Evidence of Stimulus-Dependent Correlated Activity in the Dorsal Cochlear Nucleus of Decerebrate Gerbils

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Davis, Kevin A. and Herbert F. Voigt. Evidence of stimulus-dependent correlated activity in the dorsal cochlear nucleus of decerebrate gerbils. J. Neurophysiol. 78: 229–247, 1997. Cross-correlation analysis of simultaneously recorded spike trains was used to study the internal organization of the dorsal cochlear nucleus (DCN) of unanesthetized decerebrate Mongolian gerbils. The goal was to test the model (adapted from cat) that its principal cells (type III and type IV units) receive three sources of shared auditory input: excitatory input from the auditory nerve; inhibitory input from DCN interneurons (vertical cells; type II and type III-i units) that respond vigorously to tones; and inhibitory input from ventral cochlear nucleus principal cells (D-stellate cells; wideband inhibitors) that conversely respond vigorously to noise. Records of spontaneous and/or driven activities (to long-duration tones and frozen broadband noise) were obtained for 51 pairs consisting of type II, type III, and type IV units; type III units inhibited by low-level noise were subclassified as type III-i units. Pairs were isolated with two electrodes to study the effect of differences in unit best frequencies (BFs) on correlation. All correlated pairs composed of type III and type IV units (17 of 31 pairs) showed central mounds (CMs), indicative of shared input, in their cross-correlograms. These data exhibited two important properties: pairs with similar BFs were more likely to show CMs, and the shape of the CMs was stimulus dependent. That is, CM width typically changed sharply from wide to narrow with increasing level; significantly, transition-level CMs were either a composite of these shapes or not present. The transition to only narrow CMs occurred above the thresholds of type II and type III-i units to tones, but below their thresholds to noise. Cross-correlograms derived from the tone-evoked activities of pairs involving type II units (3 of 6 pairs) showed inhibitory troughs (ITs); unexpectedly, type III-i units were involved in both IT and CM pairs, suggesting that this unit type may reflect recordings from both vertical and principal cells. Overall, the results are interpretable in terms of the model of gerbil DCN that was adapted from cat, suggesting that the model generalizes across species. Compared with cat, however, gerbil principal cell responses (predominantly type III unit properties) are less dominated by inhibition.

INTRODUCTION

The cochlear nucleus (CN) is the first structure in the central auditory pathway where neural processing of the acoustic information encoded in the auditory nerve can occur. Among the CN divisions, the dorsal CN (DCN) has the most intricate interneuronal organization (Kane 1974; Lorente de Nó 1981; Mugnaini et al. 1980a,b; Osen et al. 1990) and its neurons display the most diverse and complex responses to sound (Evans and Nelson 1973; Godfrey et al. 1975; Shofner and Young 1985). Type IV units, for example, are inhibited by tones over a wide frequency range, including high-level tones at their best frequency (BF), yet these units are excited by broadband noise (Young and Brownell 1976). Type III units also show extensive regions of inhibition in their response maps, but are excited by BF tones at all levels (Young and Voigt 1982). Both response types are recordable from DCN principal cells (pyramidal and giant cells; Adams and Warr 1976; Ding 1997; Ding et al. 1994a,b; Young 1980).

Primarily on the basis of work in cat, a conceptual model of a portion of the neural circuitry governing the responses of the DCN’s principal cells has emerged over the past two decades. This model suggests three sources of shared input to the DCN’s principal cells (predominantly type IV units in cat): excitatory input from the auditory nerve; strong inhibitory input from vertical cells, which respond vigorously to tones but weakly to noise (type II units) (Lorente de Nó 1981; Saint-Marie et al. 1991; Young 1980; Young and Brownell 1976; Young and Voigt 1982; Zhang and Oertel 1993b, 1994); and weak inhibitory input from collaterals of ventral CN principal cells, which conversely respond vigorously to noise but weakly to tones (D-stellate cells; called wideband inhibitors) (Nelken and Young 1994; Oertel et al. 1990; Smith and Rhode 1989; Winter and Palmer 1995). The generality of this model to other species, however, is unclear.

Cross-correlation analysis of the simultaneously recorded activity of pairs of DCN neurons has yielded conflicting data across species. Analysis of type IV-type IV (IV/IV) and II/IV pairs in decerebrate cat in response to long-duration tones is consistent with the model described above; these data show that type IV units with similar BFs share one or more sources of input and that type II units provide inhibitory input to type IV units (Voigt and Young 1980, 1985, 1988, 1990). In contrast, correlation studies in anesthetized rat (Gochin et al. 1989, 1990) and guinea pig (Kipke et al. 1991) did not find corroboratory evidence of inhibitory interactions; rather, these studies found prevalent functional excitatory interactions. Direct comparisons with the results from decerebrate cat, however, are difficult because, among many other methodological differences, researchers in neither of these studies used the response map scheme to classify their units; and even if they had, the use of anesthesia has a profound impact on DCN unit response properties (Evans and Nelson 1973; Fan and Voigt 1997; Gdowski and Voigt 1997).

The purpose of this work was to test critically the generalization of the conceptual model to other mammalian species by studying the interactions of pairs of response-map-identi-
fied units in a second decerebrate preparation. In particular, the gerbil DCN has many of the same neuron types organized in a laminar fashion similar to cat (Benson and Voigt 1995) and single-unit studies of its DCN reveal the same major response types as in cat (Davis et al. 1996a). Compared with cat, however, there is a relative paucity of type IV and type II units and an abundance of type III units. In addition, two unit subtypes, infrequently observed in cat, are observed in abundance in gerbil: type IV-i units are excited by low-level noise and inhibited by high-level noise; conversely, type III-i units are inhibited by low-level noise and excited by high-level noise. These data suggest that gerbil principal cells can exhibit type III unit properties because of a relatively weak type II unit inhibitory input and that type IV-i unit properties arise through vertical cells exhibiting (the reciprocal) type III-i unit response.

In this study, pairs of DCN units were isolated with the use of two microelectrodes and responses were obtained to both long-duration tones and frozen broadband noise. The results reported here suggest that type III and type IV units share one or more sources of input in response to both tones and noise and that type II and type III-i units provide inhibitory input to these units. Unexpectedly, type III-i units are involved in both shared-input and inhibitory-input pairs, suggesting that this unit type reflects recordings from both principal and vertical cells. Overall, the results are interpretable in terms of the gerbil model (adapted from cat), suggesting that the model generalizes across species and thereby provides a basis for understanding the role of the DCN in audition.

This work represents part of a Ph.D. dissertation in Biomedical Engineering presented at Boston University.

**METHODS**

**Preparation**

The animal preparation has been described previously (Davis et al. 1996a). Briefly, young adult female gerbils (3 mo old, 50–70 g) with infection-free ears were used. Gerbils were premedicated with atropine (0.04 mg/kg im), then tracheotomized and decerebrated under methohexitol sodium (65 mg/kg ip), an ultrashort-acting barbiturate anesthesia. The animal was decerebrated by complete aspiration of the brain tissue rostral to the superior colliculus; the resulting cavity was packed with gel foam to minimize bleeding and edema. Anesthesia was discontinued and the preparation was allowed to stabilize for 30 min. The DCN was accessed with the use of the transbulla approach of Frisina et al. (1982). Core body temperature was maintained at 39°C throughout the typical 14- to 16-h experiment with the use of a feedback-controlled heating blanket.

**Acoustic stimuli and recording methods**

Acoustic stimuli were presented via a closed, calibrated sound system, coupled to the animal’s left ear. A typical calibration curve was centered at ~100 dB SPL (±10 dB) over 0–23 kHz and rolled off sharply at 25 kHz. Single tone stimuli were generated by computer-controlled or manually controlled oscillators. A frozen broadband noise stimulus was digitally created with a spectrum that compensated for the nonflat calibration curve (Davis et al. 1996a). This noise signal (25-kHz bandwidth) was continuously output through a D-A converter at 100 kHz and had a period of ~1.96 s. To achieve desired sound pressure levels (dB SPL), signals were attenuated with a programmable attenuator. For tones, this attenuation was corrected for the acoustic calibration curve; for noise, this attenuation was relative to the maximum level achievable in the absence of any attenuation (~95 dB SPL re 20 μPa). All stimuli were gated on and off with the use of an electronic cosine switch with 5 ms rise-fall times.

Two independently controlled platinum-iridium (70%:30%) metal microelectrodes with platinum-black tips (2–4 μm in length) and impedances between 0.5 and 1.5 MΩ were used to record the simultaneous activity of unit pairs. The electrodes were held at a 5–10° angle with respect to each other in approximately the horizontal plane with the use of two microdrives mounted on separate micromanipulators. To insure that the electrodes intersected at the DCN (~2,000 μm deep to the surface of the cerebellum), the electrodes were initially positioned such that their tips were nearly touching and then each was retracted 2,000 μm. The manipulators were then used to place the electrodes on the exposed surface of the cerebellum. Microelectrode advances could be recorded to within 0.1 μm.

The electrode signals were individually amplified (total gain = ×20,000–50,000) and filtered (bandwidth 0.3–10 kHz). Action potentials were detected with the use of Schmitt level detectors that could be set to trigger on either the positive or negative peak of the action potentials. Two real time clocks were used to record the times of occurrence of each Schmitt level detector pulse with 1-μs resolution.

**Experimental protocol and histology**

Electrodes were individually advanced through the cerebellum into the DCN until there was background activity to broadband noise bursts. Thereafter, tone bursts at the BF of the background driving (duration 100 ms) were used as the search stimulus because type II units do not respond well to broadband noise. Once a unit was isolated on an electrode, its BF and threshold were determined. When two units were simultaneously isolated, responses (spike times) were recorded to classify both units in the response map scheme. Response maps were constructed from responses to 32-ms tone bursts presented at a rate of four per second. The frequency of the tone was changed in 0.1-octave steps starting at the approximate geometric mean of the two BF estimates, alternating above and below this frequency, for up to 50 frequencies. At each frequency, the sound pressure level was increased from 0 to 60 dB SPL (typical) in 2-dB steps. BF tone and noise-rate-versus-level functions were constructed from responses to 200-ms bursts presented once per second for up to 50 levels (0–98 dB SPL) in 2-dB steps.

Data for cross-correlation analysis were then taken. Correlation data consisted of several 110-s-long samples of spontaneous activity (SpAc), when available, and responses to 110-s-continuous tones and frozen broadband noise. The tone frequency was set equal to the geometric mean of the BFs unless one unit in the pair was spontaneously inactive; then the tone frequency was set equal to its BF to maximize the number of levels over which it fired. Data were collected for multiple sound pressure levels in 10-dB steps, typically starting at the lowest level where there was joint activity. For each stimulus condition, ~2,000 spikes were typically acquired for each train, with a maximum of 16,384 spikes allowable for each train.

In some experiments, lesions were made at the sites of interesting pairs by passing 10 μA of current for 15 s with the use of a square-wave (4-Hz) voltage input to a biphasic stimulus isolator. At the end of these experiments, the animal was killed by administering a dose of pentobarbital sodium (60 mg/kg ip), exsanguinated by perfusion with normal saline with 1% NaNO₃, and then fixed with the use of 10% formaldehyde (Formalin). After overnight immersion in the fixative at 4°C, the brain was removed from the skull,
Unit categorization and correlation analysis

Units were classified physiologically in the response map scheme as type II, type III, type III-i, type IV, type IV-i, or type IV-T on the basis of the presence and location of excitatory and inhibitory regions in the unit’s response map, on responses to BF tones and noise, and on rates of SpAc (see Davis et al. 1996a for details). The criterion for excitation or inhibition at a given stimulus condition was a 2-SD (~95% confidence limits) increase or decrease in driven rate relative to SpAc; for spontaneously inactive units (type II units), a response was said to be excitatory if the driven rate was >2.5 spikes/s. The statistically based method for generating the response maps objectively from the responses to the 32-ms-duration stimuli is described in Davis et al. (1995). Rate-versus-level curves for BF tones and noise were computed from the responses to the 200-ms-duration stimuli; driven and SpAc rates were estimated as the average rate over the last 160 ms (80%) of the stimulus duration and the last 160 ms of the 1-s trial, respectively. All rate-level curves were three-point triangular filtered. Units similar to type III units, but inhibited by low-level noise, were classified as type III-i units, and units similar to type IV units, but inhibited by high-level noise, were classified as type IV-i units (Davis et al. 1996a). Type IV-i units have highly nonmonotonic BF rate-level curves, like type IV units, but their discharge rates do not fall 2 SD below SpAc. Type IV-T unit response properties are recorded from giant cells (Ding 1997) and as such, in this paper, they are lumped together with the principal cells.

Standard cross-correlation estimation techniques (Moore et al. 1970; Perkel et al. 1967) were applied to the SpAc and stimulus-evoked activity to examine the temporal relationship between the spike trains. Cross-correlograms were computed as follows

\[
C_{ab}(k) = \frac{\#\{B \text{ spike in } [t_0 + k\Delta, t_0 + (k + 1)\Delta], A \text{ spike in } [t_0, t_0 + \Delta]\}}{N_a\Delta}
\]

where \#\{\} is the number of occurrences of the event enclosed by brackets over all \(t_0\) in the data record, \(\Delta\) is the data acquisition binwidth (1 ms), \(k\Delta\) is the binwidth of the correlogram, \(k\Delta\) is the delay time at the start of bin \(k\), \(t_0\) is an integer multiple of \(\Delta\), and \(N_a\) is the number of spikes in reference unit A (Voigt and Young 1990). If multiple 110-s data runs were collected, the numerator and denominator of Eq. 1 were accumulated before the division was performed. In the null hypothesis case in which the two units discharge independently with stationary statistics, the statistics of the bin counts in the cross-correlogram are approximately Poisson (Brillinger 1975), and the normalized correlogram defined in Eq. 1 can be shown to have a mean value equal to the average rate of the nonreference unit, \(R_b\), and a variance of \(R_b/N_a\Delta\) (see also Aertsen and Gerstein 1985; Palm et al. 1988). The variance can be made to be independent of the mean (facilitating comparison between correlograms) by performing a square root transformation yielding a final correlogram that has a mean of \(R_b\) and a variance of \(1/4N_a\Delta\) (Brillinger 1975). Correlograms in this paper are thus plotted with the use of a square root ordinate axis but with the axis relabeled to correspond to discharge rate.

Cross-correlograms are a function of individual unit firing rates; if these rates are modulated by the stimulus, the cross-correlogram may show features that reflect simply these stimulus-induced rate changes. Assuming stimulus-induced and neural interaction effects are additive, an assumption that depends on the working state of the neurons (Melson and Epping 1987), all direct stimulus effects can be eliminated from a cross-correlogram by subtracting a predictor of these effects (the resulting residual correlogram is called a difference correlogram). In response to long-duration tones, unit discharge rates become largely stationary (steady-state rates are achieved); thus a predictor is unnecessary. In response to broadband noise, however, unit discharge rates are largely nonstationary because the stimulus is continuously novel; thus a predictor is necessary. Both shift and peristimulus time predictors are computed from responses to multiple presentations of the stimulus (Perkel et al. 1967); this implies that when broadband noise is used as a stimulus, the same sequence of noise must be presented multiple times (frozen noise). Here, each 110-s-long presentation of noise had 55 complete repetitions of the same noise sequence (each ~1.96 s in duration) and noise difference correlograms were computed by subtracting a peristimulus time predictor from the raw correlogram. Typically, the mean of a difference correlogram is near zero and the variance of the bin counts is similar to that in the raw cross-correlogram because the peristimulus time predictor is much smoother than the raw cross-correlogram. To facilitate comparison to the correlograms derived from the tone-evoked data, the mean of the raw cross-correlograms was added back into the difference correlograms.

To assess the statistical significance of features in the correlograms, three horizontal lines are drawn: the middle line equals the value expected in the absence of correlation; and the top and bottom lines are approximate ±95% confidence limits (2 SD) from the mean. Cross-correlogram values will deviate from the mean because of functional interactions between the units or because of comodulation of their discharges. Similarly to Voigt and Young (1990), we consider a deviation from the mean of ±2 SD to be statistically significant and to define a significant feature to be two successive bins that deviate significantly from the mean. Features are then defined to extend continuously in either direction from the significant bins until the first of two of three correlogram values cross the mean line; this rule typically matches boundaries determined by visual inspection.

In this paper, we are only interested in short-latency transient interactions between the units, so only features within ±5 ms of the origin are considered for further analysis; the dominant feature is the one with the largest area. Consistent with Voigt and Young (1988, 1990), correlograms showing comodulation (shared input) are computed with 0.5-ms binwidths and displayed here over ±10 ms (40 bins), and correlograms showing functional (inhibitory) interactions are computed with 0.3-ms binwidths and displayed over ±10 ms (67 bins). Although feature detectability and characteristics (e.g., width, amplitude, and latency) are somewhat dependent on the binwidth chosen for the correlogram, this dependence was typically found to be weak, especially for correlograms showing functional interactions. Correlograms showing evidence of shared input were three-point-triangular filtered to reduce ambiguity at the edges of the feature.

Two different methods were used to evaluate the strength of significant features in correlograms. For correlograms showing evidence of shared input, feature amplitude (peak minus mean)–to-mean ratios were computed. For correlograms showing functional interactions, effectiveness and association values (Levick et al. 1972; Voigt and Young 1990) were computed. Effectiveness measures the likelihood of presynaptic spikes resulting in postsynaptic spikes and equals the area of the feature either above (positive) or below (negative) the mean. Association index, defined as effectiveness divided by postsynaptic firing rate, is a rate-independent probability measure with dimensions of time (Epping and Eggermont 1987; Voigt and Young 1990).
Table 1. Summary of correlation by composition of pairs

<table>
<thead>
<tr>
<th>Unit Types</th>
<th>Flat</th>
<th>CM</th>
<th>IT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>II/III</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>II/III-i</td>
<td>0</td>
<td>0</td>
<td>1*</td>
<td>1</td>
</tr>
<tr>
<td>II/IV</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>III/III</td>
<td>7</td>
<td>7*</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>III/III-i</td>
<td>7*</td>
<td>3</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>III/IV</td>
<td>6**</td>
<td>4*</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>III-i/III</td>
<td>1*</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>III-i/IV</td>
<td>1</td>
<td>1*</td>
<td>1*</td>
<td>3</td>
</tr>
<tr>
<td>IV/IV</td>
<td>1</td>
<td>6***</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>21</td>
<td>4</td>
<td>51</td>
</tr>
</tbody>
</table>

A pair is counted as showing correlation if a significant feature is observed for either spontaneous activity or tone- or noise-evoked driven activity. The type IV unit class includes type IV-T, type IV, and type IV-i units. Flat, no significant feature; CM, central mound; IT, inhibitory trough. No strictly excitatory peaks were observed. * One asterisk for each pair localized to the deep DCN (pyramidal cell layer and below).

Results

Cross-correlation data were acquired for 51 pairs consisting of type II, type III, type III-i, and type IV units in 22 experiments (Table 1). Both units in 12 of the pairs (marked by asterisks in Table 1) were localized to the deep DCN (pyramidal cell layer and below) by the histological recovery of lesions made in eight of the experiments. The distances between the units in these pairs could not be accurately estimated, however, because of the ambiguity of associating particular lesions with particular electrode tracks. It can be assumed that the units were typically in close proximity to each other on the basis of the tissue interaction effects of moving one electrode relative to the other (unit isolation would improve/degrade). On the basis of the use of a standardized electrode approach to the DCN, the depth of the recordings, and the experience of this laboratory with the recovery of horseradish peroxidase deposits in the DCN made by glass micropipette electrodes penetrating along similar trajectories (Benson and Voigt 1995; Davis et al. 1996a; Gdowski and Voigt 1997), we assume that most, if not all, of our pairs were located in the DCN.

Table 1 summarizes the occurrence of correlation between pairs of all compositions. A pair is counted as showing correlation in this table if a significant feature is observed in the cross-correlograms derived from the pair’s SpAc and/or its driven activity in response to long-duration tones or frozen broadband noise; the features will be defined below. Table 1 shows that CM correlation is often observed in pair combinations composed of type III, type III-i, and type IV units, with type III units as likely to be correlated with type IV units (4 of 10 pairs) as with other type III units (7 of 14 pairs). The table also shows that IT correlation is most often observed in pairs containing a type II unit. Finally, Table 1 shows that no strictly excitatory interactions were observed.

Figure 1 shows a summary of pair activity in relation to the BFs of the two units in the pair. Each symbol represents a pair, with the difference in unit BFs in octaves plotted against the BF of the lower-BF unit. Notice the tendency for correlated pairs (filled symbols) to be clustered close to the abscissa (the equal-BF line). Overall, 19 of the correlated pairs have BF differences ≤0.2 octaves, five have BF differences between 0.2 and 0.6 octaves, and only one correlated pair has a BF difference >0.6 octaves (an IT pair described in Fig. 10).

CM correlation: pairs involving type III, type III-i, and type IV units

The spontaneous activities (SpAc) of 20 of 44 pairs consisting of type III, type III-i, and type IV units exhibit significant correlation. Figure 2 shows SpAc-correlograms derived from three different IV/IV pairs plotted on the same set of axes. The significant feature in all three correlograms is the nearly symmetrical elevation near the origin that extends to both side of the origin. This feature, called a central mound (CM), is indicative of near-simultaneous firing of action potentials in the two spike trains and is expected where units share common excitatory or inhibitory input (Moore et al. 1970; Perkel et al. 1967). Note that the CM can have three distinct shapes: wide (Fig. 2C), narrow (Fig. 2A), or a composite of wide and narrow shapes (Fig. 2B). This feature appears to be independent of pair composition; rather, CM shape appears to be related to the SpAc rates of the units in the pair as shown in Fig. 3 (r = −0.73). That is, pairs with low SpAc rates tend to have wide CMs (black symbols), pairs with high SpAc rates tend to have narrow...
TABLE 2. Relationship between the spontaneous and stimulus-evoked correlation for pair combinations that show CMs

<table>
<thead>
<tr>
<th>Unit Types</th>
<th>Spontaneous Correlogram Shape</th>
<th>Driven Correlogram Shape</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Flat</td>
<td>CM</td>
<td>Not tested</td>
</tr>
<tr>
<td>III/III</td>
<td>Flat</td>
<td>6*</td>
<td>0</td>
</tr>
<tr>
<td>CM</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>III/III-i</td>
<td>Flat</td>
<td>7*</td>
<td>0</td>
</tr>
<tr>
<td>CM</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>III/IV</td>
<td>Flat</td>
<td>5*</td>
<td>0</td>
</tr>
<tr>
<td>CM</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>III-i/III-i</td>
<td>Flat</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CM</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>IV/IV</td>
<td>Flat</td>
<td>1*</td>
<td>0</td>
</tr>
<tr>
<td>CM</td>
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<tr>
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<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>16</td>
<td>7</td>
</tr>
</tbody>
</table>

Driven activity tested for both long-duration tones and frozen broadband noise except where indicated by asterisk (1 asterisk for each pair tested for tones only). The type IV unit class includes type IV-T, type IV, and type IV-i units. For abbreviations, see Table 1.

CMs (open symbols), and pairs with intermediate SpAc rates tend to have composite CMs (gray symbols). In this paper, a width of 5 ms (based on the separation in Fig. 3) was used to distinguish wide and composite CMs from narrow CMs. Composite CMs were distinguished from wide CMs by the presence of a distinct narrow component.

The stimulus-evoked activities of 32 pairs consisting of type III, type III-i, and type IV units were obtained in response to both long-duration tones and frozen broadband noise; five additional pairs (indicated by asterisks in Table 2) were studied with tones alone. Sixteen of these pairs have CM-correlated activity. Table 2 shows the relationship between correlograms for SpAc and driven activity. Note that if a pair had correlated SpAc, then the pair also had correlated driven activity in response to both tones and noise (15 of 15 pairs). Similarly, if a pair lacked correlated SpAc, then it also had uncorrelated driven activity (21 of 21 pairs).

Regardless of pair combination, four distinct patterns of correlation as a function of stimulus level are observed (Table 3) and these patterns are illustrated in Figs. 4–7. The organization of all figures showing correlation data is the

TABLE 3. Summary of CM correlation as a function of stimulus level

<table>
<thead>
<tr>
<th>Unit Types</th>
<th>W-F-N</th>
<th>W-C-N</th>
<th>C-N</th>
<th>N-N</th>
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<tr>
<td>III/III</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>III/III-i</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>III/IV</td>
<td>1</td>
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<td>2</td>
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<tr>
<td>III-i/IV</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>IV/IV</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>4</td>
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<td>Total</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

Symbols show the sequence of CM type for spontaneous activity and then for driven activity as the stimulus level is raised; for example, W-C-N refers to a CM feature that changes from a wide appearance for spontaneous activity to a composite and finally a narrow appearance as the stimulus level increases. W, wide CM (width >5 ms); F, flat; C, composite CM (composed of both wide and narrow components); N, narrow CM (width <5 ms). For abbreviations, see Table 1.
same. The left column shows the single-unit response properties of the units that guided the collection of the correlation data. In A, the outlines of the excitatory (bounded by the solid line) and inhibitory (bounded by the dashed lines) areas in the response map of one unit (the reference unit for the correlograms) are overlaid onto the response map of the second (nonreference) unit; the excitatory area for the second unit is filled with vertical lines, the inhibitory area is cross-hatched. The BFs of units are indicated by arrows on the plot and the crosses indicate stimulus conditions under which long-duration tone-evoked correlation data were acquired. Rate-level curves in response to BF tone (solid line) and noise bursts (bold line) and for SpAc (dashed line) for the reference and nonreference units are shown B and C, respectively. The cross-correlogram derived from the units’ SpAc is shown in F, and the correlograms derived from the activities evoked by tones (D) and broadband noise (E) at various stimulus levels are shown above. Autocorrelograms are only shown if they impact on interpretation of the primary feature.

The correlograms derived from the III/IV pair in Fig. 4 show the first pattern of CM correlation (2 pairs). The SpAc-derived correlogram shows a wide CM (Fig. 4F). Tone and noise stimulation produces two effects on the CM: the width of the CM changes from wide to narrow as a function of increasing stimulus level, and the amplitude of the CM is a nonmonotonic function of level, first decreasing until the units’ activities become decorrelated, then increasing (W-F-N in Table 3). In the second pattern (4 pairs), exhibited by the IV/IV pair in Fig. 5, a similar trend in the CM width (wide to narrow) is observed; however, low-level stimulation produces a composite CM; that is, the narrow CM feature is observed at lower stimulus levels (W-C-N in Table 3). The amplitude of the CM as a whole does not change systematically in pairs exhibiting this pattern; rather, the width component of the CM appears to decrease in amplitude (curved arrows), whereas the narrow component (straight arrows) first increases and then decreases. As illustrated by the III-i/IV pair in Fig. 6, the effects of stimulation are similar in the third pattern (7 pairs); the difference is that the composite CM is observed in the correlogram derived from the SpAc of the pair (C-N in Table 3). Finally, in the fourth pattern (3 pairs), the CM is never wide; rather, the cross-correlogram derived from the SpAc of the pair shows a narrow CM (e.g., the IV/IV pair in Fig. 7). In these pairs, the shape and width of the CM remains relatively constant as a function of stimulus level in response to both tones and noise (N-N in Table 3). The amplitude of the CM, however, is typically still nonmonotonic, increasing at low levels and then decreasing.

Dependence of CM correlation on level and stimulus type

Figure 8 shows the dependence of the CM features (width and component amplitudes) on level for tones (left) and noise (right). The bold curves with symbols represent the four pairs shown in Figs. 4–7. The shaded regions enclose the majority of the data (1 outlier in C and F is excluded), highlighting the trends in the data. CM width as a function of tone level is shown in Fig. 8A; the black squares mark the widths of pairs with correlated SpAc but untested driven activity. Fifteen of the pairs have wide or composite SpAc CMs with widths between 8.0 and 15.0 ms (average = 11.2 ms). As the tone level increases, the CM width for these pairs typically decreases slightly, then shows a sharp transition between 20 and 30 dB SPL to an average width of 3.0 ms (e.g., diamonds). For two pairs, the driven activity becomes completely decorrelated (CM width goes to 0) before the narrow CM emerges (e.g., squares). Interestingly, the transition to only narrow CMs occurs within ±10 dB of the average thresholds to tones of type II (filled arrow at top of plot) and type III-i units (open arrow). The behavior of CM widths in noise-driven data is generally similar (Fig. 8D); however, the transition from wide to narrow CMs occurs up to 30 dB below the average thresholds to excitation of type II and type III-i units (arrows). Unlike pairs with wide CMs for SpAc, CM widths for pairs with narrow SpAc CMs (5 pairs, average width = 3.2 ms) remain relatively constant as a function of level for both tones and noise (e.g., circles).

To examine the transition from wide to narrow CMs as a function of stimulus level, ratios of the feature amplitude (peak mean) to the mean correlogram value were computed separately for the “wide” and “narrow” components of the CM by assuming a linear superposition of these components. In correlograms with composite CMs (e.g., Fig. 6F), the amplitude of the wide component was defined to be the average of the correlogram values >3 ms from the center of the peak, because these limits are beyond the maximum width observed for narrow CMs (from Fig. 3). The amplitude of the narrow component was then defined to be the peak value in the correlogram minus this value. As the tone level increases, Fig. 8B shows that the wide component typically begins to decrease monotonically at ~0 dB SPL (20 dB below the average thresholds of type II and type III-i units) and is unmeasurable (only a narrow CM is observed) by 30 dB SPL. The narrow component (Fig. 8C), either alone (circles) or as part of a composite CM (crosses), typically remains relatively constant in amplitude up to 10 dB SPL, begins to increase between 10 and 20 dB SPL (around the thresholds of type II and type III-i units), reaches its peak by 30–50 dB SPL, then decreases. Similar behaviors of both the wide and narrow CM components are observed in noise-driven data (Fig. 8, E and F); however, the narrow component begins to increase (between 30 and 40 dB SPL) up to 20 dB below the threshold of type II and type III-i units.

Rate depression effects

In this study, correlation data were acquired first for SpAc, then for a level series of tone-evoked activity, and finally for a level series of noise-evoked activity. Many of the units in the pairs exhibited at least some reduction in their SpAc rates after the tone-evoked data were collected; the cause of this effect is unknown, but the rate depression could last >10 min. Typically, the rate reduction was small (<15%) and the noise-derived correlograms were unaffected. However, for 5 of the 16 CM-correlated pairs (2 IV/IV pairs, 1 II/III-i pair, and 2 III/IV pairs), the SpAc rates of one or both of the units in the pair decreased substantially (>60%) from the original value. CM width as a function of noise level was not affected in these pairs, so these data are included in Fig. 8D. CM feature amplitudes, however, were substantially larger than the means of the low-level noise-
FIG. 4. Response map and correlation data for a type III and a type IV-T unit studied simultaneously. A: response map of reference (type III) unit in correlograms (its excitatory area bounded by heavy solid line and its inhibitory regions bounded by heavy dashed lines) is superimposed onto response map of nonreference (type IV-T) unit (vertical shading, excitatory area; hatched shading, inhibitory area). Arrows: BFs. Crosses: conditions under which tone-evoked cross-correlation data were obtained. B and C: plots of discharge rate in response to 200-ms BF tones (solid line) and noise bursts (bold line) and for SpAc (dashed line) for reference type III (B) and type IV-T unit (C). BFs are indicated on plots. D–F: cross-correlograms computed from SpAc values of units (F) and their responses to long-duration (1.15-kHz) tones (D) and frozen broadband noise (E) at levels indicated on plots. Lowest labeled ordinate tick mark indicates tick spacing unless otherwise specified. SpAc-derived correlogram shows a wide CM. Pairs’ activities become decorrelated to both low-level tones and noise, but to higher-level stimuli, narrow CMs are observed. Numbers of spikes and average discharge rate for type III and type IV-T units in correlograms are as follows. SpAc: 11,127 and 6,681 spikes, 20.6 and 12.8 spikes/s; 1.15-kHz tones: 10 dB SPL, 9,904 and 6,164 spikes, 27.5 and 17.7 spikes/s; 20 dB SPL, 11,815 and 6,727 spikes, 32.8 and 18.8 spikes/s; 50 dB SPL, 16,301 and 9,095 spikes, 85.9 and 47.9 spikes/s; Noise: 20 dB SPL, 10,147 and 1,008 spikes, 36.2 and 3.6 spikes/s; 30 dB SPL, 16,079 and 2,323 spikes, 70.0 and 9.8 spikes/s; 50 dB SPL, 9,501 and 5,049 spikes, 44.3 and 23.8 spikes/s.
FIG. 5. Response map and correlation data for a IV/IV-T pair showing transition from a wide SpAc CM to a composite and then to a narrow CM as a function of increasing stimulus level. Conventions as in Fig. 4; type IV unit is reference for correlograms. In correlograms, curved arrows point to diminishing amplitude of wide component and straight arrows point to emergence of narrow component. Numbers of spikes and average discharge rate for type IV and type IV-T units in correlograms are as follows. SpAc: 3,169 and 3,610 spikes, 10.6 and 12.3 spikes/s; 15.5-kHz tones: 20 dB SPL, 1,600 and 5,107 spikes, 6.7 and 21.6 spikes/s; 40 dB SPL, 3,049 and 13,208 spikes, 12.7 and 58.8 spikes/s; 60 dB SPL, 15,701 and 14,713 spikes, 15.0 and 28.5 spikes/s; Noise: 10 dB SPL, 1,143 and 2,328 spikes, 3.2 and 6.5 spikes/s; 40 dB SPL, 5,124 and 9,749 spikes, 15.0 and 28.5 spikes/s; 70 dB SPL, 9,746 and 11,225 spikes, 43.5 and 50.1 spikes/s.

derived correlograms (e.g., Fig. 5E, 10 dB SPL), resulting in wide and narrow component feature peak-to-mean amplitude values being much larger than those in the SpAc-derived and high-level noise-derived correlograms. One possible interpretation of these results is that the strength of the shared input has increased at low noise levels. Melssen and Epping (1987), however, have shown that even in model networks where the connections have constant strength, correlation features will increase in amplitude as background activity decreases. Thus, to prevent this confounding effect from obscuring general trends, these data were not included in Fig. 8, E and F.
**FIG. 6.** Response map and correlation data for a IV-i/III-i pair showing transition from a composite SpAc CM to a narrow CM as a function of increasing stimulus level. Conventions as in Fig. 4; type IV-i unit is reference for correlograms. Numbers of spikes and average discharge rate for type IV-i and type III-i units in correlograms are as follows. SpAc: 4,756 and 10,046 spikes, 24.4 and 49.4 spikes/s; 3.3-kHz tones: 20 dB SPL, 11,932 and 9,920 spikes, 56.4 and 46.8 spikes/s; 50 dB SPL, 10,169 and 16,383 spikes, 46.4 and 75.9 spikes/s; 60 dB SPL, 6,124 and 16,276 spikes, 26.9 and 75.4 spikes/s; Noise: 30 dB SPL, 8,370 and 4,176 spikes, 35.5 and 17.7 spikes/s; 50 dB SPL, 7,898 and 7,254 spikes, 34.9 and 32.9 spikes/s; 70 dB SPL, 4,287 and 7,254 spikes, 18.8 and 55.9 spikes/s.

**IT correlation: pairs including type II and type III-i units**

Functional inhibitory interactions are observed in four pairs, including two II/III pairs (e.g., Fig. 9), one II/III-i pair, and one III-i/IV pair (Fig. 10). Despite the heterogeneity of the pair combinations, the respective single-unit response properties of the units in these pairs and their interactions exhibit many common properties. First, the excitatory area (bounded by the solid line) of the reference (II or III-i) unit partially (Fig. 9A) or completely (Fig. 10A) overlaps the low-frequency inhibitory sideband of the nonreference (III, III-i, or IV) unit. Second, the nonreference units have nonmonotonic BF rate-versus-level curves (Figs. 9C and 10C), suggesting inhibitory input at BF. Third, most of the pairs (3 of 4 pairs) have similar BFs (within 0.3 octaves); the III-i/IV pair in Fig. 10 is an exception with a BF differ-
FIG. 7. Response map and correlation data for a IV/IV-T pair showing narrow SpAc CM that remains narrow at all levels tested. Conventions as in Fig. 4 except ordinate tick spacing is 20 spikes/s; type IV unit is reference for correlograms. Numbers of spikes and average discharge rate for type IV and type IV-T units in correlograms are as follows. SpAc: 16,383 and 14,401 spikes, 96.6 and 84.9 spikes/s; 4.3-kHz tones: 10 dB SPL, 16,380 and 16,176 spikes, 82.6 and 81.6 spikes/s; 30 dB SPL, 13,633 and 16,383 spikes, 76.2 and 91.2 spikes/s; 50 dB SPL, 12,395 and 16,383 spikes, 86.5 and 114.4 spikes/s; Noise: 40 dB SPL, 11,645 and 9,017 spikes, 43.2 and 35.0 spikes/s; 50 dB SPL, 9,207 and 12,535 spikes, 36.3 and 49.4 spikes/s; 70 dB SPL, 5,017 and 16,022 spikes, 26.9 and 85.8 spikes/s.

ence of 1.8 octaves. Finally, the inhibitory features in the correlograms have similar temporal properties and dependence on level.

Figure 9 shows the correlation data for a II/III pair; recall that type II units lack SpAc and respond weakly to high-level noise. The tone-evoked correlograms (Fig. 9D) were derived from responses to tones at the type II unit’s BF; the type II unit is the reference unit for the correlograms in this figure. Note that the only significant feature in these correlograms is the asymmetric decrease in correlation to the right of the origin. This feature is called an inhibitory trough (IT) and corresponds to a decrease in the firing rate of the type III unit following spikes in the type II unit. The ITs have a latency to the onset of 1.05–1.35 ms and a duration of 2–3 ms. The effectiveness and association index measures of IT magnitude are computed over the blackened
FIG. 8. Dependence of CM width (A and D) and component amplitudes (wide, B and E; narrow, C and F) on tone and noise level, respectively. See legend for line types for different pair combinations: bold curve with squares, III/III-T data from Fig. 4; diamonds, IV/IV-T data from Fig. 5; crosses, IV-i/III-i data from Fig. 6; circles, IV/IV-T data from Fig. 7. Shaded regions enclose majority of data (1 outlier excluded in C and F) and highlight level-dependent trends. Arrows correspond to average excitatory thresholds of type II (filled arrows) and type III-i (open arrows) units to tones and noise. Black squares in A are for pairs with correlated SpAc and untested driven activity. Five pairs (1 III/III-i, 2 III/IV, and 2 IV/IV pairs) are excluded from noise amplitude plots because of significant rate suppression effects after tone-evoked data were collected (see text).
FIG. 9. Response map and correlation data for a type II and a type III unit studied simultaneously. Conventions as in Fig. 4 except that type II units lack SpAc and only respond to high-level noise. Correlogram binwidth: 0.3 ms. Tone stimulus is at BF of type II unit; stimulus levels relative to threshold of type II unit are reported (θ, see legend). Type II unit is reference for correlograms. Significant inhibitory trough (IT) features are shown in black. Effectiveness and association measures of strength of IT are given in legend. Numbers of spikes and average discharge rate for type II and type III units in correlograms are as follows. 3.73-kHz tones: 40 dB SPL, 2,323 and 13,542 spikes, 11.0 and 63.1 spikes/s; 60 dB SPL, 3,227 and 16,383 spikes, 18.1 and 91.6 spikes/s; 80 dB SPL, 2,853 and 15,334 spikes, 14.3 and 76.8 spikes/s; Noise: 70 dB SPL, 2,134 and 14,504 spikes, 10.1 and 69.4 spikes/s; 80 dB SPL, 2,544 and 15,948 spikes, 12.0 and 76.0 spikes/s.

regions of the IT and are given in the figures. Both measures show that the IT strength is only weakly dependent on stimulus level.

The correlograms derived from the activities of the III-i/IV pair are shown in Fig. 10; the tone-evoked data were acquired at the type III-i unit’s BF and the type III-i unit is the reference unit for all correlograms. Clear ITs are observed for all stimulus conditions. The leading edge of the IT derived from the SpAc (Fig. 10F, middle), however, precedes zero delay (by ~4 ms) and the feature is significant before zero delay. This extended duration of this feature most likely reflects the effect of a regularly firing reference unit; the type III-i unit has a preferred firing interval of 5 ms, indicated by the arrow in type III-i unit autocorrelogram (Fig. 10F, left). Thus the feature probably...
FIG. 10. Response map and correlation data for a type III-i/IV pair showing ITs whose strength is level dependent. Organization of figure is like that of Fig. 9; type III-i unit is reference for all correlograms. Autocorrelograms derived from SpAc of type III-i and type IV units are shown to left and right of SpAc-derived correlogram, respectively. Effectiveness and association measures of IT (shown in black) are given in legend. Numbers of spikes and average discharge rate for type III-i and type IV units in correlograms are as follows. SpAc: 1,724 and 16,383 spikes, 6.1 spikes/s and 57.9 spikes/s; 0.75-kHz tones: 40 dB SPL, 16,383 and 8,691 spikes, 51.8 and 27.5 spikes/s; 50 dB SPL, 16,383 and 3,532 spikes, 60.3 and 13.0 spikes/s; 60 dB SPL, 16,383 and 8,469 type IV spikes, 90.7 and 47.1 spikes/s; Noise: 40 dB SPL, 2,177 and 16,383 spikes, 13.4 and 98.7 spikes/s; 50 dB SPL, 2,599 and 12,113 spikes, 23.2 and 110.6 spikes/s.

reflects both a reduction in the type IV unit firing rate following the current spike in the type III-i unit and a residual reduction in its rate caused by a previous type III-i unit spike. In response to above-threshold stimuli, the type III-i unit does not exhibit such regular discharges (not shown) and the ITs are all to the right of origin; significant pre- and postinhibitory features accompany these ITs, but they are small compared with the ITs and can be expected in strictly inhibitory interactions (Bryant et al. 1973). The ITs in these correlograms have a latency-to-onset of 0.75 ms and a duration of 2–4 ms. To tonal stimulation, the effectiveness measure of IT magnitude is a nonmonotonic function of level, first decreasing and then increasing above 50 dB SPL. The association index is less dependent on level, tending to decrease slightly with increasing level.
TABLE 4. **IT timing values**

<table>
<thead>
<tr>
<th>IT Parameter</th>
<th>Range</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency to IT start</td>
<td>0.6–1.3</td>
<td>0.99 ± 0.23</td>
</tr>
<tr>
<td>Latency to IT peak</td>
<td>1.2–2.5</td>
<td>1.71 ± 0.38</td>
</tr>
<tr>
<td>Risetime</td>
<td>0.4–1.3</td>
<td>0.72 ± 0.25</td>
</tr>
<tr>
<td>Halfwidth</td>
<td>0.7–2.35</td>
<td>1.54 ± 0.41</td>
</tr>
<tr>
<td>Asymmetry</td>
<td>0.23–0.93</td>
<td>0.51 ± 0.21</td>
</tr>
</tbody>
</table>

Values are in ms. n = 20 measurements from 4 pairs. For abbreviations, see Table 1.

**Temporal parameters of the ITs**

Table 4 summarizes the temporal parameters measured (latency to IT start, latency to IT peak, and half-width) and calculated (rise time and asymmetry) for all the correlograms with significant ITs (computed as for type II/IV pairs in Voigt and Young 1990). The latency to the start of the trough is defined as the delay at which the correlogram shows a sharp drop and the peak latency is defined as the delay in the center of the bin containing the minimum of the trough. Rise times are computed as the difference between the peak and start latencies. The half-widths were measured as the difference between the delays on either side of the IT corresponding to the correlogram values equal to the average of the correlogram mean and the minimum value of the trough. Finally, asymmetry is computed as the risetime divided by half-width.

All the temporal measurements of the ITs were obtained from correlograms recomputed with a 0.1-ms binwidth and, because the timing parameters do not seem to vary consistently with stimulus level or BF difference in the data, the values are combined for all pairs in Table 4. The table shows that the average latency to the start of the ITs is 0.99 ms and the range is confined to values appropriate for a monosynaptic delay. Further, the ITs are asymmetric (mean value = 0.5) in shape. This asymmetry, where the rising phase of the IT is faster than the falling (trailing) edge, is expected of a monosynaptic, inhibitory synapse (Bryant et al. 1973; Moore et al. 1970).

**Dependence of IT correlation on stimulus level**

Figure 11 shows the dependence of effectiveness (A) and association (B) on tone level for the four pairs showing ITs in the gerbil (pairs with symbols) and, for comparison, 11 type II/IV pairs from decerebrate cat (solid lines) (Voigt and Young 1990). All these pairs were tested at two or more sound pressure levels at the BF of the unit providing the inhibitory input (the type II or type III-i unit in gerbil and the type II unit in cat); the abscissa is level with respect to this reference unit’s threshold. The solid lines are for pairs with BF differences <0.3 octaves and the dashed lines are for pairs with BF differences >0.3 octaves. The measures are computed over the filled regions defining the extent of the IT as in Figs. 9 and 10. In cases where the IT is not significant at a given level, the measures are computed over the range of delays at which the IT is present at other levels in the same pair and are plotted with crosses in Fig. 11.

Note that the strengths of the ITs in gerbil, as measured by effectiveness, are among the strongest reported in cat (Fig. 11A). This most likely reflects the fact that more spikes were collected for the pairs in cat, particularly for those pairs in which on-line analysis suggested a feature, allowing for the detection of weaker connections. For the three pairs in gerbil with BF ratios < 0.3 octaves (filled symbols), effectiveness remains relatively constant as a function of increasing level, unlike in cat, where the values tend to decrease. For the one pair in gerbil with a BF ratio >0.3 octaves (open symbols), effectiveness first decreases with level, then, simi-
lar to cat, increases with level. These differences most likely reflect differences in the discharge characteristics of the postsynaptic units; in gerbil, the postsynaptic units have primarily type III response properties, whereas in cat, the postsynaptic units all have type IV properties. When the data from gerbil and cat are plotted as association index (Fig. 11B), defined as effectiveness divided by postsynaptic discharge rate, the curves all show less dependence on level. This result suggests that most, but not all, of the dependence of effectiveness on level is caused by the changing discharge rate of the postsynaptic unit.

**Discussion**

**Association of anatomic cell types with physiological response types**

The results reported here support the hypothesis that the principal cells in gerbil DCN (type III and type IV units) receive multiple sources of shared auditory input. In particular, the level-dependent changes observed in the correlated activity of these pair types suggests that one source (presumably the auditory nerve) correlates their SpAc and other sources correlate their driven activity (to tones, presumably the vertical cells, type II and some type III-i units; and to noise, presumably the D-stellate cells, the wideband inhibitors). This conclusion is based, in part, on our current understanding of DCN anatomy and physiology because it is not possible to determine from these data the source(s) shared by the units; rather, the data can only constrain the possibilities.

Both type III and type IV unit properties are thought to be recorded from the principal cells (pyramidal and giant cells) (Adams and Warr 1976; Kane 1974; Lorente de Nó 1981; Osen 1969) for several reasons. First, intracellular recording and marking experiments in decerebrate gerbil (Ding 1997; Ding et al. 1994a,b) and antidromic stimulation studies in decerebrate cat (Young 1980) show that the principal cells can exhibit both type III and type IV response properties. Pairs involving these unit types should therefore show similar correlation features, and indeed, CM correlation is observed regardless of pair composition (Table 2) and these unit types are postsynaptic in IT correlation pairs (Table 1). Second, the CMs observed in the SpAc and driven activity of pairs involving type III-i and type IV units are restricted to pairs with similar BFs (11 of 16 pairs with BF ratios $\pm$0.2 octaves; Fig. 1). Finally, pairs consisting of these response types exhibit similar level-dependent changes (amplitude, shape, and width) in their CM-correlated activity in response to both tones and noise (Table 3, Fig. 8).

The association of type II unit properties with vertical cells is also based on several arguments. First, antidromic stimulation studies in decerebrate cat suggest that vertical cells exhibit type II responses properties (Young 1980). Second, type II units are presynaptic in pairs showing IT correlation (Figs. 9 and 10) and the ITs have the temporal properties (Table 4) expected of a monosynaptic inhibitory connection (modeling studies, Knox and Poppele 1977; Moore et al. 1970; Perkel et al. 1967; identified synapses in *Aplysia*, Bryant et al. 1973). These ITs are similar to those observed in type II/IV pairs in cat (Voigt and Young 1980, 1990) and are consistent with the expected inhibitory action of vertical cells (Saint-Marie et al. 1991; Sanes et al. 1987; Zhang and Oertel 1993b, 1994). Third, both units in an IT pair involving this unit type were recorded in deep DCN (the II/III-i pair in Table 1), where vertical cells are located (Lorente de Nó 1981; Osen et al. 1990). Finally, type II units tend to inhibit similar-BF units (3 of 3 pairs with BF ratios $\pm$0.3 octaves; Fig. 1), with the strength of this inhibition exhibiting a level dependence similar to that of type II/IV pairs in cat (Fig. 11).

The evidence suggests that the type III-i unit category may reflect recordings from several different cell types. First, type III-i units were both pre- and postsynaptic in pairs showing IT correlation (Table 1); one such unit was presynaptic to a type IV unit, suggesting a vertical cell origin, but another one was postsynaptic to a type II unit, suggesting a principal cell origin. Second, type III-i units were involved in four pairs showing CM correlation (with type III and type IV units; Table 1), suggesting a principal cell origin. Interestingly, the type III-i unit that inhibited the type IV unit was strongly inhibited by low-level noise, that is, its discharge rate was driven to zero and otherwise remained below the unit’s SpAc rate for $>30$ dB (Fig. 10B). In contrast, the other type III-i units were only weakly inhibited by low-level noise (e.g., Fig. 6C). Perhaps, then, vertical cells exhibit strongly inhibited type III-i properties, whereas principal cells exhibit weakly inhibited type III-i properties. Consistent with this hypothesis, intracellular data from marked neurons suggest that pyramidal cells can exhibit weakly inhibited type III-i properties (Ding 1997; Ding et al. 1994a). This distinction is also consistent with the proposed difference in the relative strength of the wideband inhibitor input to these cell types (Nelken and Young 1994).

**Internal organization of the DCN**

All the pairs of principal cells (type III and type IV units) in the gerbil DCN that show correlated SpAc have correlated driven activity in response to both tones and broadband noise (Table 2). These data exhibit two important properties: the units must have similar BFs to have correlated activity (Fig. 1), suggesting that the inputs are tonotopically organized; and the cross-correlograms are characterized by the presence of CMs whose properties change as a function of level. In regards to this latter observation, we first present arguments for an interpretation in which multiple sources correlate the activity of the principal cells, consistent with the conceptual model, and then explore possible candidate sources.

The observation that argues most strongly for the existence of multiple sources correlating the activities of the principal cells is the change in the shape of the CMs as a function of level (Voigt and Young 1988). For SpAc, the CMs can be either wide, composite, or narrow (Fig. 2), but at high levels of driven activity, all CMs are narrow (Fig. 8, A and D). CM features might be expected to range from wide to narrow because of a single shared input if timing became more precise with increasing level or the strength of synaptic input increased such that the postsynaptic cells were driven into depolarized states with shorter time constants. With this explanation, however, it is unlikely that intermediate-strength inputs would produce the composite...
CM shape seen in some cases (Fig. 5) or the decorrelation seen in others (Fig. 4). Decorrelation, in particular, suggests that either two sources of opposite sign (1 excitatory, 1 inhibitory) are directly competing against each other to control the output of the pair (Voigt and Young 1988), or that the source correlating the SpAc loses its effectiveness as a function of level and is replaced by a second source at higher levels. Thus we propose that SpAc is correlated by one source, most likely auditory nerve fibers, and high-level driven activity is correlated by a different source, most likely inhibitory interneurons. In support of this hypothesis, the wide component of the CM decreases in amplitude at tonal levels as low as 0 dB SPL (Fig. 8B), well below the thresholds of most type II (average = 17 dB SPL) and type III-i units (average = 16.4 dB SPL) (Davis et al. 1996a), and the narrow component increases in magnitude over levels above the type II and type III-i unit thresholds (Fig. 8C). Further, modeling studies show that much of the level-dependent behavior of pairs of principal cells to tones can be readily accounted for by the use of such a circuit (Davis and Voigt 1996).

There are several possible inputs to DCN principal cells that could correlate their SpAc. The auditory nerve is a likely candidate because it is known to be spontaneously active and to have a tonotopic projection to the DCN (Lorente de Nó 1981; Osen 1970; Rose et al. 1960); in particular, primary fibers appear to be in register with the flattened basolateral dendrites of pyramidal cells (Blackstad et al. 1984; Zhang and Oertel 1994) forming isofrequency contours in the DCN. T-stellate cells, an excitatory class of ventral CN principal cell, also appear to project tonotopically to the DCN (Doucet et al. 1996; Oertel et al. 1990; Smith and Rhode 1989; Snyder and Leake 1988; Zhang and Oertel 1994); it is not yet clear, however, whether they contact DCN principal cells. Finally, in gerbil, vertical cells exhibiting type III-i properties may also correlate the SpAc values of the principal cells. On the other hand, it seems likely that granule cells can be ruled out as a possible source. Granule cells provide excitatory input to DCN principal cells and may be spontaneously active (Hirsch and Oertel 1988; Manis 1989; Mugnaini et al. 1980a,b; Zhang and Oertel 1993b, 1994); however, granule cell axons run orthogonal to the isofrequency laminae and should therefore produce correlation between units with widely disparate BFs, and this is not observed in gerbil (present study) or cat (Voigt and Young 1988).

The most likely candidate for correlating the tone-evoked activities of the principal cells is inhibitory input from vertical cells (type II and some type III-i units). First, there is evidence that type II and type III-i units inhibit type III and type IV units (Table 1, Figs. 9 and 10). Second, the average thresholds of type II and type III-i units are lower than the level at which most pairs of principal cells show the narrow CM (Fig. 8A). Finally, the driven activities of the principal cells are more likely to show correlation if the unit BFs are similar. Consistent with these data, the local axonal terminals of vertical cells are restricted to narrow bands within the DCN that are parallel to the path of the auditory nerve (Zhang and Oertel 1993c), suggesting that these cells make tonotopic connections to the principal cells. A second candidate for correlating the tone-evoked activities is excitatory input from T-stellate cells. This possibility would account for the paucity of inhibitory interactions observed in gerbil; however, this paucity may simply reflect an electrode bias against recording from small vertical cells. Finally, inhibitory input from superficial cartwheel cells cannot be ruled out as a source (Berrebi and Mugnaini 1991; Mugnaini 1985; Osen et al. 1990; Wenthold et al. 1987; Wouterlood and Mugnaini 1984; Zhang and Oertel 1994). Cartwheel cells are a known source of complex action potentials (Ding 1997; Ding et al. 1994b; Manis et al. 1994; Zhang and Oertel 1993a). Complex-spiking neurons are excited by granule cell axons (Davis and Young 1997), but they are widely tuned and respond weakly to acoustic stimuli (Ding 1997; Ding and Voigt 1997; Parham and Kim 1995). The axonal arbors of cartwheel cells, however, appear to be confined (Zhang and Oertel 1993a); thus they could provide tonotopic input. On the other hand, inhibitory input from superficial stellate cells (Mugnaini 1985; Wouterlood et al. 1984) can most likely be ruled out because their axonal arbors are large (Zhang and Oertel 1993a); thus these cells would most likely correlate units over a wider BF range than observed.

There are many candidate sources to correlate the noise-evoked activities of the principal cells. D-stellate cells, an inhibitory class of ventral CN principal cells, are a likely candidate because these cells appear to receive inputs across a wide range of auditory nerve frequencies and thus have low thresholds to noise (Doucet et al. 1996; Doucet and Ryugo 1997; Nelken and Young 1994; Oertel et al. 1990; Smith and Rhode 1989; Winter and Palmer 1995). This would account for the low levels, up to 30 dB below the noise thresholds of most type II and type III-i units, at which pairs of principal cells show the narrow CM (Fig. 8D). The tonotopic specificity of this input, however, is currently unknown. Inhibitory input from vertical cells exhibiting type III-i unit properties is a second candidate. Type III-i units, although inhibited by low-level noise, do fire to some extent to long-duration noise of all levels and inhibit type IV units at all levels (Fig. 10). Finally, excitatory input from T-stellate cells and inhibitory input from cartwheel cells cannot be ruled out.

Comparison with other studies

Cross-correlation analysis of paired-unit activity in the DCN has yielded conflicting data across species. In the previous decerebrate cat studies (Voigt and Young 1980, 1990) and in the data reported here, inhibitory interactions were observed, but not excitatory interactions. In contrast, Gochin et al. (1989, 1990) and Kipke et al. (1991) reported that the correlograms of ~86% of their pairs in anesthetized rat and guinea pig, respectively, showed asymmetric peaks consistent with mono- or disynaptic excitation, but no inhibitory interactions were seen. Perhaps the most important methodological difference between these two groups of studies is the anesthetic state. In both the studies by Voigt and Young and the current study, atropine was used to avoid respiratory distress. Recent work suggests that atropine blocks the activity of muscarinic receptors in the DCN for prolonged periods of time (Chen et al. 1994). Muscarinic modulation of excitatory parallel fiber synapses is complex (Balogh 1996), but one possible effect of atropine could be to reduce the effectiveness of an excitatory interaction, perhaps mediated by the granule cells (Manis 1989). On
the other hand, it is known that the detectability of inhibition in the DCN is anesthesia dependent (Evans and Nelson 1973; Fan and Voigt 1997; Kaltenbach and Saunders 1987; Young and Brownell 1976); this effect can be mediated either by directly reducing the effectiveness of the inhibitory synapse or by reducing the excitatory drive to the network, which may disproportionately affect type II units that already have high thresholds. This latter effect may explain the lack of inhibition detected by both Gochin et al. and Kipke et al., who used ketamine anesthesia, which is thought to be an excitatory glutamate N-methyl-D-aspartate-receptor antagonist (Anis et al. 1983).

There is a number of other differences between the two groups of studies that could explain the differences in the observed functional interactions. For example, Gochin et al. hypothesized that their excitatory interactions reflected pyramidal cell input to other cells (observed in cat) (Smith and Rhode 1985). Such local axon collaterals, however, do not appear to be present in rodents (gerbil, Benson and Voigt 1995; Ding et al. 1994a,b; mouse, Oertel and Wu 1989); thus the lack of excitatory interactions in this study may not be surprising. On the other hand, Gochin et al. used 55-ms short-duration tones as their stimulus. Modeling studies suggest that it may be more difficult to detect inhibition when short-duration tonal stimuli are used (Davis and Voigt 1994). Finally, Kipke et al. used low-level broadband noise. It is clear that type II units would not be activated in such a study; thus the lack of inhibitory interactions may not be surprising. The results reported here suggest that ITs might have been observable in the correlograms of Kipke et al. if high-level noise had been used (e.g., Fig. 9E).

**Functional implications**

The organization of the gerbil DCN as revealed in this study involves principal cells receiving input from multiple auditory sources; further, the data imply that principal cell output is controlled by different sets of these inputs depending on the stimulus condition. A similar organization is observed in cat (Voigt and Young 1988, 1990), suggesting that some aspects of the neural computation performed in the DCN are conserved across species. An important difference between the two species, however, is that gerbil pyramidal cells predominantly exhibit type III unit response properties (Ding 1997; Ding and Voigt 1997; Ding et al. 1994a), whereas cat principal cells predominantly exhibit type IV unit properties (Young 1980). This implies that gerbil principal cell responses are less dominated by inhibition. The functional implication of this difference is unclear. In cat, the DCN has been implicated in early analysis of sound source location because its principal cells are sensitive to DAVIS, K. A., AND VOIGT, H. F. Neural modeling of the dorsal cochlear nucleus: cross-correlation analysis of short-duration tone-burst responses. *J. Neurosci.* 17: 107–122, 1997.


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