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Involvement of GABA-Mediated Inhibition in Shaping the Frequency Selectivity of Neurons in the Inferior Colliculus of the Big Brown Bat, *Eptesicus fuscus*

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Abstract

In central auditory signal processing, neural inhibition plays an important role in sharpening the selectivity of auditory neurons. The present study examines the involvement of GABA-mediated inhibition in shaping the frequency selectivity of neurons in the bat inferior colliculus (IC) using forward masking paradigm and bicuculline application. At each study session, we recorded two IC neurons with a pair of electrodes and reciprocally studied whether a sound that served as a probe to elicit response of one neuron might serve as a masker to affect the frequency tuning curve (FTC) of the other paired neuron. Among the 33 pairs of IC neurons recorded, this forward masking paradigm produces sharpening of the FTC in 29 (88%) pairs of IC neurons and broadening of the FTC in 4 (12%) pairs of IC neurons. The degree of sharpening of FTC decreases with recording depth as well as with the difference in the best frequency and recording depth between each pair of IC neurons. Although bicuculline application broadens the FTC of all IC neurons, forward masking still produces sharpening of the FTC in most IC neurons. These data suggest that population of IC neurons are highly correlated during frequency analysis such that frequency selectivity of some groups of IC neurons is improved through inhibition while the spectrum of frequency sensitivity of other groups of IC neurons is enhanced through excitation. Biological significance of these data relevant to acoustic signal processing is discussed.

Key Words: bat, GABA, inferior colliculus, frequency selectivity, impulse-frequency tuning curve

Introduction

In auditory physiology, processing of auditory information carried by sounds has been traditionally explained by neural inhibition and excitation through divergent and convergent projections within the auditory systems (24). For example, in the ascending auditory pathway, the central nucleus of the inferior colliculus (IC) receives and integrates excitatory and inhibitory inputs from many lower auditory nuclei (1, 2, 4, 22) as well as from the auditory cortex (9, 10, 23, 26). Neurotransmitters that mediate the inhibitory inputs are gamma-aminibutyric acid (GABA) or glycine (7, 22). Previous studies show that the GABA-mediated inhibition contributes significantly to auditory temporal processing and shapes multi-parametric selectivity (*e.g.*, duration, frequency, amplitude, direction, *etc.*) of IC neurons (5, 11-13,

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15-21, 27, 28, 30).

In a recent paper, the authors reported their study on the interaction of excitation and GABA-mediated inhibition on the responses of 33 pairs of IC neurons of the big brown bat, *Eptesicus fuscus* in amplitude domain using forward masking paradigm and bicuculline application (25). A pair of micro-electrodes was used to simultaneously record two IC neurons and specifically examined whether a sound that served as a probe to elicit response of one neuron might serve as a masker to modify the responses of the paired neuron as done in a previous study (14). The authors showed that when a masker was delivered at the best frequency (BF) of one IC neuron, the response of the other paired neuron was either suppressed or facilitated. The authors also showed that GABA-mediated inhibition shaped the discharge pattern and rate-level function of both IC neurons, suggesting that the signal processing in each pair of IC neurons was closely correlated. In the present paper, the role of GABA-mediated inhibition in shaping the frequency selectivity of these 33 pairs of IC neurons was presented.

Materials and Methods

The procedures for surgery of the bat were the same as described in the authors'previous paper (25). Briefly, the flat head of a 1.8 cm nail was glued onto the exposed skull of each of 7 (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. During recording, the bat was administered the neuroleptan-algesic Innovar-Vet (Fentanyl 0.08 mg/kg b.w. Droperidol 4 mg/kg b.w.), and placed inside a bat holder (made of wire mesh) that was suspended in an elastic sling inside a double-wall sound-proof room (temperature 28°-30°C). After fixing the bat's head with a set screw, small holes (100~200 μm diameters) were then bored in the skull above the IC for insertion of a 3M KCl glass electrode (impedance: 5-10 MΩ) 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 h. 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. The acoustic stimuli (4 ms with 0.5 ms rise-decay times delivered at 2 pps) were generated with an oscillator (KH model 1200, TekNet Electronics, Inc., Alpharetta, GA, USA) and a homemade electronic switch driven by a stimulator (Grass S88, Astro-Med Inc., W. Warwick, RI, USA). These stimuli were then amplified after passing through a decade attenuator (HP 350D, Hewlett-Packard Company, Palo Alto, CA, USA) before they were fed to a small condenser loudspeaker (AKG model CK 50, 1.5 cm diameter, 1.2 g) that was placed 23 cm away from the bat and 30° contralateral to the recording site in the horizontal plane. Calibration of the loudspeaker was performed with a 1/4 inch microphone (B & K 4135, B & K Components, Ltd., New York, NY, USA) placed at the position of the bat's head during recording using a measuring amplifier (B & K 2607, B & K Components, Ltd.). The output of the loudspeaker was expressed in dB SPL in reference to 20 μPa root mean square. A frequency response curve was plotted for the loud-speaker for each sound stimulation system to deter-mine the maximal available stimulus level at each frequency.

Upon isolation of an IC neuron with 4 ms sounds (0.5 ms rise-decay times), its threshold at each responsive frequency was audio-visually determined. At the threshold, the pulse amplitude on average elicited 50% response probability from the neuron. The frequency that elicited the neuron's response with the lowest sound amplitude was defined as the BF. The threshold at the BF was defined as the minimum threshold (MT). The neuron's number of impulses 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 £gm away from the 3M 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 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 m) such that the 20-dB masker decreased or increased the control response of the first neuron by at least 20%. However, if 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 impulse frequency tuning curve (impulse-FTC) was measured with the number of impulses elicited by 4

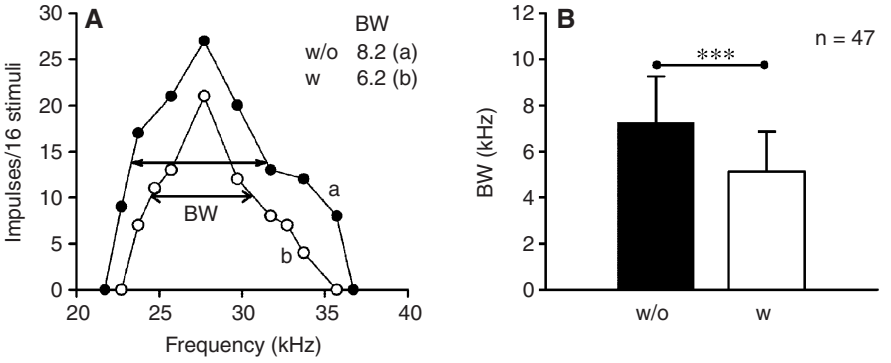

Fig. 1. A: The impulse-FTC of a representative IC neurons plotted with the number of impulses obtained with a 4 ms best frequency (BF) sound delivered at 20 dB above its minimum threshold (MT) at several selected frequencies with (w, Ab) or without (w/o, Aa) the presentation of a masker which was a BF sound set at 20 dB above the MT of the paired neuron. The sharpness of each impulse-FTC is expressed by the bandwidth (BW, shown by double-headed horizontal line) at 50% maximum at the BF. B: The average BW of the impulse-FTC of 47 IC neurons obtained with (w, unfilled bar) and without (w/o, filled bar) the presentation of a 20-dB masker (paired *t*-test, ***$P < 0.001$). The BF (kHz), MT (dB SPL), recording depth (μm) and latency (ms) of this neuron were 27.71, 48, 517, 5.

ms sounds delivered at 20 dB above the MT at several selected frequencies. For the first neuron, its impulse-FTC was measured 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 (the second) neuron, its impulse-FTC was measured with and without the presentation of a 20-dB masker (set at 20-dB above the MT of the first neuron) before and during bicuculline application. In sum, 7 impulse-FTCs (3 for the first neuron isolated by the 3M KCl electrode and 4 for the applied neuron isolated by the three-barrel electrode) were measured. For convenience of description, these two neurons are reciprocally called the paired neurons.

The sharpness of each impulse-FTC was expressed by the bandwidth of the impulse-FTC at 50% of maximal response (abbreviated as a neuron's BW, See Fig. 1). The BWs of the impulse-FTC of IC neurons obtained under different stimulation conditions were quantitatively examined and statistically compared using repeated measures ANOVA or Student's paired *t*-test at $P < 0.05$.

The involvement of GABA-mediated inhibition in shaping the frequency selectivity of IC neurons was studied by comparing the impulse-FTC of IC neurons with and without the presentation of a 20-dB masker before and during iontophoretic application of bicuculline, which is an antagonist for $GABA_A$ receptor (3). Iontophoretic application of bicuculline to a recorded neuron has been described in previous studies (20, 21). 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 +10-40 nA at 0.5 pps was applied for 1 min before data acquisition. The application current was changed to 15 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 10-15 nA. 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 nA).

Recorded action potentials were amplified (HP 465A, Polo 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-stimulustime (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.

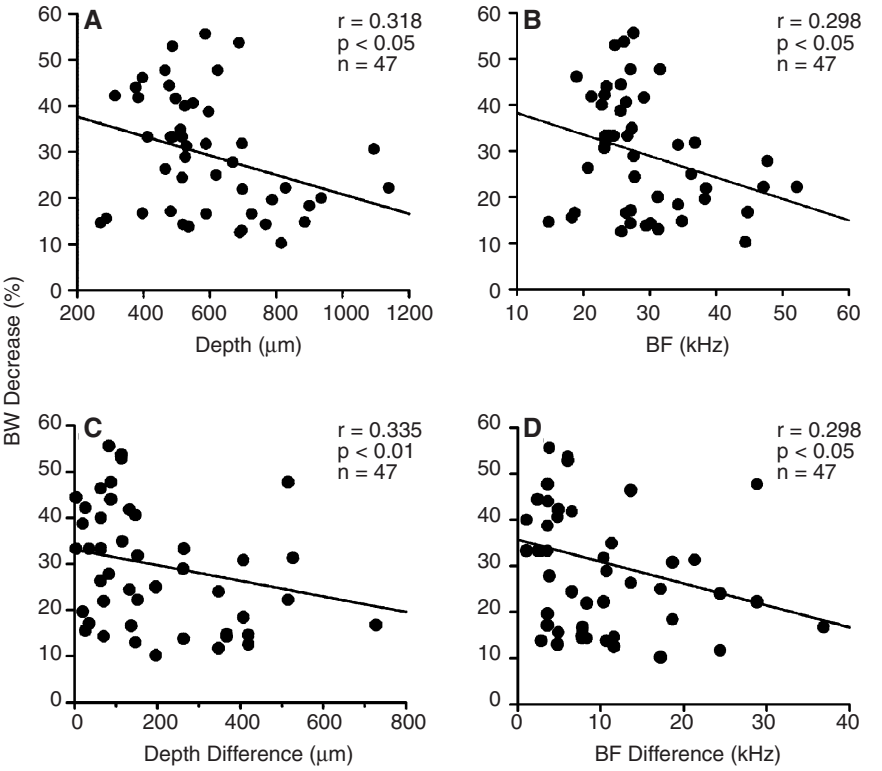

Fig. 2. Scatter plots showing the percent decrease in BW by a 20-dB masker in relation to the recording depth (A), BF (B) and the difference in recording depth (C) and BF (D) between each pair of IC neurons. n: number of neurons studied. The solid line and r represent linear regression line and correlation coefficient for each plot. p: significance level.

The total number of impulses in the PST histogram was used to quantify a neuron's response and to plot the impulse-FTC under each stimulation condition. Analysis and plotting of the impulse-FTC were performed using SigmaPlot 2,000 and InStat (in Macintosh computer).

Results

The Effects of Forward Masking on the Impulse-FTC of IC Neurons

As reported previously (25), the 33 pairs of IC neurons were tonotopically organized within the IC. They were recorded at depths of 271-1139 μm with MT between 26 and 72 dB SPL (average: 43.61 ± 10.01 dB SPL) and BF between 14.76 and 60.04 kHz (average: 30.12 ± 8.78 kHz). When a 20-dB masker was presented prior to a 10-dB probe, the impulse-FTC was sharpened in 29 (88%) pairs of IC neurons but was broadened in 4 pairs of IC neurons (12%).

The impulse-FTC of a representative IC neuron measured before and during the presentation of a 20-dB masker is shown in Fig. 1A. Clearly, the presentation of a 20-dB masker greatly sharpened the neuron's impulse-FTC as evident by a decrease in the BW from 8.2 to 6.2 kHz (24%, calculated by dividing the decrease in BW by the control BW). Among the 47 neurons studied, the average BW was significantly decreased from 7.25 ± 2.02 kHz to 5.13 ± 1.73 kHz by the 20-dB masker (Fig. 1B, *t*-test, $P < 0.001$). The percent decrease in BW in these 47 neurons by a 20-dB masker ranged between 10.2 and 55.6% (average 29.0 ± 13.0%).

Because IC neurons were recorded at different depths and had different BFs, the authors examined if sharpening of impulse-FTC of IC neurons by a 20-dB masker was correlated with recording depth and BF. Linear regression analyses of the scatter plots of percent decrease in the BW of 47 IC neurons in relation to the recording depth and BF revealed that sharpening of the impulse-FTC by a 20-dB masker significantly decreased with recording depth and BF (Fig. 2, A and B). Further analyses showed that the degree of sharpening of impulse-FTC of IC neurons by a 20 dB-masker also significantly decreased with difference in recording depth and BF between each pair of IC neurons (Fig. 2, C and D).

Sharpening of Impulse-FTC of IC Neurons by a Masker before and during Bicuculline Application

Bicuculline application broadened the impulse-FTC of 14 applied IC neurons to varying degrees

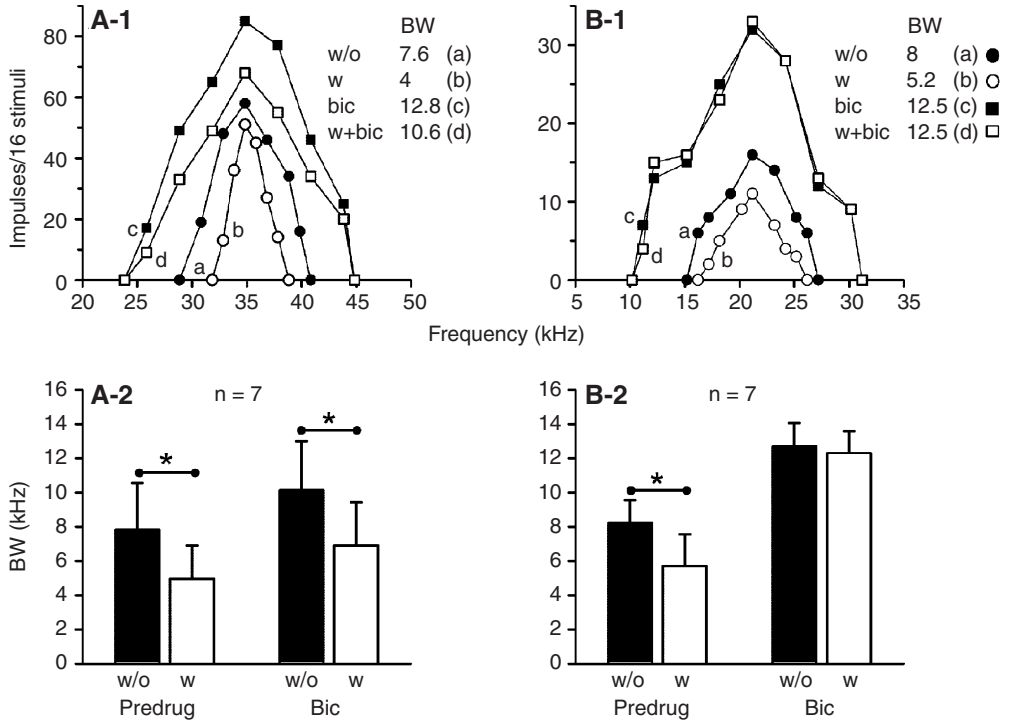

Fig. 3. A-1, B-1: The impulse-FTC of two representative IC neurons plotted under different stimulation conditions: before (filled circles, A-1a, B-1a) and during the presentation of a 20-dB masker (unfilled circles, A-1b, B-1b); with (bic, filled squares, A-1c, B-1c) bicuculline application and with bicuculline application plus a 20-dB masker (w+bic, unfilled squares, A-1d, B-1d). A-2,B-2: The average BW of these two types of IC neurons determined with (unfilled bar) or without (filled bar) the presentation of a 20-dB masker before (predrug) and during bicuculline application (Bic). paired *t*-test, $*P < 0.05$. The BF (kHz), MT (dB SPL), recording depth (μm) and latency (ms) of these two neurons were 34.84, 35, 686, 10 (A); 21.18, 36, 454, 7 (B).

(Fig. 3A-1a *vs*. A-1c; B-1a *vs*. B-1c). The presentation of a 20-dB masker affected the impulse-FTC of these 14 bicuculline-applied IC neurons in two ways.

In one way, the presentation of a 20-dB masker sharpened the impulse-FTC of 7 IC neurons both before and during bicuculline application (Fig. 3A-1a *vs*. A-1b; A-1c *vs*. A-1d). These IC neurons were mostly recorded at deeper IC (> 500 μm). The average BW of these IC neurons obtained before and during a 20-dB masker presentation differed significantly both before and during bicuculline application (Fig. 3A-2, *t*-test, Predrug and Bic, $P < 0.05$). In the other way, the presentation of a 20-dB masker sharpened the impulse-FTC of the other 7 IC neurons only before (Fig. 3B-1a *vs*. B-1b) but not during (Fig. 3B-1c *vs*. B-1d) bicuculline application. These IC neurons were mostly recorded at upper IC (< 500 μm). The average BW of these IC neurons obtained before and during a 20-dB masker presentation differed significantly only before but not during bicuculline application (Fig. 3B-2, *t*-test, Predrug *vs*. Bic, $P < 0.05$ *vs*. $P > 0.05$).

Sharpening of Impulse-FTC of IC Neurons by a Masker before and during Bicuculline Application to the Paired IC Neurons

The presentation of a 20-dB masker also affected the sharpness of the impulse-FTC of 25 IC neurons in two ways when their paired IC neurons received bicuculline application. For 19 IC neurons, sharpening of their impulse-FTCs by a 20-dB masker was further strengthened when the paired IC neurons received bicuculline application (Fig. 4A-1a *vs*. A-1b *vs*. A-1c). The average BW of the impulse-FTC of these 19 IC neurons obtained before and during presentation of a 20-dB masker with and without bicuculline application to their paired IC neurons differed significantly (Repeated measures one-way ANOVA, $P < 0.001$). A Student-Newman-Keuls multiple comparison post test showed significant difference between each set of BW ($P < 0.01$-0.001).

The presentation of a 20-dB masker also greatly sharpened the impulse-FTCs of other 6 IC neurons to varying degrees (Fig. 4B-1a *vs*. B-1b). However, the impulse-FTC of these 6 neurons was hardly sharpened by the 20-dB masker when their paired IC neurons received bicuculline application (Fig. 4B-1b *vs*. B-1c). The average BW of these 6 IC neurons obtained under three stimulation conditions differed significantly (Repeated measures one-way ANOVA, $P < 0.01$). A Student-Newman-Keuls multiple comparison post test showed that the average BW of these 6 IC

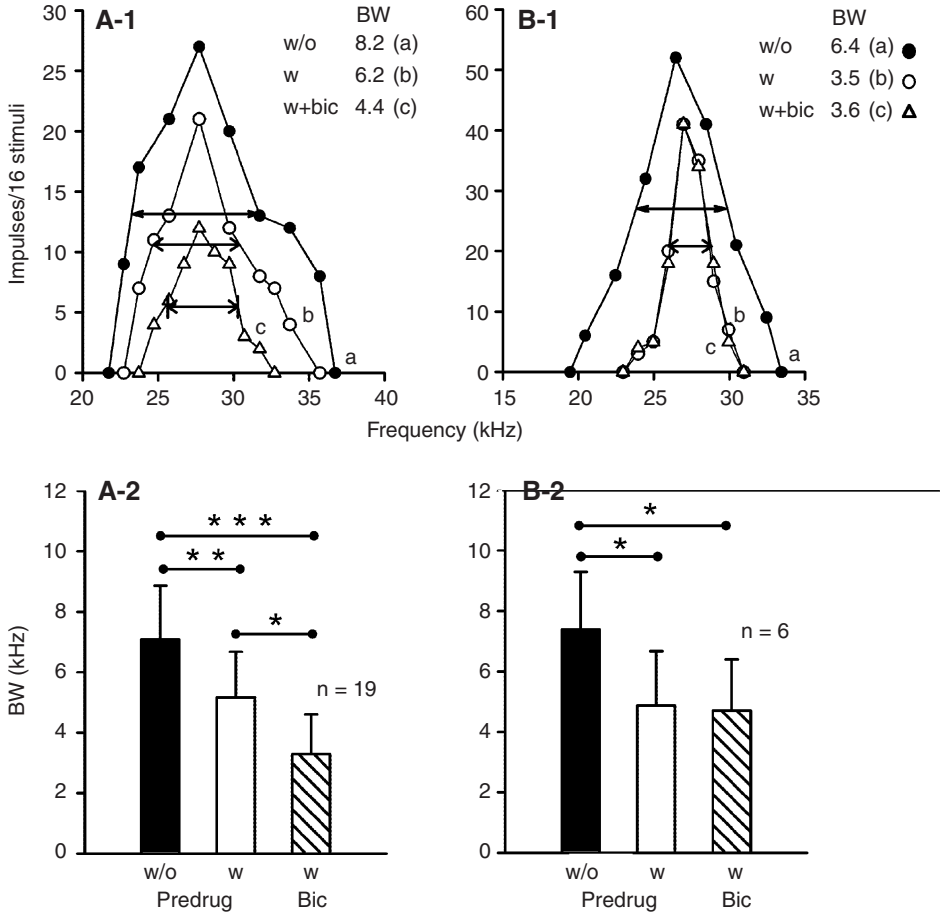

Fig. 4. A-1, B-1: The impulse-FTC of two representative IC neurons plotted under different stimulation conditions: before (filled circles, A-1a, B-1a) and during the presentation of a 20-dB masker with (w+bic, unfilled circles, A-1c, B-1c) and without (w/o, unfilled triangles, A-1b, B-1b) bicuculline application to the paired IC neurons. A-2, B-2: The average BW of these two types of IC neurons determined with (w, unfilled bar) or without (w/o, filled bar) the presentation of a 20-dB masker before (predrug) and during bicuculline application (Bic) to the paired IC neurons. Repeated measures one-way ANOVA ***$P < 0.001$; **$P < 0.01$: *$P < 0.05$. The BF (kHz), MT (dB SPL), recording depth (μm) and latency (ms) of this pair of neurons were 21.18, 36, 454, 7 (A-1); 31.26, 45, 696, 22 (A-2); 27.72, 48, 517, 5 (B-1); 26.46, 36, 549, 13 (B-2) (See text for details).

neurons obtained during the presentation of a 20-dB masker did not differ significantly before and during bicuculline application to their paired neurons (Fig. 4B-2, unfilled *vs.* shaded, $P > 0.05$). However, significant difference was observed between each of other two sets of average BW (Fig. 4B-2, filled *vs.* unfilled, filled *vs.* shaded, $P < 0.01$).

Broadening of Impulse-FTC of IC Neurons by a Masker

In this study, 4 pairs of IC neurons were recorded in which the impulse-FTC was broadened by the presentation of a 20-dB masker. The impulse-FTC of 2 pairs of IC neurons plotted under different stimulus conditions is shown in Fig. 5. Clearly, the presentation of a 20-dB masker broadened the impulse-FTC of both neurons to varying degrees (Fig. 5A-1a *vs.* A-1b; B-1a *vs.* B-1b). The impulse-FTC of both neurons also greatly increased to varying degrees during bicuculline application (Fig. 5A-1a *vs.* A-1c; B-1a *vs.* B-1c). However, the impulse-FTC measured during bicuculline application further broadened by presentation of a 20-dB masker in one neuron but not in the other neuron (Fig. 5B-1c *vs.* B-1d; A-1c *vs.* A-1d).

In parallel to these findings, the impulse-FTC of their paired IC neurons was also broadened by the presentation of a 20-dB masker (Fig. 5A-2a *vs.* A-2b; B-2a *vs.* B-2b). During bicuculline application, the impulse-FTC was further broadened only in one paired IC neuron but not in the other paired neuron (Fig. 5A-2b *vs.* A-2c; B-2b *vs.* B-2c).

Discussion

Involvement of GABA Mediated-Inhibition in Forward Masking of Frequency Selectivity of IC Neurons

In this study, two IC neurons with a pair of elec-

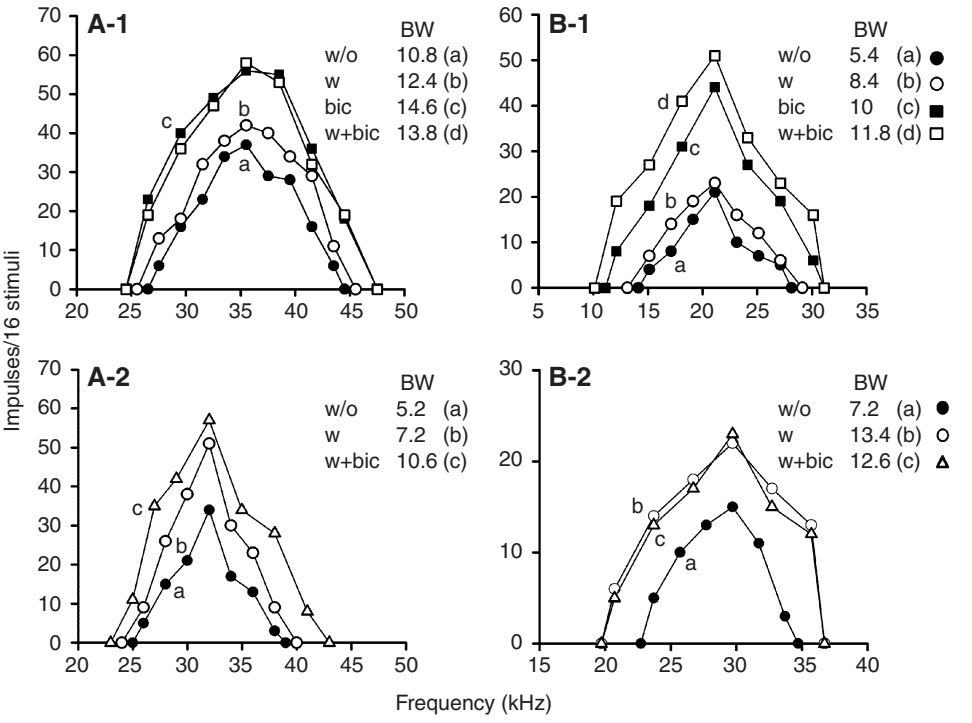

Fig. 5. The impulse-FTC of two pairs of IC neurons plotted under different stimulation conditions: with (w, unfilled circles, A-1b, B-1b) and without (w/o, filled circles, A-1a, B-1a) the presentation of a 20-dB masker; during bicuculline application (bic, filled squares, A-1c, B-1c) plus a 20-dB masker (w+bic, unfilled square; A-1d, B-1d); with (w, unfilled circles, A-2b, B-2b) and without (w/o, filled circles, A-2a, B-2a) the presentation of a 20-dB masker; presentation of a 20-dB masker when bicuculline was applied to the paired neuron (w+bic, unfilled triangles; A-2c, B-2c); The BF (kHz), MT (dB SPL), recording depth (*P*m) and latency (ms) of these four neurons were 35.52,53,710,10 (A-1); 31.98, 47, 626, 13 (A-2); 21.12, 33, 602, 16 (A-2); 29.71, 47, 682, 13 (B-2).

trodes were simultaneously recorded. The involvement of GABA-mediated inhibition in shaping the frequency selectivity of bat IC neurons were also examined using the same experimental protocols as in previous studies (14, 25). The authors specifically studied whether a sound that serves as a probe to elicit response of one neuron might serve as a masker to affect the impulse-FTC of the other paired neuron. Forward masking was found to produce sharpening of frequency selectivity of 88% of IC neurons (Fig. 1). A previous study shows that sharpening of frequency selectivity of IC neurons by a masker becomes less effective with increasing differences in the stimulus frequency between the masker and probe (18). This observation has been explained by the tonotopic organization in the IC such that the inhibition of neurons with small BF differences arrives earlier with less attenuation than neurons with large BF differences (29). In agreement with these studies, the authors showed that the degree of sharpening of frequency selectivity of these IC neurons by a masker significantly decrease with differences in the recording depth and BF (Fig. 2, C and D).

Bicucullinhe application broaden the impulse-FTC of IC neurons and modulated the effect of forward masking on the frequency selectivity of paired recorded IC neurons (Figs. 3 and 4). These observations suggest that GABAergic inhibition is one of the underlying mechanisms for this forward masking of frequency selectivity of these paired IC neurons. 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 (7). This study suggests that sharpening of frequency selectivity of IC neurons by GABA-mediated inhibition would progressively decrease along the spatial distribution gradient of $GABA_A$ receptors within the IC. Then it follows that the degree of GABA-mediated sharpening of frequency selectivity of IC neurons by a 20-dB masker would progressively decrease along the dorsoventral axis of the IC. This speculation is supported by the observation in this study that sharpening of impulse-FTC by a 20-dB masker decreases with recording depth and BF (Fig. 2, A and B).

We showed that sharpening of frequency selectivity by a 20-dB masker was observed both

before and during bicuculline application for 50% of IC neurons that were recorded at deeper IC (Fig. 3, A-1 and A-2). Conceivably this observation is due to the fact that a 20-masker may still sharpen the frequency selectivity of these IC neurons through glycine-mediated inhibition upon removal of GABA-mediated inhibition by bicuculline application. The fact that glycine-mediated inhibition sharpens frequency selectivity of IC neurons has been reported previously (17, 18). On the other hand, sharpening of frequency selectivity of other 50% neurons at upper IC by 20 dB masker was only observed before but not during bicuculline application (Fig. 3, B-1 and B-2). This might be due to the fact that GABA-mediated forward masking of frequency selectivity of these IC neurons has been completely removed during bicuculline application. Alternatively, bicuculline application had greatly increased the excitability of the applied neurons as that GABA-mediated inhibition was not strong enough to overcome the increased excitability of the applied neurons for further sharpening of frequency selectivity.

In parallel to these findings, the authors observed that the presentation of a 20-dB masker further sharpened the frequency selectivity in 76% IC neurons when bicuculline was applied to their paired IC neurons (Fig. 4A-1). This further sharpening of frequency selectivity of these IC neurons is likely due to increase excitability of the applied neuron by bicuculline application. Therefore, the strength of GABA-mediated inhibition evoked by the 20-dB masker of the applied neurons also increased. We also showed that a 20-dB masker only sharpened the frequency selectivity of 24% IC neurons before but not during bicucullien application of their paired neurons (Fig. 4B-1). Presumably, increased excitability of the applied neurons was not strong enough to increase the strength of the GABA-mediated forward masking to produce any further sharpening of the frequency selectivity of these IC neurons.

In addition, a 20-dB masker produced broadening of the FTC in 12% IC neurons (Fig. 5) was also observed. Conceivably, broadening of the impulse-FTC of these IC neurons by a 20-dB masker may be a result of removal of GABA-mediated 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

Processing of auditory information carried by sounds has traditionally been explained by neural inhibition and excitation through divergent and convergent projections within the ascending auditory system (24). The interaction of excitation and inhibition on auditory temporal processing in the IC has been studied using a probe and a masker in many previous studies (6, 8, 14, 18, 19). In these studies, however, only one neuron is recorded each time and the probe is typically the BF sound of the recorded IC neuron while a non-BF sound is used as a masker. In complementary to our previous study (25), we examined the involvement of GABA-mediated inhibition in sharpening the frequency selectivity of two simultaneously recorded IC neurons using forward masking paradigm. We specifically examined how a BF sound of one neuron might affect the frequency selectivity of the other paired neuron. Hence, the possible correlation of frequency processing in the two simultaneously recorded IC neurons may be examined.

A 20-dB masker was found to either sharpen or broaden the frequency selectivity of paired IC neurons (Figs. 1, 3-5). These data suggest that the frequency selectivity between each pair of IC neurons is closely correlated during signal processing. Because IC neurons differ in response latency and MT, frequency analysis in different sets of IC neurons would occur in different time frame during signal processing. Conceivably, when stimulated with complex sounds that occur most often in nature, individual sound frequencies would excite the response of several sets of IC neurons which in turns sharpen or broaden the frequency selectivity of other sets of IC neurons. As such, frequency selectivity of different sets of IC neurons to a specific sound frequency would be improved through inhibition while the spectrum of frequency sensitivity would be enhanced through excitation. Although our previous (25) and present studies only examined the involvement of GABA-mediated inhibition in shaping the frequency and amplitude selectivity of these IC neurons, other inhibitory transmitter such as glycine must also be involved in frequency signal analysis. Future works are necessary to determine the role of glycine-mediated inhibition in shaping the multi-parametric selectivity of these IC neurons.

Acknowledgments

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