bats (2 males, 5 females, 15-26 g body weight, b.w.). Nembutal anesthetized bats (45-50 mg/kg b.w.) with acrylic glue and dental cement one or two days before the recording session. Exposed tissue was treated with an antibiotic (neosporin, Morris Plains, NJ, USA) to prevent inflammation. During the recording session, the bat received the neuroleptanalgesic, Innovar-Vet (fentanyl 0.08 mg/kg b.w., droperidol 4 mg/kg b.w. Washing Crossing, NJ, USA) and was placed inside a bat holder (made of wire mesh) which was suspended in an elastic sling inside a sound-proof room (temperature 28°-30°C). The ceiling and inside walls of the room were covered with 3-inch convoluted polyurethane foam to reduce echoes. A local anesthetic (lidocaine, Mount Holly, NC, USA) was applied to the open wound area. After orienting the bat with its eye-snout line pointed to 0° in azimuth and 0° in elevation of the frontal auditory space, its head was immobilized by fixing the shank of the nail into a metal rod with a set-screw. Small holes were then bored in the skull above the IC for insertion of a 3M KCl glass electrode and a three-barrel electrode to record auditory responses of two IC neurons and for iontophoretic application of bicuculline to one neuron. The recording depth of each neuron was read from the scale of each microdrive (Frederick Haer & Co, David-Kopf, Tujunga, CA, USA). An indifferent electrode (silver wire) was placed at the nearby temporal muscles. Each bat was used in 1 to 5 recording sessions on separate days and each recording session typically lasted for 4-7 hours. The experiments were conducted in compliance with NIH publication No. 85-23, "Principles of Laboratory Animal Care" and with the approval of the Institutional Animal Care and Use Committee of the University of Missouri-Columbia.

Two independently controlled sound stimulation systems were used for this study. Sound generation in each system was the same as in previous studies (26). Briefly, continuous sine waves from an oscillator (KH model 1200, Brochton, MA, USA) were formed into tone pulses by a homemade tone burst generator (electronic switch) driven by a stimulator (Grass S88, West Warwick, RI, USA). Tone pulses produced by both systems were then combined with a custom-made mixer after passing through a decade attenuator (HP 350D, Palo Alto, CA, USA). They were then amplified (KH 7500, Brochton, MA, USA) before being fed to a small condenser loudspeaker (AKG model CK 50, Northridge, CA, USA, 1.5 cm diameter, 1.2 g) that was placed 23 cm away from the bat and 30° contralateral to the recording site. The loudspeaker was calibrated with a 1/4 inch microphone (B & K 4135, Nærum, Denmark) placed at the bat's ear using a measuring amplifier (B & K 2607, Nærum, Denmark). The output of the loudspeaker was expressed in dB SPL referred to 20 μPa root mean square. A frequency response curve was plotted for the loudspeaker for each sound stimulation system to determine the

maximum available stimulus level at each frequency.

Upon isolation of an IC neuron with a 4 ms tone (0.5 ms rise-decay times, at 2 pps) and a 3 M KCl glass electrode (impedance: 5-10 MΩ), its best frequency (BF) and minimum threshold (MT) were determined by changing the frequency and level of sound stimuli. The MT was defined as the sound level at which the probability of response to BF sounds was 50%. The number of impulses of this neuron in response to a BF sound at 10 dB above its MT (abbreviated as the 10-dB probe) was obtained as the control response. A three-barrel electrode (see below) was placed at least 200 µm away from the 3 M KCl electrode and was advanced to isolate a second IC neuron using a second set of sound stimulation system. After determining the BF and MT of this second neuron, a 4 ms BF sound set at 20-dB above the neuron's MT (abbreviated as the 20-dB masker) was delivered 4 ms prior to the 10-dB BF probe. When the 20-dB masker affected the control response of the first neuron, the probe-masker gap was adjusted to the optimal interval (range: 1.5 to 12 ms, average: 3.78 ± 2.2 ms) so that the 20-dB masker decreased or increased the control response of the first neuron by at least 20%. However, when the 20-dB masker did not affect the control response of the first neuron, the second neuron was abandoned. The three-barrel electrode was then advanced to isolate another neuron and the experimental procedures were repeated.

When both neurons were isolated, each neuron's RLF was then plotted with the number of impulses obtained with BF sounds delivered at MT and 10 dB increments above the MT. For the first neuron, its RLF was plotted with and without the presentation of a 20-dB masker (set at the 20-dB above the MT of the second neuron) before and during bicuculline application to the second neuron (conveniently called the applied neuron). For the applied (second) neuron, its RLF was plotted with and without the presentation of a 20-dB masker (set at 20-dB above the first neuron's MT) before and during bicuculline application. In sum, 7 RLFs were plotted (3 for the first neuron isolated by the 3 M KCl electrode and 4 for the applied neuron isolated by the three-barrel electrode). For convenience of description, these two neurons are reciprocally called the paired neurons.

Iontophoretic application of bicuculline to a recorded neuron has been described in previous studies (35, 36). Briefly, a three-barrel electrode (tip: 10-15 µm) was "piggybacked" to a 3 M KCl single-barrel electrode (tip: less than 1 µm; impedance: 5-10 MΩ) whose tip was extended about 10 µm from the tip of the three-barrel electrode. The 3 M KCl single-barrel recording electrode was used to record neural responses. One of the barrels of a three-barrel electrode was filled with bicuculline methiodide (10 mM in 0.16 M NaCl, pH 3.0). The bicuculline was prepared just prior to

each experiment and the electrode filled immediately before use. This bicuculline channel was connected *via* silver-silver chloride wire to a microiontophoresis constant current generator (Medical Systems Neurophore BH-2) that was used to generate and monitor iontophoretic currents. During bicuculline application, a 1 s pulse of +40 namp at 0.5 pps was applied for 1 min before data acquisition. The application current was changed to 10 namp during data acquisition. The other two barrels were filled with 1 M NaCl (pH 7.4), one of which was used as the ground and the other as the balanced barrel. The balance electrode was connected to a balance module. The retaining current was negative 8-10 namp. Bicuculline application was considered to have blocked $GABA_A$ receptors maximally for each neuron when three consecutive responses did not vary by more than 15% even at higher application current (60 namp).

Recorded action potentials were amplified (HP 465A, Palo Alto, CA, USA) and band-pass filtered (Krohn-Hite 3500, Brochton, MA, USA) before being sent to a window discriminator (WPI 121, Sarasota, FL, USA), an oscilloscope (Tektronix 5111, Wilsonville, OR, USA) and an audio monitor (Grass AM6, West Warwick, RI, USA). The output from the window discriminator was then sent to a computer (Gateway 2000, 486, Irvine, CA, USA) for acquisition of peri-stimulus-time (PST) histograms (bin width: 500 µs, sampling period: 100 ms) to 16 stimulus presentations. The PST histograms quantitatively describe a neuron's discharge pattern under different stimulation conditions. The total number of impulses in each PST histogram was used to quantify a neuron's response under each stimulation condition.

The values given in the text and in the figures were expressed as mean ± standard variation. The statistical significance of experimental effects was assessed using the repeated measures one-way or two-way ANOVA. In all cases, a difference at $P < 0.05$ was considered statistically significant. Analysis and plotting of the data were performed on the software of SigmaPlot 2000 and InStat (in Macintosh computer).

Results

Basic Response Properties

In total, 33 pairs of IC neurons were recorded at depths of 271-1139 µm with 79% at less than 800 µm. The recording site of each pair of IC neurons differed by 200 µm horizontally and by 5 to 727 µm vertically (68% > 100 µm, average: 231.1 ±186.9 µm). The BF of all 66 neurons ranged from 14.76 to 60.04 kHz (average: 30.12 ± 8.78 kHz) with most (75%) between 20 and 30 kHz. As in our previous studies (17, 41, 51), these neurons were tonotopically organized along
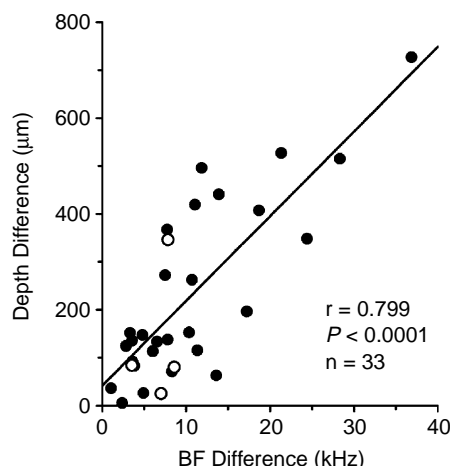
Fig. 1. A scatter plot showing the relationship between the difference in recording depth and in best frequency (BF) of 33 pairs of inferior collicular (IC) neurons. Respectively, solid and unfilled circles represent data obtained from neurons whose responses were suppressed and facilitated during forward masking. The solid line and r represent linear regression line and correlation coefficient for the distribution (P < 0.0001) (See text for details).

Table 1. The discharge patterns of 31 inferior collicular neurons determined before and during bicuculline application

Discharge pattern	predrug	bicuculline		
		P	PB	T
P	22 (71%)	7	10	5
PB	7 (23%)	0	5	2
T	2 (6%)	0	0	2
Total	31	7 (23%)	15 (48%)	9 (29%)

Numbers underlined indicate no change in discharge pattern. P: phasic responder, PB: phasic burster, T: tonic responder.
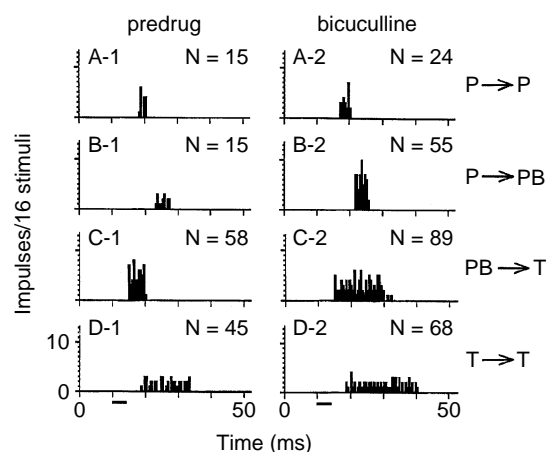

Fig. 2. Peri-stimulus-time (PST) histograms showing the discharge patterns of 4 representative IC neurons in response to a 4 ms BF sound delivered at 10 dB above the minimum threshold (MT) (abbreviated as the 10-dB probe) before (A-1, B-1, C-1, D-1) and during (A-2, B-2, C-2, D-2) bicuculline application. Note that bicuculline application did not change the discharge patterns of 2 neurons (A-1 vs. A-2, D-1 vs. D-2), but changed one phasic responder (P) into a phasic burster (PB, B-1 vs. B-2) and one phasic burster into a tonic responder (T, C-1 vs. C-2). N: number of impulses per 16 stimuli. The short horizontal bars below D-1 and D-2 represent sound stimuli. The BF (kHz), MT (dB SPL), latency (ms) and depth (μm) of these neurons were 29.12, 57, 8, 697 (A); 27.10, 59, 12, 465 (B); 60.04, 56, 6, 1121 (C); 47.17, 61, 8, 828 (D).

the dorsoventral axis of the central nucleus of the IC so that the BF increased with recording depth. The MT was between 26 and 72 dB SPL (average: 43.61 ± 10.01 dB SPL) with most (60%) lower than 50 dB SPL. The latency of these neurons in response to BF sounds at 20-dB above MT was between 5 and 16 ms (average: 8.33 ± 2.81 ms).

BF differences (kHz) between each pair of neurons ranged between 1.05 and 38.76 kHz (average: 10.21 ±8.35 kHz). They were < 5 kHz for 11 pairs (33.3%), between 5 and 10 kHz for 9 pairs (27.3%) and > 10 kHz for 13 pairs (39.4%) of neurons. The BF differences of these neurons were significantly correlated with recording depth differences such that paired neurons with small BF differences have small recording depth differences (Fig. 1, P < 0.0001).

Discharge Pattern and Bicuculline Application

Discharge patterns of all 66 neurons can be described as phasic responders (P) (n = 44, 66.7%), phasic bursters (PB) (n = 19, 28.8%) or tonic responders (T) (n = 3, 4.5%). When stimulated with 4 ms BF tones, phasic responders always discharged 1-3 impulses (Fig. 2A-1, B-1) whereas phasic bursters discharged 4-7 impulses (Fig. 2C-1). Tonic responders discharged impulses throughout or longer than the duration of presented tones (Fig. 2D-1).

The discharge patterns of 31 IC neurons were observed before and during bicuculline application. Bicuculline application produced an increase in the number of impulses of all 31 neurons. The application also changed the discharge patterns of 17 (55%) neurons from one type to another. For example, bicuculline application changed one phasic neuron into a phasic burster (Fig. 2B-1 vs. B-2) and one phasic burster into a tonic responder (Fig. 2C-1 vs. C-2). In sum, bicuculline application changed 2 phasic bursters into tonic responders, 15 phasic responders into 10 phasic bursters and 5 tonic responders (Table 1). As
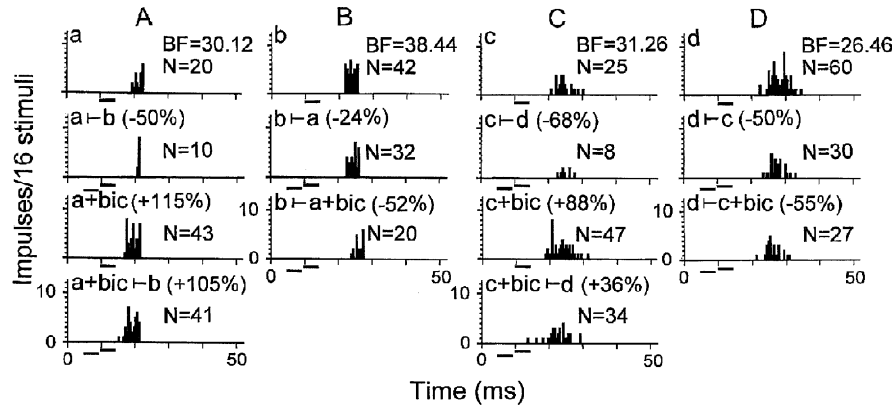
Fig. 3. The PST histograms showing the discharge patterns of two representative pairs of IC neurons whose probe-elicited responses were suppressed by a masker. The probe was the 4 ms 10-dB BF sound of the test neuron and the masker was the 4 ms BF sound of the paired neuron at 20 dB above the MT (abbreviated as the 20-dB masker). Aa, Bb, Cc, Dd: The discharge patterns of two pairs of IC neurons obtained with a 10-dB probe. AaI–b, BbI–a, CcI–d, DdI–c: the discharge pattern of each IC neuron obtained under forward masking paradigm in which the 10-dB probe was preceded by a 20-dB masker. Aa+bic, Cc+bic: The discharge patterns of neurons A and C in response to 10-dB probe during bicuculline application. A(a+bic)I–b, C (c+bic)I–d: The discharge patterns of neurons A and C obtained with a 10-dB probe during the presentation of a 20-dB masker and bicuculline application. BbI–(a+bic), DdI–(c+bic): The discharge patterns of neurons B and D obtained with a 10-dB probe during presentation of a 20-dB maker and bicuculline application to neurons A and C. The BF (kHz), MT (dB SPL), latency (ms) and recording depth (μm) of these four neurons were 30.12, 52, 9, 769 (A); 38.44, 56, 12, 698 (B); 31.26, 45, 11, 696 (C); 26.46, 36, 13, 549 (D) (see text for details).

a result, more IC neurons were phasic bursters and tonic responders during than before bicuculline application (77% *vs.* 29%). These observations are consistent with those reported in previous studies (18, 30, 35).

Suppression of Responses of IC Neurons by Masker before and during Bicuculline Application

When a 20-dB masker was presented prior to a 10-dB probe, responses of 29 (88%) pairs of IC neurons were suppressed and responses of 4 (12%) pairs were facilitated. The discharge patterns of two representative pairs of IC neurons whose responses were suppressed by a 20-dB masker are shown in Fig. 3. It is clear that the control response of each neuron was suppressed by a 20-dB masker to varying degrees (24 to 68 %, calculated by dividing the decrease in number of impulses by the control number of impulses; Fig. 3Aa *vs.* AaI–b, Bb *vs.* BbI–a, Cc *vs.* CcI–d, Dd *vs.* DdI–c).

When bicuculline application was applied to neurons A and C, the number of impulses increased by 115% and 88% (calculated by dividing the increase in the number of impulses by the control number of impulses; Fig. 3Aa *vs.* Aa+bic, from 20 to 43; Cc *vs.* Cc+bic, from 25 to 47), respectively. During bicuculline application, presentation of a 20-dB masker with the BF of the paired neuron decreased the number of impulses only slightly in neuron A (Fig. 3Aa+bic *vs.* Aa+bicI–b, decreased from 43 to 41, -4.6%) but substantially in
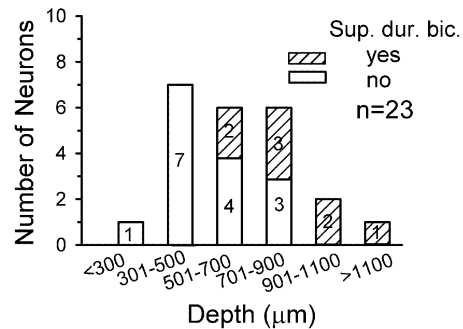

Fig. 4. Distribution of the recording depth (μm) of IC neurons whose responses were suppressed by a 20-dB masker only before but hardly during bicuculline application (unfilled) and those IC neurons whose responses were suppressed by a 20-dB masker both before and during bicuculline application (shaded).

neuron C (Fig. 3 Cc+bic *vs.* Cc+bicI–d, decreased from 47 to 34, -27.7%). However, the number of impulses of both neurons was still larger than the control number of impulses by 105% and 36%, respectively.

Among 23 bicuculline-applied neurons examined, further presentation of a 20-dB masker with the BF of the paired neuron decreased the number of impulses only slightly in 15 (65%) neurons (like as neuron A) but substantially in 8 (35%) neurons (like as neuron C). These 15 neurons were mostly recorded at upper IC (Fig. 4, unfilled) while the other 8 neurons were mostly recorded at deeper IC (Fig. 4, shaded).
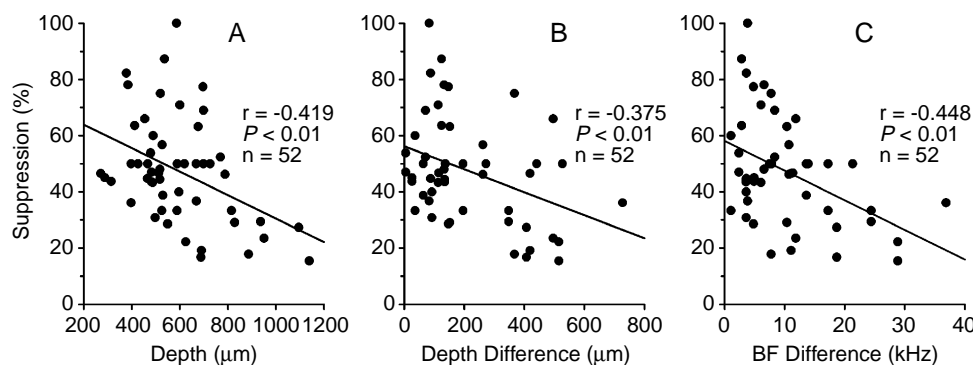
Fig. 5. Scatter plots showing percent suppression by a 20-dB masker in relation to the recording depth (A) and differences in recording depth (B) and BF (C) between each paired IC neurons. The solid line and r represent linear regression line and correlation coefficient for each distribution ($P < 0.001$).

Presentation of a 20-dB masker plus bicuculline application to neurons A and C decreased the number of impulses substantially in the paired neuron B (decreased from 32 to 20, -63%; Fig. 3BbI–a *vs.* BbI–a+bic) but only slightly in the paired neuron D (decreased from 30 to 27, -10%; Fig. 3D dI–c *vs.* DdI–c+bic). Among 27 paired IC neurons examined, further presentation of a 20-dB masker with the BF of bicuculline applied neuron decreased the number of impulses substantially in 23 (85%) paired neurons but only slightly in 4 (15%) paired neurons.

To determine how forward masking effect might be related to the BF and recording depth of all IC neurons, we obtained scatter plots of percent suppression in relation to recording depth and differences in recording depth and BF of all paired IC neurons. As shown in Fig. 5, linear regression analyses of these plots revealed that percent suppression significantly decreased with recording depth and differences in recording depth and BF of paired IC neurons (Fig. 5, A, B, C).

Suppression of Responses of IC Neurons by a Masker Is Level-Dependent

To determine the degree of forward masking in relation to stimulus level, we plotted the RLFs of IC neurons before and during the presentation of a 20-dB masker. The RLFs of a non-monotonic neuron and a monotonic IC neuron plotted before and during the presentation of a 20-dB maker are shown in Fig. 6. The number of impulses of the non-monotonic IC neuron increased with sound level to a maximum and decreased more than 25% thereafter while the number of impulses of the monotonic neuron increased with sound level (Fig. 6, A-1a, B-1a). Presentation of a 20-dB masker suppressed the responses of both neurons at all sound levels such that both RLFs lowered to varying degrees (Fig. 6, A-1a *vs.* b; B-1 a *vs.* b). The percent suppression (calculated by dividing the

difference in the number of impulses at each sound level obtained with and without the presentation of the 20-dB masker by the number of impulses obtained at each sound level) of both neurons was large at low sound level but decreased sharply within 20-30 dB above the MT (Fig. 6, A-2, B-2). As shown in Fig. 6A-3 and B-3, the average percent suppression of both types of neurons significantly decreased with sound level (One-way ANOVA, $P < 0.05$-0.0001).

Suppression of the RLF of IC Neurons by a Masker before and during Bicuculline Application

In this study, we plotted the RLF of 15 neurons with and without a 20-dB masker before and during bicuculline application. The RLF of 8 (53%) neurons elevated to varying degrees during bicuculline application (Fig. 7A-1, a *vs.* c). Presentation of a 20-dB masker with the BF of the paired neuron lowered the RLF of these neurons plotted both before and during bicuculline application (Fig. 7A-1, a *vs.* b, c *vs.* d). The percent suppression calculated both before and during bicuculline application was large at low sound level but sharply decreased to a plateau within 20-30 dB above the MT (Fig. 7, A-2, a,b). However, percent suppression was greater before than during bicuculline application at all sound levels (Fig. 7A-2, a *vs.* b). The average percent suppression of the RLF of these 8 neurons determined both before and during bicuculline application significantly decreased with sound level (Fig. 7A-3, One-way ANOVA, $P < 0.01$-0.001).

The RLF of the other 7 (47%) IC neurons also elevated to varying degrees during bicuculline application (Fig. 7B-1, a *vs.* c). However, presentation of a 20-dB masker with the BF of the paired neuron only lowered the RLF of these neurons before (Fig. 7B-1, a *vs.* b) but not during bicuculline application (Fig. 7B-1, c *vs.* d). As such, the percent suppression was large at low sound level and sharply decreased to
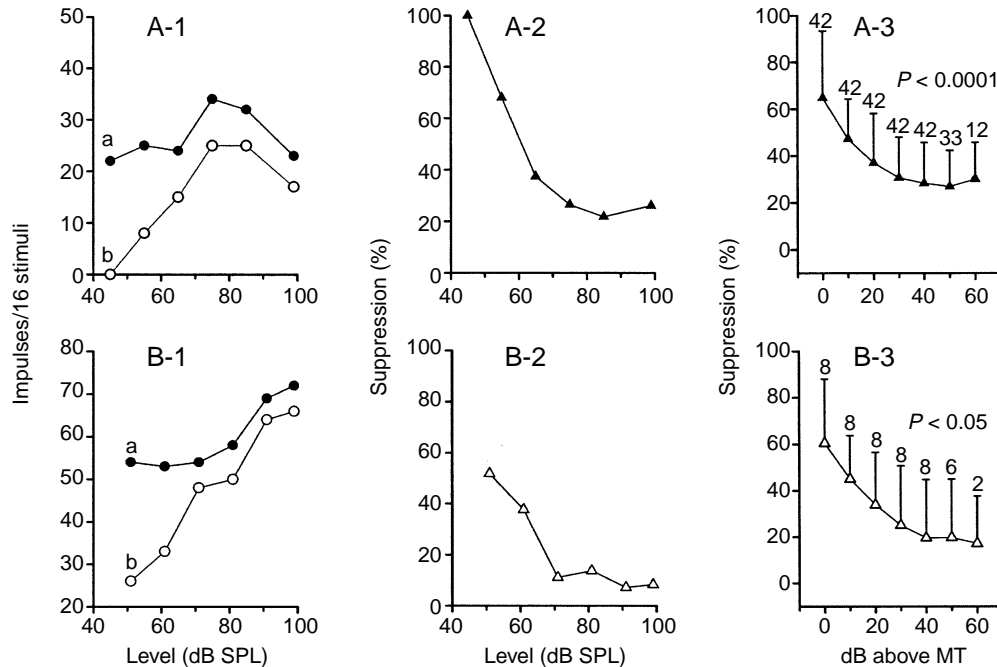
Fig. 6. A-1a, b, B-1a, b: The rate-level functions (RLF) of non-monotonic (A-1) and monotonic (B-1) IC neurons plotted with a BF tone before (filled circles, A-1a, B-1a) and during (unfilled circles, A-1b, B-1b) presentation of a 20-dB masker. A-2, B-2: Percent suppression of responses of the IC neurons by a 20-dB masker as a function of sound level. A-3, B-3: Average percent suppression of non-monotonic (filled triangles) and monotonic (unfilled triangles) IC neurons at each sound level. Each vertical bar represents half a standard deviation with the number of neurons studied shown atop. Repeated measures one-way ANOVA reveal significant differences among all data points ($P < 0.05$-0.0001).

a plateau at high sound level before bicuculline application (Fig. 7B-2a). However, the percent suppression was minimum at all sound levels during bicuculline application (Fig. 7B-2b). The average percent suppression for these 7 neurons decreased significantly with sound level only before but not during bicuculline application (Fig. 7B-3, One-way ANOVA, a *vs.* b, $P < 0.05$ *vs.* $P > 0.5$).

Suppression of the RLF of IC Neurons by a Masker before and during Bicuculline Application to the Paired IC Neurons

In this study, we also plotted the RLF of 27 IC neurons with and without a masker before and during bicuculline application to their paired neurons. Presentation of a 20-dB masker with the BF of the paired neuron lowered the RLF of all 27 neurons (Fig. 8A-1 a *vs.* b, B-1 a *vs.* b). During bicuculline application to the paired neuron, presentation of a 20-dB masker with the BF of the applied neuron further lowered the RLF of 23 (85%) neurons but hardly changed the RLF of the remaining 4 (15%) neurons (Fig. 8A-1, b *vs.* c; in contrast to B-1, b *vs.* c).

For those 23 neurons, the percent suppression by the 20-dB masker calculated both before and during

bicuculline application to the paired neurons was large at low sound level but decreased with stimulus level. However, percent suppression was smaller before than during bicuculline application to the paired neurons at all sound levels (Fig. 8A-2, a *vs.* b). The average percent suppression of the RLF of these 23 neurons determined before and during bicuculline application to their paired neurons varied significantly with sound level (Fig. 8A-3, a, b, Two-way ANOVA, $P < 0.0001$).

For those 4 neurons, the percent suppression by the 20-dB masker calculated both before and during bicuculline application to the paired neurons was also large at low sound level but was small at high stimulus level. However, percent suppression obtained before and during bicuculline application to the paired neurons was hardly different at all sound levels (Fig. 8B-2, a *vs.* b). The average percent suppression of the RLF of these 4 neurons determined both before and during bicuculline application to their paired neurons decreased significantly with increasing sound level (Fig. 8B-3, a,b, Two-way ANOVA, $P < 0.05$).

Facilitation of the RLF of IC Neurons by a Masker before and during Bicuculline Application

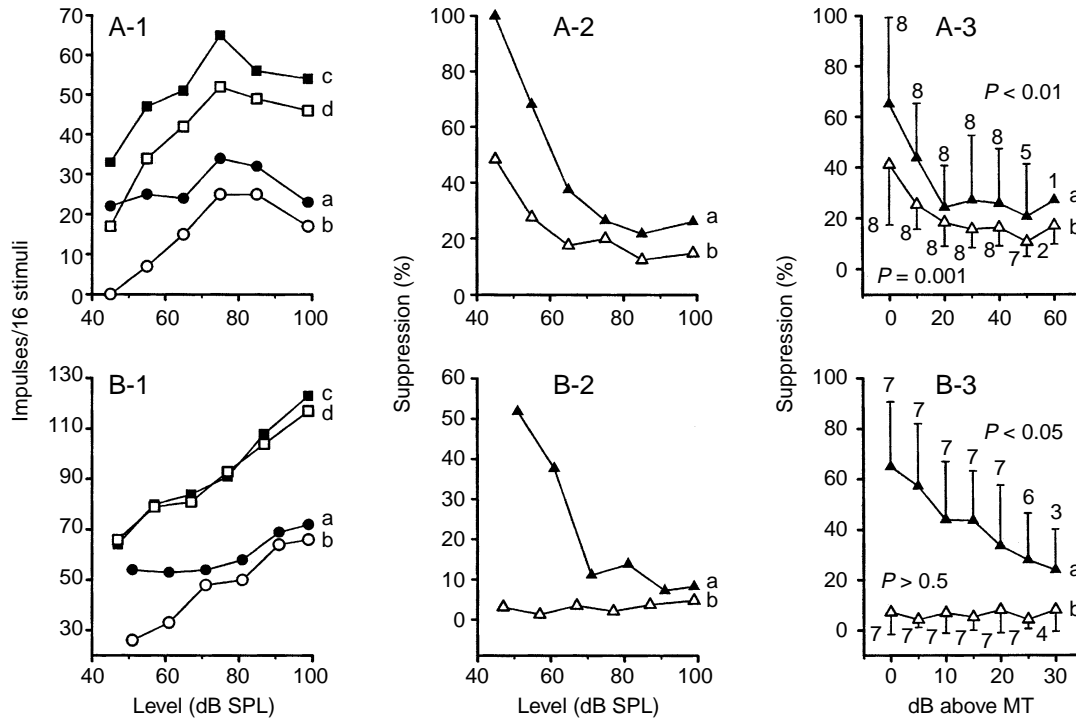The discharge patterns of two representative

Fig. 7. A-1, B-1: The RLFs of two IC neurons plotted with (unfilled circles and squares) and without (filled circles and squares) a 20-dB masker before (A-1, a *vs.* b, B-1, a *vs.* b) and during (A-1, c *vs.* d, B-1, c *vs.* d) bicuculline application. Note that the RLFs of both neurons greatly elevated during bicuculline application (A-1, a *vs.* c; B-1, a *vs.* c). However, presentation of a 20-dB maker during bicuculline application only lower the RLF of one neuron (A-1, c *vs.* d) but not the other neuron (B-1, c *vs.* d). A-2, B-2: Percent suppression of these two neurons as a function of sound level determined before (filled triangles, A-2a, B-2a) and during (unfilled triangles, A-2b, B-2b) bicuculline application. A-3 and B-3: Average percent suppression at each sound level determined before (filled triangles, A-3a, B-3a) and during (unfilled triangles, A-3b, B-3b) bicuculline application. Repeated measures one-way ANOVA revealed significant differences among data points in A-3a, A-3b and B-3a ($P < 0.01$-0.05) but not among data points in B-3b ($P > 0.5$). The BF (kHz), MT (dB SPL), latency (ms) and recording depth (µm) of these two neurons were 31.26, 45, 11, 696 (A); 44.36, 51, 6, 815 (B) (See text for details).

pairs of IC neurons whose number of impulses increased during presentation of a 20-dB masker are shown in Fig. 9. It is clear that the control number of impulses of each neuron increased to varying degrees by a 20-dB masker (18 to 43%, calculated by dividing the increase in number of impulses by the control number of impulses. Fig. 9Aa *vs.* a<−b, Bb *vs.* b<−a, Cc *vs.* c<−d, Dd *vs.* d<−c).

Bicuculline application increased the number of impulses of the applied neurons A and C by +83 and +131% (Fig. 9Aa *vs.* Aa+bic, Cc *vs.* Cc+bic). Presentation of a 20-dB masker with the BF of the paired neuron further increased the number of impulses only slightly in neuron A (from 64 to 67, +4.7%, Fig. 9 Aa+bic *vs.* Aa+bic <−b) but substantially in neuron C (from 30 to 40, +33%, Fig. 9 Cc+bic *vs.* Cc+bic <−d). As such, the number of impulses of both neurons was larger than the control number of impulses by 91% and 208 %, respectively.

As for the paired neurons that did not receive

bicuculline application, presentation of a 20-dB masker with the BF of the applied neuron increased the number of impulses by +18% in neuron B and +27% in neuron D (from 17 to 20 in Fig. 9B, b *vs.* b<−a, from 11 to 14 in Fig. 9, Dd *vs.* Dd<−c). The number of impulses further increased by +65% in neuron B and +7% in neuron D when bicuculine was applied to neurons A and C (from 20 to 33; Fig. 9Bb<−a *vs.* b<−a+bic, from 14 to 15; Fig. 9D, d<−c *vs.* 9Dd<−c+bic).

Fig. 10 shows the RLFs of two pairs of IC neurons whose responses were facilitated by the presentation of a 20-dB masker. The RAFs of the first pair of IC neurons elevated to varying degrees by a 20-dB masker (Fig. 10A-1, a *vs.* b, A-2, a *vs.* b). Bicuculline application increased the number of impulses and elevated the RLF of the applied neuron (Fig. 10A-1, a *vs.* c). However, presentation of a 20-dB masker only further elevated the RLF of the applied neuron but not its paired neuron (Fig. 10A-1, c *vs.* d; in contrast to A-2, b *vs.* c).
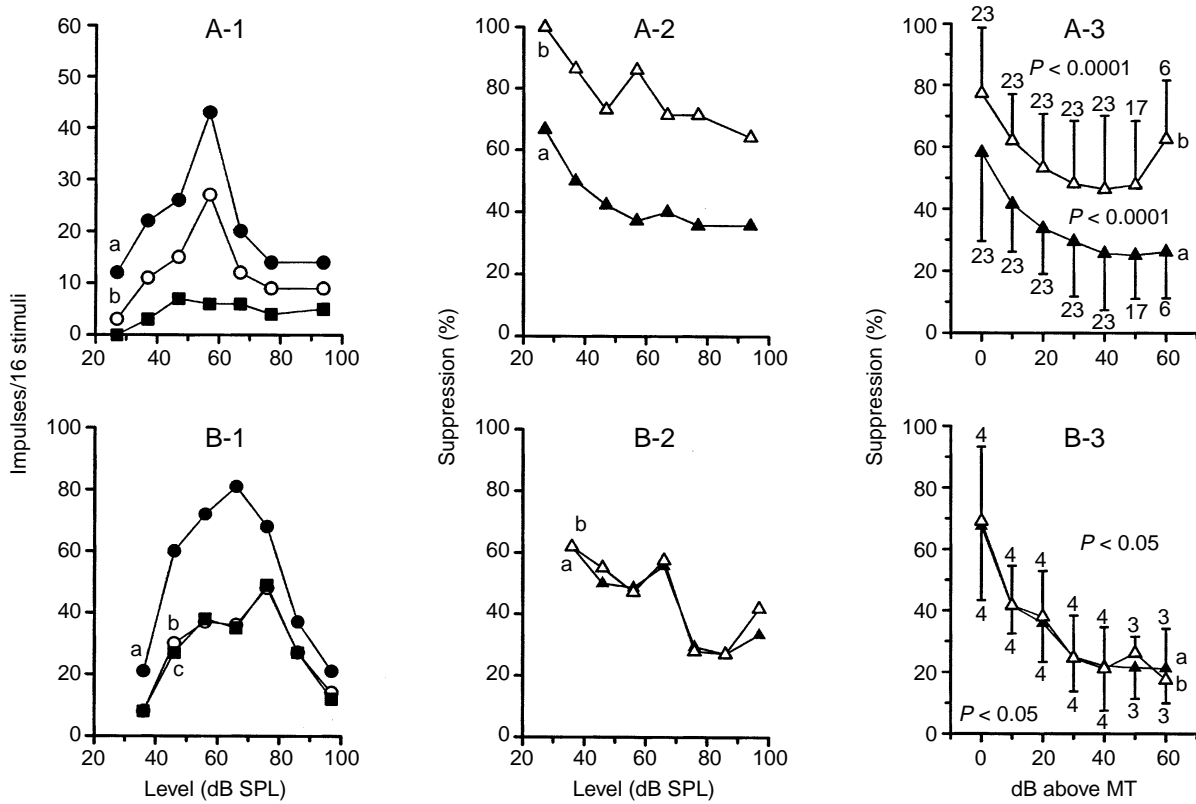
Fig. 8. A-1, B-1: The RLFs of two IC neurons plotted with (unfilled circles) and without (filled circles) a 20-dB masker before (A-1, a *vs.* b, B-1, a *vs.* b) and during (A-1, b *vs.* c, B-1b *vs.* c) bicuculline application to their paired neurons. Note that presentation of a 20-dB maker during bicuculline application to the paired neuron only further lower the RLF of one neuron (A-1, b *vs.* c, unfilled circles *vs.* flled squares) but not the other neuron (B-1, b *vs.* c). A-2, B-2: Percent suppression of these two neurons at each sound level determined before (filled triangles, A-2a, B-2a) and during (unfilled triangles, A-2b, B-2b) bicuculline application to the paired neurons. A-3 and B-3: Average percent suppression as a function of sound level determined before (filled triangles, A-3a, B-3a) and during (unfilled triangles, A-3b, B-3b) bicuculline application. Repeated measures tested by two-way ANOVA revealed significant differences among all data points ($P < 0.05$-0.0001). The BF (kHz), MT (dB SPL), latency (ms) and recording depth (µm) of this pair of neurons were 34.28, 48, 9, 529 (A-1); 31.26, 45, 11, 696 (A-2); 20.68, 27, 15, 466 (B-1); 26.46, 36, 13, 549 (B-2) (see text for details).

The RLFs of the second pair of IC neurons also elevated to varying degrees by a 20-dB masker (Fig. 10B-1, a *vs.* b, B-2, a *vs.* b). Bicuculline application increased the number of impulses and elevated the RLF of the applied neuron (Fig. 10B-1, a *vs.* c). However, presentation of a 20-dB masker hardly affected the already elevated the RLF of the applied neuron but further elevated the RLF of its paired neuron (Fig. 10B-1, c *vs.* d in contrast to B-2, b *vs.* c).

Discussion

Discharge Pattern and Bicuculline Application

Using the big brown bat, *Eptesicus fuscus*, as the mammalian model auditory system, we specifically studied how the interaction of excitation and GABAergic inhibition shapes the temporal response properties and

RLF of two simultaneously recorded IC neurons using bicuculline application. We observed that bicuculline application increased the number of impulses, discharge duration, elevated RLFs and changed discharge patterns of most IC neurons (Figs. 2, 3, 7-10); similar to previous studies in bats, cats, guinea pigs, rats (10, 14, 18, 20, 27, 29-31, 35, 47, 52).

However, the effect of bicuculline application on the temporal response properties varied among individual IC neurons (Fig. 2). A previous study has suggested that at least three separate GABAergic circuits are responsible for shaping the discharge patterns, RLFs and dynamic regulation of excitability of most IC neurons (42). For example, it has been suggested that phasic responders and phasic bursters are due to different time course of GABAergic inhibition following the neuron's excitatory responses to sound stimulation (38). Partial or complete removal
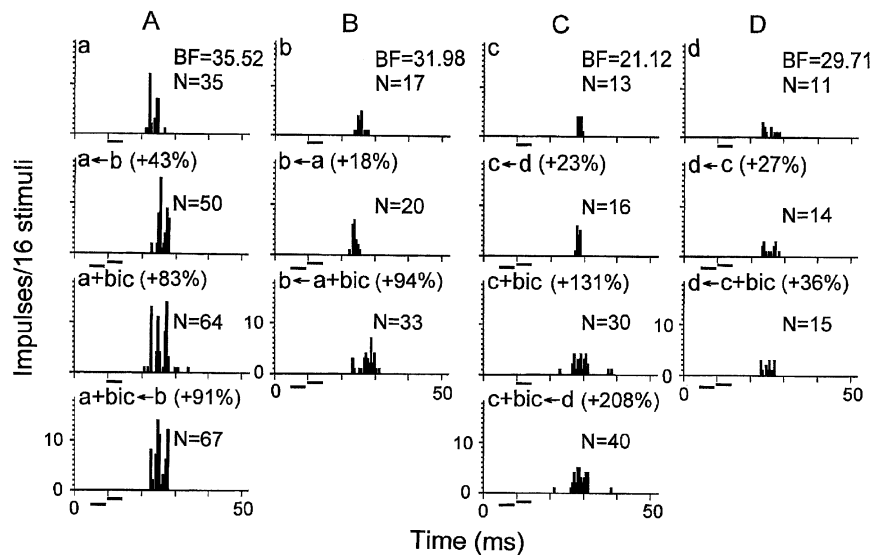
Fig. 9. The PST histograms showing the discharge patterns of two representative pairs of IC neurons whose responses were facilitated by a 20-dB masker. Aa, Bb, Cc, Dd: The discharge patterns of two pairs of IC neurons in response to a 10-dB probe. Aa<−b, Bb<−a, Cc<−d, Dd<−c: The discharge patterns of these neurons obtained with a 10-dB probe and a 20 dB masker. Aa+bic, Cc+bic: The discharge patterns of neurons A and C in response to a 10-dB probe during bicuculline application. A (a+bic)<− b, C(c+bic)<−d: The discharge patterns of neurons A and C obtained with a 10-dB probe BF and a 20-dB masker during bicuculline application. Bb<−(a+bic), Dd<−(c+bic): The discharge patterns of neurons B and D obtained with a 10-dB probe and a 20-dB maker during bicuculline application to neurons A and C. The BF (kHz), MT (dB SPL), latency (ms) and recording depth (μm) of these four neurons were 35.52, 53, 10, 710 (A); 31.98, 47, 13, 626 (B); 21.12, 33, 16, 602 (C); 29.71, 47, 13, 682 (D).
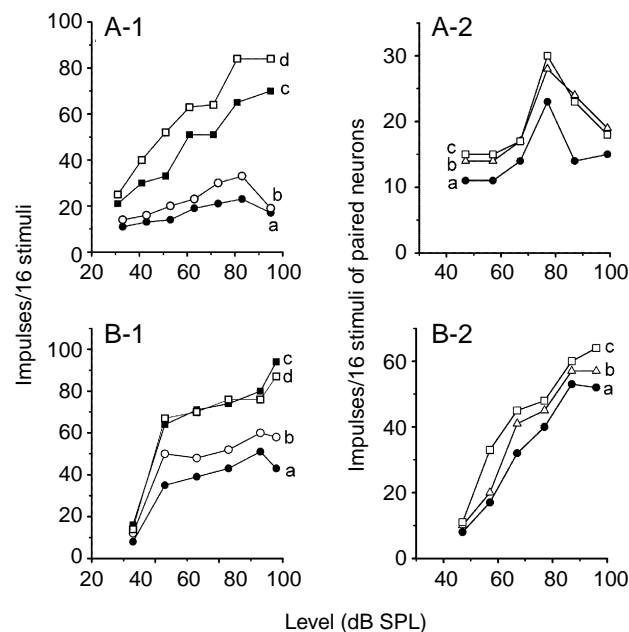

Fig. 10. A-1 and B-2: The RLFs of two IC neurons plotted with (filled circles and squares) and without (unfilled circles and squares) a 20-dB masker before (A-1, a vs. b, B-1, a vs. b) and during (A-1, c vs. d, B-1c vs. d) bicuculline application. The RLFs of both neurons greatly elevated during bicuculline application (A-1, a vs. c; B-1, a vs. c). Presentation of a 20-dB masker elevated the RLF of both neurons before bicuculline application (A-1, a vs. b, B-1, a vs. b). However, presentation of a 20-dB masker during bicuculline application only further elevated the RLF of one neuron (A-1, c vs. d) but not the other neuron (B-1, c vs. d). A-2 and B-2: The RLFs of the paired neurons plotted before (A-2a, B-2a, filled circles) and during presentation of a 20-dB masker with (A-2a, B-2c, unfilled squares) and without (A-2b, B-2b, unfilled triangles) bicuculline application to neurons A-1 and B-1. The BF (kHz), MT (dB SPL), latency (ms) and recording depth (μm) of these four neurons were 21.12, 33, 16, 16, 602 (A-1); 29.71, 47, 13, 682 (A-2); 35.52, 53, 10, 710 (B-1); 31.98, 47, 13, 626 (B-2)(See text for details).

of GABAergic inhibition upon bicuculline application would allow the phasic responders and phasic bursters to respond to large or entire portion of stimulus duration. As a result, the phasic responders and phasic bursters change into phasic bursters or tonic responders (Fig. 2B-1 *vs.* B-2, C-1 *vs.* C-2, Table 1).

One the other hand, the reasons that bicuculline application did not affect the discharge patterns of 14 IC neurons (Fig. 2A-1 *vs.* A-2, D-1 *vs.* D-2, Table 1 numbers underlined) may be due to the following. Firstly, intrinsic membrane properties shape the discharge patterns of these neurons. Therefore, GABAergic inputs may modulate the excitatory response of these neurons but not their discharge patterns. Secondly, these IC neurons may receive GABAergic inhibitory inputs from neurons with tonic activity which do not respond to sound stimuli and only modulate the overall excitability of these IC neurons. Thirdly, these IC neurons simply inherited the discharge patterns from lower-order auditory nucleus so that bicuculline application would have little affect on their discharge patterns. For example, some neurons in the ventral nucleus of the lateral lemniscus (VNLL) discharged phasically to sound stimulation (9). Conceivably, the discharge patterns of IC neurons that receive their inputs directly from these VNLL neurons will not be modified during bicuculline application. Fourthly, these neurons may receive predominant glycinergic rather than GABAergic inhibitory inputs, so their discharge patterns may change during strychnine rather than bicuculline application. The fact that strychnine application changes the discharge pattern of IC neurons has been reported previously (28, 30, 31).

GABAergic Inhibition Underlies Suppression of Responses of IC Neurons by a Masker

Previous studies have shown that the number of impulses of auditory neurons to a sound pulse is decreased if the sound pulse is presented shortly after or before another one (*i.e.* forward and backward temporal masking, 4, 5, 21, 22, 33, 37, 40). In agreement with these studies, we observed that the number of impulses of most IC neurons decreased and the RLF lowered during the presentation of a 20-dB masker (Figs. 3, 6). In addition, we observed that bicuculline application increased the number of impulses and elevated the RLFs (Figs. 2, 3, 7-9). These observations suggest that GABAergic inhibition is one of the underlying mechanisms for this forward masking of response of these paired IC neurons.

Consonant with our previous study (25), the degree of suppression of responses of IC neurons by a 20-dB masker decreased significantly with sound level (Fig. 6). This level-dependent suppression might be due to the fact that the strength of GABAergic inhibition

evoked by the 20-dB masker was counterbalanced by progressively increased strength of excitation with sound levels. In other words, a progressively increase in the strength of excitation decreased the effectiveness of GABAergic inhibition evoked by the 20-dB masker. Similar observations have been reported for GABA-mediated corticofugal modulation of auditory sensitivity of IC neurons (24, 53).

We observed that the degree of suppression by the 20-dB masker with the BF of paired neurons was greater for most bicuculline applied neurons before than during bicuculline application at all sound levels (Fig. 7A-2). Conceivably, bicuculline application had increased the excitability of the applied neurons so the GABAergic inhibition evoked by the 20-dB masker with the BF of paired neuron became less effective to suppress the response of the applied neurons. In parallel to this finding, increased excitability of the applied neurons during bicuculline application also inevitably increased the strength of the GABAergic inhibition evoked by the 20-dB masker with the BF of the applied neurons. Hence, the degree of suppression by the 20-dB masker was greater for most paired neurons during than before bicuculline application to the applied neurons (Fig. 8, A-2, A-3).

A previous study of this bat species indicates that neurons with $GABA_A$ receptors are mostly distributed in the dorsomedial region but are sparsely distributed in the ventrolateral region which is mostly distributed with neurons containing glycine receptors (12). In the present study, we showed that suppression of responses of IC neurons by the 20-dB masker is most likely mediated through GABAergic inhibition (Figs. 2, 3, 7-9). The combined observations in these two studies suggest that neurons at upper IC would receive more GABAergic inhibitory inputs than neurons at the deeper IC. If this were true, the strength of GABAergic inhibition evoked by the 20-dB masker would progressively decrease along the spatial distribution gradient of $GABA_A$ receptors within the IC. Then it follows that the degree of GABA-mediated masking of responses of IC neurons would progressively decrease along the dorso-ventral axis of the IC. Indeed, this speculation is evident by our observation that suppression of the responses of IC neurons by a 20-dB masker significantly decreased with the recording depth (Fig. 5A).

In this study, we showed that response suppression by a 20-dB masker was observed only before but not during bicuculline application for one group of IC neurons (*e.g.*, Figs. 3A, 3 D, 7B-1 8B-1) but was observed both before and during bicuculline application for another group of IC neurons (*e.g.*, Figs. 3B, 3C, 7A-1, 8A-1). We also showed that the former group of IC neurons was mostly recorded at upper IC while the latter group of IC neurons was mostly recorded at

deeper IC (Fig. 4). Conceivably, presentation of a 20-dB masker could no longer evoke GABAergic inhibition for neurons in the upper IC because bicuculline application had removed the GABAergic inhibition of these neurons. Conversely, a 20-masker may still suppress the responses of neurons in the deeper IC through glycinergic inhibition even though bicuculline application might have removed GABAergic inhibition of these neurons. Future works are needed to confirm this speculation.

Previous studies show that sharpening of frequency tuning and spatial selectivity of IC neurons by a masker becomes less effective with increasing differences in the stimulus frequency between the masker and probe (32, 54). Consonant with these studies, we observed that suppression of responses of IC neurons by a masker also significantly decreased with BF differences between each pair of IC neurons (Fig. 5C). This observation has been explained by the fact that IC neurons are tonotopically organized such that the inhibition of neurons with small BF differences arrives earlier with less attenuation than neurons with large BF differences whether the origin of the inhibitory inputs originates extrinsically or intrinsically (54). Since we observed that differences in recording depth and BF between each pair of IC neurons are closely correlated (Fig. 1), then it follows that degree of suppression of responses of IC neurons by a 20-dB masker would also significantly decrease with differences in the recording depth (Fig. 5B).

Facilitation of Responses of IC Neurons by a Masker

In this study, we only recorded 4 pairs of IC neurons whose responses were facilitated by a masker (Figs. 9, 10). We do not know if this small sample size was an indication of predominant role of inhibition in signal processing in the IC or was simply due to sampling bias. Conceivably, facilitation of responses of these IC neurons by a 20-dB masker may be a result of removal or lesson of inhibition of these IC neurons through the activation of an inhibitory interneuron. Alternatively, it may be the result of recruitment of stronger excitation than inhibition to these IC neurons.

Possible Biological Significance of the Present Study

Previous studies have examined the interaction of excitation and inhibition on auditory temporal processing in the IC using a probe and a masker (11, 13, 14, 19, 32, 46, 47, 54). In these studies, only one neuron is recorded each time and the probe is typically the BF sound of the recorded IC neuron while an off-BF sound is used as a masker. Different from these studies, we examined the interaction of excitation and GABAergic inhibition on the responses of two simultaneously recorded IC neurons using forward masking paradigm. We specifically studied whether a sound that served as a probe to elicit response of one neuron might serve as a masker to modulate the responses of the other neuron. For this reason, this procedure provides us an opportunity to examine how a BF sound of one neuron might affect the response of the other neuron in amplitude domain.

We showed that the auditory response of an IC neuron was either suppressed or facilitated by a 20-dB masker whose frequency was the BF of the paired neuron (Figs. 3, 9). The suppression or facilitation of the response of one IC neuron by excitation of the paired neuron would inevitably increase the difference in the degree of excitation and therefore the response magnitude between the paired neurons. Because the area of suppression and facilitation of a neuron is always within the excitatory FTC of the paired neuron (25), all these observations suggest that the paired IC neurons are closely correlated during signal processing. Because IC neurons differ in response latency and MT, suppression or facilitation of responses of different sets of IC neurons would occur in different time windows and sound levels during signal analysis. Conceivably, when stimulated with complex sounds, individual sound frequencies would excite the response of several sets of IC neurons while suppresses or facilitates the responses of other sets of IC neurons. As a result, auditory selectivity of different sets of IC neurons to a specific signal parameter would be improved through response suppression while overall sensitivity would be enhanced through response facilitation in different time windows.

Although we studied the interaction of excitation and GABAergic inhibition on temporal response properties and RLF of IC neurons of the big brown bat, the data obtained from this study may be applicable to other mammalian species as well since the auditory system of the bat is fundamentally similar to that of other mammals. For example, the effect of interaction of excitation and inhibition on central auditory responses observed in this study may serve as the underlying mechanism for the psychophysical phenomena of temporal masking.

References

1. Adams, J.C. Ascending projections to the inferior colliculus. *J.*

Comp. Neurol. 183: 519-538,1979.

2. Aitkin, L. The Auditory Midbrain: Structure and Function in the Central Auditory Pathway. Clifton, NJ: Humana Press, 1986.

3. Bormann, J. Electrophysiology of GABA$_A$ and GABA$_B$ receptor subtypes. *Trend Neurosci*. 11: 112-116, 1988.

4. Brosch, M. and Schreiner, C.E. Time course of forward masking tuning curves in cat primary auditory cortex. *J. Neurophysiol*. 77: 923-943, 1997.

5. Calford, M.B. and Semple, M.N. Monaural inhibition in cat auditory cortex. *J. Neurophysiol*. 73: 1876-1891, 1995.

6. Casseday, J.H., Ehrlich, D. and Covey, E. Neural tuning for sound duration: role of inhibitory mechanisms in the inferior colliculus. *Science* 264: 847-850, 1994.

7. Casseday, J.H., Ehrlich, D. and Covey, E. Neural measurement of sound duration: control by excitatory-inhibitory interaction in the inferior colliculus. *J. Neurophysiol*. 84: 1475-1487, 2000.

8. Cooper, J.R., Bloom, F.E. and Roth, R.H. The biomedical basis of neuropharmacology. Oxford University Press, New York, 1982.

9. Covey, E. and Casseday, J.H. The monaural nuclei of the lateral lemniscus in an echolocating bat: parallel pathways for analyzing temporal features of sound. *J. Neurosci*. 11: 3456-3470, 1991.

10. Ebert, U. and Ostwald, J. GABA alters the discharge pattern of chopper neurons in the ventral cochlear nucleus. *Hear. Res*. 91: 160-166, 1995.

11. Ehret, G. and Merzenich, M.M. Complex sound analysis (frequency resolution, filtering and spectral integration) by single units of the inferior colliculus of the cat. *Brain Res. Rev*. 13: 139-163, 1988.

12. Fubara, B.M., Casseday, J.H., Covey, E. and Schwartz-Bloom, R.D. Distribution of GABA$_A$, GABA$_B$ and glycine receptors in the central auditory system of the big brown bat, *Eptesicus fuscus. J. Comp. Neurol*. 369: 83-92, 1996.

13. Fuzessery, Z.M. and Feng, A.S. Frequency selectivity in the anuran medulla: excitatory and inhibitory tuning properties of single neurons in the dorsal medullary and superior olivary nuclei. *J. Comp. Physiol. A* 150: 107-119, 1983.

14. Fuzessery, Z.M. and Hall, J.C. Role of GABA in shaping frequency tuning and creating FM sweep selectivity in the inferior colliculus. *J. Neurophysiol*. 76: 1059-1073, 1996.

15. Herbert, H., Aschoff, A. and Ostwald, J. Topography of projections from the auditory cortex to the inferior colliculus in the rat. *J. Comp. Neurol*. 304: 103-122, 1991.

16. Huffman, R.F. and Henson, O.W. The descending auditory pathways and acoustico-motor systems: connections with the inferior colliculus. *Brain Res. Rev*. 15: 295-323, 1990.

17. Jen, P.H.S. and Schlegel, P. A. Auditory physiological properties of the neurons in the inferior colliculus of the big brown bat, *Eptesicus fuscus. J. Comp. Physiol. A* 147: 351-363, 1982.

18. Jen, P.H.S. and Feng, R.B. Bicuculine application affects pulse duration tuning characteristics of bat inferior collicular neurons. *J. Comp. Physiol. A* 184: 185-194, 1999.

19. Jen, P.H.S. and Zhang, J.P. Corticofugal regulation of excitatory and inhibitory frequency tuning curves of bat inferior collicular neurons. *Brain Res*. 841: 184-188, 1999.

20. Jen, P.H.S. and Zhang, J.P. The role of GABAergic inhibition on direction-dependent sharpening of frequency tuning in bat inferior collicular neurons. *Brain Res*. 862: 127-137, 2000.

21. Jen, P.H.S. and Zhou, X.M. Temporally patterned pulse trains affect duration tuning characteristics of bat inferior collicular neurons. *J. Comp. Physiol. A* 185: 471-478, 1999.

22. Jen, P.H.S. and Wu, C.H. The role of GABAergic inhibition in shaping the response size and duration selectivity of bat inferior collicular neurons to sound pulses in rapid sequences. *Hear. Res*. 202: 222-234, 2005.

23. Jen, P.H.S. and Wu, C.H. Duration organization selectivity in the inferior colliculus of the big brown bat, *Eptesicus fuscus. Brain Res*. 1108: 76-87, 2006.

24. Jen, P.H.S., Chen, Q.C. and Sun, X.D. Corticofugal regulation of

auditory sensitivity in bat inferior colliculus. *J. Comp. Physiol. A* 183: 683-697, 1998.

25. Jen, P.H.S., Wu, F.J. and Chen, Q.C. The effect of two-tone stimulation on responses of two simultaneously recorded neurons in the inferior colliculus of the big brown bat, *Eptesicus fuscus. Hear. Res*. 174: 281-289, 2002.

26. Jen, P.H.S., Sun, X.D., Chen, D.M. and Teng, H.B. Auditory space representation in the inferior colliculus of the FM bat, *Eptesicus fuscus. Brain Res*. 419: 7-18, 1987.

27. Jen, P.H.S., Wu, C.H., Luan, R.H. and Zhou, X.M. GABAergic inhibition contributes to pulse repetition rate-dependent frequency selectivity in inferior colliculus of the big brown bat, *Eptesicus fuscus. Brain Res*. 948: 159-164, 2002.

28. Klug, A., Park, T.J. and Pollak, G.D. Glycine and GABA influence binaural processing in the inferior colliculus of the mustache bat. *J. Neurophysiol*. 74: 1701-1713, 1995.

29. Koch, U. and Grothe, B. GABAergic and glycinergic inhibition sharpens tuning for frequency modulations in the inferior colliculus of the big brown bat. *J. Neurophysiol*. 80: 71-82, 1998.

30. LeBeau, F.E., Rees, A. and Malmierca, M.S. Contribution of GABA- and glycine-mediated inhibition to the monaural temporal response properties of neurons in the inferior colliculus. *J. Neurophysiol*. 75: 902-919, 1996.

31. LeBeau, F.E., Malmierca, M.S. and Rees, A. Iontophoresis *in vivo* demonstrates a key role for GABA$_A$ and glycinergic inhibition in shaping frequency response areas in the inferior colliculus of guinea pig. *J. Neurosci*. 21: 7303-7312, 2001.

32. Lu, Y. and Jen, P.H.S. GABAergic and glycinergic neural inhibition in excitatory frequency tuning of bat inferior collicular neurons. *Exp. Brain Res*. 14: 331-339, 2001.

33. Lu, Y. and Jen, P.H.S. Interaction of excitation and inhibition in inferior collicular neurons of the big brown bat, *Eptesicus fuscus. Hear. Res*. 169: 140-150, 2002.

34. Lu, Y., Jen, P.H.S. Binaural interaction in the inferior colliculus of the big brown bat, *Eptesicus fuscus. Hear. Res*. 177: 100-110, 2003.

35. Lu, Y., Jen, P.H.S. and Zheng, Q.Y. GABAergic disinhibition changes the recovery cycle of bat inferior colliculus neurons. *J. Comp. Physiol. A* 181: 331-341, 1997.

36. Lu, Y., Jen, P.H.S. and Wu, M. GABAergic disinhibition affects the responses of bat inferior collicular neurons to temporally patterned sound pulses. *J. Neurophysiol*. 79: 2303-2315, 1998.

37. Moriyama, T., Hou, T.Z., Wu, M. and Jen, P.H.S. Responses of inferior collicular neurons of the FM bat, *Eptesicus fuscus*, to pulse trains with varied pulse amplitudes. *Hear. Res*. 79: 105-114, 1994.

38. Nelson, P.G. and Erulkar, S.D. Synaptic mechanisms of excitation and inhibition in the central auditory pathway. *J. Neurophysiol*. 26: 908-923, 1963.

39. Oliver, D.L., Winer, J.A., Beckius, G.E. and Saint Marie, R.L. Morphology of GABAergic neurons in the inferior colliculus of the cat. *J. Comp. Neurol*. 340: 27-42, 1994.

40. Phillips, D.P., Hall, S.E. and Hollett, J.L. Repetition rate and signal level effects on neuronal responses to brief tone pulses in cat auditory cortex. *J. Acoust. Soc. Am*. 85: 2537-2549, 1989.

41. Pinheiro, A.D., Wu, M. and Jen, P.H.S. Encoding repetition rate and duration in the inferior colliculus of the big brown bat, *Eptesicus fuscus. J. Comp. Physiol. A* 169: 69-85, 1991.

42. Pollak, G.D. and Park, T.J. The effects of GABAergic inhibition on monaural response properties of neurons in the mustache bat's inferior colliculus. *Hear. Res*. 65: 99-117, 1993.

43. Roberts, R.C. and Ribak, C.E. An electron microscopic study of GABAergic neurons and terminals in the central nucleus of the inferior colliculus of the cat. *J. Neurocytol*. 16: 333-345, 1987.

44. Saldana, E., Feliciano, M. and Mugnaini, E. Distribution of descending projections from primary auditory neocortex to inferior colliculus mimics the topography of intracollicular projections. *J. Comp. Neurol*. 371: 15-40, 1996.

45. Shneiderman, A. and Oliver, D.L. EM autoradiographic study of

the projections from the dorsal nucleus of the lateral lemniscus: A possible source of inhibitory inputs to the inferior colliculus. *J. Comp. Neurol*. 286: 28-47, 1989.

46. Suga, N. Sharpening of frequency tuning by inhibition in the central auditory system: tribute to Yasuji Katsuki. *Neurosci. Res*. 2: 287-299, 1995.

47. Vater, M., Habbicht, H., Kossl, M. and Grothe, B. The functional role of GABA and glycine in monaural and binaural processing in the inferior colliculus of horseshoe bats. *J. Comp. Physiol. A* 171: 541-553, 1992.

48. Winer, J.A. Decoding the auditory corticofugal systems. *Hear. Res*. 211: 1-8, 2006.

49. Wu, C.H. and Jen, P.H.S. The role of GABAergic inhibition in shaping duration selectivity of bat inferior collicular neurons determined with temporally patterned sound trains. *Hear. Res*. 215: 55-65, 2006.

50. Wu, C.H. and Jen, P.H.S. GABA-mediated echo duration selectivity of inferior collicular neurons of *Eptesicus fuscus*, determined

with single pulses and pulse-echo pairs. *J. Comp. Physiol. A* 192: 985-1002, 2006.

51. Wu, M. and Jen, P.H.S. Encoding of acoustic stimulus intensity by inferior collicular neurons of the big brown bat, *Eptesicus fuscus*. *Chinese J. Physiol*. 34: 145-155, 1991.

52. Yang, L., Pollak, G.D. and Resler, C. GABAergic circuits sharpen tuning curves and modify response properties in the mustache bat inferior colliculus. *J. Neurophysiol*. 68: 1760-1774, 1992.

53. Zhou, X.M. and Jen, P.H.S. Corticofugal inhibition compresses all types of rate intensity functions of inferior collicular neurons in the big brown bat. *Brain Res*. 881: 62-68, 2000.

54. Zhou, X.M. and Jen, P.H.S. Neural inhibition sharpens auditory spatial selectivity of bat inferior collicular neurons. *J. Comp. Physiol. A* 186: 389-398, 2000.

55. Zhou, X.M. and Jen, P.H.S. The role of GABAergic inhibition in shaping directional selectivity of bat inferior collicular neurons determined with temporally patterned sound trains. *J. Comp. Physiol. A* 188: 815-826, 2002.