Auditory Response Properties in the Superior Paraolivary Nucleus of the Gerbil

OLIVER BEHREND, ANTJE BRAND, CHRISTOPH KAPFER, AND BENEDIKT GROTHE
Max-Planck-Institute of Neurobiology, D-82152 Martinsried, Germany

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Behrend, Oliver, Antje Brand, Christoph Kapfer, and Benedikt Grothe. Auditory response properties in the superior paraolivary nucleus of the gerbil. J Neurophysiol 87: 2915–2928, 2002; 10.1152/jn.01018.2002. The ascending auditory pathway is characterized by parallel processing. At the brain stem level, several structures are involved that are known to serve different well-defined functions. However, the function of one prominent brain stem nucleus, the rodent superior paraolivary nucleus (SPN) and its putative homologue in other mammals, the dorsomedial periolivary nucleus, is unknown. Based on extracellular recordings from anesthetized gerbils, we tested the role of the SPN in sound localization and temporal processing. First, the existence of binaural inputs indicates that the SPN might be involved in sound localization. Although almost half of the neurons exhibited binaural interactions (most of them excited from both sides), effects of interaural time and intensity differences (ITD; IID) were weak and ambiguous. Thus a straightforward function of SPN in sound localization appears to be implausible. Second, inputs from octopus and multipolar/stellate cells of the cochlear nucleus and from principal cells of the medial nucleus of the trapezoid body could relate to precise temporal processing in the SPN. Based on discharge types, two subpopulations of SPN cells were observed: about 60% of the neurons responded to pure tones with sustained discharges, with irregular spike patterns and no phase-locking. Only four neurons showed a regular spike pattern (“chopping”). About 40% of the neurons responded with phasic ON or OFF discharges. First spike latency observed in neurons with sustained discharges was significantly shorter than that of ON responders, but had a considerably higher trial-latency observed in neurons with sustained discharges. Although almost half of the neurons exhibited binaural interactions (most of them excited from both sides), effects of interaural time and intensity differences (ITD; IID) were weak and ambiguous. Thus a straightforward function of SPN in sound localization appears to be implausible. Second, inputs from octopus and multipolar/stellate cells of the cochlear nucleus and from principal cells of the medial nucleus of the trapezoid body could relate to precise temporal processing in the SPN. Based on discharge types, two subpopulations of SPN cells were observed: about 60% of the neurons responded to pure tones with sustained discharges, with irregular spike patterns and no phase-locking. Only four neurons showed a regular spike pattern (“chopping”). About 40% of the neurons responded with phasic ON or OFF discharges. Average first spike latency observed in neurons with sustained discharges was significantly shorter than that of ON responders, but had a considerably higher trial-latency observed in neurons with sustained discharges. Again, ON responders showed a significantly higher temporal precision in the phase-locked discharge compared with the sustained responders. High variability was observed among spike-rate-based modulation transfer functions. Histologically, a massive concentration of cytological markers for glycineergic input to SPN cells was demonstrated. Application of glycine or its blockade revealed profound effects of glycineergic inhibition on the auditory responses of SPN neurons. The existence of at least two subpopulations of neurons is in line with different subsets of SPN cells that can be distinguished morphologically. One temporally less precise population might modulate the processing of its target structures by providing a rather diffuse inhibition. In contrast, precise ON responders might provide a short, initial inhibitory pulse to its targets.

INTRODUCTION

One of the most striking features of the mammalian auditory system is its high degree of parallel processing in the ascending pathways, which can already be observed at the level of the brain stem. The textbook picture that each of these pathways fulfills an explicit function related to a specific acoustic cue is certainly simplified in that at least some nuclei might be involved in encoding different aspects of a sound (Casseday et al. 2000; Grothe 2000). However, at least specific rules of processing (subtraction of inhibition from excitation, coincidence detection etc.) and in some cases specific functions can be attributed to the main auditory brain stem nuclei. Some nuclei such as the lateral and medial superior olive (LSO, MSO) are involved in binaural processing, others seem to be involved in temporal processing of monaural inputs, like the ventral nucleus of the lateral lemniscus (VNLL) (Covey and Casseday 1991) or in monaural spectral integration for sound elevation coding, such as the dorsal cochlear nucleus (May 2000).

There is, however, one prominent auditory brain stem structure the function of which we do not know at all: the superior paraolivary nucleus (SPN) in rodents or its potential homologue, the dorsomedial periolivary nucleus (DMPO) described in carnivores (Harrison and Feldman 1970; Houtgast and Aoki 1994; Irving and Harrison 1967; Moore 1988; Osen et al. 1984; Smith et al. 1991) and bats (Grothe et al. 1994; Zook and Casseday 1982; Zook and DiCaprio 1988). The SPN is a part of the superior olivary complex (SOC). In rodents, the SPN is a very prominent structure located medially or mediodorsally to the MSO and dorsolaterally to the medial nucleus of the trapezoid body (MNTB) (Harrison and Warn 1962; Kudo et al. 1990; Kuwabara and Zook 1992; Nordeen et al. 1983; Ollo and Schwartz 1979; Saint Marie and Baker 1990; Schofield 1991; Schofield and Cant 1991; Willard and Martin 1983). SPN neurons are driven by direct excitatory inputs from both cochlear nuclei (CN) and project directly to the auditory midbrain, making it a potentially fast and important part of the ascending auditory system (for review: Thompson and Schofield 2000). Based on the connection pattern and the immunohistochemistry of SPN cells, we propose two hypotheses that we will test during the course of this study.

The first hypothesis is that the SPN—or at least a significant proportion of its neurons—is directly involved in sound localization. This hypothesis is based on the finding that the SPN receives bilateral inputs from the VCN (ventral cochlear nucleus) and unilateral input from the ipsilateral medial nucleus...
of the trapezoid body (MNTB). The MNTB input is driven by the contralateral ear and is glycnergic, hence inhibitory (Smith et al. 1998; Wenthold et al. 1987). Therefore one might expect interaural time difference (ITD) sensitivity based on binaural excitation (E/E) and/or interaural intensity difference (IID) sensitivity based on the interaction of ipsilateral excitation and contralateral inhibition (E/I). In fact, Spitzer and Semple (1995) and Batra et al. (1997a,b) found several ITD-sensitive neurons in a nondefined mediiodorsal area of the SOC, partly exhibiting patterns not expected in MSO neurons (e.g., so-called “trough type” and putative second-order “irregular” ITD functions).

The second hypothesis states that SPN neurons are involved in processing temporal aspects of sounds (independent of putative ITD sensitivity). This hypothesis is mainly based on the cell types providing excitatory and inhibitory inputs to the SPN. Excitatory inputs derive from posteroventral cochlear nucleus (PVCN) octopus and multipolar/stellate cells (review: Thompson and Schofield 2000). In vivo and in vitro studies have shown that these cells are well suited to transmit precise temporal information (Ferragamo et al. 1998; Gardner et al. 1999; Rhode and Greenberg 1994; Rhode et al. 1983a,b; Smith and Rhode 1989). Moreover, the inhibitory input derives from MNTB principal cells (Banks and Smith 1992; Kuwabara et al. 1991; Sommer et al. 1993) and is supposedly glycnergic (Wenthold et al. 1987). Principal cells of the MNTB are innervated from cochlear nucleus globular bushy cells by single synapses with outstandingly accurate signal transmission (Calyces of Held) (Brew and Forsythe 1995; Forsythe and Barnes-Davies 1993; Moster 1968; Ramon y Cajal 1907; Smith et al. 1998; Taschenberger and von Gersdorff 2000). Hence, the SPN is likely to be a target of precisely timed excitatory and inhibitory inputs. Taken together, these input patterns suggest either complex filtering properties due to the interaction of excitatory and inhibitory inputs (compare: Grothe 1994; Kuwada and Batra 1999) or very precise transmission of temporal information to the auditory midbrain. Because many SPN cells are GABergic (Thompson and Schofield 2000) and some glycnergic (Saint Marie and Baker 1990), the SPN could provide fast and temporally precise inhibition to neurons in the inferior colliculus (IC) in both hemispheres.

Here we describe our findings from extracellular recordings, pharmacological manipulations and antibody staining in the gerbil SPN. Parts of the data have been presented in abstract form.

**METHODS**

Auditory responses from 62 single neurons were recorded in 24 Mongolian gerbils, *Meriones unguiculatus*. The animals were anesthetized by an initial intraperitoneal injection of ketamine (10 mg/100 g)/rompun (2%). During surgery and the recording session, the drugs were applied continuously by intramuscular injection (0.15/0.25 ml/h). Skin and tissue covering the upper part of the skull was cut and carefully pushed aside laterally, and a metal rod was mounted on the frontal part of the skull using UV-sensitive dental-restorative material (Charisma, Heraeus Kulzer, Dormagen, Germany). The rod was used to reproducibly secure the gerbil’s head in a stereotactic device during recordings. For electrode penetrations, the muscles and dermis layer over the foramen magnum were carefully pushed aside laterally, and a small opening was cut into the dura mater. During the recording session, Ringer solution was frequently applied to the opening to prevent dehydration of the brain.

During recordings, the animal was placed on a heating cushion (36°C) in a sound-attenuated chamber. Typical recording periods were 10–14 h. The animals' position in the recording chamber was standardized by stereotactical landmarks on the surface of the skull (intersections of the bregmoid and lambdoid sutures with the sagittal suture in horizontal alignment). To properly adjust the electrode trajectory relative to the brain stem, the animal was rotated rostrally by 60° (see gerbil brain atlas) (Loskota et al. 1974; Spitzer and Semple 1995). Micromanipulators were used to position the recording electrode according to landmarks on the brain surface and a reference point used for all penetrations.

Depending on the recording electrode used, different strategies were applied to anatomically localize recording sites. When multibarrel electrodes were used, the balancing channel contained horseradish peroxidase (HRP) that was iontophotically injected (720 nA for 8 min, Sigma) after recordings of a neuron were finished. When single-barrel electrodes were used, fluorescent latex beads (Lumofluor) were pressure-injected (2 psi for 50 ms) through a glass pipette cut to a diameter of 10 μm positioned at the same point where the last unit was recorded. This allowed an anatomical reconstruction of the actual recording sites. The accuracy of the position of the marking electrodes was tested in three of the animals by additional penetrations using different colors of fluorescent latex beads and measuring the relative positions of the different injections. The maximal deviation between different electrodes was about ±80 μm.

At the end of the experiment the animals were killed and perfused intracardially with heparinized 0.9% saline for 5 min followed by 4% paraformaldehyde and 1.25% glutaraldehyde for 40 min. The brain was then removed and stored in sucrose for kryoprotection (10, 20, and 30% solutions were applied successively, and the brain remained in each solution until it sank). Finally, the brain was embedded in egg yolk and mounted on a cryostat to obtain frontal sections of the SOC (each 25 μm). After HRP injections, the slices were counterstained with diaminobenzidine and cytochrome. To verify recording sites, the sections were analyzed by light microscopy (for location of HRP staining) or fluorescent microscopy (for location of latex bead injections).

**Neural recordings and stimulus presentation**

The recording of action potentials and stimulus generation was controlled by custom-made software (Spide; D. Molter, Zoologisches Institut der LMU, München, Germany, and B. Warren, University of Washington, Seattle, WA).

**Neural recordings**

Single-unit responses were recorded extracellularly using glass pipettes filled with 2 M sodium acetate (impedance, 10–30 MΩ), and an electrometer (Electro 705, World Precision Instruments). The recording electrodes were advanced under remote control, using a motorized micromanipulator (DC3314, World Precision Instruments) and a piezodrive (PM-10−1, World Precision Instruments). Recorded signals were fed into a 50/60-Hz noise eliminator (Humbug, Quest Scientific), a 0.7- to 3-kHz band-pass filter (spike conditioner PC1, Tucker Davis Technologies, System II) and a spike discriminator (SD1, Tucker Davis Technologies, System II). Only action potentials from single neurons with a signal to noise ratio of >5 were recorded. Subsequently, action potentials were registered using an event timer (ET1, Tucker Davis Technologies; temporal accuracy, 2.5 μs) and a DSP-Board (Tucker Davis Technologies, System II) before storage for off-line analysis.

**Acoustic stimuli**

Acoustic stimuli were delivered using a Tucker Davis Technologies System II, comprising 16-bit D/A converters (DA3-2; sampling rate...
250 Hz), anti-aliasing filters (FT-6; cutoff 100 kHz), and two digital attenuators per channel (PA4). Stimuli were presented via an electrostatic speaker driver (ED1, Tucker Davis Technologies, System III) and two electrostatic speakers (Tucker Davis Technologies, System III) or a headphone buffer HB6 (Tucker Davis Technologies, System II) and two Beyer Dynamics speakers (model DT 990). Both systems were fitted to the ear via 3-mm-diam probe tubes. Both sets of earphones including the tubes were calibrated using a 1/4-in microphone (Reintorpi VS), a measuring amplifier (MV 302, Microtech, Gefell, Germany) and a waveform analyzer (Stanford Research Systems, SR770 FFT network analyzer).

Recording procedure

To search for acoustic responses, pure tones, sinusoidally amplitude modulated tones (SAM; modulation frequency, 10–1,000 Hz; modulation depth, 100%), upward frequency modulated sounds (500 Hz to 50 kHz), or white noise stimuli were delivered binaurally. The stimulus duration was 100 ms, the rise–fall time was 5 ms to cover 5–10 times the tone period of the lowest stimulus frequency used (unless otherwise stated). Except while searching for neurons and generating tuning curves, the stimulus amplitude was 20 dB above threshold at a neuron’s best frequency (BF). To determine the threshold at the BF of an isolated single neuron, a frequency-tuning curve was measured using 40-ms pure tones. Then binaural properties were examined by presenting pure tones, SAM, or noise stimuli at various ITDs or IIDs. Sensitivity to IIDs was measured with the stimulus intensity kept constant at one ear and systematically varied at the other ear (over a range of ≥40 dB). Sensitivity to static ITDs was tested with pure tones (low-frequency neurons; BF <2 kHz), trains of tone pulses (5 pulses, 5-ms pulse duration; rise–fall time, 0.5 ms; variable inter-stimulus interval of 1–20 ms), or SAM stimuli. All stimuli were presented at each neuron’s BF. The stimulus delay was constant at one ear and varied at the other ear in 50–200-μs steps covering a range of up to ±6 ms (or 1 full cycle of a SAM stimulus).

The temporal pattern coding of SPN neurons was tested using SAM stimuli at different modulation frequencies. The carrier frequency was set to each neuron’s BF. The modulation frequency of the SAM stimuli covered a range from 20 to 1,000 Hz in 11 logarithmic steps. The modulation depth was 100%. At least 10 repetitions per stimulus were presented in a random order with an inter-stimulus interval of ≥250 ms to avoid adaptation effects.

Pharmacology

“Piggy back” multibarrel electrodes (Harvey and Caspary 1980) were used for iontophoretic application of glycine and the glycine receptor antagonist strychnine. The tip of a five-barrel glass electrode was cut to a total diameter of ~20 μm. The recording electrode was glued to the multibarrel so that the tip of the recording electrode protruded ~5–15 μm beyond the tip of the multibarrel. Typically, three barrels were filled either with glycine (0.5 M, pH 4) or strychnine (10 mM, pH 3.5). One barrel was filled with HRP to mark recording sites. The remaining barrel was filled with sodium acetate (2 M) to serve as a balancing channel. The drug and the balancing electrodes were connected via silver chloride wires to a micro-iontophoresis system (npi electronics, Neurophore MVCS) that was used to generate and monitor ejection currents (glycine 10–40 nA; strychnine ≥240 nA) and retention currents (~24 nA). The sum channel that was connected to the balancing electrode was used to offset current effects.

Data analysis

Data were analyzed off-line using individual spike times, peri-stimulus-time histograms (binwidth, 1 ms), and inter spike intervals (binwidth, 0.5 ms). As a measure for sharpness of frequency tuning Q10db values were calculated using the formula Q10db = BF/tuning-width 10 dB above threshold. To quantify neuronal discharges evoked by SAM stimuli and to assess the degree to which these responses correlated with the phase of the modulation frequency, modulation transfer functions (MTFs) based on spike rate and vector strength (VS) were plotted. For calculating MTFs, the response to the first cycle was excluded from the analysis. If the first cycle was <10 ms, the first 10 ms of the response were excluded. The VS was calculated as described by Goldberg and Brown (1969). Only statistically significant VS values that fulfilled the P < 0.05 criterion in the Rayleigh test (Batschelet 1991) were used. To set the criterion for cutoffs, a 50% drop in spike rate based MTFs was used. Accordingly, for VS based MTFs the modulation rate at which the VS dropped <0.3 or became insignificant was regarded as a cutoff. Values were chosen for comparison with previous studies about SAM filtering (e.g., Grothe et al. 2001). Following this procedure, neurons could be classified as all-pass, low-pass, high-pass, or band-pass.

Immunohistochemistry

For glycine-receptor immunohistochemistry animals were perfused (5 min) through the heart with artificial cerebrospinal fluid containing (in mM): 125.0 NaCl, 4.0 KCl, 1.2 KH2PO4, 1.3 MgSO4, 26.0 NaHCO3, 15.0 glucose, and 2.4 CaCl2. Brains were removed immediately, frozen in liquid nitrogen, and stored at −80°C. Brains were sectioned at 25 μm on a cryostat, thaw mounted on slides, and fixed in 4% paraformaldehyde (5 min). Sections were incubated for 1 h in 0.5% Triton X-100 with 10% normal goat serum (NGS; Sigma) in 0.1 M phosphate-buffered saline (PBS). Sections were incubated overnight with a rabbit polyclonal antibody against the glycine-receptor α1 subunit (Chemicon International) diluted 1:100 in PBS and containing 10% NGS and 0.5% Triton X-100 at 4°C. Immunoreactive sites were visualized using secondary antibodies coupled to Cy3 (dilution 1:300; Dianova). Immunofluorescence was imaged using a Leica confocal microscope (≈25 optical sections with a 1-μm increment were obtained per specimen). Digital image stacks were contrast adjusted and merged using Adobe Photoshop 5.0. For gephrin immunohistochemistry, animals were perfused through the heart with Ringer solution containing 0.02% Heparin (5 min) followed by a fixative containing 4% paraformaldehyde, 0.2% glutaraldehyde, and 0.2% picric acid in 0.1 M PBS (30 min). Brains were postfixed for 3 h in the same fixative at 4°C. Brains were sectioned at 30-μm increments on a vibratome. The sections were then incubated in 0.05% Triton X-100 and 10% NGS in 0.1 M PBS for 2 h. Sections were incubated overnight with a mouse monoclonal antibody against gephrin (mAb7a, Alexis Biochemicals) diluted 1:100 in PBS and containing 10% NGS and 0.05% Triton X-100 at 4°C. Immunoreactive sites were visualized using secondary antibodies coupled to biotin (dilution 1:200; Dianova) and the avidin-biotin-diaminobenzidine (DAB) method (Vector). DAB-stained sections were analyzed and photographed on a Reichart and Jung Polyvar light microscope. Photographs were digitized with a slide scanner (Polaroid). Digitized images were contrast adjusted and inverted to better visualize gephrin-positive sites (Adobe Photoshop 5.0).

All experiments were approved according to the German Tier schutzgesetz.

RESULTS

Responses were recorded from 62 SPN neurons of which 22 were directly verified as SPN cells via marker injections at the recording site. The locations of the other 40 neurons were stereotactically reconstructed as within the SPN using marker injections at other recording positions in the same animal (taking into account a confirmed accuracy of ≥80 μm). The recording sites where distributed across the entire dorsoventral and mediolateral extent of the nucleus. Figure 1A depicts a recording site (marked with HRP) in the SPN as visible in a frontal section. The outline of the gerbil SPN is indicated in Fig. 1B.
Spontaneous activity

One-third (21/62) of the SPN neurons recorded from showed a very low rate of spontaneous activity (<1 spike/s). Another third (17/62) displayed a moderate amount of spontaneous activity (1–10 spikes/s), and the remaining third (24/62) a high degree of spontaneous activity (>10 spikes/s).

Tuning characteristics

Within our sample of SPN neurons, 82% (51/62) responded to pure tones. A minority of 18% (11/62) did not respond to pure tones and could only be driven by white noise (4/62) or brief frequency modulated pulses (7/62). BFs (stimulus frequency at which the lowest sound pressure elicited a response) of the 51 neurons responsive to pure tones ranged from 700 Hz to 37 kHz, covering most of the gerbil audiogram (Ryan 1976). However, the distribution of BFs showed a bias to frequencies <6 kHz (Fig. 2). Thresholds varied from 2 to 52 dB SPL. The typical tuning curve was V-shaped with a steeper slope at the high-frequency flank. Broad frequency tuning is indicated by low Q10dB values, ranging from 1.0 to 16.8 with an average of 3 (SD: 2.9). Q10dB values >5 were observed exclusively in neurons with BFs ≥4 kHz.

Rate-level functions of 49 neurons were tested over a range of ≤40 dB, using binaural stimulation (IID = 0), irrespective of the binaural properties of the cell. In 86% of the cells (42/49), raising sound pressure level caused monotonic increases in discharge rate. Only 14% (7/49) of the neurons exhibited nonmonotonic rate-level functions.

Response patterns

Of the cells that responded to pure tones, 59% (30/51) showed sustained discharge patterns when tested at their BF, 20 dB above threshold. Fifteen of these neurons showed smooth PST histograms without strong onset effects or pauses (Fig. 3A), whereas 9 displayed primary-like discharge patterns. These 24 cells exhibited no regularity in the interspike interval histogram (Fig. 3B). Of the remaining six sustained neurons, four exhibited some regularity in the interspike interval that was not correlated to the stimulus frequency (“chopping”; Fig. 3, C and D). One cell showed a pause after a strong onset but otherwise no regularity. Only one of the 30 sustained responders phase-locked to pure tones, although 6 of the sustained neurons had BFs <2 kHz. None of the five other neurons showed phase-locking at any frequency throughout the tuning curve.

Phasic discharge patterns in response to pure tones were found in 21 neurons (41% of the 51 neurons which responded to pure tones), 18 showing a discharge related to the stimulus onset (Fig. 4A), and 3 showing a discharge to the stimulus offset (Fig. 4B). Figure 5 displays the distribution of discharge patterns of the 51 SPN neurons responding to pure tones.
Response latencies

The following section demonstrates that ON neurons showed a higher temporal acuity in their response to pure tones when compared with sustained responders.

When measured at BF, 20 dB above threshold, the mean first spike latency of sustained responses to pure tones was 3.4 ± 1.7 (SD) ms (n = 30). However, a remarkable variation across the population of neurons with latencies ranging from 0.6 to 7.8 ms was observed. In 54% of these neurons, the first spike latency decreased as a function of intensity with an average ratio of 0.20 ms/dB. The remaining neurons showed no systematic change in latency for increasing stimulus intensities. The average jitter of the first spike latency of ON neurons was 588 ± 816 μs (n = 18), which was considerably lower than in neurons with sustained discharges. Accordingly, in 44% of the ON neurons (8/18) a jitter <100 μs was observed (Fig. 6).

The difference in the average latency between sustained and ON responders was found to be 5.1 ± 2.5 ms (n = 18) ranging from 0.9 to 11.2 ms. In 62% of these neurons, latency decreased as a function of intensity (trading ratio: 0.11 ms/dB). The remaining neurons showed no systematic change in latency intensities. The average jitter of the first spike latency of ON neurons was 588 ± 816 μs (n = 18), which was considerably lower than in neurons with sustained discharges. Accordingly, in 44% of the ON neurons (8/18) a jitter <100 μs was observed (Fig. 6).

The difference in the average latency between sustained and ON responders was highly significant (t-test; P = 0.008), and the difference in the jitter between cell subsets was weakly significant (t-test; P = 0.08).

Binaural response characteristics

Roughly half of the SPN neurons within our sample showed clear binaural interactions, although no significant sensitivity to IIDs and ITDs within the behaviorally relevant range of gerbils could be found.

The binaural characteristics of 48 neurons were assessed. Previous studies showed that binaural stimuli must be carefully chosen to prevent a misinterpretation of complex binaural characteristics (Grothe et al. 1997). Therefore neurons were examined with a variety of paradigms to characterize inputs from each ear as exciting or facilitating (E), inhibiting (I), or neither one (O). Note that the following classification relates to the overall effect from each ear, i.e., does not address unilateral combinations of excitatory and inhibitory inputs. Out of the 48 cells tested, 25% were driven by the contralateral ear without any effect of ipsilateral stimulation (O/E) and 31% were characterized E/O (Fig. 7). Hence, monaural neurons represented slightly more than half of the recorded SPN neurons. The remaining neurons (44%) exhibited binaural interactions, mostly as binaural excitation or facilitation (E/E; 35%; 17/48). Only four neurons were characterized as being excited by stimuli at one ear and inhibited by stimuli at the other ear, each type (E/I and I/E) was found in two neurons. However, the IID


![FIG. 5. Distribution of discharge types in response to pure tones.](image)

![FIG. 6. Comparison of the accuracy of the 1st spike of a tone-evoked response ("jitter") of neurons with phasic ON and sustained discharge patterns.](image)

![FIG. 7. Distribution of overall binaural properties (E, excitatory; I, inhibitory; O, no effect). The 1st letter indicates ipsilateral effects; the 2nd letter indicates contralateral effects.](image)
sensitivity of these cells was weak, and IID functions never dropped <50% of the maximal discharge rate.

All but one of the E/E cells had monotonic rate-level functions for binaural stimulation at an IID of zero. Changing IIDs had only moderate effects on these cells. Four E/E neurons showed a monotonic increase in spike rate when the stimulus intensity was kept constant at either the ipsilateral or the contralateral ear (20 dB above the threshold for binaural stimulation) and systematically increased at the opposite ear resulting in a manifold increase of spike rate at 0 IID compared with -20 IID (minimal effect of the attenuated ear, Fig. 8, top left). This behavior was in line with their monotonic rate-level functions (Fig. 8, top right) and indicates a strong facilitating effect of binaural stimulation. These cells showed no signs of inhibition. In 9 of the 17 E/E neurons, changing the stimulus intensity at one ear up to 30 dB above threshold (+10 dB IID) did not have any effect on the response to stimulus presentation at the opposite ear (Fig. 8; middle left). Four cells showed weak increases for more positive IIDs (Fig. 8; bottom left).

Of the 17 E/E cells recorded, 5 had BFs < 2 kHz, and they might be expected to show some ITD sensitivity to ongoing pure tones. Figure 9A shows the ITD functions of these five neurons. Two of them showed some ITD sensitivity in the physiologically relevant range for the gerbil (±120 μs; gray areas in Fig. 9). However, this 20% change in spike rate across the relevant ITD range is rather insignificant when compared with the E/E neurons in the gerbil MSO (Brand et al. 2002; Spitzer and Semple 1995). One of these two neurons showed increasing spike rates for ipsilateral stimuli leading contralateral stimulation, whereas the other neuron showed the opposite effect.

Neurons that did not phase-lock to SAM or pulses at an ITD of 0 ms never displayed phase-locked responses, regardless of the ITDs presented (not shown). Hence, phase-locking did not benefit from binaural time disparities. Accordingly, the only neuron in this sample that showed phase-locking to pure tones had a VS of -0.5 for all ITDs tested. ITD sensitivity to the stimulus envelope was tested in six neurons using SAM stimuli at different modulation frequencies. Figure 9B illustrates the SAM responses of these neurons at the highest modulation frequency that elicited a robust (>0.5 spikes/cycle) and significantly phase-locked response. No cyclic ITD sensitivity was apparent, and only minimal changes in the discharge rate were observed within the relevant range of ITDs. In five of those neurons, ITD sensitivity was tested over a larger time scale, such that all interaural phase disparities of a complete SAM cycle were covered. Again, no ITD sensitivity was detected (Fig. 9D; gray area indicates physiological range of ITDs). Three E/E neurons were additionally tested for ITD sensitivity to trains of short tone pulses with steep rise-fall times (0.5 ms), but again no significant ITD sensitivity was observed (Fig. 9C).

Responses to SAM tones

A considerable variability in MTFs was observed among neurons, and typically ON neurons showed sharper rate based filter functions and a higher degree of phase-locking. However, some sustained neurons were capable of phase-locking to SAM stimuli ≤1.000 Hz modulation frequency.

Of the 51 SPN neurons that responded to pure tones, 39 were tested with SAM stimuli (20- to 1,000-Hz modulation frequency). None of these neurons phase-locked to pure tones and two-thirds of them (26/39) had BFs >3 kHz. Within this sample, all 39 neurons responded to SAM stimulation. The majority (26/39) of the neurons showed an ongoing synchronized response to SAM stimuli with a VS of >0.3 (P < 0.05; Rayleigh test) to at least some modulation frequencies. All but one of the sustained responders tested (20/21), yet only 6 of 18 neurons with a phasic ON or OFF discharge belong to this group of neurons, which showed a significant ongoing response to SAM stimulation. The remaining 13 neurons responded to SAM like they responded to pure tones (10 ON, 2 OFF, and 1 “chopper” neuron), irrespective of the modulation frequency. Typical responses to SAM stimuli and the corresponding rate and VS-based modulation transfer functions (MTFs) are shown in Fig. 10 for an ON and a sustained responder.

To quantify the precision of phase-locking to SAM stimuli, the average VS for the 26 phase-locking neurons was calculated at a modulation frequency of 114 Hz (this modulation frequency was chosen for its proximity to 100 Hz for reasons of comparison; Grothe et al. 2001; recall that the step size used to measure MTFs was logarithmic). Of the 26 neurons, the averaged VS at 114 Hz was 0.58 ± 0.19. The average
maximal VS at the best modulation frequency for each neuron was 0.68 ± 0.15. Interestingly, this value varied for different subpopulations within the 26 neurons sampled: neurons that responded with an on discharge to pure tones had significantly higher VS values (0.78 ± 0.134) than sustained responders (VS 0.67 ± 0.14; \( P < 0.05; \) Mann-Whitney \( U \) test).

To assess the temporal filter characteristics of SPN neurons, we measured the 50% cutoffs of the rate-based MTFs and the modulation frequency at which VS dropped to 0.3 or became insignificant (see METHODS; Fig. 11, A and B). Flat rate-based MTFs that never fell <50% of the maximal response were seen in 16 of the 27 neurons with ongoing responses to SAM. We classified these neurons as all-pass. All of these were sustained responders when stimulated with pure tones. Of only four remaining sustained neurons, two showed low-pass, one high-pass and one band-pass characteristics in their rate MTF. Neurons with an on discharge to pure tones showed mainly band-pass filter characteristics (5/6), only one on neuron responded at high modulation frequencies only. Here again, the filter pattern seems to be related to the neural discharge type. The averaged upper 50% cutoff of the low-pass and band-pass neurons was 477 ± 266 Hz.

The VS-based MTFs of sustained responders to pure tones showed band-pass (4/20), low-pass (8/20), all-pass (5/20), and high-pass (3/20) filter characteristics for SAM stimuli. The MTFs based on VS for on responders showed mainly low-pass (4/6) and, in two cases, band-pass characteristics. Thus about one-third of the SPN neurons tested reflected the temporal stimulus pattern up to a modulation frequency of 1,000 Hz, with some degree of phase-locking. Table 1 summarizes filter characteristics in rate- and VS-based MTFs.

Table 2 depicts the relationship of the most obvious features described so far in relation to the basic response patterns. Most obvious is the temporal precision of on responders. Binaural properties seem not to relate to particular subgroups within our sample of SPN neurons.

**Pharmacology**

SPN neurons receive very strong glycinergic inputs. Figure 12 depicts a typical SPN neuron that has been stained with antibodies against gephyrin, a protein anchoring the glycine receptor in the postsynaptic membrane. Given the strength of the antibody staining, the influence of glycinergic inputs on the auditory response characteristics of SPN neurons was investigated. Glycine (or its receptor antagonist strychnine) was applied iontophoretically to single neurons during the recording of acoustic responses. The neural discharges before, during, and after application of glycine and/or strychnine in a total of 14 SPN cells were recorded. Both drugs significantly influenced discharge rates and, in some cases, the VS-based MTFs and the ITD sensitivity of SPN neurons. Interestingly, discharge patterns in response to pure tones remained unchanged by pharmacological ma-
nipulation. In all tested cells, glycine significantly inhibited stimulus evoked responses, in three of them no response at all could be elicited during and for a short period after the drug application (Fig. 13).

In seven neurons, effects of the glycine antagonist strychnine could be observed. In all cases, strychnine caused an increase in acoustically evoked responses (up to twofold relative to control). The effect of strychnine on the spontaneous discharge rate was found to be even stronger (average of 2.6 times control) and lasted several minutes after the application. In two cells (both sustained responders), the effect of strychnine on the discharge to SAM was tested. In both cases, phase-locking to low SAM frequencies was unchanged. However, the ability to phase-lock to modulation frequencies >400 Hz was significantly enhanced (Fig. 14), shifting the cutoff in the VS-based MTF to >1,000 Hz. Another effect of glycine inhibition on temporal processing is shown in Fig. 15. This E/E neuron was tested for sensitivity to ITDs in the envelope of SAM stimuli (tested at 75-, 125-, and 175-Hz modulation frequency; carrier frequency: 3.1 kHz). Note that the ITDs presented relate to the modulation frequency and are far beyond the physiological range. Under control conditions, the neuron showed no ITD-sensitivity in the spike rate (Fig. 15; top left). However, the VS showed a cyclic function indicating good phase-locking when the binaural inputs were roughly in phase and low phase-locking when they were out of phase (top right). Partial blocking of glycine inhibition via application of strychnine (middle) increased the spike rate but lowered the degree of phase-
locking. The basic ITD sensitivity remained unchanged. Application of glycine, however, strongly inhibited the response rate, and binaural excitation could only overcome the inhibitory effect when elicited in phase, hence, when excitatory inputs coincided (bottom left). Although the ITD sensitivity created by experimentally induced inhibition in this neuron was far from being relevant for sound localization, it indicates that inhibitory inputs might significantly alter and potentially sharpen the sensitivity of SPN neurons to temporal stimulus properties.

**DISCUSSION**

The SPN is a prominent SOC structure that rivals the size of the three so-called principal nuclei of the SOC, namely LSO, MSO, and MNTB. Our investigation addressed the potential relation of the gerbil SPN to either sound localization or temporal processing. The basic findings were that, first, almost half of the SPN neurons showed signs of binaural interactions, although ILD and ITD functions of binaural SPN neurons turned out to be shallow and ambiguous. Simple binaural processing as it occurs in MSO or LSO neurons can therefore be excluded as a function of SPN. However, binaural interactions might modulate SPN responses to complex sounds. Second, SPN neurons respond to pure tones with a variety of discharge patterns dominated by sustained and phasic on discharges. Overall, the temporal acuity of cells with on responses turned out to be superior compared with sustained responders, and they showed sharper filter characteristics for SAM stimuli. These cells might provide a precise inhibitory pulse to their target structures. Cells with sustained responses to pure tones showed weaker temporal acuity although some neurons showed some phase-locking to SAM stimuli presented with high modulation frequencies. These cells might provide a more diffuse inhibition to their targets, more likely to be of a modulatory nature than involved in precise temporal processing. Hence, SPN consist of at least two distinct groups of neurons, a finding that is in line with the different sources of excitatory inputs. Iontophoretic application of glycine or its antagonist strychnine indicated a major role of inhibitory inputs in creating responses of SPN neurons. This result is supported by the massive occurrence of gephyrin and glycine-receptors on SPN cell membranes which is in line with earlier findings of strong glycinergic and GABAergic inputs to guinea pig SPN neurons (Helfert et al. 1989).

**Temporal processing**

One hypothesis tested was that SPN neurons are involved in processing of temporal aspects of sound. This hypothesis was largely based on substantial inputs from ventral cochlear nucleus (VCN) octopus and multipolar/stellate cells as well as inhibitory projections from the MNTB.

Octopus cells for instance have a very low input resistance (Golding et al. 1999; Oertel et al. 2000) and very short time constants (Gardner et al. 1999), resulting in sharp onset responses with only one spike per stimulus (Golding et al. 1995). In the octopus cell region, onset neurons are able to accurately phase-lock to the cyclic envelope of SAM stimuli at rates of roughly \( \pm 800 \text{ Hz} \) (Rhode and Greenberg 1994; Rhode et al. 1983a,b). We found a significant proportion of SPN cells with an on response to resemble PVCN octopus cell inputs in respect to the low jitter, when the rather long stimulus rise-fall time (5 ms) is taken into account. Additionally, the ability of these SPN cells to phase-lock to SAM stimuli is in line with octopus cell inputs (Rhode and Greenberg 1994).

PVCN inputs from multipolar/stellate cells would also be well suited for precise temporal processing (Ferragamo et al. 1998; Gardner et al. 1999). For PVCN multipolar cells, regular chopping responses to pure tones and SAM stimuli are reported in several mammals, including gerbils (Frisina et al. 1990a,b; Smith and Rhode 1989). However, we found only few neurons that we classified as chopper, and, compared with VCN neurons, they showed a rather weak regularity in their interspike interval.

An inhibitory input that indicates precise temporal processing in SPN neurons derives from glycinergic MNTB principal cells (Kuwabara et al. 1991; Sommer et al. 1993), matched by a strong presence of gephyrine and glycine-receptors on the cell membranes of gerbil SPN cells. MNTB cells receive their input from VCN bushy cells that accurately follow the tempo-

<table>
<thead>
<tr>
<th>Filter Properties in Response to SAM</th>
<th>VS-MTF</th>
<th>Rate MTF</th>
<th>VS-MTF</th>
<th>Rate MTF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ON</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Band-pass</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Low-pass</td>
<td>4</td>
<td>—</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>High-pass</td>
<td>—</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>All-pass</td>
<td>—</td>
<td>—</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td>6</td>
<td>6</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

**TABLE 1.** Filter properties in response to SAM

<table>
<thead>
<tr>
<th>FILTER</th>
<th>VS-MTF</th>
<th>RATE MTF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Band-pass</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Low-pass</td>
<td>4</td>
<td>—</td>
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<tr>
<td>High-pass</td>
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<tr>
<td>All-pass</td>
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<td><strong>S</strong></td>
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<td>6</td>
</tr>
</tbody>
</table>

SAM, sinusoidally amplitude modulated; VS, vector strength; MTF, modulation transfer function.
nervous system of sounds (Joris et al. 1994) and convey this information via the calyx of Held onto MNTB cells (Brew and Forsythe 1995, Taschenberger and von Gersdorff 2000). As a consequence, MNTB cells also reliably convey temporal structures (Gardner et al. 1999; Smith et al. 1998). Indeed, glycinergic inhibition deriving from MNTB has been shown to participate in precise temporal filtering in bat MSO neurons. Combined with well timed excitatory inputs it creates precise ON, OFF responses and participates in building precise filter properties for the temporal structure of sounds, including SAM (Grothe 1994; Grothe et al. 1997, 2001). Similarly, OFF responders in the medial region of the rabbit SOC show very precise filter properties for SAM stimuli (Kuwada and Batra 1999). Moreover, in the rabbit and the bat SOC, these neurons show the highest vector strength in response to SAM stimuli (Kuwada and Batra 1999; Grothe et al. 2001). However, within our sample, only three SPN neurons showed OFF discharges, and these neurons did not phase-lock to SAM stimuli at all. Interestingly, this is in sharp contrast to a remarkably uniform population of neurons recently described in the rat SPN. There, almost all neurons exhibited monaurally evoked OFF responses with sharp low-pass filtering (Kulesza et al. 2002). Moreover, in the gerbil SPN the blockade of glycinergic inhibition did not change the response properties to pure tones as described for bat MSO cells (Grothe et al. 1994). Nevertheless, glycinergic inhibition seems to play a role in temporal processing. On the one hand, we observed increased selectivity of coincident inputs when glycine was present, on the other hand blocking glycinergic inhibition allowed some cells to respond to much higher modulation frequencies with a phase-locked response. Differences between this and other studies concerning, e.g., the homogeneity of cell types or the abundant existence of OFF cells in the rat SPN, might be due to different recording electrodes or anesthesia. We cannot exclude the possibility that we missed a specific population of cells with higher temporal precision. However, using identical recording procedures and

### TABLE 2. Relationship between basic response properties and most obvious features of SPN neurons

<table>
<thead>
<tr>
<th>Neuron Type</th>
<th>n</th>
<th>Latency &lt;3 ms, %</th>
<th>RLF Monotone, %</th>
<th>Binaural, %</th>
<th>SAM VS &gt; 0.7, %</th>
<th>SAM Filtering, %</th>
<th>Tuning Q(SAM) &lt; 5, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jitter &gt; 100 μs</td>
<td>26</td>
<td>60</td>
<td>96.2</td>
<td>41</td>
<td>50</td>
<td>65</td>
<td>81.5</td>
</tr>
<tr>
<td>Jitter &lt; 100 μs</td>
<td>4</td>
<td>50</td>
<td>100</td>
<td>67</td>
<td>66</td>
<td>15</td>
<td>0</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jitter &gt; 100 μs</td>
<td>10</td>
<td>20</td>
<td>100</td>
<td>40</td>
<td>No ongoing response</td>
<td>20</td>
<td>75</td>
</tr>
<tr>
<td>Jitter &lt; 100 μs</td>
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<td>37.5</td>
<td>87.5</td>
<td>37.5</td>
<td>100</td>
<td>26.6</td>
<td>60</td>
</tr>
<tr>
<td>OFF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>67</td>
<td>67</td>
<td>No ongoing response</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chopper</td>
<td>4</td>
<td>0</td>
<td>75</td>
<td>50</td>
<td>67</td>
<td>25</td>
<td>50</td>
</tr>
</tbody>
</table>

Relationship of the basic response properties found in the superior paraolivary nucleus (SPN). Discharge pattern in response to pure tones is used as the main criterion. Values give the percentage of all cells included in one row (for instance all sustained responders with jitter >100 μs). SAM VS > 0.7 indicates how many neurons showed a vector strength >0.7 for at least one modulation rate tested. SAM filtering: this column displays neurons that showed any kind of filtering (lowpass, highpass or bandpass) in either VS-MTFs or rate-MTFs. RLF, rate level function.

**FIG. 12.** Glycinergic inputs to SPN. Massive staining for glycine-receptors (A) as well as for the glycine-receptor clustering protein gephyrin (B) indicates extensive glycinergic inhibitory inputs to cell bodies (open arrows) and dendrites (filled arrows) of SPN neurons. Scale bar: 20 μm

**FIG. 13.** Application of glycine suppresses responses of SPN neurons to tones. Top: PSTH from a neuron with a sustained response to binaural stimulation. Middle: the response could be blocked completely with glycine (after 10 s of iontophoretic application with 40 nA) and recovered fully after the application was stopped (bottom). The binwidth of the PSTHs is 1 ms. Responses to 10 stimulus presentations are shown.
often within the same electrode penetrations, we recorded from neurons in neighboring structures (e.g., MSO) displaying an extreme temporal resolution in the microsecond range (Brand et al. 2001) and phase-locking off neurons outside the SPN. Also, the uniformity in the rat described by Kulesza and colleagues (Kulesza et al. 2002) somewhat contradicts the anatomical diversity of SPN neurons and the fact that different CN cell populations project to SPN neurons (Schofield 1991, 1995; Schofield and Cant 1992, 1999). For instance, pure onset cells in the rat CN were described to project to the SPN (Friauf and Ostwald 1988). Moreover, Finlayson and Adam (1997) have demonstrated a variety of responses in the rat SPN, most commonly sustained (primary-like) and on type, i.e., a pattern of cell types much like the gerbil SPN. Again, the fact that no on/off discharges at all were observed in Finlayson’s study on rats gives rise to speculation as to what extent the selection of recording electrodes biases the neuron types recorded. Still, species-specific variation in the physiology of the SPN could be expected between the rat and the gerbil (Saldana and Berrebi 2000). For instance, the presence of cholinergic cells indicates that the gerbil SPN is part of the olivocochlear system. However, in rats, no such cells are described (Aschoff and Ostwald 1988; Osen et al. 1984; Vetter and Mugnaini 1992; Vetter et al. 1991, 1993; White and Warr 1983). A high potential for species-specific evolution of the SPN is emphasized by findings in another mammal such as the mustached bat, Pteronotus parnellii. Here, the SPN was even found to be merged with the MSO (Grothe et al. 1992; Vater 1995).

Therefore species-specific differences in the general function of the SPN and in the combination of subsets of response properties might well reflect evolutionary adaptations. This might not come as a surprise because the medial region of the SOC has been shown to be, together with the ventral region of the lateral lemniscus, the region of the ascending auditory system that displays the highest variability among mammals (Covey and Casseday 1995; Grothe 2000). We need to learn more about the specific needs of the gerbil in terms of its hearing capabilities. So far one can only speculate whether, e.g., the adaptation to hear low frequencies as it occurred in several desert rodents (Rosowski et al. 1999), elicited a different function of SPN in gerbils compared with the SPN of rats.

**Binaural processing**

We found ~40% of SPN cells to be influenced by binaural inputs, most of them by binaural excitation. Traditionally, E/E neurons are associated with ITD detection as demonstrated for MSO neurons (Goldberg and Brown 1969; Spitzer and Semple 1993; Yin and Chan 1990). Because Finlayson and Adam (1997) predominantly observed E/E neurons in the rat SPN, we felt encouraged to speculate on binaural processing and, in particular, sound localization in the SPN of the gerbil. One might think that IID coding in the LSO and ITD coding in the MSO should be sufficient and additional binaural processing not necessary. However, it has been shown that, although starting in the LSO, IID sensitivity of many IC neurons is modified by inputs from the dorsal nucleus of the lateral lemniscus (Li and Kelly 1992) and a de novo IID sensitivity is created in other IC neurons (Park and Pollak 1994). Similarly, ITD functions of many IC neurons do not simply reflect single MSO inputs (McAlpine et al. 1998), ITD tuning gets sharper in the ascending auditory system (Fitzpatrick et al. 1997), and there is sensitivity to dynamic stimuli not seen in the MSO (Spitzer and Semple 1993). Hence, it seems feasible to assume that binaural cells other than those of MSO and LSO might considerably contribute to binaural characteristics of IC neurons.

The gerbil has evolved good low-frequency hearing to match the requirements of the desert biotope and therefore has to use ITDs of low-frequency sounds. The biased distribution of BFs...
in the gerbil SPN indeed emphasizes the role of low-frequency hearing in this animal. Spitzer and Semple (1995) recorded four ITD-sensitive low-frequency neurons anatomically confirmed to be in the SPN of the gerbil, and Batra and colleagues (1997a,b) described ITD-sensitive cells in the medial portion of the SOC that might well include SPN. Yet, our sample of 16 low-frequency neurons included only one unit that exhibited phase-locking to pure tones, and none of the binaural cells exhibited a significant ITD sensitivity. Addressing the differences in our recordings, it is noteworthy that first, the entire partition of ITD-sensitive SPN neurons in the sample of Spitzer and Semple is recorded at the lateral margin of the SPN, in close vicinity to LSO or MSO. Second, different electrode types were in use in the two studies (discussed earlier).

**Tonotopy and cell subsets**

The SPN shares the tonotopic order of its principal input regions (Friauf 1992; Saldana and Berrebi 2000; Thompson and Thompson 1991), which is anatomically reflected by the flattened dendritic trees of SPN neurons, aligned to the rostro-caudal axis of the nucleus.

The monotonic rate-level functions and V-shaped tuning curves we found to be typical for SPN neurons largely resemble characteristics of their CN inputs. The distribution of best frequencies of SPN neurons in the gerbil is clearly biased to frequencies $<6$ kHz. Because our reconstruction of recording sites does not indicate any bias to a specific region within the SPN, this bias seems to be real and spectral integration might therefore be ruled out as a major function of the gerbil SPN.

One might consider neurons with ON and sustained discharges as two different populations, and the physiological results presented here support such an assumption. Subpopulations of SPN cells have been demonstrated to differ in morphology, projections, or input sources (Schofield 1991, 1995; Schofield and Cant 1992, 1995). In particular, olivocochlear projections originate within a subset of cells that was considered to form a distinct population among the SPN neurons. Typical SPN responses (ON) displayed short adaptation time constants and a nonsignificant overall trend to long time constants was apparent in the recovery from adaptation (Finlayson and Adam 1997). This characteristic might match the olivocochlear projections of the SPN and might give rise to a quick feedback adjustment of auditory processing at lower levels when new stimulus configurations are detected.

**Conclusion**

In accordance with the connection patterns as well as the existence of different cell types in the SPN (compare Thompson and Schofield 2000), the physiology of SPN neurons does not indicate a homogeneous population of cells. Some cells with shallow MTFs and/or ambiguous binaural response characteristics are likely to play a role in modulation of the ascending and descending auditory pathway rather than providing a specific filter for temporal or spatial stimulus characteristics. Other cells showing long-jitter ON responses might provide a fast, synchronized inhibitory input to both midbrain hemispheres that correlates with the onset of stimuli or transient changes in ongoing stimuli.


