Directionality Derived From Pinna-Cue Spectral Notches in Cat Dorsal Cochlear Nucleus

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Imig, Thomas J., Nikolai G. Bibikov, Pierre Poirier, and Frank K. Samson. Directionality derived from pinna-cue spectral notches in cat dorsal cochlear nucleus. J. Neurophysiol. 83: 907–925, 2000. We tested two hypotheses to determine whether dorsal cochlear nucleus (DCN) neurons are specialized to derive directionality from spectral notches: DCN neurons exhibit greater spectral-dependent directionality than ventral cochlear nucleus (VCN) neurons, and spectral-dependent directionality depends on response minima (nulls) produced by coincidence of best frequency (BF) and spectral-notch center frequency. Single-unit responses to 50-ms noise and tone bursts were recorded in barbiturate-anesthetized cats (BFs: 4–37 kHz). Units were classified using BF tone poststimulus time histograms. Pauser, onset-G (type II interneurons), and some chopper units were recorded from the DCN. Primary-like, onset-CIL (onset other than onset-G), and most choppers in the sample were recorded from the VCN. Many pauser and onset-G units were highly directional to noise. Chopper, onset-CIL, and primary-like units (collectively referred to as C-O-P units) were not. The difference in directionality depends on a monaural mechanism as pausers were more directional to monaural noise than C-O-P units. Contralateral inhibition produced a small increase in pauser directionality to noise simulation but had no effect on directionality of C-O-P units. Pauser and C-O-P units exhibited similar low directionality to BF tone, showing that the difference in noise directionality between groups depends on spectral cues. These results show that spectral-dependent directionality is a DCN specialization. Azimuth functions of highly directional units exhibited response nulls, and there was a linear relationship between BF and azimuth in this frequency range. These results show that DCN spectral-dependent directionality depends on response nulls produced by coincidence of unit BF and spectral-notch center-frequency.

INTRODUCTION

Cats and other mammals are capable of localizing the source of broadband sounds with considerable accuracy. Sound localization is important for survival, and neural mechanisms have evolved that use two available acoustic cues for location. Binaural time and level disparity (ITD and ILD, respectively) cues are available to the brain as a consequence of the separation of the two ears on either side of the head, and they are most important for left-right (azimuthal) localization. Spectral (pinna) cues derive from diffraction of high-frequency broadband sounds primarily with the pinna and are most important for up-down (vertical, elevational) and front-back localization (Middlebrooks and Green 1991). The head-related transfer function (HRTF) describes the free-field to tympanic-membrane spectral transformation and there is a unique HRTF associated with each sound direction (e.g., in cats; Musicant et al. 1990; Rice et al. 1992).

Many neurons in the cat’s auditory midbrain (inferior colliculus, IC) and forebrain (medial geniculate body and auditory cortex) are sensitive to the azimuth of noise bursts. They respond well to some sound directions and poorly to others over a broad range of SPL (Aitkin and Martin 1987; Barone et al. 1996; Clarey et al. 1992, 1995; Imig et al. 1990; Rajan et al. 1990). Some such neurons derive azimuth sensitivity from binaural disparity cues as their responses to monaural noise stimulation are insensitive to azimuth (Poirier et al. 1996; Samson et al. 1994, 1996). Others derive directionality from monaural spectral cues as they are sensitive to the azimuth of noise bursts presented binaurally and monaurally (Imig et al. 1997; Poirier et al. 1996; Samson et al. 1993, 1996). These findings show that midbrain and forebrain neurons are differentially sensitive to binaural-disparity and monaural-spectral directional cues.

Different functional groups of cochlear nucleus (CN) neurons may provide input to separate spectral and binaural directional pathways. Each auditory nerve fiber bifurcates on entering the CN. The ascending branch terminates in the anteroventral cochlear nucleus (AVCN), and the descending branch terminates in the posteroventral (PVCN) and dorsal cochlear nucleus (DCN). AVCN neurons provide input to the binaural disparity pathway. Their axons provide bilateral input to the superior olivary nuclei, the lowest level where ITD and ILD sensitive neurons are found in the ascending auditory pathway (Yin and Chan 1988). DCN neurons may represent the beginning of a pathway that is sensitive to spectral directional cues. Spectral notches are salient features of the HRTF. Discharge rates of some DCN neurons are inhibited when the center frequency of a spectral notch coincides with the neuron’s best frequency (Joris 1998; Nelken and Young 1994; Spirou and Young 1991; Young et al. 1992a,b). These observations have been made using earphones coupled to the ears, but such neurons would presumably be sensitive to spectral notches in broadband sounds presented under free-field conditions. The sensitivity of VCN neurons to spectral notches has not been described in detail, although Young et al. (1992a) noted in an abstract that spectral notches did not inhibit VCN neurons. Nevertheless VCN choppers may have physiological properties appropriate for notch inhibition as they exhibit inhibitory side bands that are nearly as strong as those of DCN neurons (Rhode and Greenberg 1994).

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The effect of anesthesia on response properties of DCN neurons raises questions regarding their potential role as the beginning of a spectral-directional pathway. Spectral-dependent directionality has been observed in the midbrain and forebrain of pentobarbital-anesthetized cats (Imig et al. 1997; Poirier et al. 1996; Samson et al. 1993, 1996). In contrast, DCN notch inhibition has been described mainly in unanesthetized, decerebrate cats (Nelken and Young 1994; Spirou and Young 1991; Young et al. 1992a,b). Barbiturate anesthesia causes significant changes in DCN neuron response properties as compared with unanesthetized conditions (Rhode and Kettner 1987; Young and Brownell 1976), although its effect on notch inhibition is unknown. Spectral notches also can inhibit DCN neurons in α-chloralose anesthetized cats, although barbiturate may alter response properties to a greater extent than α-chloralose (Joris 1998). Consequently the potential role of DCN neurons as a source of spectral-dependent directionality that is transmitted to higher levels of the auditory system in barbiturate-anesthetized cats is uncertain.

Nelken and Young (1994) presented a model for notch inhibition in DCN projection neurons (type IV cells). According to the model, type IV cells receive inputs from two types of inhibitory neurons, type II cells and from a wideband inhibitor (WBI), although only WBI input plays an important role in notch inhibition. Whether notch inhibition recorded under conditions of barbiturate anesthesia is consistent with this model is unknown.

Our long-term goal is to identify mechanisms that underlie the spectral-dependent directionality of midbrain and forebrain neurons. These experiments focus on identification of possible sources of spectral-dependent directionality in the CN using identical experimental conditions (including pentobarbital anesthesia and free-field stimulation) as those used to identify spectral-dependent directionality in midbrain and forebrain neurons. There are three specific goals. The first is to test the hypothesis that DCN neurons exhibit greater spectral-dependent directionality than VCN neurons. The second is to test the hypothesis that spectral notches cause inhibition of discharge rates and thus result in directional responses. The third is to test the hypothesis that a WBI has a major role in notch inhibition in DCN projection neurons. The results support these hypotheses. Some of these data have been presented in preliminary form (Imig et al. 1998).

METHODS

Twelve healthy, young, adult cats with clean external ears, translucent tympanic membranes, and low-threshold single-unit responses were used in the experiments. Three were used in acute best-frequency mapping experiments and nine in chronic single-unit recording experiments with the goal to obtain more data from each animal during multiple recording sessions than might have been possible during a single session. All husbandry and experimental procedures were carried out using protocols approved by the Institutional Animal Care and Use Committee of the Kansas University Medical Center.

Surgical implant of a stainless steel chronic recording chamber was carried out using inhalation anesthesia (0.8–1.5% isoflurane in O2) and standard aseptic procedures under the supervision of an Accreditation for Accreditation of Laboratory Animal Care–accredited veterinarian. Postoperative discomfort was ameliorated with analgesics. The chamber was positioned stereotaxically over a craniotomy and fastened to the skull with dental acrylic and stainless steel screws. A stainless steel tube, used to secure the animal’s head to a support frame during recording sessions, also was attached to the skull. The chamber was sealed with a stainless steel cap at times other than during recording sessions to protect the craniotomy from mechanical damage and infection. The dura mater was covered with a broad-spectrum antibiotic ophthalmic ointment (bacitracin) before sealing the chamber.

Cats were allowed to fully recover from the surgery before the first recording session and thereafter single-unit recording-sessions were scheduled at ≥2-week intervals. Animals were anesthetized during chronic recording sessions to prevent movements. Anesthesia was induced with isoflurane in O2 and atropine (0.1 mg/kg im) was injected. Isoflurane was replaced with pentobarbital sodium (initial dose, 10 mg/kg iv) which was infused continuously intravenously throughout the recording session at a rate sufficient to eliminate pinna reflexes and spontaneous movements (~8.5 mg · kg⁻¹ · h⁻¹). Dexamethasone (2 mg/kg iv) was injected to reduce the possibility of cerebral edema. Application of ophthalmic ointment prevented corneal drying. Tracheal intubation ensured a patent airway. Breathing and heart rates were monitored during the recording session, and temperature was maintained using a thermostatically controlled heating pad. After the recording session, animals were kept warm until they awakened from the anesthesia. Marking lesions were placed during terminal recording sessions. Each animal was given a lethal dose of anesthetic at the end of the terminal recording session, perfused through the heart with a 10% solution of formal saline, and the brain processed using standard methods (Barone et al. 1996).

Single-unit recordings were carried out in an electrically shielded, anechoic, sound-isolation chamber. The anesthetized cat rested in a sling with its head rigidly fixed by clamping the head-support tube. The head was positioned with the horizontal Horsley-Clarke plane tilting forward and down at an angle of ~18° from horizontal, which approximates the head position of an alert cat looking forward. The ears were pulled to an upright position using strings that were attached to the outer surfaces of each pinna. Sterility was maintained within the recording chamber throughout the procedure. Single-unit activity was recorded using paralene-insulated, tungsten electrodes (Frederick Haer) with impedances of 1–5 MΩ measured at 1 kHz in the brain. Details concerning single-unit recording, computer control of data collection, and data analysis have been described previously (Barone et al. 1996; Samson et al. 1993).

Auditory waveform synthesis, acoustic calibration, stimulus timing and sequencing, and data collection were controlled by a PDP 11/73 computer. Stimulus waveforms were generated at an output sample rate of 100 kHz using a 16-bit D/A converter (Boys Town National Research Hospital), low-pass filtered at 40 kHz (Kemo VBF/8, ~180 dB/octave) to prevent aliasing, attenuated with computer controllable attenuators, and amplified. Each loudspeaker was calibrated by placing a microphone (B&K type 4133 1/2-in.) at the center of the loudspeaker array, aiming it at the loudspeaker, and performing a fast Fourier transform (FFT) on the impulse response. Tables of maximum SPLs attainable at different frequencies were derived from FFT data and stored in a computer disk file for use during experiments.

A random-number generator produced a frozen, broadband-noise waveform with a flat spectrum (0–50 kHz) and random amplitude distribution. The actual spectrum of the noise delivered to the animal was shaped by the sound system (mainly the loudspeaker). Stimulus envelopes for all stimuli were 50 ms in duration and had linear rise/fall times of 5 ms. Stimuli were presented at a rate of 5/s for most units and 3.3/s for a few.

Monaural stimulation was simulated using ear plugging. Injection of ear mold compound (Ear Mold Impression Material, All American Mold Lab) into the concha and ear canal occluded the ear and attenuated sound reaching the tympanic membrane. Attenuation varied between 32 and 70 dB in the range of 4–32 kHz (Samson et al. 1993).

Best frequencies (BFs, center frequency of the excitatory range at
10–20 dB above threshold) and frequency response areas were obtained by presenting tone bursts from a loudspeaker at +30 or +60° of azimuth (+30 or +60°A, direction in the horizontal plane passing through the interaural line). Poststimulus time histograms for BF stimuli were constructed using 10–200 stimulus repetitions. Timing of unit discharges was recorded with a resolution of 0.01 ms. Analyses of spike counts were based on the number of spikes in a 60-ms time window that began at stimulus onset and terminated 10 ms after stimulus offset.

An array of high-frequency loudspeakers (Radio Shack 40-1310B) with similar frequency response characteristics allowed the free-field presentation of sounds whose directions could be varied in azimuth and elevation (Fig. 1). Loudspeakers in the array were aimed at the interaural midpoint and located at a distance of 0.79 m from it. An aluminum tubing frame supported loudspeakers along a vertical meridian (vertical array) of an imaginary sphere centered on the cat’s head. The vertical array consisted of seven loudspeakers spaced at 22.5° intervals (±67.5, ±45, ±22.5, and 0°). A horizontal array of 13 loudspeakers spaced at 15° intervals along a 180° arc of the equator was attached to the vertical support. Sound direction could be varied in elevation by presenting sound from different loudspeakers and could be varied in azimuth the same way or by rotating the frame about its vertical axis. The loudspeakers had a usable frequency range between 4 and 40 kHz. Output increased from 4 kHz to a peak at 8 kHz at 20 dB/octave, decreased by 5 dB/octave up to 35 kHz and then decreased at 60 dB/octave. Loudspeakers with lower frequency output were also available for use below 4 kHz.

**Measurement of directionality**

The term directionality refers to the extent to which a unit’s responsiveness is azimuth dependent. Directionality was calculated from a unit’s responses to an azimuth-level stimulus set composed of noise or BF-tone bursts that varied in azimuth and SPL. Stimuli were presented from each one of seven azimuths (±90, ±60, ±30, and 0°A) and in some cases also at intermediate azimuths (±75, ±45, and ±15°A). At each direction, SPL was varied from near threshold up to 70 or 80 dB SPL in 5-, 10-, or 20-dB steps. Ten (or in a few cases, 20) repetitions were presented at each azimuth-level combination.

Responses to each azimuth-level stimulus set were normalized (percentage of maximum) and displayed as an azimuth-level response area (ALRA, Fig. 2, A and D). Typical of CN units, this unit responded at lower SPLs on the right (ipsilateral to the recording site in the right CN) than on the left side of the head showing azimuth dependence of response thresholds for both noise and BF-tones. The noise ALRA (D) showed substantial azimuth-dependence of unit responsiveness. Responsiveness was near maximal throughout the ipsilateral quadrant and minimal at −15°A. Such strong directional variation in responsiveness was not apparent in the tonal ALRA (A).

Two measures of unit responsiveness were used to assess directionality. To calculate the first one, ALRA data at each azimuth were plotted as functions of level re: threshold. BF-tone level-response functions had similar, weakly nonmonotonic profiles showing that responsiveness to tones was rather similar at each azimuth (B). Greater differences in responsiveness were seen in the noise level-response functions (E). A normalized threshold response (NTR) was calculated for each level-response function by averaging interpolated responses in 1-dB steps over the range of 20–29 dB re: threshold. The 2- to 29-dB range is delimited in B and E by vertical interrupted lines. The NTR values were normalized and plotted as a function of azimuth (NTR, C and F). Azimuth function modulation provides an index of directionality: Modulation(%) = 100%*(R_{max} - R_{min})/R_{max}; R_{max} = maximum response and R_{min} = minimum response.

NTR azimuth function modulation was greater for noise (69%, F) than for BF-tonal stimulation (12%, C). Although data were collected at 15° intervals in the case of this unit, data were collected at 30° intervals for others. For the purpose of statistical comparisons, measurement of directionality was restricted to data at 30° intervals as these were available for all units. This restriction caused a significant underestimation of NTR directionality for noise stimulation in the case of this unit (69 vs. 33%) but no effect on the NTR directionality for BF-tonal stimulation (12 vs. 12%).

Excitatory response thresholds were used to align level-response functions in the vast majority of units, but in three units alignment at certain azimuths was based on threshold for inhibition of spontaneous rate of discharge (SR; e.g., Fig. 13). This unit was most responsive to noise bursts presented at the midline and in the left quadrant (A), and SR was inhibited by noise bursts presented at 60 and 90°A on the right side of the head (B).

A second measure of directionality was based on the gross response (GR), which is equal to the sum of responses to all stimulus SPLs. This measure was used in previous studies (Imig et al. 1997; Poirier et al. 1996; Samson et al. 1993, 1994, 1996), and we use it here for comparison with the NTR measure. As is the case for NTR modulation, GR modulation for the unit in Fig. 2 was greater for noise than for BF tones (75% F vs. 41% C, respectively). Unlike the NTR measure, the GR measure has the advantage that it is unnecessary to obtain thresholds at each azimuth. A disadvantage is that azimuth-dependent threshold differences affect GR modulation, whereas they have little effect on the NTR measure. Thus threshold increases on the contralateral side of the head (e.g., A) produce a decrease in GR magnitude at these locations that is not seen in the NTR function (C). In RESULTS we first compare unit responses using the NTR measure and then compare GR and NTR measures.

**NTR sample**

Calculation of NTR over a broader range of level would provide presumably more accurate estimates of responsiveness as more re-
Responses would be included in each estimate. Nevertheless NTR modulation was quite similar whether measured over a 10 dB (20–29 dB) or 20 dB (20–39 dB) range (n = 445, mean absolute difference, 3.9 ± 3.3%, mean ± SD), and the two measures were strongly correlated (r = 0.98). The 20- to 29-dB range was preferable to ranges that extended to higher levels because it allowed inclusion of more units in the analysis. Using the 20- to 29-dB range required that a unit be tested with stimuli $29 \text{ dB}$ above threshold at each of the seven azimuths. Units that met this criterion were included within the NTR sample. Some units failed to meet the criterion because of high thresholds at one or more azimuths (e.g., Fig. 8G) and these comprised the non-NTR sample. We were quite conservative in selection of the NTR sample. If we could not confidently identify a threshold at each of the seven azimuths, the unit was rejected even if there was clear spectral inhibition at some azimuths where NTR measures were available (e.g., Fig. 8G and 8H). Use of ranges that extended to higher levels would have restricted the NTR sample further.

Fifty units were tested at least twice using identical azimuth-level stimulus sets (binaural noise, monaural noise, binaural BF tone, or monaural BF tone) and repeated ALRAs for the vast majority appeared very similar. Comparison of azimuth function modulation for repeated responses provided an indication of response reliability. NTR modulation of repeated measures differed by an average of 6.7 ± 7.1%, and the repetitions were strongly correlated (r = 0.92). GR modulation showed similar results (mean absolute difference, 5.4 ± 4.8%, r = 0.92). This provides reasonable assurance that directionality was usually stable over time. In the following analyses, response measures are based on averages of repetitions when they are available.

RESULTS

Single-unit waveforms were identified by their responses to noise burst search stimuli that varied in sound pressure level (SPL, from 0 to 80 dB) and azimuth (–90 to +90° in 30° steps). Tone bursts that varied in frequency and SPL also were presented at many recording sites. Rate-level functions for BF tones and azimuth-level response areas for BF-tones and/or noise bursts were obtained for 190 well-isolated single units,
although most analyses were restricted to 129 units in the NTR sample that were categorized into one of five poststimulus time histogram (PSTH) classes. BFs of the NTR sample ranged from 4.2 to 37 kHz.

**FIG. 3.** Pauser post-stimulus time histograms (PSTHs) and frequency response areas (FRAs). Binaural stimulation was used for data in each panel. **A**: pauser PSTH. **B**: build-up PSTH. Bar below the time scale shows the 50-ms stimulus duration. Time bins of 1 ms are used for the PSTHs although spike times were recorded with a resolution of 0.01 ms. Spike times are not corrected for the 2.4 ms that it takes sound to travel 0.79 m from the loudspeaker to the ear. **C–H**: FRAs of pauser units. Iso-response contour plots show the response (number of spikes) normalized as a percentage of maximum. Points in each panel show the frequency-SPL combinations that were used to construct each FRA. Some FRAs were characterized by nonmonotonic rate-level functions and displayed a circumscribed island of higher responsiveness near threshold (CI, **C–E** and **H**). Others exhibited monotonic rate-level functions to BF-tonal stimulation (**F** and **G**). Spontaneously active units showed inhibitory side bands (**C, G, and H**).

**PSTH classification**

PSTHs of responses to BF tone bursts presented at 20–80 dB above threshold were used to classify functional groupings...
of CN neurons. The PSTH categories described by Rhode and colleagues in the cat CN (Rhode and Greenberg 1992; Rhode and Smith 1986a,b) were deemed appropriate as our data were collected using identical anesthetic conditions.

Pauser PSTHs were characterized by a silent period (pause) that separated an initial peak from a later discharge (Fig. 3A). The duration of the pause (typically \( \geq 10 \) ms) varied among units. A few pausers exhibited only late period firing (build-up pattern, \( B \)) or both patterns depending on SPL. Pausers commonly exhibited chopper (multipeaked) responses, some only at near threshold levels and others at higher levels as well. BF-tonal responses of some pausers were nonmonotonic functions of level (e.g., Fig. 2B), typically reaching a peak at 10–20 dB above threshold, decreasing and often increasing again. There was considerable variation in the magnitude of response decrement. Frequency response areas (FRAs) of these units are referred to as nonmonotonic and were characterized by a circumscribed island (CI) of higher responsiveness near threshold BF, delimited by lower responsiveness at higher SPLs (CI, Fig. 3, C–E, and H). In some cases there were multiple excitatory frequency domains, especially at higher SPLs (C and E). Responses of other pausers to BF-tonal stimulation were monotonic functions of level (\( F \) and \( G \)). Inhibition of spontaneous rate (SR) provided evidence for side-band inhibition in all spontaneously active pausers (\( C \), \( G \), and \( H \)). Intracellular staining has revealed that pauser PSTHs represent responses of DCN fusiform cells the axons of which project to higher levels of the auditory system (Rhode et al. 1983b).

Onset-G units responded to stimulus onset with an onset burst that gradually decreased throughout the duration of the discharge (e.g., Fig. 4A). All lacked SR. Some onset-G PSTHs exhibited two peaks during the first 5 ms of the response at certain SPLs that gave a chopper appearance to the PSTH, although they did not exhibit the regularity of discharge characteristic of choppers (see following text). Most onset-G units (8/11) exhibited nonmonotonic FRAs (\( B \)). Intracellular staining has revealed that onset-G PSTHs represent responses of inhibitory interneurons (type II cells) the axons of which terminate within the CN (Rhode 1999).

Pauser and onset-G responses have been found almost exclusively in the DCN (Rhode 1999; Rhode and Greenberg 1992; Rhode and Smith 1986a,b). Histological localization of single-unit recording sites was not practicable in our experiments due to the use of chronic recording preparations, but tonotopic sequences provided an independent criterion for assigning recording site locations to either the DCN or VCN. Electrodes passed from caudodorsal to rostroventral through the CN at a 30° angle from vertical in the sagittal plane. Recording sites were marked with electrolytic lesions in three BF-mapping experiments. Often electrodes penetrated the DCN before entering the VCN. These penetrations recorded high-to-low BF sequences in each division consistent with earlier reports (e.g., Rose et al. 1959). Only one tonotopic sequence was encountered if an electrode penetration was terminated before reaching the VCN or if it missed the DCN and passed only through the VCN. In double-tonotopic sequence penetrations, pauser and onset-G units were found exclusively during the first sequence, i.e., in the DCN (Table 1).

Primary-like units (Fig. 5A) were found almost exclusively during the second tonotopic sequence (Table 1), consistent with their known location in the VCN (Rhode and Greenberg 1992). The primary-like NTR sample of 25 units included 9 primary-like with notch units (not illustrated). These showed a 0.2- to 2-ms pause in firing after the initial peak in the PSTH (bins of 0.1 ms were used during the analysis, but 1-ms bins are used in the illustrated PSTHs). Onset units (excluding onset-G type) were characterized by a precisely timed discharge after stimulus onset. The small sample includes two onset-chopper (onset-C) units that discharged one to four spikes per tone burst (\( C \)). It also included one onset-I response that consisted of a single spike following tone-burst onset, and four onset-L responses that consisted of an onset spike followed by a low rate of discharge throughout the duration of the tone-burst and a low rate of spontaneous activity (I and L refer to the shape of the PSTH). We refer to this small group of onset-C, onset-I, and onset-L units collectively as onset-CIL units. Onset-CIL units were found exclusively during the second tonotopic sequence (Table 1) consistent with previous findings of these responses in the VCN (Rhode and Greenberg 1992).

Chopper units exhibit multipeaked PSTHs (Fig. 5B) and

<table>
<thead>
<tr>
<th>Unit Group</th>
<th>No. in DCN (First Tonotopic Sequence)</th>
<th>No. in VCN (Second Tonotopic Sequence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pauser</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Onset-G</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Primary-like</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Chopper</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Onset-CIL</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

DCN, dorsal cochlear nucleus; VCN, ventral cochlear nucleus.
regular discharges with coefficients of variation (CV, SD/mean interval) of <0.35 (Young et al. 1988). Some choppers showed regular firing over the entire stimulus duration \((n = 19)\), others only over the initial part \((n = 5)\) or final part of the discharge \((n = 1)\). Choppers are found in both the DCN and VCN (Rhode and Greenberg 1992). Extrapolation from double-tonotopic sequences suggests that 73\% (11/15) of the chopper sample was found in the VCN and 27\% (4/15) in the DCN (Table 1).

Most chopper, onset-CIL and primary-like units (collectively referred to as C-O-P units) exhibited monotonic FRAs \((D–F)\), although two choppers exhibited weakly nonmonotonic responses (not illustrated).

More pauser than C-O-P units were spontaneously active in the NTR sample (Table 2). Of 61 pausers tested with noise stimulation, 42 (69\%) were spontaneously active and SR averaged 17.3\% of the maximum response to noise. Of 59 C-O-P units tested with noise, 26 (44\%) were spontaneously active with SRs averaging 11\% of their maximum response to noise. The overall average SR relative to noise maximum response was significantly greater for pausers (12\%) than for C-O-P

![FIG. 5. Primary-like, chopper, and onset-chopper post stimulus time histograms (A–C) and frequency response areas (D–F). Binaural stimulation. See Fig. 3 for further details.](http://jn.physiology.org/)

### TABLE 2. Comparison of SR of pauser and C-O-P units in the NTR sample

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Unit Group</th>
<th>No. of Units Tested</th>
<th>No. of Units With SR</th>
<th>Percent of Units With SR, %</th>
<th>Average Normalized SR, %</th>
<th>Overall Average SR, %</th>
<th>(t)-Test ((P))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noise</td>
<td>Pauser</td>
<td>61</td>
<td>42</td>
<td>69</td>
<td>17.3</td>
<td>11.9</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>C-O-P</td>
<td>59</td>
<td>26</td>
<td>44</td>
<td>11.0</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td>BF tone</td>
<td>Pauser</td>
<td>24</td>
<td>20</td>
<td>83</td>
<td>11.1</td>
<td>9.2</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>C-O-P</td>
<td>22</td>
<td>10</td>
<td>44</td>
<td>10.2</td>
<td>4.6</td>
<td></td>
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</table>

These data were obtained from responses to azimuth-level stimulus sets. The average spontaneous rate of discharge (SR) for units with non-zero SR is shown as a percentage of the maximal response to noise or best frequency (BF) tones (Average Normalized SR). Noise maximal response was based on responses to an azimuth-level data set. BF-tone maximal response was based either upon an azimuth-level data set or upon a rate-level function at a single azimuth. Overall average is the average SR for the entire group including units with zero and non-zero SR. The \(t\)-test compares the overall averages for pauser and C-O-P groups. NTR, normalized threshold response; C-O-P, chopper, onset-CIL, and primary-like units.
units (5%). Comparable differences were seen in these two groups when they were tested with BF tones.

**Pauser and onset-G units are more directional than C-O-P units**

NTR modulation of CN units in response to binaural and monaural noise stimulation was distributed broadly across BF (Fig. 6). Modulations >50% were found only in units with BF >8 kHz. Onset-G and pauser units exhibited the highest modulations. All five onset-G units that were responsive to noise stimulation exhibited relatively high directionality (NTR modulation >45%, Fig. 6) evidenced by a striking diminution of responsiveness at one or more azimuths (response nulls, Fig. 7). Pausers exhibited a wide range of directionality to noise stimulation (Fig. 6). Many pausers exhibited low directionality and lacked response nulls (e.g., Fig. 8A, NTR mod. 13%). Others showed higher directionality and response nulls that could be located anywhere throughout the frontal field (Figs. 2D, 8, B–H, and 13A).

There was no obvious relationship between pauser directionality and FRA architecture. Units with nonmonotonic FRAs could exhibit low directionality (FRA, Fig. 3C; ALRA, Fig. 8A; 13%, NTR modulation) or high directionality (FRA, Fig. 3H; ALRA, Fig. 13A; 92% NTR modulation). Correspondingly, pausers with monotonic FRAs also could exhibit low directionality (FRA, Fig. 3F; ALRA not illustrated; 10% NTR modulation), or high directionality (FRA, Fig. 3G; ALRA, Fig. 8E; 88% NTR modulation).

Chopper, primary-like and onset-CIL units exhibited lower directionality than pauser and onset-G units (Fig. 6). A typical example is shown in the responses to noise bursts of a primary-like with notch unit (Fig. 9). Responsiveness was rather similar at each azimuth, and consequently the NTR azimuth function shows relatively little (19%) modulation.

Mean NTR modulation for binaural noise stimulation was higher for pauser (35%) and onset-G groups (62%) than for units (5%). Comparable differences were seen in these two groups when they were tested with BF tones.

**FIG. 6.** Scatter plots comparing unit BF and NTR modulation to noise stimulation. Top: binaural stimulation. PSTH type, n, mean NTR modulation (%) ± SD: pauser, 54, 34.9 ± 20.5; onset-G, 3, 61.6 ± 14.2; primary-like, 25, 19.9 ± 8.5; chopper, 24, 20.6 ± 9.0; onset-CIL, 6, 22.8 ± 4.5. Bottom: monaural stimulation. Pauser, 26, 35.2 ± 22.2; onset-G, 2, 86.7 ± 14.3; primary-like, 5, 19.1 ± 4.9; chopper, 4, 23.91 ± 12.6; onset-CIL, 5, 26.1 ± 7.7.

**FIG. 7.** Examples of onset-G unit ALRAs for noise stimulation. A: binaural noise stimulation. B and C: monaural noise stimulation. p values are 0.94, 0.26, and 0.11 for the units in A–C, respectively. ↑, response nulls. Gray scale intervals are shown in Fig. 3C.
primary-like (20%), chopper (21%), and onset-CIL groups (23%, see legend of Fig. 6). Binaural noise NTR modulation for pauser, primary-like, and chopper groups was compared using a one-way, mixed model, ANOVA. Onset-G and onset-CIL units were excluded from the analysis because of small sample size. The ANOVA revealed that there were significant (P < 0.0001) differences among classes. Tukey-Kramer post hoc tests showed that mean NTR modulation of pauser units was significantly greater than that for primary-like (P < 0.0001) or chopper units (P < 0.0002). There was no significant difference between mean NTR modulation for primary-like and chopper units. ANOVA did not reveal any significant differences between the mean BF for pausers (14.4 kHz), choppers (14.5 kHz), or primary-like (16.0 kHz) groups, show-

FIG. 8. Examples of pauser ALRAs for noise stimulation. Units are arranged in order of ascending BF. A: low directionality unit lacks a response null. B–H: response nulls are indicated by arrows. Response null is the minimum of the NTR azimuth function. Nulls in G and H are estimates as NTR values could not be calculated at some azimuths. Binaural noise stimulation except for D, which was monaural noise. Gray scale intervals are shown in Fig. 3C.
ing that BF differences cannot account for these results. Monaural responses of pauser and onset-G groups also exhibited higher modulation than monaural responses of primary-like, chopper, or onset-CIL groups, but the small sample size precludes statistical comparison (see legend of Fig. 6).

Because choppers, primary-like, and onset-CIL groups all showed relatively low NTR modulation, we combined them (C-O-P group) and compared them with pausers. Onset-G units were excluded from this analysis because they are presumably interneurons and our primary interest was in comparing directionality of CN outputs. Pausers exhibited significantly greater mean NTR modulation than C-O-P units under both binaural and monaural conditions (Table 3). Differences in NTR modulation between pauser and C-O-P groups cannot be attributed to differences in BFs between the two samples as means were not significantly different. There was no significant modulation difference between pauser and C-O-P groups for BF-tonal stimulation. These results lead to the following conclusions.

First, pausers are significantly more directional in their response to binaurally presented noise bursts than are C-O-P units. Second, similar findings obtain for monaurally presented noise bursts, showing that differential sensitivity derives at least in part from monaural mechanisms. Third, pauser and C-O-P units show no directionality differences in response to BF-tone bursts. This shows that greater pauser directionality to noise stimulation depends on spectral cues as these are present in noise but not in BF tones.

Although the pauser group derives greater directionality from spectral cues than the C-O-P group, comparison of noise and tone NTR directionality in units tested with both stimuli shows that both groups derive significant directionality from spectral cues. Under both binaural and monaural conditions, pauser and C-O-P groups showed significantly greater NTR modulation to noise than to BF tone bursts (Table 4).

**Effect of contralateral inhibition on directionality**

Evidence for contralateral inhibition came from comparison of unit responses to binaural and monaural ipsilateral stimulation. Unit responses to monaural stimulation were often greater in magnitude than their responses to binaural stimulation leading to the conclusion that sound reaching the contralateral ear had an inhibitory or suppressive effect on the response. Contralateral inhibition is seen in the responses of a pauser to which two binaural and two monaural noise stimulus sets were alternately presented (Fig. 10A). Gross responses were obtained at each azimuth by averaging over SPL. Monaural responses were larger than binaural responses at each azimuth. Monaural responses were also larger than binaural responses recorded from another pauser unit presented alternately with monaural and binaural stimulus sets (noise, B; 27 kHz BF-tones, C). The response differences in each case are rather small, but their consistency makes them convincing. For each stimulus set, responses were averaged over both SPL and azimuth. Pausers had slightly larger monaural responses to noise (5.46 spikes/stimulus) than binaural responses (5.03 spikes/stimulus).
spikes/stimulus, \( P < 0.01, n = 24 \), paired \( t \)-test). Pauser monaural responses to BF tones (7.90 spikes/stimulus) were also slightly larger than their binaural responses (7.53 spikes/stimulus, \( P < 0.0001, n = 20 \)). Monaural and binaural C-O-P responses were not significantly different for noise (\( n = 15 \)) and there were too few comparisons to BF tones (\( n = 4 \)) to evaluate. Spontaneous activity was suppressed during contralateral monaural noise stimulation (simulated by occluding the ipsilateral ear) in six pausers that were tested, with suppression beginning \(< 20 \) ms after stimulus onset.

Contralateral inhibition had a small but significant effect on pauser NTR directionality. Pausers exhibited slightly greater average modulation to binaural (43%) than to monaural (39%) noise stimulation (Table 5, \( P < 0.01 \)), showing that the magnitude of the effect of contralateral inhibition was small. Pauser NTR modulation to BF-tonal stimulation was not significantly different under monaural and binaural conditions. Neither did C-O-P units show significant monaural/binaural NTR modulation differences.

Comparison of GR modulation and NTR modulation

GR modulation was greater than NTR modulation for noise and BF tones for most units (e.g., Figs. 2 and 9) although there were a few exceptions in cases of units that responded only with an inhibition of SR at particular azimuths (e.g., NTR modulation, 91.8%, GR modulation, 74.5%, Fig. 13, A and B). Average GR modulation (mean ± SD, 44.6 ± 13.9%) was greater than the average NTR modulation (25.1 ± 16.8%) for all units in the NTR sample in response to binaural stimulation (noise and BF tone combined). Similar results were obtained for monaural stimulation (GR modulation, 42.4 ± 16.0%; NTR modulation, 25.5 ± 19.1%). GR and NTR modulation showed moderate positive correlation for noise stimulation (binaural, \( r = 0.51 \); monaural, \( r = 0.59 \)) but very weak correlation for BF-tonal stimulation (binaural, \( r = 0.04 \); monaural, \( r = 0.02 \)).

GR and NTR measures both showed significant modulation differences in comparing monaural and binaural stimulation thus revealing that contralateral inhibition produced a small increase in directionality of pausers to noise stimulation (Table 5). Similarly, both measures revealed greater modulation to noise than to tones for pausers and C-O-P units (Table 4). In contrast, unlike the NTR measure, the GR measure is insensitive to differential spectral directionality among different functional groups of CN units. ANOVA showed no significant differences in mean GR modulation among pausers, choppers, and primary-like units for binaural stimulation, and there was no significant difference between pausers and C-O-P units in their mean GR modulation to noise (Table 3).

### TABLE 4. Comparison of NTR and GR modulation to noise and BF tones

<table>
<thead>
<tr>
<th></th>
<th>Noise NTR Modulation, %</th>
<th>BF NTR Modulation, %</th>
<th>( t )-Test</th>
<th>Noise GR Modulation, %</th>
<th>BF GR Modulation, %</th>
<th>( t )-Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Binaural</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pauser</td>
<td>19</td>
<td>45.3</td>
<td>14.8</td>
<td>0.0001</td>
<td>52.7</td>
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<tr>
<td>C-O-P</td>
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<td>23.8</td>
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<td>0.002</td>
<td>48.5</td>
<td>41.1</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>0.01</td>
<td>45.6</td>
<td>37.6</td>
</tr>
<tr>
<td>C-O-P</td>
<td>7</td>
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<td>14.6</td>
<td>0.02</td>
<td>47.4</td>
<td>40.3</td>
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</tbody>
</table>

Each unit in this analysis provided modulation values for both noise and BF-tone burst stimulation. Statistical comparisons were made using paired \( t \)-tests.

C-O-P unit class breakdown: binaural stimulation (chopper = 9, primary-like = 9, onset-CIL = 1), monaural stimulation (chopper = 4, primary-like = 1, onset-CIL = 2).

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**FIG. 10.** Monaural and binaural GR azimuth functions for 2 pausers that show contralateral inhibition. Binaural and monaural stimulus sets were delivered alternately, and the numbers in the legend indicate the sequential order of data collection. Units were more responsive to monaural than to binaural stimuli indicating the presence of contralateral inhibition. A: noise stimulation, unit 9706-32. B: noise stimulation, unit 9804-11. C: BF tonal stimulation, unit 9804-11.
TABLE 5. Comparison of NTR and GR modulation to monaural and binaural stimulation

<table>
<thead>
<tr>
<th></th>
<th>Pauser</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Binaural NTR</td>
<td>Monaural NTR</td>
<td>$P&lt;\text{modulation, %}$</td>
<td>Binaural GR</td>
<td>Monaural GR</td>
<td>$P&lt;\text{modulation, %}$</td>
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<tr>
<td>Noise</td>
<td>19</td>
<td>43.4</td>
<td>39.2</td>
<td>0.01</td>
<td>49.1</td>
<td>43.0</td>
<td>0.001</td>
</tr>
<tr>
<td>BF tone</td>
<td>19</td>
<td>14.9</td>
<td>15.6</td>
<td>NS</td>
<td>38.5</td>
<td>38.7</td>
<td>NS</td>
</tr>
<tr>
<td>C-O-P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noise</td>
<td>10</td>
<td>22.1</td>
<td>23.3</td>
<td>NS</td>
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<td>44.0</td>
<td>0.08</td>
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<td>10.3</td>
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<td>36.2</td>
<td>37.5</td>
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</table>

The distribution of C-O-P unit classes for noise is primary-like = 2, chopper = 4, onset-CIL = 4. The distribution of unit classes for BF tones is primary-like = 1, chopper = 4. Statistical comparisons were made using paired t-tests. NS, not significant ($P > 0.2$), NA, not applicable, i.e. number of observations was too small for statistical comparison.

Spectral notches (SNs) produce response nulls

Notches occur in high-frequency spectra as a result of diffraction of sound with the cat’s pinna, and center frequency varies as a function of sound source location in both azimuth and elevation (Musianc et al. 1990, Rice et al. 1992). Pausers are inhibited by SNs centered on their BF (Joris 1998; Nelken and Young 1994; Young 1992a,b), suggesting that response nulls in ALRAs (e.g., Figs. 7 and 8) occur when a SN is centered on a unit’s BF. Although we did not directly measure SNs present in the sound reaching the ear, Rice et al. (1992) showed that their spatial distribution is fairly consistent among individual cats. Therefore we compared the location of response nulls in our data with the location of SNs as previously described.

SNs of a given center frequency in the range of 8–16 kHz are distributed in the frontal field along a curving line that sweeps downward and toward the ear. Spatial receptive fields (SRFs) of two pausers with high-directional responses and BFs in this range were obtained using a vertical array of loudspeakers positioned at 22.5° intervals (Fig. 1). SRFs of both units showed a response null that paralleled the expected SN trajectory. The most complete example was an 11-kHz BF pauser the ALRA of which shows a broad response null that reaches a minimum at $−15°A$ (Fig. 11A). Elevation-level response areas (ELRAs) were obtained at intervals of $15°A$, and representative examples are illustrated that show that response null elevations varied depending on azimuth. There is a prominent null at $−22.5°$ of elevation ($−22.5°E$) for the ELRA at 45°A ($B$), and a somewhat less prominent one at the same elevation at 15°A ($C$). At $−15°A$ ($D$), separate primary and secondary nulls are present at 0° and $−45°E$. At $−45°A$, there are nulls at $+22.5$ and $−45°E$ ($E$).

The ELRA data have been plotted as a SRF based on the GR, the sum of responses to each SPL presented at each azimuth-elevation direction ($F$). The 75% iso-response contour delimits a receptive field core. This is bounded by a curving band of lower responsiveness that separates it from regions of higher responsiveness in the lower field. The band corresponds in location to response nulls seen in the ALRA and the ELRAs. The locus of the 11-kHz SN (Rice et al. 1992) has been superimposed on the SRF. It closely parallels the low response band, suggesting that unit discharges represent the SN as a response null.

The unit responded at locations in the upper ipsilateral quadrant at 10 dB above threshold (20 dB SPL, not illustrated). It responded throughout the entire frontal field at higher levels, although at each SPL there were regions of lower responsiveness that bordered the high-response receptive field core ($G$ and $H$). Response nulls ($A−E$) correspond to areas of reduced responsiveness in SRFs for individual stimulus levels as was the case in the average SRF.

Trajectories for right ear notches with center frequencies in the range of 9–13 kHz intersect the horizontal plane such that lower center frequencies are located further from the ear than higher center frequencies (SN data, Fig. 12). If a response null occurs when a SN is centered on a unit’s BF, then the relationship between response null azimuth and unit BF should parallel the relationship between SN azimuth and center frequency. Inspection of ALRAs shows that response nulls of units with BFs between 8.5 and 10 kHz (Figs. 2D and 8, $B$ and $C$) are located further away from the ear than nulls of units with BFs between 11 and 13 kHz (Figs. 7, $A$ and $B$, and 8, $D$ and $E$). Figure 12 shows the relationship between BF and the response null azimuth for 31 units in which a clear response null could be identified (NTR modulation >30%). For units with BFs between 8.5 and 13 kHz, there is a linear relationship between BF and response null azimuth. The linear regression line for these data closely parallels the slope of the line connecting the SN data points, although it is displaced $−12°$ toward the contralateral ear. These results strongly suggest that SNs cause response nulls and high directionality in units with BFs of 8.5–13 kHz. For units with BFs of $\geq 14$ kHz, there is no simple relationship between BF and response null azimuth.

Response null locations were usually stable over time. Repeated ALRAs under either monaural or binaural conditions were obtained for 14 units with nulls. Repeated measurements showed no change in response null location in most units (12/14). One unit that exhibited a null during the first run but not the second showed the biggest change in the entire NTR sample. A minor change in responsiveness in a second unit resulted in nulls at adjacent locations ($−30$ and $−60°$) during repeated runs of binaural stimulation. Most (7/9) units studied with both binaural and monaural stimulation exhibited response nulls at the same location under both conditions. Two units exhibited response nulls in different locations for monaural and binaural stimulation (Fig. 12, labeled Mon. and Bin. and connected together with lines). In the first case of a 10-kHz unit, the differences were minor. It showed nulls at $−30$ and $−60°$ for repeated runs of binaural stimulation and at $−60°$ for monaural stimulation. The second case of a 22-kHz unit showed a null at $0°$ for monaural stimulation and $−60°$ for binaural stimulation. These data show that response null locations in most units are not influenced by contralateral inhibition.

An example of a 17-kHz BF pauser that is selective for both azimuth and elevation is illustrated in Fig. 13. The average
SRF (D) shows a receptive field core (75% contour) that is located from 30 to −60°A and from 0 to 22.5°E. It is delimited above, below, and to the right by an area of lower responsiveness. The ALRA (A) shows a response null to the right of the receptive field core and the ELRA at 0°A (C) shows response nulls above and below the core.

**Mechanisms of notch inhibition**

Nelken and Young (1994) presented a model for notch inhibition based on the responses of type IV and type II cells that have been characterized in decerebrate unanesthetized cats, and a hypothetical WBI. Type IV cells are fusiform cells.
in the DCN that project axons to higher levels of the auditory system. Some exhibit notch inhibition. Fusiform cells have pauser PSTHs in barbiturate-anesthetized cats (Rhode and Kettner 1987). Type II cells are inhibitory interneurons. They are characterized by very low or nonexistent SR, and by relatively poor responses to noise as compared with BF tones. Onset-G units have similar properties and presumably correspond to type II cells. The relative noise ratio, $r$, is defined as the maximal discharge to noise divided by the maximal discharge to BF tones. Type II units typically exhibit $r$ values of $\leq 0.3$ (Davis et al. 1996; Joris 1998; Rhode 1999; Shofner and Young 1985; Young and Voigt 1982). Figure 14 compares the maximum number of spikes discharged to noise bursts and BF-tone bursts. All choppers and primary-like units and almost all pausers responded well to noise and tones. A high proportion of onset-G units (6/11) and one pauser (which was not included in the NTR sample, A) had $r < 0.3$. $r$ was $< 0.3$ for 3/129 units in the NTR sample, and all had onset-G PSTHs.

FIG. 12. There is a linear relationship between the azimuthal location of response nulls on the horizontal plane and BFs in the range of 8–13 kHz. Linear regression line parallels the azimuth locations of spectral notches (SNs) with center frequencies in the same frequency range (SN data from Rice et al. 1992). A response null is the minimum value of an NTR azimuth function. Response null estimates (est) came from units that did not meet the NTR criterion yet showed clear response nulls (e.g., Fig. 8, G and H). Two units showed different response nulls for monaural and binaural stimulation. These are labeled Mon. and Bin. and are connected together with interrupted lines. A 10-kHz BF unit had response nulls at $-30$ and $-60^\circ$A for 2 binaural stimulus sets and at $-30^\circ$ for 1 monaural stimulus set. An average of $-45^\circ$ was used for the calculation of the regression line.

FIG. 13. A 17-kHz pauser is selective to azimuth and elevation of noise bursts. A: ALRA for monaural noise stimulation. B: data from A are plotted as a function of level re: threshold. Noise stimulation produces an inhibition of spontaneous activity at 60 and $90^\circ$ of azimuth. C: elevation level response area at 0° azimuth. D: spatial receptive field for the gross response. Data in C and D were obtained using binaural noise burst stimulation. Gray scale intervals are shown in Fig. 3C.
One onset-G approached the criterion ($r = 0.31$). The WBI is hypothesized to respond much more vigorously to noise than to tones. Onset choppers in our sample were much more responsive to noise than BF tones ($Oc, B$) and some researchers have argued that onset choppers are the WBI (Joris and Smith 1998; Winter and Palmer 1995).

According to the Nelken-Young model, type IV cells receive two sources of inhibitory input. Type II inhibitory input is activated predominantly by narrowband stimuli such as BF tones, whereas input from the WBI is activated predominantly by broadband stimuli such as noise. Assuming that $R_{\text{max}}$ for noise is inversely proportional to the inhibitory strength of WBI input to a pauser, that the strength of notch inhibition is determined by the strength of WBI input, and that NTR modulation is a measure of notch inhibition, then the model postulates a negative correlation between NTR modulation and $R_{\text{max}}$. Figure 15, top, compares noise $R_{\text{max}}$ and NTR modulation for all pausers in the NTR sample. The correlation is rather weak ($r = -0.42$), but the negative slope of the regression line is significantly different from 0 ($P < 0.0005$). Correspondingly, $R_{\text{max}}$ for BF tones can be assumed to be inversely proportional to the strength of type II inhibitory input that a pauser receives. Figure 15, bottom, compares $R_{\text{max}}$ for BF tones and NTR modulation for noise stimulation. The correlation is weaker ($r = -0.27$), but again the regression line has a negative slope that is significantly different from 0 ($P < 0.04$).

These results support the model prediction that NTR modulation depends on WBI input but additionally suggest that type II inhibition makes a significant contribution.

**DISCUSSION**

These results show that pauser and onset-G units commonly exhibit greater spectral-dependent directionality than other classes of CN neurons in barbiturate anesthetized cats. Pausers are projection neurons (Rhode et al. 1983b) and onset-G units are interneurons (type II cells) the axons of which do not project to higher levels of the auditory system (Rhode 1999). Type II cells were initially identified in unanesthetized, decerebrate cats based on the criteria that included low SR and relatively weak responses to noise as compared with tones (Young and Brownell 1976; Young and Voigt 1982). Most units in our sample meeting the Type II criteria exhibited onset-G PSTHs, although one pauser also met the criterion. The pauser may represent a variant type PSTH for a type II interneuron (Shofner and Young 1985) or a projection neuron that responds poorly to noise (Joris 1998).

**Notch inhibition contributes to pauser directionality**

Spectral notches have been shown to inhibit the responses DCN projection neurons in decerebrate, unanesthetized cats (Nelken and Young 1994; Spirou and Young 1991; Young et al. 1992a,b) and in $\alpha$-chloralose anesthetized cats (Joris 1998). Inhibition is strongest when the center frequency of a spectral notch corresponds with best frequency (Young et al. 1992a,b). Responses of some pausers in the present study showed azimuth-dependent decrements in responsiveness (response nulls).
Directionality. The 11-kHz BF unit (Fig. 11, D and E) shows two response nulls, but only the upper one shows a correspondence with an 11-kHz spectral notch. Response nulls above and below an area of higher responsiveness of a 17-kHz BF unit (Fig. 13D) do not clearly correspond to locations of 17-kHz notch frequencies (Rice et al. 1992) but rather to a steep drop-off in the spectrum.

Our results (Fig. 12) showed a 12° difference between the observed and expected null locations based on acoustic measurements of Rice et al. (1992). Differences in head and pinna position in the two experiments would be expected to cause a disparity as changes in pinna orientation produce corresponding shifts in spectral notch locations with respect to the contralateral head (Young et al. 1996). Rice et al. (1992) held cats’ heads with the Horsley-Clarke plane in the horizontal plane. In our experiments, the Horsley-Clarke plane was tilted forward and down at about a 18° angle, approximating the position that a cat normally holds its head while looking straight ahead. This would have the effect of shifting spectral notch center frequencies toward more contralateral locations in our experiments with respect to their locations as measured by Rice et al. (1992). The pinna also was pulled to a more upright position in our experiments, whereas it was allowed to remain in its relaxed position by Rice et al. (1992).

Use of different loudspeakers to present sounds from different directions raises the question of whether these results may be an artifact of differences in loudspeaker frequency response characteristics. Several observations argue against this. First, similar response nulls were seen when single loudspeaker responses were compared with multiple loudspeaker responses. We regularly compared unit responses to one loudspeaker located at different azimuths with responses to multiple loudspeakers located at different azimuths to be certain that a response null was not the result of an equipment problem, and, barring an occasional equipment problem, the agreement was always excellent. An example of this type of comparison for a cortical unit has been published previously (Samson et al. 1993). Second, frequency response curves for the loudspeakers were rather smooth and had no notches. Spectral notches in HRTFs are much more abrupt than any fluctuations in loudspeaker frequency response. Third, response nulls showed good correlation with expected spectral notch distribution. This would not be expected if nulls were the result of loudspeaker frequency response characteristics.

Response of onset-G units to noise

A substantial minority of onset-G units in our sample responded relatively well to noise at certain azimuths (ρ > 0.3). This finding may at first appear inconsistent with published reports of type II response properties, but in fact it is not. Noise stimuli in our experiments were presented in the free field and thus contain spectral notches due to the HRTF. Type II cells are characterized by an excitatory frequency domain that is flanked by strong inhibitory domains. These cells do not discharge to broadband noise with a relatively flat spectrum presumably because energy in the inhibitory domains dominates the response. On the other hand, type II cells have been shown to respond to notch noise when the center frequency of the notch is located off-BF in an inhibitory side band (Nelken and Young 1994). Such a stimulus reduces energy in inhibitory relative to excitatory domains and shifts the balance of excitatory and inhibitory inputs toward net excitation, and thus disinhibition causes the cell to discharge. Onset-G units in our sample probably discharged to free-field noise presentation because of this effect.

Onset-G cells that were responsive to free-field noise stimulation exhibited response nulls. In the case of two cells with BF of 12 and 13 kHz (Fig. 7), a systematic azimuth-dependent shift in spectral notch center frequency provides an explanation for the null. As sound direction changes from contralateral to ipsilateral, spectral notch center frequency moves through the frequency response area beginning in the low-frequency inhibitory domain, progressing to the excitatory domain, and then entering the high-frequency inhibitory domain. When SN center frequency is within the inhibitory domains, disinhibition causes the cell to discharge. When the notch is centered at BF, there is decreased energy in the excitatory relative to the inhibitory domains shifting the excitatory/inhibitory balance toward inhibition, and thus the cell ceases to discharge.

Contributions of WBI and type II neurons to pauser directionality

Spirou and Young (1991) provided an explanation of notch inhibition based on inhibitory input from type II cells. Type II cells of lower BF are preferentially connected with type IV cells of higher BF (Voigt and Young 1990). A spectral notch centered on the BF of a type IV cell decreases energy in its excitatory frequency domain, and simultaneously the notch will be centered over the upper inhibitory frequency domain of type II cells that provide inhibitory input to the type IV cell. Disinhibition of the type II cell causes it to discharge thus inhibiting the type IV cell. Responsiveness of some onset-G cells to free-field noise stimulation suggests that according to the theory, onset-G inhibition could be one source of notch inhibition in pausers.

Although this theory has certain attractive features, Nelken and Young (1994) pointed out a number of problems with it. First, pauser notch inhibition occurs at too low a level to be accounted for by type II inhibition. Second, notch inhibition occurs over too wide a frequency range to be accounted for by
inhibitory domains in type IV frequency response areas that are presumably the result of type II input. Third, type II neurons are relatively unresponsive to notch noise so that they should produce rather minimal inhibitory input to type IV cells under such stimulus conditions. These authors postulated the existence of a second inhibitory input to type IV cells, the WBI, to account for notch inhibition. In contrast to type II cells, the WBI is presumed to be strongly driven by broadband noise (including notch noise). According to this model, strength of WBI inhibitory input to a type IV cell is correlated negatively with its maximal discharge to broadband noise and positively correlated with strength of notch inhibition. Consequently maximal discharge to noise and strength of inhibition to notch noise should be correlated negatively. Nelken and Young (1994) presented evidence for such a negative correlation in their experiments, and our data also support a similar relationship, although measures of maximal discharge rate and strength of inhibition were made somewhat differently.

Type II inhibitory input is activated predominantly by narrowband stimuli such as BF-tones, and thus a type IV cell’s maximal response to BF stimulation should be negatively correlated with the strength of type II input it receives. Nelken and Young (1994) found that the maximal discharge of type IV cells to BF stimulation was correlated positively with strength of notch inhibition, although the relationship was not statistically significant, and interpreted these findings as showing that type II inhibition is unrelated to strength of notch inhibition. Our results show a weak, but statistically significant negative correlation between maximal discharge to BF tones and pauser directionality. This supports the idea that type II inhibition makes a significant contribution to pauser directionality although less important that the WBI input. Given that notch inhibition is a major contributor to pauser directionality, it is curious that type II inhibition appears to contribute to directionality, but it does not contribute to notch inhibition. There are a number of factors that could account for this apparent discrepancy. First, responses of DCN neurons are significantly affected by anesthesia so that neural circuitry creating notch inhibition functions differently under anesthetized and unanesthetized conditions. Second, other spectral features besides notches could contribute to NTR modulation. Perhaps type II inhibition is related to modulation dependent on these other features but not notch-dependent modulation. Finally, differences in stimulus duration may contribute to the discrepancy. Our stimuli were 50 ms in duration and those of Nelken and Young (1994) were 200 ms. Rapid adaptation of onset-G responses suggests that their inhibitory input to DCN projection neurons also may be rapidly adapting. It is possible that their inhibitory contribution would be most apparent in the initial part of the response to noise and thus would have a greater effect on responses to shorter than to longer duration stimuli.

VCN neurons exhibit low directionality

Primary-like and onset-CIL units were found almost exclusively in the VCN, consistent with earlier reports (Rhode and Smith 1986a,b; Shofner and Young 1985). Chopper responses were recorded from both the DCN and VCN. Extrapolation from the distribution of such responses in penetrations with two tonotopic sequences suggests that most were recorded from the VCN. We expected to find a higher proportion of choppers in the DCN than we did because choppers are the most frequently encountered type of PSTH in the DCN (Rhode and Smith 1986b). Nevertheless PSTH patterns of choppers in our sample are consistent with the assumption that most were recorded from the VCN. DCN choppers often have relatively wide response modes in their PSTHs, and although these were found in our sample, they were much less common than PSTHs with narrow modes. It is possible that differences in classification criteria could account for the relatively low proportion of DCN choppers in our sample. Under conditions of barbiturate anesthesia, DCN projection neurons appear to exhibit a continuum of PSTH patterns that vary from pauser/build-up responses at one extreme to chopper responses at the other. Units with response patterns between these extremes may exhibit pauser responses at most SPLs and chopper responses at a few or chopper responses at most SPLs and pauser responses at a few. We classified a unit as a pauser even if it exhibited chopper responses at most SPLs and pauser responses at a few. The apparent use of a narrower range of SPLs for classification of PSTHs by Rhode and colleagues may have resulted in classification of some cells as choppers that we would have classified as pausers.

PVCN choppers have inhibitory side bands that are stronger than all other classes of CN neurons except for pausers (side band strength was not assessed in onset-G units) (Rhode and Greenberg 1994). Nevertheless our data suggest that choppers are not a major source of projections from the CN that carry spectral-dependent directional information as their directionality is not greater than that of primary-like or onset-CIL units.

Pauser and onset-G units are much more directional to noise stimulation than chopper, primary-like, or onset-CIL units. Assuming that choppers, primary-like, and onset-CIL units represent the output of the VCN and that pausers represent the output of the DCN, this finding shows greater spectral-dependent directionality of DCN than VCN outputs. Axons of DCN neurons travel to the contralateral IC via the dorsal acoustic stria (DAS). Sutherland et al. (1998b) transected the DAS in cats, thus depriving their auditory systems of DCN output. The accuracy of unconditioned reflexive orientation to sound directions that varied in elevation, a localization task that is dependent on spectral cues (Huang and May 1996; Martin and Webster 1987; May and Huang 1996; Middlebrooks and Green 1991), was impaired permanently. Although DAS-lesioned cats cannot accurately orient to vertical sound location, they do have the ability to discriminate between noise bursts originating from a single loudspeaker and noise bursts alternating between two vertically displaced loudspeakers (Sutherland et al. 1998a). This shows that a neural representation of spectral cues, sufficient to distinguish between sounds presented from different vertical locations, is present in VCN outputs. Whether such information is also sufficient for vertical sound localization using other behavioral paradigms than the unconditioned reflex is unknown.

Contribution of contralateral inhibition to pauser directionality

Contralateral inhibition caused a modest increase in pauser modulation to noise stimulation and therefore monaural spectral inhibition and contralateral inhibition have complementary
effects on unit directionality. On the other hand, contralateral inhibition had no significant effect on pause directionality to BF tones. The effect of contralateral inhibition was limited to the DCN in our data. We found no significant effect on either response magnitude or directionality to noise or tones in the C-O-P sample, although the sample size is so small that the effect might have been missed if actually present.

The contralateral inhibition that we observed in the responses of DCN neurons is weaker than that seen in unanesthetized decerebrate (Young and Brownell 1976) or α-chloralose-anesthetized cats (Joris and Smith 1998). Contralateral noise stimulation causes inhibition of responses of auditory nerve fibers that is more similar to the magnitude of inhibition that we observed in the DCN (Rice et al. 1995). Nevertheless it seems unlikely that the effect of contralateral inhibition on DCN neurons in our data simply reflects auditory nerve input. Contralateral inhibition of auditory nerve fibers mediated by olivocochlear efferents has an onset latency is 100–200 ms (Warren and Liberman 1989), which is too long to account for the inhibition of responses to 50-ms stimuli used in our experiments. Middle ear muscle reflex contraction also seems unlikely to account for the inhibition as these have little effect on high-frequency stimuli and would be expected to affect all CN units not just pausers in the DCN. It seems most likely that contralateral inhibition in our results involves a direct connection between the cochlear nuclei (Joris and Smith 1998) and is attenuated by barbiturate anesthesia.

Comparison of GR and NTR measures

Spectral inhibition produced by noise stimulation increases both NTR and GR modulation (e.g., Fig. 2F), consistent with finding a moderate positive correlation between NTR and GR modulation. GR and NTR modulation showed virtually no correlation for BF-tonal stimuli presented monaurally or binaurally, and no correlation should be expected, as there are no common response features such as spectral inhibition that influence both response measures. In paired comparisons of unit responses to noise and tone stimulation and to monaural and binaural stimulation, both GR and NTR exhibited similar statistical differences in mean modulation. On the other hand, pausers showed significantly greater NTR modulation to noise stimulation than other groups of CN units but showed no significant differences in GR modulation (Table 3). Although NTR and GR response magnitude are both affected by spectral inhibition, GR magnitude is affected additionally by azimuth-dependent threshold differences and SR. Given two units with identical response properties except that one exhibits SR, the spontaneously active unit would be expected to show less GR modulation than the other. This effect can be appreciated by considering the primary-like unit in Fig. 9. If this unit was not spontaneously active, then the maximal GR value (60°A) would decrease somewhat because responses at 5 and 10 dB SPL would decrease from the spontaneous rate to 0. On the other hand, the minimum GR value (~60°A) would show an even greater decrement because responses at 10 different levels (5–50 dB) would decrease from the spontaneous rate to 0. Consequently GR modulation for a unit lacking SR would be greater than if SR were present.

Pausers exhibit significantly greater SR than C-O-P units. The effect of SR would be expected to attenuate GR modulation of the pauser group to a greater extent than the C-O-P group, and this is what is seen. In response to BF tones, GR modulation is less for pausers than for C-O-P units. BF tone NTR modulation is similar for the two groups. SR would be expected to have a similar effect on noise responses. Thus GR modulation differences between the two groups due to spectral inhibition would be reduced by the SR effect. The effect of SR on GR modulation makes this a less appropriate measure of directionality differences between these groups than NTR modulation.

Overview

These results show that DCN neurons are more directional than VCN neurons, but the extent to which DCN output contributes to spectral-dependent directionality of neurons at higher levels of the auditory system remains unknown. Certainly there are some differences. Some cells at higher levels exhibit multiple excitatory frequency domains (Imig et al. 1997), a pattern of frequency organization that does not appear to be commonly found in the DCN under barbiturate anesthesia. Many units at higher levels that exhibit spectral-dependent directionality to monaural noise stimulation receive inhibitory input from the opposite ear, i.e., they are EI cells. Although many DCN neurons also receive EI input, the inhibition is much weaker in the DCN than at higher levels (Poirier et al. 1996; Samson et al. 1993, 1996). Finally, many cells at higher levels appear to respond to noise bursts over more restricted ranges of azimuth than was the case in the DCN, and at many directions, there was no response regardless of SPL. Such complete inhibition of responses was rather uncommon in the DCN. Further work is needed to determine whether and to what extent higher level neurons that exhibit spectral-dependent directionality reflect activity of DCN neurons.