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Xie, Ruili, John Meitzen, and George D. Pollak. Differing roles of inhibition in hierarchical processing of species-specific calls in auditory brainstem nuclei. *J Neurophysiol* 94: 4019–4037, 2005. First published August 31, 2005; doi:10.1152/jn.00688.2005. Here we report on response properties and the roles of inhibition in three brain stem nuclei of Mexican-free tailed bats: the inferior colliculus (IC), the dorsal nucleus of the lateral lemniscus (DNLL) and the intermediate nucleus of the lateral lemniscus (INLL). In each nucleus, we documented the response properties evoked by both tonal and species-specific signals and evaluated the same features when inhibition was blocked. There are three main findings. First, DNLL cells have little or no surround inhibition and are unselective for communication calls, in that they responded to ~97% of the calls that were presented. Second, most INLL neurons are characterized by wide tuning curves and are unselective for species-specific calls. The third finding is that the IC population is strikingly different from the neuronal populations in the INLL and DNLL. Where DNLL and INLL neurons are unselective and respond to most or all of the calls in the suite we presented, most IC cells are selective for calls and, on average, responded to ~50% of the calls we presented. Additionally, the selectivity for calls in the majority of IC cells, as well as their tuning and other response properties, are strongly shaped by inhibitory innervation. Thus we show that inhibition plays only limited roles in the DNLL and INLL but dominates in the IC, where the various patterns of inhibition sculpt a wide variety of emergent response properties from the backdrop of more expansive and far less specific excitatory innervation.

INTRODUCTION

The ways that neurons in the auditory system process species-specific communication calls has been of interest for over 30 yr. Particular attention has been focused on forebrain structures in anurans (Fuzessery and Feng 1983), songbirds (Boettiger and Doupe 1998; Theunissen and Doupe 1998), and on the cortices of primates (Rauschecker and Tian 2000; Wang 2000; Winter and Funkenstein 1973) and bats (Esser et al. 1997; Kanwal 1999), because these species have a rich vocal repertoire. Only recently have studies begun to evaluate how species-specific communication calls are processed and represented in subcortical nuclei (Bauer et al. 2002; Klug et al. 2002; Pollak et al. 2003b; Portfors 2004; Suta et al. 2003). Such studies are significant because they not only reveal how lower nuclei process this information, but also because they provide insights into which response features might be created in lower nuclei and which are emergent properties of the cortex.

A subcortical nucleus of particular importance is the inferior colliculus (IC). The IC is a nexus in the auditory system because it is the common target of the projections from the majority of lower auditory nuclei (Casseday 2002; Pollak and Casseday 1986; Roth et al. 1978), from the opposite IC through its commissure (Aitkin and Phillips 1984; Malmierca et al. 1995, 2003; Moore et al. 1998), and from descending projections of the auditory cortex (Huffman and Henson 1990; Winer et al. 1998; Zhou and Jen 2000). The IC also provides the principal source of innervation to the medial geniculate body and thus indirectly to the auditory cortex (Clarey 1992; Wenstrup et al. 1994; Winer 1992).

Here we report on some response transformations that occur in three brain stem nuclei of Mexican free-tailed bats. The three nuclei are the IC, the dorsal nucleus of the lateral lemniscus (DNLL), and the intermediate nucleus of the lateral lemniscus (INLL). Each is a successively higher auditory nucleus, where the IC is the highest region, the DNLL is situated just below the IC, and the INLL is located just ventral to the DNLL. Both the DNLL and INLL send inhibitory projections to the IC. Particular attention was given to evaluating tuning curves of neurons in each nucleus, the degree to which lateral inhibition sharpens the tuning curves in each nucleus, and the role that inhibition, especially lateral inhibition, plays in shaping the responses of neurons in each nucleus to species-specific calls.

The impetus for this study follows from two previous studies that investigated the responsiveness of IC (Klug et al. 2002) and DNLL neurons (Bauer et al. 2002) in bats to species-specific calls. Most IC neurons are selective for calls in that they respond to only a subset of a repertoire of natural calls (Klug et al. 2002) and fail to respond to other calls, although the calls to which they fail to respond have suprathreshold energy in their excitatory tuning curves. This selectivity is largely caused by inhibition, because pharmacologically blocking inhibitory receptors results in a dramatic decrease in selectivity due to an increase in the cell's responsiveness to calls to which the neurons were unresponsive before inhibition was blocked. DNLL neurons, in contrast, are unselective for calls and respond to any call so long as the call has energy that stimulates its excitatory tuning curve. Moreover, the responses of DNLL cells to any complex signal, including species-specific calls, can be accurately predicted simply by convolving the responses evoked by tone bursts with the spectrogram of each signal. Thus processing in the DNLL is apparently accomplished largely by the linear integration of excitation, which suggests that inhibition, especially lateral inhibition, plays little or no role in shaping responses of DNLL neurons.

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This report evaluates several issues concerned with the hierarchical processing of acoustic information in the INLL, DNLL, and IC that either were not addressed by previous studies or were raised but not answered by them. In this study, we document the response properties of DNLL neurons evoked by both simple (tonal) and complex stimuli (species-specific signals) and evaluate the same features when inhibition was blocked by iontophoretic application of antagonists of $GABA_A$ receptors and/or glycine receptors. As mentioned above, previous studies suggest that inhibition plays little or no role in shaping the responses of DNLL neurons to monaural stimulation, a suggestion inconsistent with the excitatory and inhibitory innervation of the DNLL, and one that we resolve in this study. We evaluated the same features in INLL and IC neurons, both before and while inhibition was blocked. Thus we evaluate *1*) the ways in which DNLL and INLL neurons respond to both simple and complex signals; *2*) the roles that inhibition plays in shaping responses to simple and complex stimuli in the DNLL compared with the roles that inhibition plays in shaping responses of INLL neurons; and *3*) how the processing in the DNLL and INLL compares to the more complex processing in the IC, with particular attention given to comparing the roles of inhibition in the three nuclei. We show that inhibition plays only limited roles in the DNLL and INLL but dominates in the IC, where the various patterns of inhibition sculpt a wide variety of emergent response properties from the backdrop of more expansive and far less specific excitatory innervation.

METHODS

Surgical and recording procedures

Surgical and pharmacological procedures, electronic equipment, sound generation, and criteria for isolating single neurons are the same as those described in previous publications (Bauer et al. 2002; Klug et al. 2002). In brief, each Mexican free-tailed bat, *Tadarida brasiliensis mexicana*, was anesthetized with isoflurane inhalation (IsoFlo, Abbott Laboratories), and surgically prepared by reflecting the muscles and skin overlying the skull. Lidocaine (Abbott Laboratories) was applied topically to all open wounds. The surface of the skull was cleared of tissue, and a foundation layer of cyanoacrylate and small glass beads was placed on the surface. A small hole was made in the skull over the IC using landmarks visible through the skull. The bat was transferred to a heated recording chamber, where it was placed in a restraining cushion constructed of foam molded to the animal's body. The restraining cushion was attached to a platform mounted on a custom made stereotaxic instrument (Schuller et al. 1986). A small metal rod was cemented to the foundation layer on the skull and attached to a bar mounted on the stereotaxic instrument to ensure a uniform positioning of the head. A ground electrode was placed between the reflected muscle and the skin.

After the animal was fixed in the stereotaxic instrument, the electrode was positioned over the IC while viewed with an operating microscope. The electrode was advanced to a depth of ~300 μm to ensure that recordings were obtained from neurons in the central nucleus of the IC. The electrode was subsequently advanced from outside of the experimental chamber with a piezoelectric microdrive (Burleigh 7121W). Several criteria were used to determine when the electrode was in the IC and when it exited the IC and entered the DNLL and subsequently the INLL. As the electrode was advanced through the IC, there was an abrupt change in the best frequency (BF; the frequency to which the unit or cluster of units was most sensitive) of the background activity at a depth of ~1,500–1,600 μm. This change signaled that the electrode had left the IC and entered the DNLL. For the next 300–400 μm, both the multiunit activity and the single units encountered displayed prominent sustained activity in response to contralateral tone bursts, and this activity was strongly suppressed when tone bursts were presented simultaneously to the ipsilateral ear. A second abrupt change in BF and a change from binaural to monaural activity that was only influenced by sound to the contralateral ear signaled that the electrode left the DNLL and entered the INLL. To ensure that these changes in BF, as well as discharge patterns and binaural properties, indicated DNLL and INLL locations, we verified the electrode location from histological sections in several experiments after making small lesions by passing 5 μA of current for 10–15 min. If killed, the bat was removed from the stereotaxic apparatus and from the cushion. It was overdosed with the inhaled anesthetic IsoFlo and perfused immediately with 4% formaldehyde. After removal from the skull, the brain was placed in a 30% sucrose solution for 24–48 h for the purpose of cryoprotection. The brain was sectioned at 50 μm thickness on a freezing microtome, and the brain slices were counterstained with cresyl violet. Electrode positions within the DNLL or INLL were confirmed through visualization of the small lesion. The histological sections confirmed that the response features were reliable indicators of electrode location, as they were in previous studies of the DNLL in this bat and in mustache bats.

Recordings were begun after the bats recovered from the anesthetic, and thus all data were obtained from awake animals. The bats typically lay quietly during the remainder of the experiments. If they showed signs of discomfort, doses of the neuroleptic ketamine hydrochloride (1/40 dilution, 0.01 ml injection; Vetamine, Mallinckrodt Veterinary), were administered. All experimental procedures were in accordance with a protocol approved by the University of Texas Institutional Animal Care Committee.

Electrodes

"Piggyback" multibarrel micropipettes were used for recordings and iontophoresis of drugs (Havey and Caspary 1980). Multibarrel electrodes were pulled from a five-barrel blank (A-M Systems) and blunted to 15–20 μm. A single barrel pipette was attached to the five-barrel pipette and glued with cyanoacrylate so that the tip of the single barrel pipette protruded 10–15 μm from the blunted tip of the five-barrel pipette. The single-barrel micropipette was used for recording single unit activity and was filled with buffered 1 M NaCl and 2% Fast green (pH 7.4) to enhance the visibility of the electrode. One barrel of the five-barrel pipette was the balancing barrel and was filled with buffered 1 M NaCl and 2% Fast green. The other barrels were filled with solutions of bicuculline methiodide (Sigma, St. Louis, MO), an antagonist of $GABA_A$ receptors, and with the glycine receptor antagonist, strychnine HCl (both were 10 mM in 0.165 M NaCl, pH 3.0; Sigma). In some experiments, one barrel was also filled with L-glutamic acid (500 mM in dH_2O, pH 9–10; Sigma). Drugs were retained in the electrode with a 15- to 20-nA retention of opposite polarity compared with the ejection current. For bicuculline and strychnine, retention currents were negative, and ejection currents were positive, while for glutamate, retention currents were positive and ejection currents negative. The drug and balancing barrels were connected via silver-silver chloride wires to a six-channel microiontophoresis constant current generator (Medical Systems Neurophore BH-2) that was used to generate and monitor ejection and retention currents. The sum channel was used to balance current in the drug barrels and reduce any influence of passing positive or negative current during iontophoresis. The recording barrel was connected by a silver-silver chloride wire to a Dagan AC amplifier (model 2400).

Acoustic stimuli

Tone bursts were digitally generated by a G4 Macintosh computer with custom built hardware and software. Tone bursts had 0.2-ms rise-fall times and durations ranging from 2.0 to 50.0 ms depending on

the particular experiment. All tone bursts were set to the same peak intensity that corresponded to 70 dB SPL when measured between 20–25 kHz. The species-specific calls consisted of a suite of 10 Mexican free-tailed bat vocalizations (Fig. 5) that were previously recorded. These were the same suite of calls used in previous studies (Bauer et al. 2002; Klug et al. 2002). Eight of the 10 vocalizations were communication signals of various behavioral contexts [Social Calls (SC 1–8)], and the remaining two vocalizations were echolocation calls (EC 9–10). The calls were all at the same peak intensity that corresponded to the peak intensity of tone bursts and stored as AIFF files. Thus a library of 10 species-specific sounds was created and stored for later playback. All stimuli were uploaded from the Macintosh G4 into a custom made Downloadable Arbitrary Waveform Generator through a 24-bit digital interface (National Instruments DIO-24) and a digital distributor just before that particular sound's presentation. The acoustic signals were sent to custom-made electronic attenuators. The outputs of the attenuators were fed to earphones biased with 200 V DC. The design of the earphones was originally described by Schuller (1997), and each was tested for frequency-intensity response. These earphones are flat ±5 dB from about 10 kHz to 80 kHz. At the start of each experiment, the earphones were inserted into the funnel formed by the bat's pinnae and positioned adjacent to the external auditory meatus. The pinnae were folded onto the housing of the microphones and wrapped with Scotch tape. The acoustic isolation with this arrangement is ≥40 dB.

Data acquisition and processing

After a cell was isolated, its BF and threshold at BF were obtained, followed by rate-level functions and tuning curve. Quality values (Q values) were calculated by dividing the neuron's BF by the bandwidth of the tuning curve at a specified level above threshold. The suite of 10 species-specific calls was presented at 30–50 dB above the neuron's threshold at BF to ensure that each call had suprathreshold energy that encroached on the neuron's tuning curve (Bauer et al. 2002; Klug et al. 2002). Peristimulus time histograms (PSTHs) or raster displays were generated from 20 presentations of each stimulus (bin width was 1.0 ms) presented pseudo-randomly at a rate of 4/s. Thresholds to tones were determined audiovisually. The criterion for a threshold response evoked by each species-specific call was three or more spikes evoked by 20 presentations the call.

Cells were typically held for periods of 45–60 min. After recording a cell's responses to tones and the 10 calls, pharmacological agents were iontophoretically applied, and the responses to the same signals were recorded again. Before evaluating responses while inhibition was blocked by bicuculline or bicuculline and strychnine, we first applied an ejection current that routinely caused a substantial change in responsiveness, typically 20–40 nA. We recorded responses to BF tones until a substantial increase in spike count was obtained and stabilized. Once responses were stable, the complement of tone bursts and communication calls was presented again, and the same response features were obtained for comparison with those obtained before the application of drugs. The ejection current was switched off, and the cell was allowed to recover. Recovery was complete when both the shape and maximum spike count of the rate-level function returned to their predrug values. Because recovery times were usually 30–90 min and most neurons were held for 45–60 min, most neurons were lost before recovery was attained. We allowed ≥45 min before searching for another neuron in those instances.

RESULTS

This report describes the responses of 48 INLL, 30 DNLL, and 179 IC cells that were evoked by both tone bursts and by a suite of 10 species-specific calls. Particular attention is directed at the roles of inhibition and how response features in each nucleus are either changed or are unaffected when inhibitory inputs are blocked by the iontophoretic application of bicuculline or strychnine. We begin with the DNLL because its neuronal population is more homogeneous and simpler than the populations in the INLL or IC. In the subsequent sections dealing with the INLL and IC, we describe the responses to the same stimuli that were used to evaluate the DNLL and point out the differences and/or similarities in the response properties of INLL and DNLL neurons, and those of IC neurons compared with the neuronal populations of the INLL and DNLL.

Basic features of DNLL neurons

The average BF of the 30 DNLL neurons was 24.6 ± 6.2 kHz (range, 13–43 kHz). The DNLL population is homogeneous because all the DNLL cells we recorded displayed four tone evoked response features. *1*) They responded to tone bursts with a sustained discharge train that lasted as long as the duration of the tone burst that evoked it. Moreover, the majority of DNLL neurons displayed an onset-chopping sustained pattern, where the cells initially discharged at a regular interval that was unrelated to the stimulus period followed by a series of irregularly spaced discharges. *2*) DNLL cells were binaural, being excited by sound at the contralateral ear and inhibited by sound at the ipsilateral ear, and thus had excitatory–inhibitory (EI) response properties. *3*) The rate-level functions were monotonic, where they exhibited increasing spike counts with intensity that typically plateaued at 30–40 dB above threshold. *4*) Their tuning curves were all moderately sharp, with an average Q_{10dB} of 6.3 ± 2.0 ($n = 25$) and an average Q_{30dB} of 2.6 ± 1.0 ($n = 26$). The above features are in agreement with previous studies of the DNLL in this species and are shown in Fig. 1.

In a previous study we also showed that DNLL cells were unselective for species-specific calls in that DNLL neurons responded to most or all of the 10 calls presented at 30–50 dB above BF threshold, so long as the call had energy that encroached on its excitatory tuning curve (Bauer et al. 2002). This lack of selectivity for calls was confirmed here. As shown in Fig. 2*A*, when calls were presented at 30–40 dB above BF threshold, 83% (19/23) of DNLL neurons responded to all 10 calls.

EFFECTS OF BLOCKING INHIBITION ON TONE-EVOKED RESPONSES AND TUNING CURVES. We next evaluated whether or not DNLL cells have surround inhibitory regions that flank their excitatory tuning curves. If the excitatory tuning curves of DNLL neurons are sharpened by surround inhibition, their tuning curves should expand when inhibition is blocked, as tuning curves do in IC neurons. However, when inhibition was blocked the tuning curves of DNLL cells were either unchanged or broadened only slightly. These features are shown by the neuron in Fig. 3. The first point to be made is that when glycinergic inhibition was blocked by strychnine, there was no change in the width of the tuning curve nor was there an increase in response magnitude. If anything, spike counts declined slightly with strychnine. The second point is that when GABAergic inhibition was blocked with bicuculline after the cell recovered from strychnine, the blockage of GABAergic inhibition caused the spike counts to increase by ~100–300%. The main point, however, is that the width of the tuning

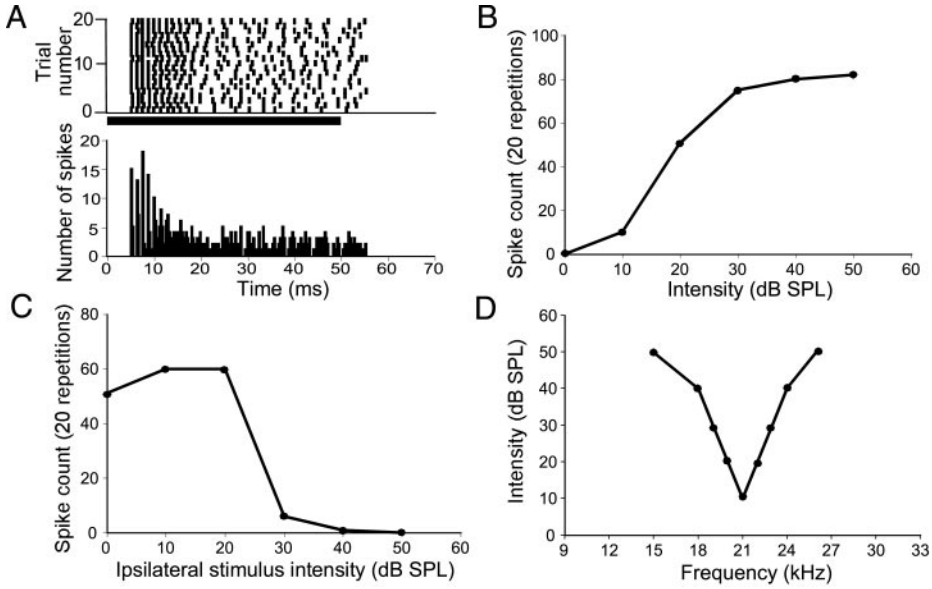

FIG. 1. Response properties of a dorsal nucleus of the lateral lemniscus (DNLL) neuron. *A*: raster (*top*) and poststimulus time histogram (PSTH) display showing chopping features of a sustained response typically seen in DNLL cells with best frequency (BF) tone bursts. Tone duration was 50 ms at 50 dB SPL. *B*: monotonic rate-level function where the spike rate saturates at ~30 dB above threshold. Tones durations were 2.0 ms at 21 kHz (BF). *C*: interaural level disparity (ILD) function generated by simultaneously presenting a BF tone at 20 dB SPL (10 dB above threshold) to the contralateral (excitatory) ear and tones of various intensities at the ipsilateral ear. Notice that the cell was completely inhibited when the ipsilateral intensity was 30 dB SPL, an ILD of 10 dB. *D*: tuning curve of the same neuron.

curve was virtually the same before inhibition was blocked as it was while inhibition was blocked. The effects of blocking GABAergic, glycinergic, or both inhibitory receptors on tuning were evaluated in 13 DNLL neurons. In 9/13 neurons, the tuning was unchanged, whereas in 4/13 neurons, the tuning curve expanded just slightly. These features are shown in Fig. 4*A*, which shows the Q_{30dB} values of the 13 neurons before and while inhibition was blocked.

The results from blocking inhibition suggest that DNLL cells have little or no surround inhibition, but these experiments cannot provide definitive proof of its absence. The reason is that blocking inhibition can only reveal frequency

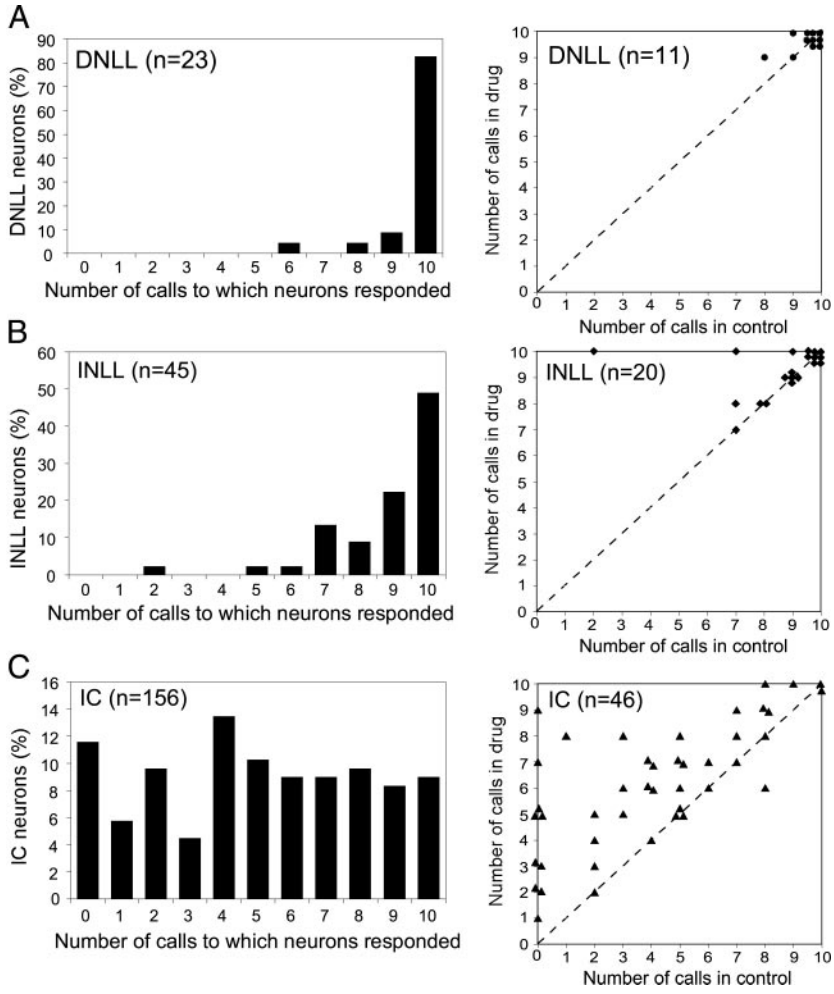

FIG. 2. Graphs showing the number of calls to which (*A*) DNLL, (*B*) intermediate nucleus of the lateral lemniscus (INLL), and (*C*) inferior colliculus (IC) cells responded. Graphs on the *right* show the number of calls to which each DNLL, INLL, and IC neuron responded in the control and when inhibition was blocked. All calls were presented at 30–50 dB above BF threshold.

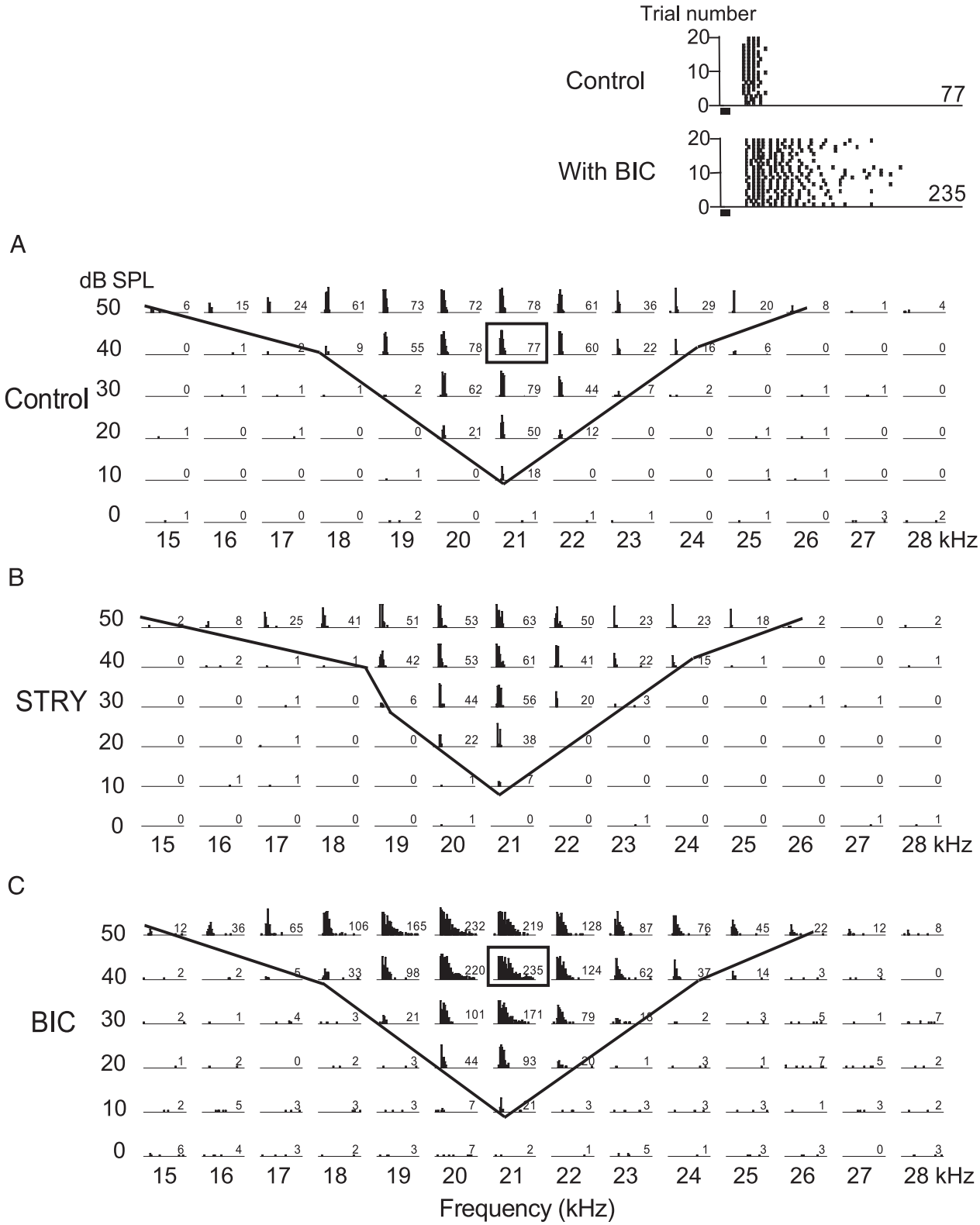

FIG. 3. Tuning of a DNLL neuron was not changed by blocking inhibition. Tuning curves before inhibition was blocked (Control, *top*) and during blockage of glycinergic inhibition with strychnine (*middle*). The cell was allowed to recover, bicuculline was applied to block GABAergic inhibition, and the tuning curve obtained during blockage of GABAergic inhibition panel (*bottom*). All tones were 2.0 ms in duration. *Inset*: raster displays of responses evoked by tones indicated in the tuning curves (boxed histograms) before and while GABAergic inhibition was blocked. Ejection current was 70 nA for strychnine and 50 nA for bicuculline. Same cell as in Fig. 1.

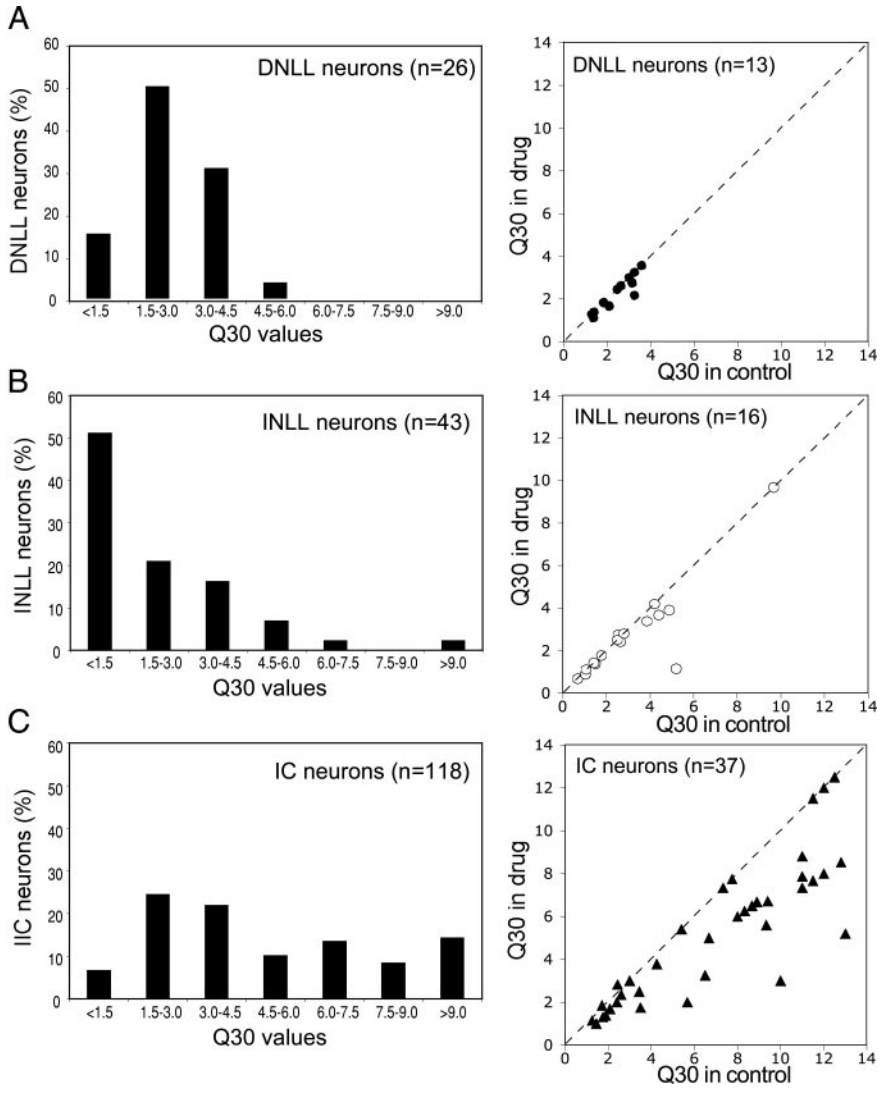

FIG. 4. Distribution of Q_{30dB} values of the DNLL (*A*), INLL (*B*), and IC (*C*) neurons in our sample. Graphs on the *right* show changes in Q_{30dB} values of DNLL, INLL, and IC neurons caused by blocking inhibition.

regions in which tones evoke an excitation that is completely suppressed by inhibition evoked by the same frequencies. This technique, however, cannot reveal whether there are frequencies that flank the excitatory tuning curve but which evoke only pure inhibition, because when inhibition is blocked, there is no excitation that would be unmasked. The presence of a pure inhibition, however, would be revealed when tone bursts are presented while a carpet of background activity is produced by the iontophoretic application of glutamate. Under these conditions, tone evoked inhibition is evident as a gap in the background activity that is time-locked to the stimulus.

We tested for surround inhibition with iontophoresis of glutamate in 11 other DNLL neurons. In all of the DNLL neurons, tones within the excitatory tuning curve evoked both an initial excitatory discharge followed by a gap produced by the inhibition that followed the excitation. An example is shown in Fig. 5. Presumably, it was this trailing inhibition that was blocked by bicuculline and caused the increase in spike count and response duration shown in Fig. 3. However, the most notable feature was the absence of any gaps evoked by frequencies outside of the excitatory tuning curve, showing that there was no surround inhibition in this DNLL neuron.

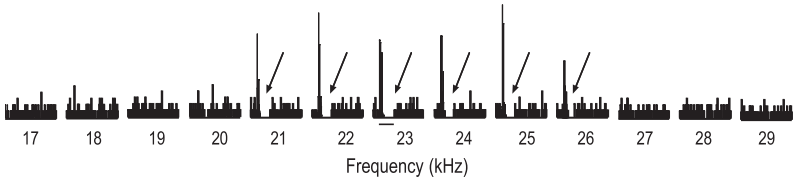

FIG. 5. DNLL cell showing absence of lateral inhibition. Background activity was generated by iontophoresis of glutamate, while tone bursts of 2.0-ms duration were presented at 60 dB SPL (30 dB above threshold). Tone burst frequencies of 21–26 kHz evoked an initial discharge followed by a gap in the background activity caused by a period of inhibition (arrows). Frequencies evoking excitation correspond to the range of excitation that would comprise the tuning curve at 60 dB SPL (30 dB above BF threshold). Note that there were no gaps on either side of the excitatory region, showing that the neuron had no surrounding inhibitory regions. Time bar is 20 ms.

Comparable results were obtained from the 10 other DNLL cells in which surround inhibition was evaluated by creating background activity with glutamate.

EFFECTS OF BLOCKING INHIBITION IN DNLL NEURONS ON RESPONSES TO SPECIES-SPECIFIC CALLS. The above results, coupled with the results from the previous studies on DNLL processing of species-specific calls, are consistent with the hypothesis that processing in the DNLL is determined predominantly by a linear integration of excitatory inputs. We evaluated this issue directly by presenting the same suite of 10 species-specific calls that Bauer et al. 2002 presented in the previous report, and recorded the responses from 11 DNLL neurons evoked by those calls before and while inhibition was blocked. Blocking inhibition increased response magnitude but did not change the selectivity for the calls nor did it change the relative responsiveness to each call. These features are shown in Fig. 6*A*, where the responses evoked by each call are shown before and while inhibition was blocked by bicuculline. Notice that the neuron was relatively unselective because it responded to 9 of the 10 calls both before and while inhibition was blocked. The spike counts evoked by each call before and during blockage of inhibition are plotted graphically in Fig. 6*B*. The important feature is that the shapes of the two graphs are similar, showing that the relative responsiveness of each call was unchanged. The neuron, for example, responded most vigorously to call SC2, did not respond to call SC5, and responded with the smallest spike count to call SC9, and this result was obtained before and while inhibition was blocked. That inhibition had no influence on the relative responsiveness to each call even more evident when the normalized spike counts in the two conditions were graphed, as shown in Fig. 6*C*. Similar results were obtained for the 10 other DNLL neurons. The changes or more appropriately the lack of changes in the number of calls to which each neuron responded when inhibition was blocked are shown in Fig. 2*A*. Taken together, these results show that DNLL neurons have little or no surround inhibition and that processing in the DNLL is determined largely by excitation, where inhibition acts mainly to reduce response magnitude.

Basic features of INLL neurons

Response features of INLL neurons were more diverse than those in the DNLL, and this was found for most of the response features that we evaluated. The majority (85%, 41/48) of INLL neurons were monaural, excited by stimulation of the contralateral ear, and unaffected by stimulation of the ipsilateral ear alone or when presented simultaneously with stimulation of the contralateral ear. However, 15% (7/48) of INLL cells were binaural and were EI (excited by contralateral and inhibited by ipsilateral stimulation). Thus in contrast to the DNLL, where every cell was EI and thus binaural, the aural features of INLL population were a mixture of mostly monaural and a smaller number of binaural, EI cells. The binaural INLL cells were surprising because previous studies of the INLL in another species of bat reported that all neurons in this nucleus were monaural (Covey and Casseday 1991; Huffman and Covey 1995).

The average BF of the sample from the INLL was 22.7 ± 9.1 kHz ($n = 45$), with a range of 8–54 kHz. Most INLL cells (73%, 35/48) responded to tone bursts with a sustained discharge pattern, and a smaller percentage (27%, 13/48) responded only to the onset of the tone (Fig. 7). Two types of sustained response patterns were observed. One type displayed an onset-chopping sustained pattern, similar to the pattern of DNLL neurons. The other was a primary-like pattern, where the tone bursts evoked an initial high firing rate that adapted to a lower rate for the duration of the stimulus. Two types of onset

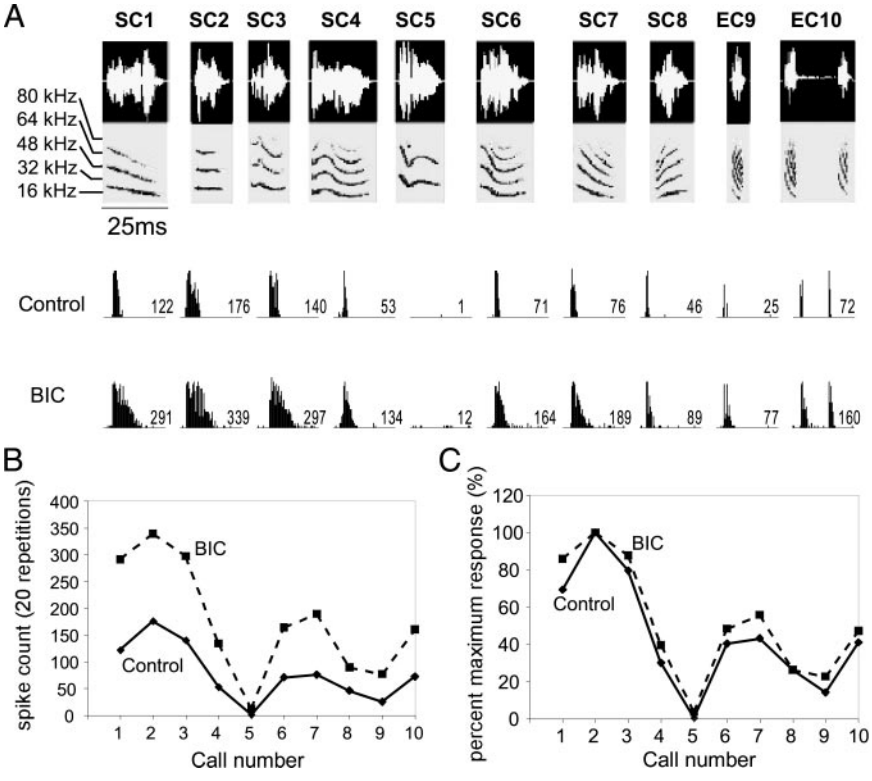

FIG. 6. DNLL neuron showing that inhibition did not shape its selectivity for species-specific calls. *A*: spectrograms and envelopes of the 10 calls are shown together with the response evoked by each call both before and while GABAergic inhibition was blocked by bicuculline. Blocking inhibition caused spike-counts to increase. Number next to each histogram is the spike-count evoked by that call. *B*: plots of spike counts evoked by each call before and while inhibition was blocked by bicuculline. *C*: plot of normalized spike counts showing that relative response to each call was the same before and during application of bicuculline. Thus the neuron responded most vigorously to call SC2 and least vigorously to SC5 in the control condition, and that relationship, as well as the relative responsiveness to the 8 other calls, was preserved while inhibition was blocked by bicuculline. All calls were 30 dB above BF threshold. Ejection current was 50 nA.

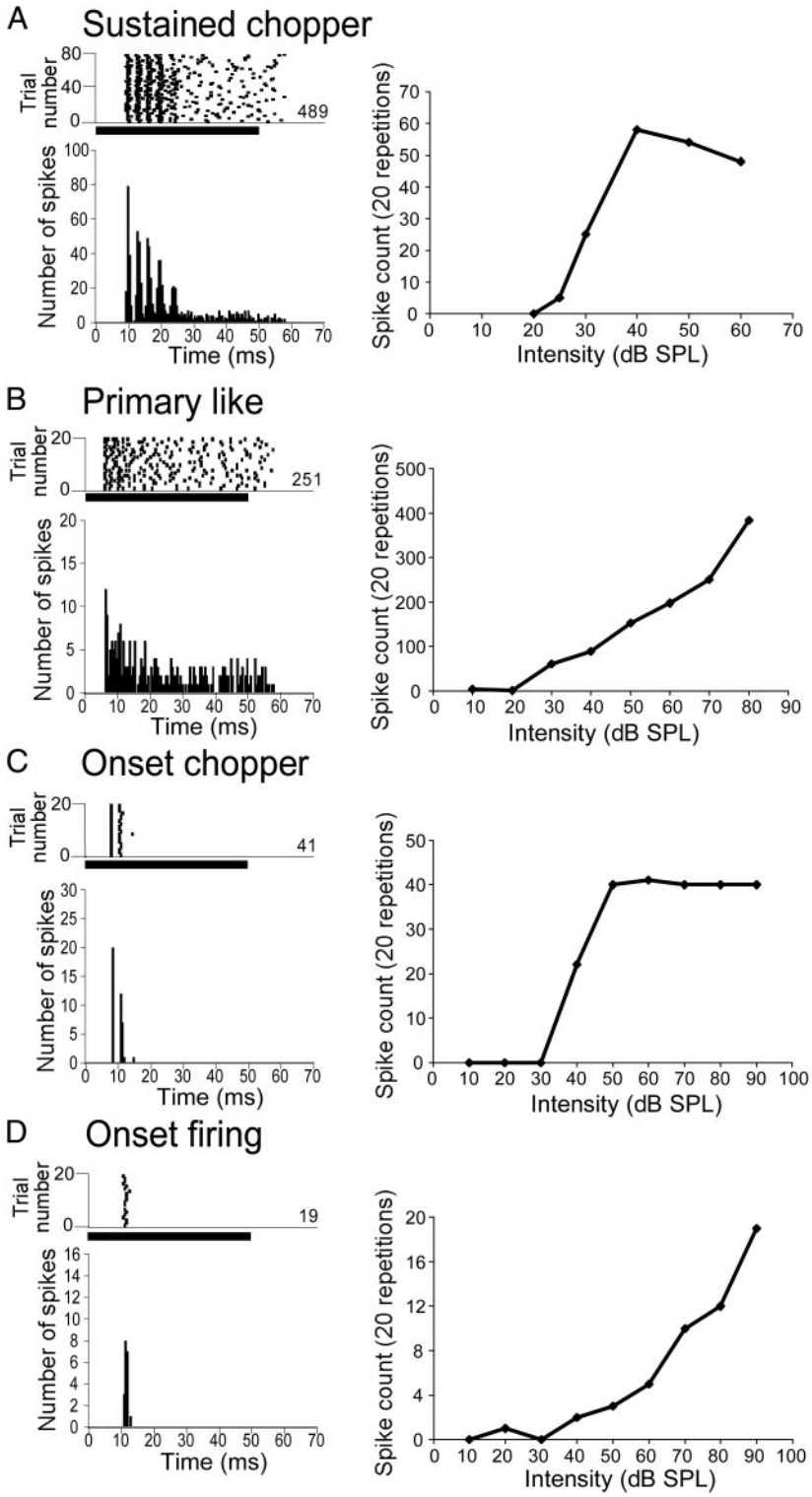

FIG. 7. INLL neurons respond to BF tone bursts with 1 of 4 temporal discharge patterns and with monotonic rate-level functions. Tone bursts were 50 ms in duration and 30 (*A*), 70 (*B*), 80 (*C*), and 60 dB SPL (*D*).

neurons were also found. One type was an onset chopper, where the neurons fired one to five regularly spaced discharges at the onset of the signal and failed to fire to the remainder of the signal duration. The other onset type also fired only at the onset of the signal, but the discharges did not have a temporal regularity. Both types were also seen in previous studies of the INLL (Covey and Casseday 1991) and are shown in Fig. 7.

All INLL cells, like DNLL cells, had monotonic rate-level functions (Fig. 7). The monotonic functions in the majority of INLL cells had a plateau, where the spike counts reached a maximum at a certain intensity, usually 20–30 dB above threshold, and remained constant at higher intensities. In a smaller number of neurons the functions did not plateau, but rather the spike counts continued to increase at every intensity we presented.

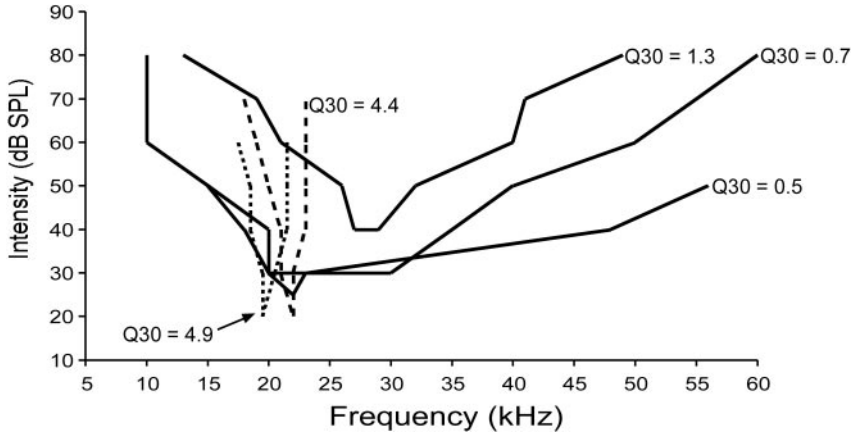

FIG. 8. Tuning curves from 5 INLL neurons. Most INLL neurons were broadly tuned, as shown by tuning curves with solid lines. A smaller number were more sharply tuned as shown by the tuning curves with dashed lines. Q_{30dB} value of each tuning curve is shown.

The most distinctive feature, and the one that characterized the majority of INLL cells, was the width of their tuning curves at 30–50 dB above threshold. Of the tuning curves obtained from 36 INLL cells, 30 (83%) were broadly or very broadly tuned, and only 6 (17%) were narrowly tuned (Fig. 8). In the broadly tuned cells, the tuning at 30–40 dB above threshold encompassed a frequency range that spanned one to three octaves. The average Q_{30dB} of the broadly tuned INLL cells was 1.4 ± 0.60. The tuning of these broadly tuned INLL cells was substantially broader than the tuning curves of DNLL or IC cells. Six cells in our sample were narrowly tuned with V-shaped tuning curves comparable to DNLL and IC cells (Fig. 8). The average Q_{30dB} value of these cells was 5.0 ± 0.8 ($n = 6$). As we show below, the underlying excitatory innervation of one "narrowly tuned cell" actually was the broadest of any cell we had ever seen and encompassed the entire hearing range of this animal.

RESPONSES EVOKED IN INLL NEURONS BY SPECIES-SPECIFIC CALLS. The majority of INLL cells responded to most or to all of 10 species-specific calls we presented, and thus like the DNLL cells, were, in general, unselective for calls. On average, INLL cells responded to 8.8 ± 1.3 calls ($n = 45$) when presented at 30–50 dB above threshold. The distribution of the number of calls to which the INLL neurons in our sample responded is shown in Fig. 2*B*. The lack of selectivity for calls was not surprising because most INLL cells were broadly tuned, and thus some energy in each call encroached on their excitatory tuning regions. Furthermore, as we show below, these cells appear to have little or no inhibitory surrounds.

Most INLL neurons (93%, 39/42), like DNLL cells, responded similarly to time-reversed calls and to the same calls presented in their normal temporal sequence (data not shown). Only 7% (3 of 42) responded differently to forward and reversed calls.

EFFECTS OF BLOCKING INHIBITION IN THE INLL ON TONE-EVOKED RESPONSES AND SPECIES-SPECIFIC CALLS. Inhibition played little or no role in shaping response properties in almost all INLL cells. We evaluated changes in the responses to calls caused by blocking inhibition in 20 neurons, and in 16 of those neurons we also evaluated changes in tuning. In 19 of 20 neurons, there were either no changes in the number of calls to which the neurons responded ($n = 16$) or there were only small changes, where they responded to 1–3 additional calls when inhibition was blocked (Fig. 2*B*). The minor roles of inhibition in the INLL are further illustrated by the 16 cells in which changes in both responses to calls and in tuning were recorded before and while inhibition was blocked. When inhibition was blocked in 15 of these neurons, there were either no changes in response magnitude, discharge pattern, in the extent of their tuning curves, and in the responses to the species-specific calls, or there was only an increase in response magnitude with no other changes either in tuning or selectivity for calls. The lack of change in the response to calls when inhibition was blocked is shown in Fig. 2*B*, and the similarity in tuning before and while inhibition was blocked is shown in Fig. 4*B*.

This remarkable lack of inhibitory influences is further illustrated by the three neurons in Figs. 9 and 10. The neuron in Fig. 9*A* was a very broadly tuned INLL cell in which the application of both strychnine and bicuculline failed to have any influence on either response magnitude, tuning, or on the responses to species-specific calls. The complete absence of any changes while inhibition was blocked was seen in 5 of 16 cells in which we obtained tuning curves and responses to calls. This was a most surprising finding because we had never before seen neurons in any nucleus whose properties were virtually unchanged when inhibition was blocked. This absence of effects was not caused by a failure to eject drugs because of blockage of the ejection barrels, because the resistance of the barrels were routinely monitored. It was also not caused by any ineffectiveness of the particular batch of drugs, because we documented substantial changes in IC cells with the same electrodes in the same penetrations and with the same ejection currents. Finally, we used long periods (20–30 min) of high ejection currents in these cells, all without affecting the cells discharge properties.

These cells, however, were not devoid of GABA receptors. In several cells we also ionotophoretically applied GABA while presenting BF tone bursts, as shown in Fig. 9*Bb*. In all cases, GABA completely suppressed discharges, although bicuculline had no effect. Presumably, these cells had $GABA_B$ receptors that were activated by GABA, but did not have $GABA_A$ receptors, and thus bicuculline had no effects on these cells. We conclude that these neurons lacked $GABA_A$ receptors, and thus these receptors play no role in shaping their response features, although a potential, but unknown role for $GABA_B$ receptors cannot be ruled out.

Ten other INLL cells (10/16) responded similarly when inhibition was blocked, except in these cells, response magnitude increased, although other features, which include tuning

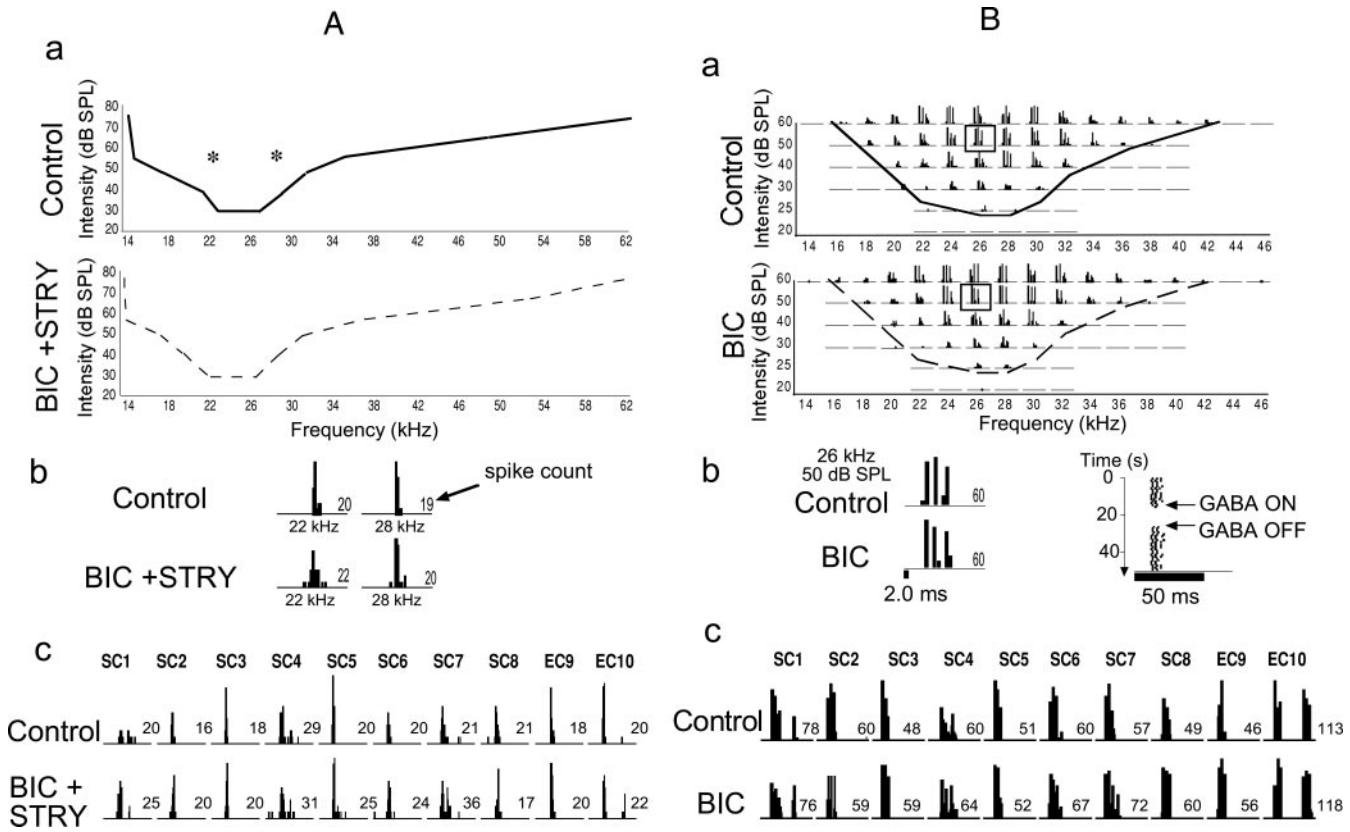

FIG. 9. Two INLL neurons in which blocking inhibition had virtually no effects on tuning, response magnitude, or selectivity for calls. *Aa*: broadly tuned INLL cell in which application of both bicuculline and strychnine had no effect on its tuning curve. *Ab*: PSTHs evoked by frequency-intensity combinations shown by asterisks in tuning curves before and while inhibition was blocked. *Ac*: responses evoked by 10 calls before and while inhibition was blocked by bicuculline and strychnine. Ejection currents were 40 nA for strychnine and 40 nA for bicuculline. *Ba*: INLL cell showing PSTHs evoked by each frequency-intensity combination before and while GABAergic inhibition was blocked by bicuculline. *Bb*: PSTHs on *left* show larger version of responses evoked by tones indicted in tuning curves. Raster display on *right* shows that responses evoked by BF tone bursts could be completely blocked by application of GABA, even though bicuculline had no effects on responsiveness. *Bc*: responses evoked by 10 calls before and while inhibition was blocked by bicuculline. Calls were presented at 35 dB above BF threshold. Ejection current was 40 nA.

and the number of calls to which they responded, were unchanged (Fig. 10).

Only 1 of 16 INLL cells showed a substantial change in all response features when inhibition was blocked, but those changes were extraordinary. As shown in Fig. 11, in the control condition, the tuning curve was narrow and the cell responded to tones with an onset response. The cell also was selective for the suite of calls, where it responded to only 2 of the 10 calls, and it responded weakly to both of those calls. Blocking glycinergic inhibition caused an expansion of the tuning curve, especially at high intensities, and also caused an increase in the number calls to which the neuron responded, from two calls before inhibition was blocked to nine calls. When both glycinergic and GABAergic inhibition were blocked, there was an additional increase in response magnitude, and the cell now responded vigorously to all 10 of the calls. Moreover, there were additional changes in tuning, where thresholds were substantially lowered for frequencies from ~30 to 80 kHz. When both GABA and glycinergic inhibition were blocked, the neuron fired to frequencies from ~15 to 99 kHz, which encompassed most, if not all, of the animal's hearing range (Bartsch and Schmidt 1993; Vater and Siefer 1995), whereas it originally responded only to frequencies ranging from ~20 to 28 kHz.

Summary of INLL and DNLL response features

To summarize, DNLL cells had V-shaped tuning curves with little or no surround inhibition, and they responded to all or most of the species-specific calls, and thus were unselective for calls. Inhibition apparently acted to reduce response magnitude and had little or no influence on their tuning or on their selectivities for calls. Most INLL cells had wider or much wider tuning curves than DNLL cells, and their tuning curves had no surround inhibition, a feature they share with DNLL neurons. INLL cells were also similar to DNLL cells in that blocking inhibition had little or no influence on their tuning, responses to tones, or on their responses to calls. The exception was one sharply tuned INLL cell whose response features were strongly shaped by inhibition.

Features of IC neurons

The BFs of the IC neurons in our sample ranged from 12 to 42 kHz ($n = 147$), with an average of 23.3 ± 5.1 kHz, and were similar to the BFs of the DNLL and INLL neurons in our sample. However, the neuronal population of the IC is markedly different from those of the INLL and DNLL. The most distinctive feature of the IC population is its diversity, where IC neurons displayed a wide variety of different response

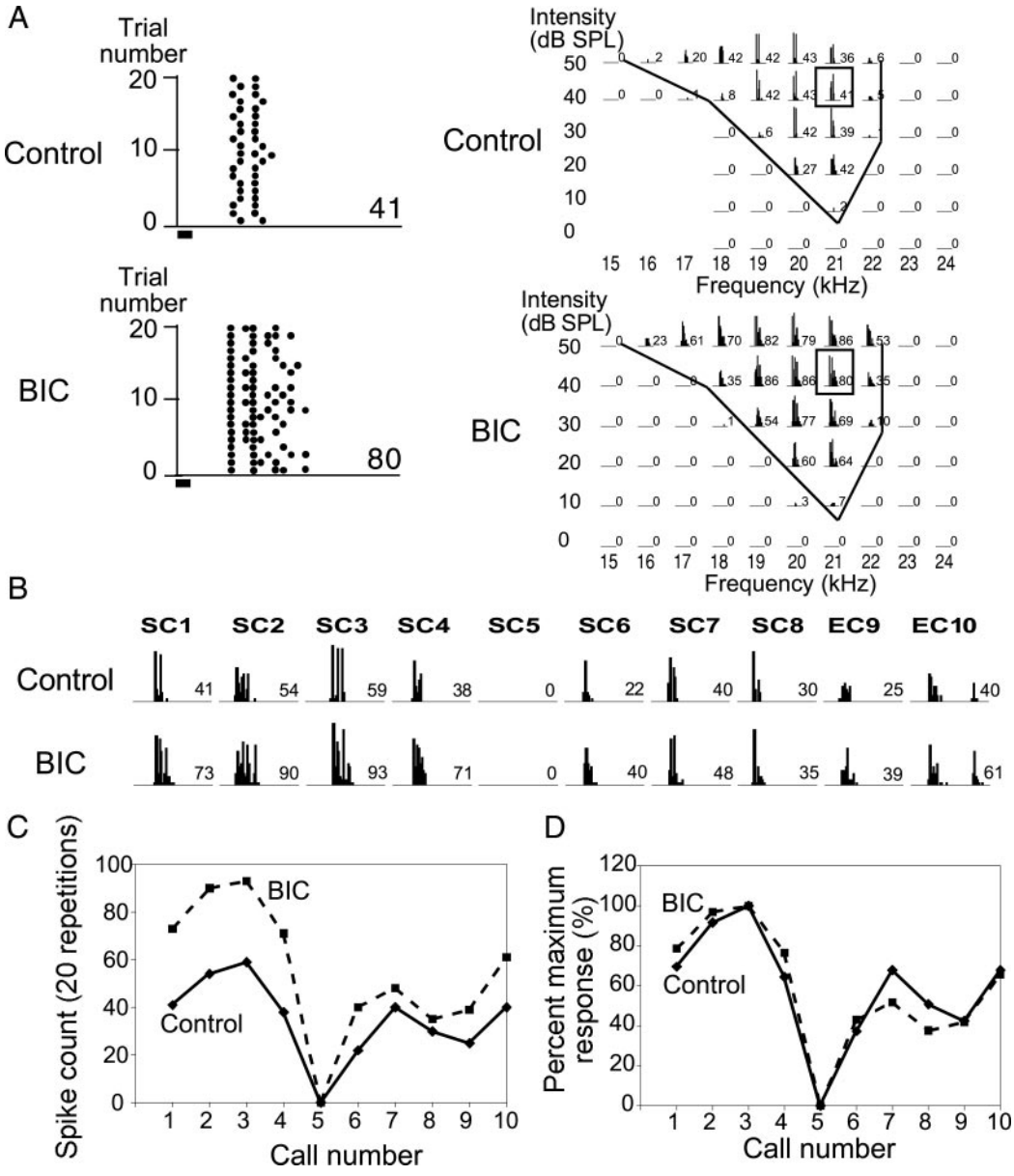

FIG. 10. *A*: INLL cell in which bicuculline increased response magnitude while leaving other response properties unaffected. *Right*: sharply tuned INLL cell whose tuning curve was not broadened by bicuculline, although the spike-counts evoked by all frequency-intensity combinations increased markedly. *Left*: enlarged versions of the increase in spike count evoked by the frequency-intensity combination indicated in tuning curve. *B*: responses to the 10 calls evoked before and during application of bicuculline (45 nA). Calls were presented at 40 dB above BF threshold. *C*: spike counts evoked by calls before (control) and during application of bicuculline (BIC). *D*: normalized spike counts evoked by calls before (control) and during application of bicuculline (BIC).

features to tonal stimuli and to the species-specific calls. The diversity was also seen in the various changes in IC response features that obtain when inhibition was blocked, showing that inhibition in the IC plays a far more prominent role in shaping response properties than it does in the INLL or DNLL. Indeed, it seems that the wide diversity of response properties expressed by the IC population is due largely to the particular pattern of inhibition that innervates each neuron, which more or less uniquely shapes its response features.

The diverse properties were evident from responses evoked by BF tones. Two main types of temporal discharge patterns were evoked by BF tone bursts: *1*) onset patterns in which cells discharged one or a few spikes at the onset of the signal and *2*) sustained patterns in which the discharges were evoked throughout the duration of the signal. Onset responses were more common (52%, 93/179) than sustained patterns (29%, 52/179). These, however, were not the only types that we observed. Sixteen cells (9%) had high rates of spontaneous activity and responded to tone bursts with inhibitory gaps in the spontaneous background. Four cells responded to offsets, and two responded with ON-OFF responses. However, 12 cells (7%) were unresponsive to any frequency–intensity combination of tone bursts that we presented, although 10 of these cells responded to downward FM sweeps. Most of these patterns have been described in previous studies of the IC of this bat (Bauer et al. 2000; Bodenhamer and Pollak 1981; Burger and Pollak 2001; Hurley and Pollak 2001; Pollak et al. 1977, 1978).

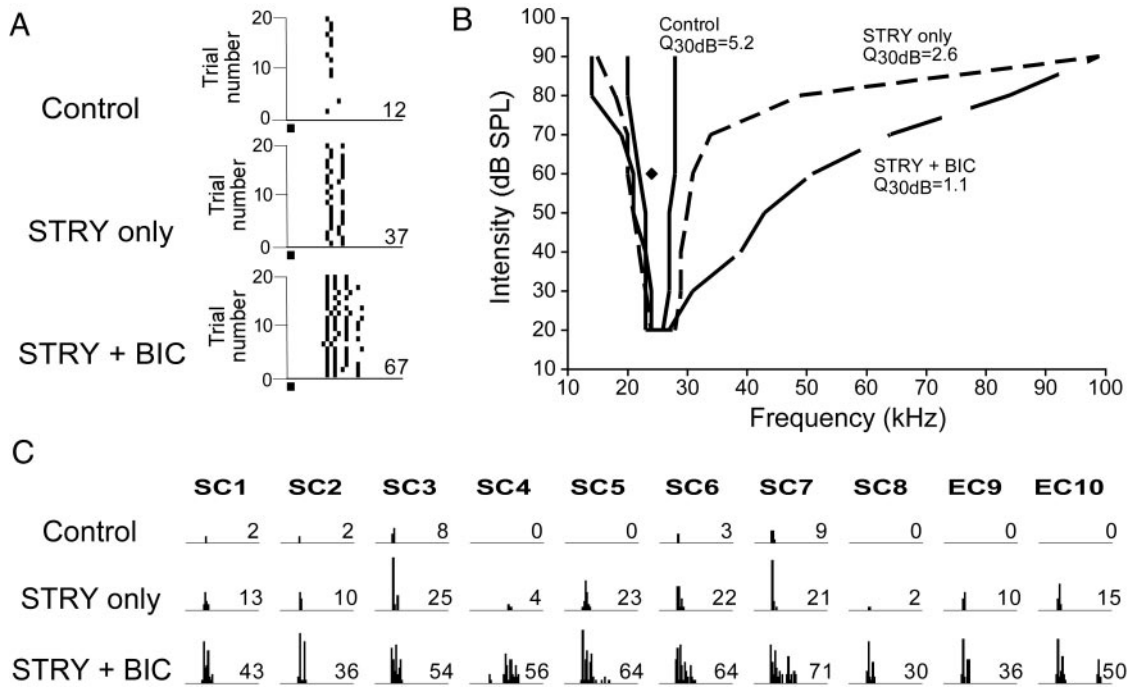

FIG. 11. Sharply tuned INLL cell in which all response features were changed by application of strychnine and bicuculline. *A*: rasters showing spike count increases when strychnine alone and bicuculline and strychnine were applied. Tone bursts were 24 kHz (BF) at 60 dB SPL (40 dB above threshold). *B*: tuning curve broadened markedly when glycinergic inhibition was blocked by strychnine. Even greater changes occur when both strychnine and bicuculline were applied. *C*: changes in both response magnitude and selectivity for calls when strychnine and when strychnine and bicuculline were presented together. Calls were presented at 60 dB SPL, 40 db above BF threshold. Ejection currents were 25 nA for strychnine and 50 nA for bicuculline.

Several types of rate-level functions were also found and included monotonic functions that reached a plateau and monotonic functions that did not plateau. In addition, many cells had nonmonotonic functions and others had upper-threshold functions, the extreme form of a nonmonotonic rate-level function in which the neuron stopped firing at higher intensities. Nonmonotonic functions were slightly more common than monotonic functions. The number of cells displaying each type of rate-level function is shown in Table 1.

As with other response properties, the shapes and widths of tuning curves varied among the IC population (Fig. 12). Classical V-shaped tuning curves were found in 87.5% (126/144). The average Q_{10db} among these cells was 8.5 ± 5.7 and the average Q_{30dB} was 4.7 ± 2.9. Eighteen cells (12.5%) had upper threshold rate-level functions, and their tuning curves were typically bounded as an island of activity evoked by a limited range of frequencies at moderate intensities, with no activity at higher or lower intensities (Fig. 12*E*). Tuning curves having these features have been called type "O" in the cat IC (Ramachandran et al. 1999).

As we mentioned previously, most IC cells were selective for the suite of 10 calls that we presented. Selectivity, however, varied markedly from neuron to neuron, where a few neurons responded to all 10 of the calls, whereas others responded only some of the calls and yet others responded to none of the calls. A graph showing the distribution of selectivities of all the neurons in our sample is shown in Fig. 2 (*bottom*). IC neurons responded to 5.2 ± 3.0 of the 10 calls (n = 156).

TABLE 1. *Number and percentage of IC cells having different types of rate level functions*

Types of Rate Level Function	Nonplateau Monotonic	Plateau Monotonic	Nonmonotonic	Upper Threshold
Number of IC cells	16	65	40	26
Percentage	11%	44%	27%	18%

N = 147. IC, inferior colliculus.

EFFECTS OF BLOCKING INHIBITION ON TONE-EVOKED RESPONSES AND TUNING CURVES. Blocking inhibition had a substantial influence on the response properties in almost all IC neurons. In almost every IC cell, blocking inhibition caused an increase in spike count. In many cells, the increase was accompanied by a change in response pattern from an onset to a sustained response, and the magnitude change in these cells was substantial. In other cells, including both onset and sustained neurons, the temporal discharge pattern was not changed. These cells were still onset or sustained while inhibition was blocked, and the spike count increases were caused by an increase in the discharge probability.

Tuning curves in 47 neurons were measured before and while inhibition was blocked, and representative examples are shown in Fig. 12. Thirty-seven of those neurons originally had V-shaped tuning curves, whereas seven were O type and three failed to respond to tones. The distribution of changes in Q_{30dB} caused by blocking inhibition for the 37 V-type neurons is shown in Fig. 4*C* and contrasts markedly with the near absence of changes in tuning in DNLL and INLL cells. The average change in Q_{10dB} was –3.1 ± 4.4 and Q_{30dB} was –1.5 ± 1.8 (the minus sign indicates that tuning broadened). When we consider all 47 neurons, the tuning curves in a minority of neurons (23%, 10/47) were unaffected by blocking inhibition (Fig. 12*A*), but the curves of most neurons (76%, 37/47) broadened when inhibition was blocked, showing that surround inhibition acted to sharpen the tuning curves of most IC cells. Substantial

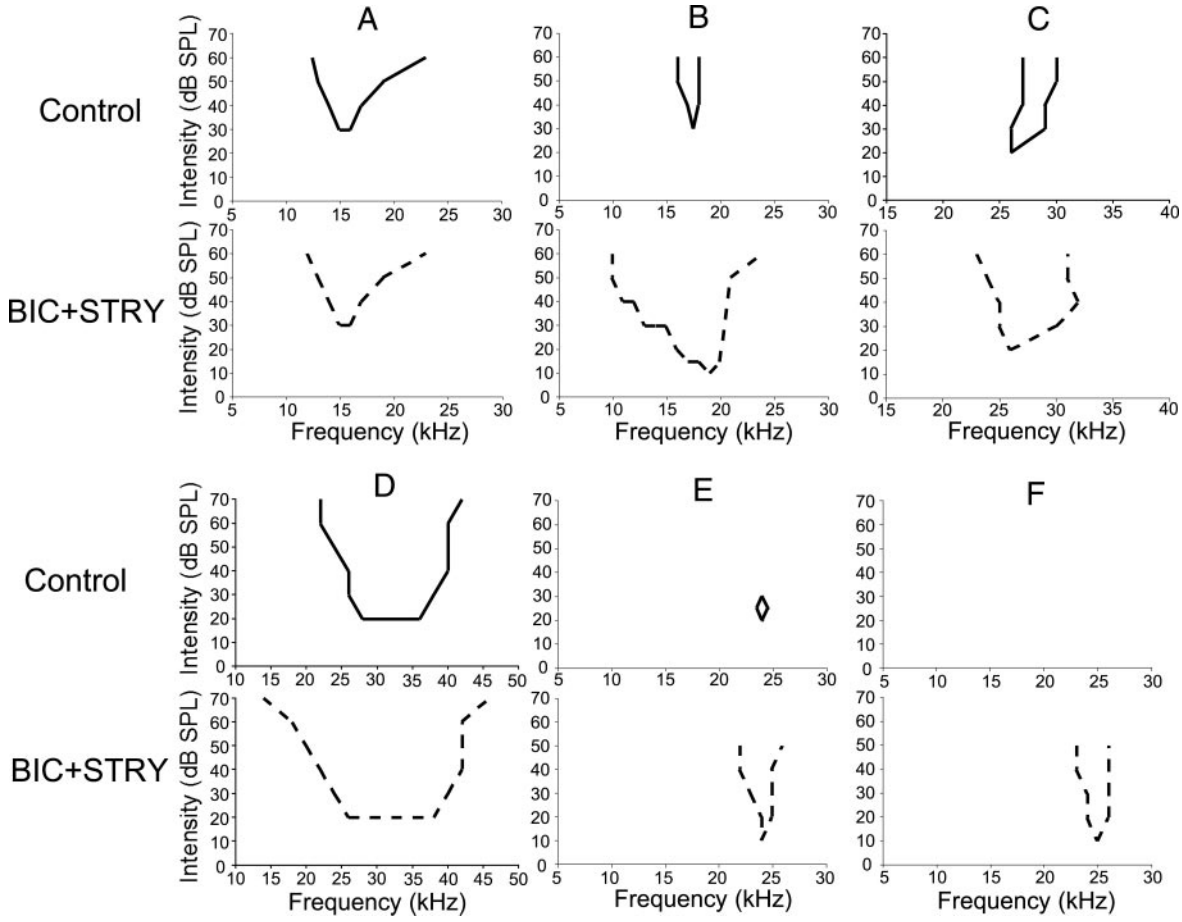

FIG. 12. Tuning curves from 6 IC neurons before and while inhibition was blocked by bicuculline and strychnine.

changes occurred in cells that had O-type tuning curves. In seven of seven cells with O-type cells, the upper threshold feature was eliminated, and the tuning curves were changed from an island-like O-type into a traditional V-shaped tuning curve (Fig. 12*E*). Finally, the most dramatic changes were seen in those IC cells that were unresponsive to tones, and thus had no tuning curves. We blocked inhibition in three of these cells, and in all cases, blocking inhibition converted an unresponsive cell into one that had a classical V-type tuning (Fig. 12*F*).

While substantial widening of tuning was commonly observed when inhibition was blocked in the IC, the extent of surround inhibition may have been underestimated in at least some of those cells. As described previously, blocking inhibition cannot reveal any pure surround inhibition, whereas the method of creating a carpet of background activity with glutamate can. We therefore evaluated the extent of surround inhibition in 16 IC cells with glutamate and found that, in 7 cells (44%), the range of frequencies that evoked inhibition at 30–50 dB above threshold was far wider than any of the tuning curve expansions that we observed when inhibition was blocked. This is shown in Fig. 13, which shows an IC neuron with a BF of 13 kHz and a fairly narrow, V-shaped, excitatory tuning curve. The remarkable feature of this cell is that inhibitory responses, as revealed by the gaps in the glutamate generated background activity, were evoked by frequencies ranging from as low as 19 kHz to as high as 55 kHz, a range that spanned about three octaves.

INHIBITION SHAPES SELECTIVITY FOR CALLS IN IC NEURONS. As reported previously (Klug et al. 2002; Pollak et al. 2003b), inhibition plays a prominent role in shaping the selectivities for calls in most IC neurons, and this was confirmed in this study. Representative examples are shown in Fig. 14. The six neurons shown in this figure are the same neurons whose tuning curves are shown in Fig. 12. These six neurons shown two features: *1*) that blocking inhibition increased the number of calls to which IC neurons responded (decreased selectivity) and *2*) that the change in the number of calls that evoked responses when inhibition was blocked varied from neuron to neuron. In a minority of neurons, such as the neuron in Fig. 14*A*, blocking inhibition hardly changed selectivity. The tuning curve of this neuron did not expand when inhibition was blocked (Fig. 12*A*), suggesting little or no surround inhibition. In contrast, the tuning curves of the four neurons shown in Fig. 14, *B* and *E*, expanded markedly, and correspondingly, they responded to many more calls when inhibition was blocked. The most dramatic change was seen for the neuron that was originally unresponsive to tone bursts and to any of the calls (Fig. 14*F*). Blocking inhibition unmasked a V-shaped tuning curve and allowed the neuron to respond to 9 of the 10 calls. The changes in the number of calls to which the 46 IC cells in our sample responded because of blocking inhibition are shown in Fig. 2*C* and illustrates the dominant role that inhibition plays in sculpting responsiveness to complex signals in the IC of these animals.

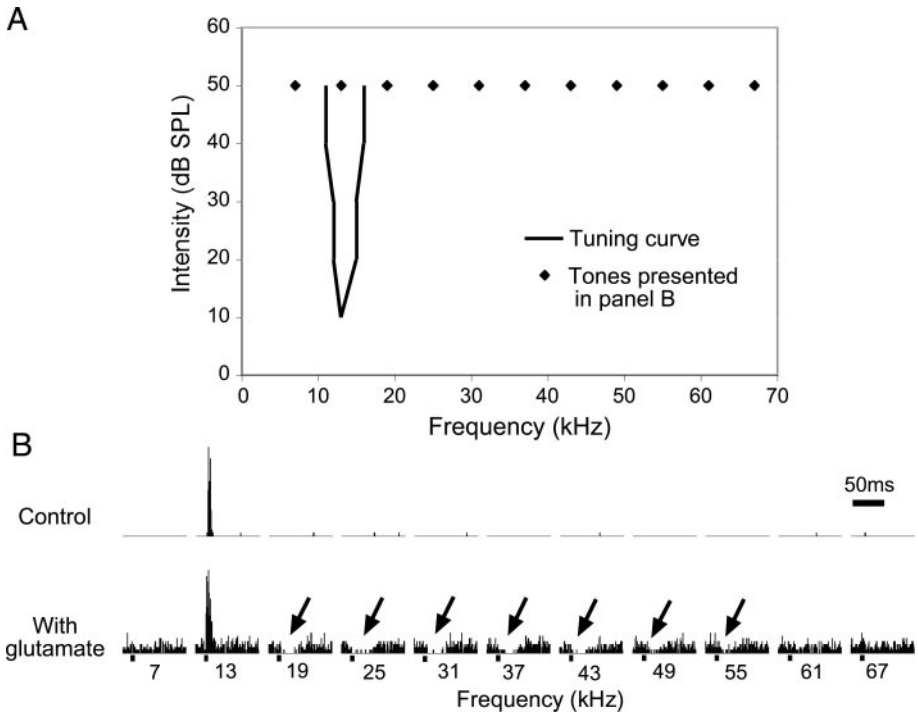

FIG. 13. Wide extent of surround inhibition in an IC cell. *A*: sharp tuning curve generated with 5.0-ms tone bursts at 1.0-kHz increments. The diamonds running horizontally show frequencies of tone bursts presented at 50 dB SPL during application of glutamate. *B*: *top*: (Control) responses evoked by tone bursts at 50 dB SPL (40 dB above BF threshold) at frequencies indicated by diamonds in *A*. Tone burst duration was 5.0 ms. Frequency increments are 6.0 kHz. *Bottom*: background activity generated by iontophoresis of glutamate while the same tone bursts were presented. Sharp tuning is shown by excitatory response that was evoked by only 1 frequency, 13 kHz. Frequencies that evoked inhibition are shown as gaps in the carpet of glutamate-evoked background activity (arrows) and range from 19 to 55 kHz.

DISCUSSION

There are four main findings of this study. First, we confirmed that DNLL cells have little or no surround inhibition. While GABAergic inhibition apparently reduces response magnitude, neither GABAergic nor glycinergic inhibition has any substantive influence on shaping response features evoked

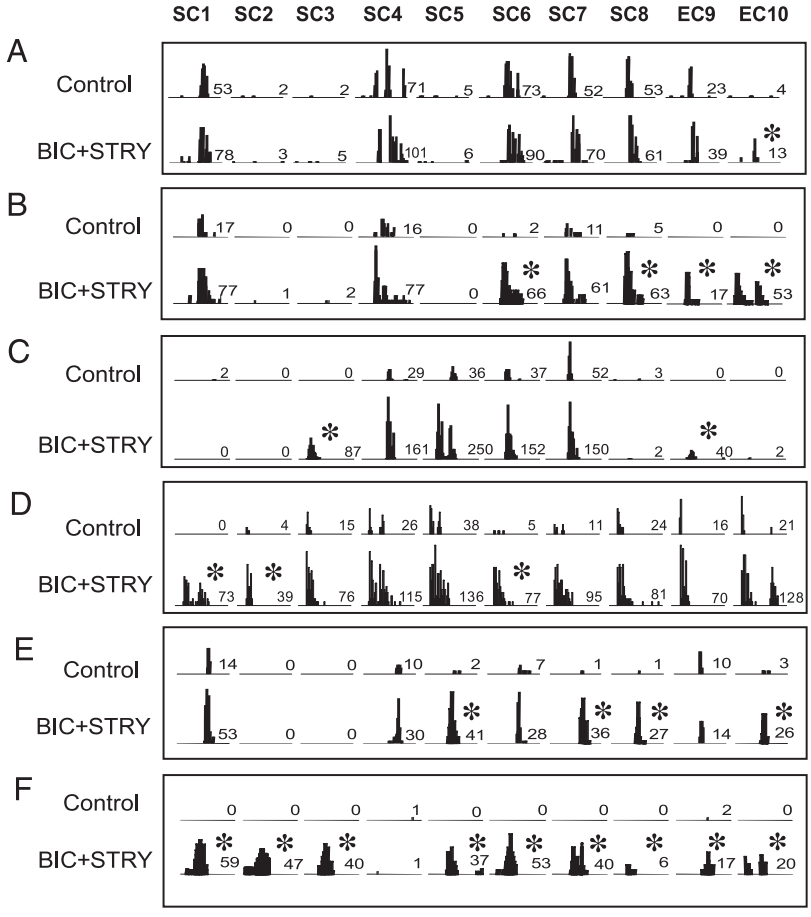

FIG. 14. Responses evoked by 10 species-specific calls in 6 IC cells before and while inhibition was blocked by bicuculline and strychnine. Asterisks show calls to which neuron responded while inhibition was blocked but not in the control condition, before inhibition was blocked. *A*: neuron in which blocking inhibition increased spike counts but had little influence on the selectivity for calls. The tuning curve of this neuron is shown in Fig. 12*A*. *B–D*: 3 IC neurons in which blocking inhibition not only increased response magnitude but also allowed the neurons to respond to more calls than they did before inhibition was blocked. *E*: upper threshold neuron whose tuning curve is shown in Fig. 12*E*. In the control condition, the neuron responded weakly to 4 calls but responded strongly to 8 calls when inhibition was blocked. *F*: neuron that did not respond to any tone burst or to any of the calls in the control condition. Blocking inhibition allowed the cell to respond 9 calls. Calls were presented at 30–40 dB above BF threshold to all neurons.

by tonal or species-specific signals. This lack of inhibitory sculpting, in turn, provides additional support for the hypothesis that information processing in the DNLL is accomplished largely by a linear integration of excitatory inputs. Second, we showed that most INLL neurons are characterized by wide tuning curves, and those INLL cells, like DNLL neurons, are unselective for species-specific calls. Also in common with the DNLL, responses to communication and echolocation calls in most INLL neurons are not shaped by inhibitory innervation, and their responses also appear to be caused by an integration of excitatory inputs. The third finding is that a minority of INLL cells are sharply tuned, and those cells, like the broadly tuned INLL cells, are unselective for calls. A small portion of sharply tuned cells are highly selective for calls, and their responses are strongly shaped by inhibition, because blocking inhibition unmasks a broad excitation that encompasses much, if not all, of the animal's hearing range. The fourth finding is that the IC population is strikingly different from the populations in either the INLL or DNLL. Where DNLL and INLL neurons are unselective and respond to most or all of the calls in the suite we presented, the majority of IC cells are selective for calls, and many are highly selective. Moreover, the selectivity for calls in almost all IC cells, as well as other response properties, are strongly shaped by inhibitory innervation. Inhibition dominates in the IC and creates response properties that are so heterogeneous that we cannot identify a simple set of response properties that are shared by the majority of IC neurons and thus would characterize a neuron as an IC neuron.

Monaural compared with binaural processing in the DNLL

We have shown that inhibition has little or no influence on sculpting DNLL response properties, a finding consistent with previous studies of the DNLL in this and other species of bats (Burger and Pollak 2001; Yang and Pollak 1994b; Yang et al. 1996). It is important to note that the response features that were uninfluenced by inhibition are responses that were evoked by monaural stimulation of the contralateral ear. However, high-frequency DNLL cells are binaural and are driven by stimulation of the contralateral ear and are inhibited by stimulation of the ipsilateral ear (Brugge et al. 1970; Covey 1993; Kelly et al. 1998; Yang and Pollak 1997, 1998; Yang et al. 1996). The ipsilaterally evoked inhibition is both glycinergic and GABAergic and acts to create unique binaural properties in the DNLL (Yang and Pollak 1994c). Those properties endow DNLL neurons with emergent features for the processing of multiple sound sources in space and/or for directional selectivity for moving sounds (Pollak et al. 2003a; Yang and Pollak 1994a,c). Thus DNLL cells appear to be unselective and therefore are generalists for coding "what" the sounds are, but the same cells are far more complex in their coding for "where" the sounds are located in space or whether they are moving and the direction of movement.

Consequences of wide tuning of INLL cells for processing in the IC

One notable feature of the INLL is the extreme that many INLL cells displayed in terms of the lack of inhibitory influences on their response features and in the widths of their tuning curves. Whereas blocking inhibition in some INLL cells increased response magnitude without affecting other response features, an effect similar to that seen in the DNLL, blocking both glycinergic and GABAergic inhibition in other INLL cells had no effects at all on their response properties. In those cells, even the response magnitude was unchanged. This total lack of any change in responsiveness when inhibition was blocked was never seen in any other neuron in any other nucleus that we had studied in this or in any previous study, and we consider it both unusual and remarkable.

The second extreme feature of INLL cells was the broadness of their tuning. To be sure, the fact that many INLL cells were excited by a range of frequencies that spanned two or even three octaves and encompassed a frequency range of 30–40 kHz is impressive. But even more impressive is the sharply tuned INLL cell in which blocking inhibition caused the excitatory tuning curve to expand and encompass the entire hearing range of the animal, from $<$12 to $\geq$99 kHz. This was, by far, the most remarkable expansion of tuning we have ever seen or that has been reported in any previous study.

The INLL sends predominately inhibitory but also some excitatory projections to the IC (Vater et al. 1992b; Winer et al. 1995), and broadly tuned INLL cells must have a significant impact on their targets in the IC. The impacts of those projections, however, were not apparent with most techniques we used to study IC cells. For example, IC tuning curves expand when inhibition is blocked, but the expansion is typically several kilohertz on either or both sides of the original excitatory tuning curve. Expansion of IC tuning curves by 20–30 kHz when inhibition is blocked has not been observed previously. However, if some IC cells receive inhibitory innervation from the INLL that is broader than their excitatory innervation, blocking inhibition would cause their tuning curves to expand but the surround frequencies that evoked pure inhibition would not be evident. One indication that inhibitory tuning may be wider than excitatory tuning in some IC neurons is seen in the experiments in which a background activity is generated by iontophoresis of glutamate. Our results show that at least some IC neurons have very wide, pure inhibitory surrounds (e.g., Fig. 13). Whether those inhibitory surrounds are a consequence of inhibitory innervation from widely tuned INLL cells is a distinct possibility, although these experiments were not designed test this possibility.

Comparative considerations

Anatomical studies conducted on a wide variety of bats and other mammals have all shown that the structural and connectional features of the mammalian auditory system have a common ground plan, with a similar complement of nuclei, similar connections, similar cell types, similar neurochemistry, and similar synaptic morphologies (Casseday 2002; Grothe 2000; Grothe et al. 1994; Pollak and Casseday 1986; Pollak et al. 1995; Vater et al. 1992b; Winer et al. 1995). Consistent with a basic mammalian ground plan, some of the most prominent results we obtained in the DNLL, INLL, and IC are similar to the findings reported in previous studies of these nuclei in a variety of mammals. However, other results we obtained are not. Below we consider the DNLL, INLL, and IC and point out features in each nucleus that vary among mammals and appear to be species-specific and features in each nucleus that are common to both bats and other mammals.

The DNLL is a conservative nucleus, since the response features that we observed in high-frequency neurons are similar to the features reported in studies of the DNLL in other bats, in cats, rats, and gerbils (Aitkin et al. 1970; Brugge et al. 1970; Covey 1993; Kelly et al. 1998; Markovitz and Pollak 1993, 1994). DNLL neurons tuned to high frequencies in all of these animals are EI, have the same complement of inputs, including GABAergic inputs from the opposite DNLL through the commissure of Probst, and the same projections (Chen et al. 1999; Glendenning et al. 1981; Huffman and Covey 1995; Oliver and Shneiderman 1989; Shneiderman et al. 1988; Yang et al. 1996; Zhang et al. 1998). Of particular significance is that the effects of ipsilaterally evoked inhibition operate in the same way in the DNLL of bats (Yang and Pollak 1994a,c) and in high-frequency neurons in the gerbil DNLL (Zahn 2004). In short, those response features that have been studied are similar among species, or at least, there is no evidence of any substantive differences.

The INLL, in contrast, appears to be species-specific, and markedly so. Although chopper and primary-like discharge patterns that we observed in Mexican free-tailed bats were also seen in the INLL of the big brown bat (Covey and Casseday 1991), the most prominent response feature of INLL reported here, the wide tuning curves, were not seen in the INLL in the big brown bat (Covey and Casseday 1991; Haplea et al. 1994). Moreover, recent studies of the INLL in the mustache bat have shown that the majority of INLL neurons in that animal are combination sensitive (Nataraj 2005; Portfors and Wenstrup 2001a). Those neurons integrate excitation from one frequency band and inhibition from another frequency band in a nonlinear manner to produce responses that depend on both the combination of frequencies in a signal and on the temporal relationships of those frequencies. The results found in this study show that inhibition plays, at best, a minor role in shaping INLL responses, and the lack of virtually any change in response selectivity to the suite of calls we presented when inhibition was blocked show that INLL neurons in Mexican free-tailed bats are not combinatorial, as they are in mustache bats. The INLL has received almost no attention in other mammals and thus we cannot comment on how INLL neurons in bats compare with those of the other mammals. Nevertheless, we point out that the INLL is the largest and most well developed of the nuclei of the lateral lemniscus in all bats, but is far less prominent in other mammals. This disparity in the relative development of the INLL among mammals also suggests that the INLL has prominent species-specific features.

Basic response features of IC neurons in bats

Bats are diverse mammals, both in terms of the number of species and the variety of ecological niches that the various species occupy. Consistent with their diversity, pronounced adaptations have been seen in the IC of the more specialized bats, such as the pallid (Fuzessery 1996, 1997; Fuzessery and Hall 1996), vampire (Schmidt 1991) and mustache bats (Leroy and Wenstrup 2000; Mittmann and Wenstrup 1995; Portfors and Wenstrup 2001b). We have not, however, observed any feature in the IC of Mexican free-tailed bats that could be considered to be a special adaptation for echolocation. Rather, we find that the basic response features in the IC of free-tailed bats are strikingly similar to the response features that have been found in the IC of other mammals. As in the free-tailed bat, IC neurons in a wide variety of bats and other mammals have monotonic and nonmonotonic rate-level functions (Faingold et al. 1991; Pollak and Park 1993; Ramachandran et al. 1999; Sivaramakrishnan et al. 2004; Syka et al. 2000), have more or less sharply tuned neurons (Haplea et al. 1994; LeBeau et al. 2001; Ramachandran et al. 1999), have a large population of binaural EI neurons that display time-intensity trading (Klug et al. 2000; Li and Kelly 1992; Pollak 1988; Yin et al. 1985), exhibit a wide range of latencies (Haplea et al. 1994; Park and Pollak 1993; Syka et al. 2000), and express other features such as duration tuned neurons (Brand et al. 2000; Faure et al. 2003; Fuzessery and Hall 1999), and neurons that respond preferentially to low rates of sinusoidal amplitude modulations (Burger and Pollak 1998; Casseday et al. 1997; Joris et al. 2004) and to the direction of FM sweeps (Fuzessery and Hall 1996; Koch and Grothe 1998).

Not only are these universal features of the IC, but most of these features are also shaped by inhibition at the IC, suggesting that the processing that generates those features may also be common among most mammals. Two basic response features, frequency tuning and binaural EI properties, show the putative communality of processing. Consistent with the results shown in this study, the tuning curves of many IC neurons in several types of bats (Vater et al. 1992a; Yang et al. 1992), as well as in the IC of rats and guinea pigs, have been shown to expand when inhibition is blocked (LeBeau et al. 2001; Palombi and Caspary 1996). Similarly, the features of binaural EI neurons have been shown to change in numerous ways when inhibition is blocked at the IC or when the contralateral DNLL is reversibly inactivated (Burger and Pollak 2001; Faingold et al. 1989, 1991, 1993; Klug et al. 1995; Li and Kelly 1992; Vater et al. 1992a).

The only mammal in which blocking inhibition at the IC fails to cause an expansion of tuning curves is the cat (Ramachandran et al. 1999). Moreover, the cat is the only mammal in which blocking inhibition at the IC fails to change the binaural properties of any neuron (Davis et al. 1999). Indeed, the only changes in IC cells that occur when inhibition is blocked are an overall increase in response magnitude and some interesting, yet subtle changes in the effects of noise on type O neurons (Davis et al. 2003). The conclusion drawn is that almost all processing in the cat occurs in lower nuclei and the results of that processing are largely inherited by IC neurons (Davis 2002; Ramachandran et al. 1999). The role of inhibition at the IC in cats appears to be largely for adjusting response magnitude. If this is correct, one can only conclude that while similar response properties occur in the IC of cats and other mammals, the ways in which those response properties are created in the cat's IC differ markedly from every other mammal in which the roles of inhibition have been investigated in vivo with iontophoretic application of drugs that block inhibitory receptors.

Communication call selectivity in the IC

In the section above, we outlined our reasons for concluding that while there are some species-specific features, the most basic response properties of IC neurons and the roles that inhibition plays in shaping those features are, for the most part, similar among mammals. This conclusion also seems to apply

to the processing of species-specific communication calls in the IC. There has only been one other previous report on the responses of communication calls in the IC of a mammal other than Mexican free-tailed bats and that was in the guinea pig IC (Suta et al. 2003). Their results are in some ways markedly different from those we report here, but there are a number of similarities as well.

The most marked difference is that guinea pig IC cells are unselective for calls, where ~80% of the cells responded to all or almost all of the calls they presented and only 3% failed to respond to any of the calls. This lack of selectivity contrasts with the high degree of selectivity of IC neurons in Mexican free-tailed bats, where the vast majority of IC cells were selective, and many of them were highly selective. The selectivity in Mexican free-tailed bats is not caused by variations in tuning among neurons because comparable selectivity occurs among isofrequency IC neurons. On the other hand, Suta et al. (2003) pointed out that, while isofrequency IC neurons in the guinea pig do not show variations in selectivity, they show pronounced variations in the way they respond to a particular call. That is, the population of isofrequency neurons respond to a particular call with a variety of temporal discharge patterns. The authors attributed the different discharge patterns evoked by a call to differences in the inhibitory innervation received by individual isofrequency neurons. In short, they attribute variations in IC temporal discharge patterns evoked by the same call to inhibition, whereas we attribute variations in call selectivity to inhibition. Taken together, the results suggest that inhibition can shape responses in different ways leading to species-specific differences in call processing.

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