Interdependence of Spatial and Temporal Coding in the Auditory Midbrain

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Koch, U. and B. Grothe. Interdependence of spatial and temporal coding in the auditory midbrain, J. Neurophysiol. 83: 2300–2314, 2000. To date, most physiological studies that investigated binaural auditory processing have addressed the topic rather exclusively in the context of sound localization. However, there is strong psychophysical evidence that binaural processing serves more than only sound localization. This raises the question of how binaural processing of spatial cues interacts with cues important for feature detection. The temporal structure of a sound is one such feature important for sound recognition. As a first approach, we investigated the influence of binaural cues on temporal processing in the mammalian auditory system. Here, we present evidence that binaural cues, namely interaural intensity differences (IIDs), have profound effects on filter properties for stimulus periodicity of auditory midbrain neurons in the echolocating big brown bat, Eptesicus fuscus. Our data indicate that these effects are partially due to changes in strength and timing of binaural inhibitory inputs. We measured filter characteristics for the periodicity (modulation frequency) of sinusoidally frequency modulated sounds (SFM) under different binaural conditions. As criteria, we used 50% filter cutoff frequencies of modulation transfer functions based on discharge rate as well as synchronicity of discharge to the sound envelope. The binaural conditions were contralateral stimulation only, equal stimulation at both ears (IID = 0 dB), and more intense at the ipsilateral ear (IID = −20, −30 dB). In 32% of neurons, the range of modulation frequencies the neurons responded to changed considerably comparing monaural and binaural (IID = 0) stimulation. Moreover, in ∼50% of neurons the range of modulation frequencies was narrower when the ipsilateral ear was favored (IID = −20) compared with equal stimulation at both ears (IID = 0). In ∼10% of the neurons synchronization differed when comparing different binaural cues. Blockade of the GABAergic or glycinergic inputs to the cells recorded from revealed that inhibitory inputs were at least partially responsible for the observed changes in SFM filtering. In 25% of the neurons, drug application abolished those changes. Experiments using electronically introduced interaural time differences showed that the strength of ipsilaterally evoked inhibition increased with increasing modulation frequencies in one third of the cells tested. Thus glycinergic and GABAergic inhibition is at least one source responsible for the observed interdependence of temporal structure of a sound and spatial cues.

INTRODUCTION

In most physiological studies, the neuronal encoding of the temporal pattern of sounds has been investigated independent of the spatial properties of the sound. In contrast binaural processing has been discussed rather exclusively in the context of sound localization. Most of the studies were performed under the assumption that different sound features are processed by different sets of neurons. Yet many psychophysical experiments do not support a narrow concept of parallel processing but provide evidence that the temporal sound pattern is not analyzed independent of binaural cues. Temporal analysis and binaural processing rather contribute to each other (Bernstein and Trahiotis 1985; Cherry 1953; Kidd et al. 1995; Kollmeier and Koch 1994). However, little is known about the underlying physiological mechanisms.

The processing of the temporal structure of sounds, which is an important cue for auditory feature detection including speech, has been studied extensively. In the ascending auditory system, neurons progressively increase their selectivity for the periodicity of temporal structured sounds, that is, they respond best to lower modulation frequencies and tuning gets narrower (for review, see: Langner 1992; Schulze and Langner 1997). This increase in selectivity might be due to active neuronal filter mechanisms. However, this response behavior has only been tested independent of the spatial properties of the sound. Recent studies indicate that neuronal processing of sound location and sound pattern are mutually dependent, suggesting an interdependence of filter mechanisms for periodic stimuli and binaural processing. First, spatial receptive fields of neurons in the inferior colliculus (IC) of the big brown bat (Eptesicus fuscus) depend on the stimulus type presented (Grothe et al. 1996). Second, filter properties for sinusoidally amplitude modulated (SAM) sounds of auditory midbrain neurons in the northern leopard frog (Rana p. pipiens) are affected by the azimuthal position of an open-field sound source or by interaural time differences in a closed-field experiment (van Stokkum and Melssen 1991; Xu et al. 1996). Third, the azimuthal position of a sound source influences filter characteristics for sinusoidally frequency modulated (SFM) sounds of many neurons in the IC of the big brown bat (Koch and Grothe 1997). Fourth, neurons in the medial superior olive (MSO) of the free-tailed bat (Tadarida brasiliensis) change their tuning for the periodicity of SAM sounds depending on interaural intensity differences (IIDs) (Grothe et al. 1997b).

There is strong evidence that GABAergic and glycinergic inhibition narrows tuning for SAM or SFM sounds of neurons in the MSO, the dorsal nucleus of the lateral lemniscus (DNLL), and the IC (Grothe 1994; Koch and Grothe 1998; Yang and Pollak 1997). On the other hand, inhibition has been shown to be essential for processing IIDs at different levels of the auditory system including the IC (Boudreau and Tsuchitani 1968; Klug et al. 1995; Moore and Caspary 1983; Park and Pollak 1993, 1994). The IC, the focus of this study, receives inhibitory and excitatory projections from a large number of
monaural and binaural nuclei (for review, see Oliver and Huerta 1992). This set of binaural projections provides an opportunity to selectively change the interaural intensity or time difference using dichotic stimulation. This way, it is possible to test whether filters for the periodicity of sounds are dependent on the relative weight or timing of ipsi- and contralateral excitation and inhibition.

Here, we present data from single neuron recordings in the IC of the big brown bat, E. fuscus, an insectivorous bat that uses frequency modulated echolocation calls. Previous studies revealed sharp tuning to SFM sounds in IC neurons under monaural conditions (Casseday et al. 1997). Moreover, GABAergic and glycineergic inhibition increases selectivity for the modulation frequency of SFM sounds and changes the response pattern under monaural stimulus conditions (for more details, see Koch and Grothe 1998). Additionally, we previously have shown a major impact of the spatial position on these tuning characteristics under open-field conditions (Koch and Grothe 1997). In this study, we tested the tuning to the modulation frequency of SFM stimuli under various binaural conditions (closed-field) and performed the same tests during iontophoretic application of GABA and glycine receptor antagonists. In this way, we were able to address the following questions: is there a significant dependency of periodicity coding on binaural cues when pinna effects are excluded by using closed field stimulation? How does GABAergic and glycineergic inhibition contribute to the dependency of periodicity coding on binaural cues at the level of the IC? And if so how does the relative timing of ipsi- and contralateral excitation and inhibition influence temporal filter properties of IC neurons?

METHODS

Surgical procedure

Eight big brown bats (E. fuscus) were used in this study. Before surgery animals were injected subcutaneously with the neuroleptic thalamonal (Janssen; per 100 g body wt; 1 ml of 0.05 mg fentanyl and 2.5 mg droperidol) and additionally anesthetized with metofane (Janssen) by inhalation until no nociceptive response could be evoked. During surgery, the animal’s head was secured in a head holder with a bite bar. The local anesthetic bupivacain (Curasan) was injected under the skin covering the skull. An incision was made across the midsagittal line of the skull and muscles and skin were reflected. The surface of the skull was cleared of tissue. A layer of cyanoacrylate adhesive was applied to the surface of the skull, and a rod was cemented onto the skull overlying the cortex using dental cement. Before the first recording session, a small hole was drilled in the skull above the IC. The location of the IC was identified visually using landmarks on the skull. Open wounds were treated with 1% H2O2.

Recording sessions started 2 days after surgery and were performed every day for 8–14 days, each session lasting 3–6 h. Between recording sessions, bats were housed in individual cages with free access to water and food. Before each recording session, bats were injected subcutaneously with 0.15–0.2 ml of the neuroleptic thalamonal. Bats then were transferred to a heated, sound-proof recording chamber where they were restrained in a cushioned holder molded to their body. The restraining cushion was attached to a custom-made stereotaxic instrument. The rod mounted on the animal’s skull was secured to the stereotaxic instrument. The ground electrode was placed between the reflected muscle and the skull. The recording electrode was advanced from outside of the experimental chamber using a remote controlled hydraulic microdrive (Wells). To ensure positioning of the electrode within the central nucleus of the IC, neurons were only recorded at depths between 150 and 1,800 μm. The tonotopic organization of the central nucleus of the IC served as an additional indicator for the position of the electrode. Recording sessions lasted until the bat showed any sign of discomfort. Animals were anesthetized with pentobarbital and perfused after the last recording session, and the brain was removed for sectioning. The lesion generated by the multibarrel electrode was used to verify that the position of the electrode was within the central nucleus of the IC.

Electrodes

“Piggy back” multibarrel electrodes (HAVEY and Caspary 1980) were used for recording and drug application. A single-barrel micropipette was pulled to a tip diameter of <1 μm. A five-barrel micropipette (H-configuration, Science products) was pulled and the tip broken to a total diameter of 15–20 μm. The single-barrel pipette was positioned so that the tip of the recording electrode protruded ~10 μm beyond the tip of the multibarrel electrode and attached with cyanoacrylate to the multibarrel electrode. The single-barrel electrode was filled with 2 M NaCl and used for recording the extracellular neural response. Action potentials were measured by an electrometer (Model Electro 705; World Precision Instruments), amplified and band-pass filtered (Tektronix, 5112), discriminated by a custom-made window discriminator, and fed into a DSP-board (Tucker-Davis-Technology). Spike time resolution was 2.6 μs.

One barrel of the multibarrel electrode was filled with 2 M Na-acetate and used for balancing currents. The other four barrels were filled with bicuculline methiodide (5 mM, pH: 3), strychnine (10 mM, pH: 3.5), GABA (0.5 M, pH: 3.5), glycine (0.5 M, pH: 3.5), or glutamate (1 M, pH: 8) (all drugs: Sigma). Adjustment of pH was achieved by titrating with 1 M HCl or 1 M NaOH.

The drug electrodes and the balancing electrode were connected via silver chloride wires to a microiontophoresis system (Medical Systems, Neurophore BH-2), which was used to generate and monitor ejection (10–40 nA; for glutamate: ~5 to ~20 nA) and retention currents (~15 nA; for glutamate: ~15 nA). The sum channel that was connected to the balancing electrode was used to eliminate current effects.

Acoustic stimuli and data acquisition

Acoustic stimuli were digitally generated by using two DSP boards, 16-bit D/A converters (sampling rate, 377 kHz) and attenuators from Tucker-Davis Technologies. Sounds were amplified (Toellner) and fed into custom-made earphones (Schlegel 1977) that were placed into the funnels of the bat’s ears.

The search stimulus was a 100-ms SFM sound with 0.5-ms rise/fall time presented every 600 ms. Center frequency, modulation depth, and modulation frequency were frequently varied while searching. On encountering activity of a single neuron, the optimal center frequency (19.1–69.1 kHz), modulation depth (between ±2 and ±25 Hz) and threshold of the SFM stimulus to drive the neuron were determined audiovisually. For all subsequent recordings stimuli 20 dB above threshold at the contralateral ear were used. SFM signals first were presented monaurally to the contralateral ear at best modulation depth using a range of modulation frequencies (10–600 Hz). The same range of stimuli then was presented binaurally by changing the ipsilateral sound level to create interaural intensity differences (IIDs) of 0 and ~20 dB (ipsilateral ear louder). To demonstrate the existence of GABA(A) or glycine receptors, GABA or glycine was applied until the response to a stimulus was inhibited completely. To test the effects of GABAergic and glycineergic inhibition on SFM coding, the receptor antagonists bicuculline or strychnine were applied. After initializing drug application the neuron’s response to a test tone modulated with 50 or 100 Hz was monitored continuously. Drug application usually caused an immediate increase in discharge rate. Recordings did not
start before discharge rate to the test stimulus had stabilized. The same tests then were presented as under predrug conditions. After each drug application, the retention current was turned on, and the neuron was allowed to recover until its discharge rate to the test stimulus dropped to levels of predrug conditions. Recovery usually took 5–15 min. At least 10 repetitions of each stimulus were presented for recordings. Ten stimulus repetitions are on the lower side for quantifying responses. However, the length of the pharmacological experiments (including recovery times) and the state of the animal, which was only slightly sedated, required to shorten the experimental protocol. To determine the time course of ipsilaterally evoked inhibition, two different experiments were designed. In one set of experiments, glutamate was applied iontophoretically to the neuron to create a stimulus independent discharge activity. The stimulus then was presented to the ipsilateral, mostly inhibitory ear with a range of modulation frequencies and sound intensities. This sound presentation usually resulted in a gap in the glutamate-evoked activity, which was created by the inhibitory action of the ipsilateral stimulus.

In another set of experiments, a sound modulated with various modulation frequencies (25–200 Hz) was presented to the contralateral excitatory ear. For monaural stimulation, this stimulus evoked a phase-locked response in the neuron. When the stimulus was presented binaurally with a slightly different modulation frequency at the two ears (difference = 5 Hz = beat frequency), an ongoing interaural time difference (ITD) of the FM phase was created, a so-called “binaural beat.” The time course of ipsilateral inhibition could be observed by determining the ITDs where the contralaterally evoked discharge had been suppressed. The duration of the binaural beat stimuli was 1 s. To determine whether the time course of inhibition was also dependent on the sound level, various IIDs (IID = 0 to IID = −30) were tested.

**Data analysis**

The definition of a neuron’s filter characteristics was based on the total number of spikes (0–120 ms after stimulus onset) evoked by each stimulus for each binaural condition. Discharge rate was normalized to its maximum for each binaural condition. By plotting normalized spike count versus modulation frequency we determined the modulation transfer function (MTF) based on spike count. The upper and lower cutoff frequencies were defined as the modulation frequencies where the MTF dropped to 50% of its maximum. Differences in SFM tuning for different stimulus conditions were calculated according to the following equation: change(bin − mon) = [cutoff(bin) − cutoff(mon)]/[cutoff(mon)/100]%. To illustrate changes in the response pattern, we generated cycle histograms that showed the number of spikes as a function of modulation phase.

Additionally, we calculated the synchronization coefficient (SC) (Goldberg and Brown 1969) for each neuron’s response to different SFM stimuli. The SC is a measure of how precisely the neuronal discharge is locked to a certain phase of each modulation cycle. It ranges from 0 (no phase-locking) to 1 (perfect phase-locking). For neurons that responded twice to each modulation cycle of the SFM stimulus, the SC was computed separately for the response to the upward and downward part of each modulation cycle. In most neurons, this response pattern was dependent on the modulation frequency (Fig. 1). Second, over the population of neurons tested, phase-locking of the response varied profoundly. For example, at a modulation frequency of 50 Hz, the SC of the neurons varied between 0.14 (almost no synchronization) and 0.99 (nearly perfect synchronization). About 80% of the neurons exhibited significant phase-locking (P ≤ 0.01).

For monaural stimulation most neurons (86%) showed SC-based low-pass filter characteristics or still exhibited significant phase-locking when the spike number dropped below a level that allowed a statistical significant calculation of the SC (all-pass filter characteristics). If a neuron’s response was bidirectional, we calculated the SC separately for the response to the upward and downward component of each modulation cycle and took the SC of the larger response for comparison. The response behavior of IC neurons to monaural stimulation with SFM sounds and the influence of GABAergic and glycine receptors are described in more detail in Koch and Grothe (1998).

**SFM tuning of neurons depends on the binaural stimulus conditions**

In this study, we first compared the response to SFM stimuli for different binaural conditions. The results show that presenting a SFM stimulus binaurally (IID = 0) compared with monaurally changed SFM tuning in many IC neurons. Figure 1 shows an example of a neuron that was tested for its SFM tuning properties under both conditions [monaural and binaural (IID = 0)]. In this case, the neuron’s response was equally

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**RESULTS**

Only IC neurons that under optimal stimulus conditions responded throughout the entire stimulus duration of SFM sounds were included in this study (n = 85). Each neuron’s response behavior to SFM sounds was analyzed in the following way. First, the MTF based on discharge rate was calculated and the modulation frequency determined where the response had dropped to 50% of the maximal response (upper and lower cutoff frequency). Second, for a subset of neurons, the SC was calculated to determine the precision of phase-locking of the response to each stimulus cycle (see METHODS).

These results were compared between monaural stimulation and two different binaural stimulations with an IID = 0 dB and an IID = −20 dB favoring the ipsilateral ear. To analyze the contribution of GABAergic and glycinergic inhibition on binaural response properties to SFM sounds, the same tests were performed while iontophoretically blocking the GABA_A or glycine receptors with bicuculline or strychnine, respectively.

**Response properties of neurons to monaural stimulation with SFM sounds**

For monaural stimulation, SFM tuning differed largely between neurons. SFM tuning was defined as the range of modulation frequencies neurons responded to robustly (with ≥50% of their maximal discharge rate). Most neurons displayed band-pass (63%) or low-pass (33%) filter characteristics for modulation frequency. Upper cutoff frequencies ranged between 40 and >500 Hz. All lower cutoff frequencies were <100 Hz. Furthermore, the temporal response pattern to SFM sounds differed between neurons. First, calculating cycle histograms showed that neurons responded either once (unidirectional) or twice (bidirectional) to each modulation cycle, presumably to the upward and downward part of each modulation cycle. In most neurons, this response pattern was dependent on the modulation frequency (Fig. 1). Second, over the population of neurons tested, phase-locking of the response varied profoundly. For example, at a modulation frequency of 50 Hz, the SC of the neurons varied between 0.14 (almost no synchronization) and 0.99 (nearly perfect synchronization). About 80% of the neurons exhibited significant phase-locking (P ≤ 0.01). For monaural stimulation most neurons (86%) showed SC-based low-pass filter characteristics or still exhibited significant phase-locking when the spike number dropped below a level that allowed a statistical significant calculation of the SC (all-pass filter characteristics). If a neuron’s response was bidirectional, we calculated the SC separately for the response to the upward and downward part of each modulation cycle and took the SC of the larger response for comparison. The response behavior of IC neurons to monaural stimulation with SFM sounds and the influence of GABAergic and glycine receptor mediated low-pass filter characteristics or still exhibited significant phase-locking when the spike number dropped below a level that allowed a statistical significant calculation of the SC (all-pass filter characteristics).
Under both conditions when tested for modulation frequencies $\leq 75$ Hz. Additionally, the number of cycles the neuron responded to decreased for increasing modulation frequencies ($\geq 100$ Hz) until only the response to the first modulation cycle remained. Figure 2A shows the MTFs of the same neuron based on total discharge rate. Compared with monaural stimulation, the upper cutoff frequency decreased by 65 Hz (about $\sim 45\%$) for binaural stimulation. In this neuron, the decrease of the upper cutoff frequency corresponded to its binaural response characteristics in the way that it received excitation from the contralateral and inhibition from the ipsilateral ear (EI neuron). As in many cases, calculating the upper cutoff frequency based on the number of spikes/cycle only displayed a small change of upper cutoff frequencies between monaural and binaural stimulation (Fig. 2B). However, because the response of the neuron as shown in the histograms in Fig. 1 (and the MTFs in Fig. 2A) substantially differed between monaural and binaural stimulation for modulation frequencies $>75$ Hz, we chose to analyze SFM tuning differences on the bases of total discharge rate. Furthermore for this neuron, the precision of phase-locking was independent of whether the sound was presented monaurally or binaurally (IID = 0; Fig. 2C). For a detailed analysis on changes in phase-locking for different binaural conditions, see following text.

In total, 85 neurons were tested for SFM tuning changes based on discharge rate comparing monaural and binaural (IID = 0) stimulation. In about one-third of the neurons (32%) it responded unidirectionally to modulation frequencies $>75$ Hz.
the upper cutoff frequency shifted by >25% (Fig. 3A). Seventeen neurons (20%) responded to substantially higher modulation frequencies (≥25%) during binaural compared with monaural stimulation. Ten neurons (12%) decreased their upper cutoff frequency for binaural compared with monaural stimulation. Additionally, minor changes of the upper cutoff frequency (10% but <25%) could be observed in 27% of the neurons tested. Again, as many neurons increased as decreased their upper cutoff frequency.

We also observed changes of lower cutoff frequencies in about a quarter of the neurons that exhibited band-pass filter characteristic. However, because changes usually occurred at very low modulation frequencies (<50 Hz), we did not attempt to thoroughly quantify those changes because our stimulus step size was too large for those modulation frequencies.

For 52 neurons, we also determined SFM tuning properties at an IID = −20 (ipsilateral ear 20 dB louder), which is well within the physiologically relevant range of our experimental animal. We then compared SFM tuning properties of neurons for binaural stimulus presentation with IID = 0 and IID = −20. Figure 4 displays the response of a neuron to an IID = 0 (left) and an IID = −20 (right). When the stimulus was presented with an IID = 0, the neuron showed a phase-locked response up to a modulation frequency of 200 Hz and an uncorrelated response to higher modulation frequencies ≥250 Hz. At a modulation frequency of 25 Hz, the response was biphasic, at high modulation frequencies monophasic (see phase histograms as insets).

![FIG. 3. Distribution of upper cutoff frequency changes for monaural vs. binaural (IID = 0) stimulation (A) and for binaural stimulation with IID = 0 vs. IID = −20 (B). Changes by >25% are shaded in dark gray.](http://jn.physiology.org/)

![FIG. 4. PSTHs of a neuron’s response to various modulation frequencies. Stimulation was binaural at IID = 0 (left) and IID = −20 (ipsilateral ear more intense; right). This neuron responded with a phase-locked response up to modulation frequencies of 150 Hz for IID = 0 but only ≤50 Hz for IID = −20. At low modulation frequencies, the response was biphasic, at high modulation frequencies monophasic (see phase histograms as insets).](http://jn.physiology.org/)
Upper cutoff frequency was highest for sounds with an IID of 5. Changes in the discharge rate of individual neurons to different binaural sound conditions (monaural, IID 0) were compared. A significant difference in SFM tuning between monaural and binaural stimulation for various groups of neurons (EE and EI) was found. Interestingly, upper cutoff frequencies also increased in a large number of EI neurons during binaural stimulation. This suggests that a complex interaction of inhibitory and excitatory projections causes SFM tuning changes as well as differences in the apparent binaural properties of neurons.

Temporal response patterns are affected by binaural stimulus properties

For a subset of neurons (n = 42) SFM tuning changes were analyzed based on the temporal response pattern of the neurons. The precision of phase-locking was compared between monaural and binaural stimulation as shown in Fig. 6. In this case, phase-locking was considerably better for binaural than for monaural stimulation, particularly for modulation frequencies <150 Hz (Fig. 6, A and B). However, the cycle histograms show that this change in SC could also be partially due to a change in the response from bidirectional to unidirectional (Fig. 6D). Because the responses to the upward and downward part of the modulation cycle could not be separated clearly, we calculated the SC for the entire response. Analyzing the response to SFM sounds based on spike count, this neuron responded to higher modulation frequencies for binaural than for monaural stimulation (Fig. 6C).

In Fig. 7A, changes in phase-locking between monaural and binaural stimulation are quantified. Each line represents the difference of the SC between monaural and binaural stimulation as shown in Fig. 6. In almost half of the neurons tested (22/52), the upper cutoff frequency decreased by >25% when stimulation was changed from IID = 0 to IID = -20. For about one-third of the neurons the upper cutoff frequency decreased by 80 Hz when stimulation was changed from IID = 0 to IID = -20. Synchronization coefficients were identical for low modulation frequencies (there were not enough spikes to calculate a significant SC for IID = -20 at rates >50 Hz). Only for modulation frequencies <250-Hz phase-locking was significant (—, Rayleigh-test = P ≤ 0.01; •••, Rayleigh test = P > 0.01).

SFM tuning is related to the neurons’ EI properties

We also tested whether there is a systematic interdependence of differences in SFM tuning between monaural and binaural (IID = 0) stimulation, and the general binaural response characteristics of individual neurons. Discharge rates between different binaural conditions (monaural, IID = 0, and IID = -20) at the modulation frequency that elicited the maximal response were compared. A change in the discharge rate of >25% in the spike rate between two binaural conditions was defined as a change evoked by additional excitation or inhibition. According to this scheme, neurons were classified as EI (contralateral excitation, ipsilateral inhibition), EE (excitation from both ears), EO (contralateral excitation), and EI (excitation from contra- and ipsilateral; inhibition from ipsi- and contralateral; strongest response for IID = 0). Almost all neurons (9/10) for which the upper cutoff frequency decreased considerably (less than -25%) were EI neurons (Table 1). For the majority of EE and EI F neurons, the upper cutoff frequencies increased by >10% for binaural compared with monaural sound presentation. Measuring changes in upper cutoff frequency the populations of EI neurons and EE/EIf neurons were significantly different (Mann-Whitney U test: P < 0.05). No significant difference could be found between the populations of EO and EI or EE/EIf neurons. Interestingly, upper cutoff frequencies also increased in a large number of EI neurons during binaural stimulation. This suggests that a complex interaction of inhibitory and excitatory projections causes SFM tuning changes as well as differences in the apparent binaural properties of neurons.

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In Fig. 7A, changes in phase-locking between monaural and binaural stimulation are quantified. Each line represents the difference of the SC between monaural and binaural stimulation for each neuron. Positive values indicate better phase-locking for binaural than for monaural stimulation. Over the population of neurons, a distinct change of the SC (≥0.25) was only observed in eight neurons. Interestingly, in all except one neuron, the change was from IID = 0 to IID = -20.

**Table 1. Distribution of SFM tuning changes of neurons with different binaural response characteristics**

<table>
<thead>
<tr>
<th>Change of Cutoff Point, %</th>
<th>EE and EIf</th>
<th>EI</th>
<th>EO</th>
</tr>
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<tbody>
<tr>
<td>≤ -25</td>
<td>1</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>&gt; -25 and ≤ -10</td>
<td>3</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>&gt; -10 and &lt;10</td>
<td>5</td>
<td>22</td>
<td>6</td>
</tr>
<tr>
<td>≥10 and &lt;25</td>
<td>4</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>≥25</td>
<td>8</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

Magnitude of sinusoidally frequency modulated (SFM) tuning changes for monaural compared with binaural stimulation for various groups of neurons with different binaural response properties. In the majority of EE and EH neurons upper cutoffs increased for binaural compared to monaural stimulation. A considerable decrease of upper cutoff frequencies (25%) was almost exclusively observed in EI neurons. Applying the Mann-Whitney U test, the population of EI neurons differed significantly from the population of EE/EIf neurons (P < 0.05). Neither of the populations was significantly different from the population of EO neurons. EI, contralateral excitation, ipsilateral inhibition; EE, excitation from both ears; EO, contralateral excitation; EIf, excitation from contra- and ipsilateral, inhibition from ipsi- and contralateral; strongest response for interaural intensity difference (IID) = 0.
neuron, phase-locking was better for binaural than for monaural stimulation. Additionally, phase-locking differed substantially for modulation frequencies only <150 Hz.

The modulation frequency eliciting best synchronization and the synchronization cutoff frequency, defined as the modulation frequency where the SC dropped <0.3, were determined for monaural and binaural stimulation if spike count was high enough to calculate the SC. For many neurons (10/18), the modulation frequency with best synchronization was substantially higher (>25%) for binaural than for monaural stimulation. In contrast, for 9 of 12 neurons, the synchronization cutoff frequency was roughly equivalent for monaural and binaural stimulation (Fig. 7C).

A small number of neurons changed their response pattern from uni- to bidirectional for different binaural stimulus conditions. For example, at a modulation frequency of 50 Hz, 5 of 61 neurons, that phase-locked at this modulation frequency, responded unidirectionally during monaural and bidirectionally during binaural (IID = 0) stimulation. In three neurons that responded bidirectionally during monaural stimulation, the second response to each modulation cycle was suppressed during binaural stimulation.

**Ipsilateral inhibition changes the response pattern of neurons**

To test whether synaptic inhibition changes the temporal response pattern of neurons, two different experiments were performed. First, the GABA_A receptor antagonist bicuculline was applied iontophoretically to the neurons that changed its response pattern (uni- or bidirectional) depending on the binaural conditions. Blocking GABAergic inhibition prevented this change in response pattern in five neurons. During drug application, these neurons responded bidirectionally independent of the binaural conditions.

In a second experiment, glutamate was applied iontophoretically, causing the neurons to increase their discharge rate independent of the acoustic stimulus. During glutamate application, the same range of modulation frequencies was presented as before but only to the ipsilateral, thus inhibitory ear. In all cases, ipsilateral sound presentation resulted in an inhibition of glutamate-evoked activity. In five of nine neurons, this inhibition was phase-locked when low modulation frequencies (≤50 Hz) were used. Figure 8 shows the result of an experiment where the phase-locked inhibition coincided with the suppression of the second response during binaural sound presentation. The *top histogram* shows the response of the neuron when the stimulus was presented only to the ipsilateral ear (Fig. 8A). The activity of the neuron was increased artificially by glutamate application. Therefore inhibition evoked by stimulating the ipsilateral ear can be directly viewed as a gap in the increased activity. For this neuron, the inhibition was phase-locked to the modulation frequency (30 Hz). The *middle histogram* shows the response of the same neuron to contralateral, thus monaural stimulation (Fig. 8B). The neuron responded to both...
the upward and downward part of the modulation cycle. The bottom histogram shows that during binaural stimulation (IID = 0 dB) the neuron responded only once per modulation cycle (Fig. 8C). The comparison of the three histograms indirectly suggests that the inhibition evoked by the ipsilateral ear (Fig. 8A) coincided with the second discharge to each modulation cycle for monaural stimulation (Fig. 8B), thereby suppressing the second, contralaterally evoked discharge.

GABAergic and glycinergic inhibition is involved in binaural changes of SFM tuning

Several neuronal mechanisms might be responsible for changes in SFM tuning induced by ipsilateral stimulation. IC neurons receive multiple inhibitory projections from lower auditory nuclei. These inhibitory inputs might be responsible for the observed interdependence of SFM tuning and IIDs. To test this idea, we blocked GABAergic or glycinergic inhibition by applying the antagonists bicuculline (blocks GABAA receptors) or strychnine (blocks glycine receptors) under different binaural stimulation.

Several patterns of inhibitory influences on SFM tuning could be observed. For example, the neuron depicted in Fig. 9 showed a low-pass filter for monaural stimulation and a band-reject filter for binaural stimulation; i.e., a highly reduced response to a small range of modulation frequencies (~90 Hz) within the usual response range. The upper cutoff frequency increased by 275 Hz for binaural compared with monaural stimulation. This is consistent with the observation that this neuron received excitatory input from both the ipsi- and contralateral ear (EE neuron). Bicuculline application caused this neuron to discharge with very high rates for both conditions up to high modulation frequencies (~200 Hz). No difference between monaural and binaural (IID = 0) stimulation could be
observed anymore. Normalizing the response rate as depicted in Fig. 9B shows that for monaural stimulation, the neuron did not respond to modulation frequencies >50 Hz except for a small on response. For binaural stimulation, the neuron responded with a phase-locked response at 190 Hz. However, there was a gap (band reject) at 90 Hz modulation frequency where the neuron did not respond. Application of bicuculline abolished these filter effects and the neuron responded up to modulation frequency of 200 Hz for monaural and binaural stimulation.

For the neuron displayed in Fig. 10, SFM tuning sharpened under binaural (IID = 0) compared with monaural stimulation, which is consistent with the EI-response properties of this neuron. For monaural stimulation, the neuron responded with a sustained response up to a modulation frequency of 125 Hz. For binaural stimulation, the neuron did not respond to modulation frequencies <50 Hz. Strychnine application rendered this neuron responsive for modulation frequencies ≤125 Hz and above for monaural and binaural stimulation. The MTFs in Fig. 10B show that differences in SFM tuning between monaural and binaural stimulation completely disappeared during strychnine application. This neuron did not lose its direction selectivity during strychnine application in contrast to the previous neuron that responded unidirectionally under predrug conditions and bidirectionally during bicuculline application (Figs. 9C and 10C). However, over the population of neurons tested, no systematic effect on direction selectivity between GABA and glycine could be observed. For a more detailed analysis, compare Koch and Grothe (1998).
For the population of cells tested with bicuculline (\(n = 40\)) or strychnine (\(n = 19\)), several groups of neurons can be described. The diagrams in Fig. 11 depict differences in SFM tuning based on firing rate between monaural and binaural stimulation under predrug and drug conditions. Positive values indicate increased upper cutoff frequencies during binaural stimulation. Blocking GABAergic inhibition four different effects could be seen. In \(\approx 25\%\) of the neurons, bicuculline abolished or greatly diminished binaural differences in SFM tuning (Fig. 11A, top). Under predrug conditions, most of these neurons broadened SFM tuning during binaural stimulation. In contrast, for another group of neurons (25%) SFM tuning was broader for binaural condition during bicuculline application (Fig. 11B, top). For about one-quarter of the neurons, bicuculline application had virtually no effect on their binaural SFM tuning (Fig. 11C, top). The remaining neurons (\(\approx 25\%\)) showed a reversed relationship of SFM tuning and binaural conditions under bicuculline application compared with predrug conditions (Fig. 11D), which means that differences in upper cutoff frequencies comparing binaural and monaural stimulation changed from positive to negative or vice versa. Four neurons exhibited changes in upper cutoff frequencies that were \(>80\%\) comparing monaural and binaural stimulation and are not included in the graphs. For three of these neurons, tuning differences were diminished greatly during bicuculline application. During strychnine application three different effects could be observed. About 25% of the neurons did not show binaural SFM tuning differences (Fig. 11A, bottom) during strychnine application anymore. However, in contrast to bicuculline application, strychnine was only effective in neurons that sharpened SFM tuning for binaural compared with monaural stimulation (negative values). In four neurons, binaural SFM tuning differences increased during drug application (Fig. 11B, bottom). In the remaining neurons, strychnine application did not cause any changes in binaural SFM tuning differences (Fig. 11C, bottom). No reversed response behavior could be observed during strychnine application.
Ipsilateral inhibition gets stronger for higher modulation frequencies

Because some neurons changed their temporal response pattern in the way that at some modulation frequencies the response was unidirectional for binaural stimulation and bidirectional for monaural stimulation, we argued that the timing of ipsilateral inhibition might be an important factor for the tuning properties.

To precisely measure the temporal occurrence and duration of ipsilateral inhibition, we presented SFM sounds as “binaural beats.” Several modulation frequencies were tested (25/30–200/205 Hz) with a 5-Hz modulation frequency difference between the two ears. This created an interaural phase difference (IPD) that changed continuously as the stimulus progressed and allowed us to determine at which IPDs the ipsilateral induced inhibition suppressed contralateral evoked excitation and to measure the timing and strength of the ipsilaterally evoked inhibition.

There are two pieces of evidence that ipsilateral inhibition was involved in the reduction of the response at certain IPDs: first, all neurons tested were increasingly inhibited when the intensity at the ipsilateral ear was increased gradually. Second, the maximal response during a binaural beat stimulus was equal to the response evoked by monaural stimulation. This excludes mechanisms solely based on the coincidence of two excitatory inputs.

In most neurons (14/16), inhibition was phase-locked to each modulation cycle. For higher sound intensities at the ipsilateral ear, the inhibition lengthened and got stronger (Fig. 12A). Figure 12B shows the response of a neuron to a “binaural beat” SFM stimulus that was modulated for 50/55, 100/105, and 200/205 Hz at the contralateral/ipsilateral ear respectively.

For this neuron, inhibition evoked by the ipsilateral side was weak at 50 Hz. It gradually strengthened for higher modulation frequencies, and at 200 Hz, a strong biphasic inhibition could be observed. At higher modulation frequencies, the duration of inhibition remained the same although the length of each stimulus phase decreased, leading to a higher duty cycle of inhibitory input. To determine of what nature the observed ITD sensitivity of this neuron was, the mean phase angles were calculated (50/55 Hz: 0.31; 100/105 Hz: 0.36; 200/205 Hz: 0.26) according to Yin and Kuwada (1983). Determining the intercept of the regression line with the ordinate yields to a characteristic phase (CP) of 0.36. This indicates that this neuron’s ITD sensitivity is neither based on a pure EE (CP = 0) nor a pure EI (CP = 0.5) interaction (Batra and Fitzpatrick 1997). For this neuron, excitation and inhibition are most likely present from ipsi- and contralateral. This neuron decreased its upper cutoff frequency when the sound was presented with an IID = –20 compared with monaural stimulation (Fig. 12C).

DISCUSSION

The present study presents evidence that binaural cues, namely interaural intensity differences, have profound effects on filter properties for stimulus periodicity of auditory midbrain neurons. According to our analysis, changing the binaural stimulus conditions does not merely scale SFM tuning linearly.
for conventional SFM tuning under monaural and binaural stimulation (C neurons, the synchronization of the response as well as the interaural intensity differences (IIDs). Second, in depends on the binaural stimulus conditions, in this case the neurons tested for IID for monaural versus binaural stimulation, and in about half of the main findings. First, in about one-third of the IC neurons tested binaural inhibitory inputs. This conclusion is based on four effects are partially due to changes in strength and timing of response type of the neuron. Our data also indicate that these modifies it nonlinearly, partially dependent on the binaural characteristic phase of 0.36, which suggests that this neuron is neither a pure EE (excitation from both ears) nor a pure EI (contralateral excitation, ipsilateral inhibition) type and receives excitation and inhibition from both ears. A similar dependency of response characteristics for periodic stimuli on sound location has been reported before but in a different class of vertebrates. In the northern leopard frog’s torus semicircularis, the amphibian homologue of the mammalian IC, more than half of the neurons sharpened their tuning for the modulation frequency of SAM sounds when a free-field loudspeaker was rotated from the contralateral hemisphere into the ipsilateral hemisphere (Xu et al. 1996). Similar results from the grass frog midbrain have demonstrated that most neuron’s selectivity for the temporal characteristic of a sound and its tuning for interaural time disparities (ITD) are intricately coupled (Melssen and van Stokkum 1988; Melssen et al. 1990; van Stokkum and Melssen 1991). However, the tympanic membrane of these animals acts as a pressure gradient receiver comparing sound pressure reaching the tympanic membrane through the external ear and the Eustachian tube from both sides. As a consequence, frequency tuning of auditory nerve fibers in these animals is already dependent on the spatial position of the stimulus (Feng and Shofner 1981; Narins et al. 1988). Therefore changes in SAM tuning of frog IC neurons might be at least partially a reflection of the peripheral response properties. However, similar results also were obtained from IC neurons in the big brown bat, the animal used in the present study.

SFM tuning based on firing rate changes for different binaural situations

Most studies that investigated response characteristics of IC neurons to periodic stimuli used monaural sound presentations exclusively (Casseday et al. 1997; Langner and Schreiner 1988; Schuller 1979). On the other hand, most studies investigating the binaural properties of IC neurons only used pure tones or broadband noise. Consequently, these independent sets of data cannot be related to each other. The present study, however, indicates that neuronal processing of periodic stimuli and the analysis of IIDs are not accomplished by two completely independent mechanisms but rather influence each other.

In a different set of experiments, we previously showed that the azimuthal position of a free-field speaker influences the tuning for the modulation frequency of SFM sounds (Koch and Grothe 1997). Using the same criterion for changes in the tuning to the modulation frequency (≥25%), ~55% of the neurons showed position-dependent filtering. This is an equivalent number of neurons as we found in the present study comparing differences in SFM tuning between IID = 0 and IID = −20. This indicates that the frequency-dependent attenuation of the pinna only plays a minor role in determining SFM tuning of IC neurons and that neuronal processing is the main factor. It also demonstrates that the differences in SFM tuning in the present study are most likely not due to different total energy levels that exist for different binaural conditions in our present, more artificial experimental design.

A similar dependency of response characteristics for periodic stimuli on sound location has been reported before but in a different class of vertebrates. In the northern leopard frog’s torus semicircularis, the amphibian homologue of the mammalian IC, more than half of the neurons sharpened their tuning for the modulation frequency of SAM sounds when a free-field loudspeaker was rotated from the contralateral hemisphere into the ipsilateral hemisphere (Xu et al. 1996). Similar results from the grass frog midbrain have demonstrated that most neuron’s selectivity for the temporal characteristic of a sound and its tuning for interaural time disparities (ITD) are intricately coupled (Melssen and van Stokkum 1988; Melssen et al. 1990; van Stokkum and Melssen 1991). However, the tympanic membrane of these animals acts as a pressure gradient receiver comparing sound pressure reaching the tympanic membrane through the external ear and the Eustachian tube from both sides. As a consequence, frequency tuning of auditory nerve fibers in these animals is already dependent on the spatial position of the stimulus (Feng and Shofner 1981; Narins et al. 1988). Therefore changes in SAM tuning of frog IC neurons might be at least partially a reflection of the peripheral response properties. However, similar results also were obtained from IC neurons in the big brown bat, the animal used in the present
study. There neurons sharpened their receptive field when pulse repetition rate of pure tones was increased (Wu and Jen 1996). Moreover, receptive fields of individual neurons in the big brown bat IC differ for different stimuli (Grothe et al. 1996). Interestingly, in the present study, only a small number of neurons could be classified as true EE neurons when a SFM stimulus was used. Most neurons responded only weakly by ipsilateral stimulation alone and also exhibited some inhibition from the ipsilateral side. A possible explanation could be that IC neurons integrate projections from the presumed EI and EE neurons of the MSO and lateral superior olive (LSO). It is possible that by using pure tone stimulation, this integration remains occluded in many cases. Another study that used binaural SAM stimulation reported a similar small percentage of true EE neurons (Batra et al. 1989). Despite species-specific differences that certainly exist, all these results indicate that processing of sound location and sound pattern is not independent from each other.

**Synchronization and response pattern changes with different IIDs**

In the present study, only 10% of the neurons changed their precision of synchronization to the modulation cycles when the stimulus was presented binaurally compared with the degree of phase locking in response to monaural sound presentation. In our study, most of these neurons synchronized better under binaural than under monaural stimulation. In contrast, under free-field conditions, we observed a change in synchronization in 50% of the neurons (Koch and Grothe 1997). The discrepancy might be explained by the different analysis used. In the free-field study, the SC was calculated the same way regardless of whether the response was uni- or bidirectional. A considerable difference exists to neurons of the rabbit IC. There most neurons synchronized significantly better to SAM sounds when they were presented as binaural beat stimuli compared with contralateral stimulation only (Batra et al. 1989). However, neurons in the rabbit IC synchronized to much higher modulation frequencies compared with the neurons in the present study. On the other hand, in the frog IC there are no significant differences in the degree of synchronization due to different binaural test conditions (Xu et al. 1996). Again, there seem to be profound species-specific differences.

**GABA and glycine affects binaural tuning in different ways**

There are several potential mechanisms that could accomplish IID-dependent changes in SFM tuning of IC neurons. Data from the MSO of the free-tailed bat (T. brasiliensis) demonstrate that in the majority of neurons SAM tuning is dependent on IIDs (Grothe et al. 1997b), whereas in LSO neurons, these parameters are processed independently (Grothe et al. 1997a). This suggests that this interdependency might be at least partially created at much earlier stages of binaural processing. However, in this study, we present evidence that GABAergic and glycinergic inhibition is involved in changing SFM tuning at the level of the IC. Therefore at least some of these changes are likely to be created within the IC.

Our results indicate that GABAergic and glycinergic inhibition differ in their effects on changing SFM tuning for different binaural conditions. A schematic of the major GABAergic and glycinergic projections to the IC is shown in Fig. 13. The major source of GABAergic inhibition to IC neurons is the dorsal nucleus of the lateral lemniscus (DNLL). Neurons in the DNLL stain for GABA and provide strong bilateral projections to both ICs (Adams and Mugnaini 1984; Roberts and Ribak 1987a,b; Thompson et al. 1985; Vater et al. 1992). Many neurons in the DNLL respond with a phase-locked discharge up to high modulation frequencies of SAM sounds (Yang and Pollak 1997). Moreover, DNLL neurons are excited by contralateral stimulation and inhibited by ipsilateral stimulation (Covey and Casseday 1991; Yang and Pollak 1997).

As depicted in Fig. 11A (top), bicuculline was most effective in abolishing SFM tuning differences in neurons that broadened their tuning for binaural stimulation. This suggests that GABAergic inhibition is stronger at high modulation frequencies for contralateral stimulation than for binaural stimulation. This is in agreement with findings that contralateral stimulation excites neurons in the ipsilateral DNLL, which in turn exert GABAergic inhibition on neurons in the ipsilateral IC. As the sound intensity at the ipsilateral ear increases (binaural stimulation), neurons in the ipsilateral DNLL are increasingly inhibited and cease to inhibit IC neurons at higher modulation frequencies. In a number of neurons, blocking GABAergic inhibition broadened SFM tuning for binaural stimulation (Fig. 11B, top). This effect might be due to inhibitory GABAergic inputs from the contralateral DNLL. In this DNLL neurons do not respond to contralateral stimulation alone; however, they do start to exert inhibition on IC neurons during binaural stimulation. Another GABAergic projection arises from the contralateral IC. In vitro recordings of IC neurons have shown that stimulation of the commissure elicits short and long latency inhibitory postsynaptic potentials (IPSPs) that can be blocked by bicuculline (Moore et al. 1998; Smith 1992).

In contrast, blocking glycinergic inhibition was only effective in abolishing differences in SFM tuning in neurons that sharpened their SFM tuning for more negative IIDs (Fig. 11A, bottom). This might be due to the prominent glycinergic projection from the ipsilateral LSO (Glendenning et al. 1992; Saint Marie and Baker 1990; Saint Marie et al. 1989), which is profound species-specific differences.
excited by stimulating the ipsilateral ear and inhibited by stimulating the contralateral ear (Tsuchitani 1977). Another glycinergic projection arises from the monaural nuclei of the lateral lemniscus on the ipsilateral side (Gonzalez-Hernandes et al. 1996; Vater et al. 1997). However, neurons in the ventral nucleus of the lateral lemniscus (VNLL) and the intermediate nucleus of the lateral lemniscus (INLL) receive input only from the contralateral ear. Hence their impact on SFM tuning should not change for binaural stimulation because the intensity at the contralateral ear was kept constant in the present study.

Ipsilaterally evoked inhibition gets stronger at higher modulation frequencies: a possible neuronal mechanism for creating low-pass filters

As already suggested by Melssen and Epping (1992), relative timing of excitation and inhibition might be an important factor in changing periodicity tuning for different IIDs. Well understood is the impact of delayed inhibitory inputs on SAM coding in the MSO (Grothe 1994, Grothe et al. 1997b) and the DNLL (Yang and Pollak 1997) where the response to one cycle is suppressed by inhibition evoked by the preceding cycle. In combination with temporal summation of inhibition at very high repetition rates, which has been shown at different levels of the auditory system and for hippocampal neurons, this creates a very effective low-pass filter mechanism for periodic sounds (Buhl et al. 1995; Davies and Collinridge 1996; Fuzeessey 1997; Grothe and Sanes 1994). Moreover, the effect and duration of ipsilaterally induced inhibition has been shown to increase with increasing intensity of the ipsilateral signal (Park et al. 1996; Sanes 1990; Wu and Kelly 1992). Our data indicate that inhibition strengthens at higher modulation frequencies and the duration of inhibition stays the same in absolute terms and hence increases relative to the duration of the modulation cycle. Additionally, the absolute duration increases for higher sound intensities. Therefore different IIDs might contribute to the filter effect through the mechanism of time-intensity trading. Increasing the stimulus intensity at one ear results in shorter delays of excitation and inhibition in many IC and LSO neurons that can be compensated for by artificially introducing interaural time differences (Irvine et al. 1995; Park et al. 1996; Pollak 1988; Yin et al. 1985). On the contrary, one other study suggests that in the IC of the free-tailed bat inhibition is only little involved in low-pass filtering the neuronal response to SAM sounds (Burger and Pollak 1999). This indicates that other neuronal filter mechanisms apart from inhibition, which are presently unknown, must be effective in that case.

Unfortunately because inhibitory and excitatory inputs to each IC neuron are plentiful, it seems impossible to determine the temporal and binaural changes of each input and to dissect out their contributions to the entire response behavior of each neuron.

We also are aware of the fact that the amount of cycling of the response to a binaural beat stimulus depends on the precision of phase-locking of the excitatory and inhibitory inputs. However, phase-locking decreased for increasing modulation frequencies during contralateral (mostly excitatory) stimulation (Fig. 12A). Therefore the inhibitory input is most likely to be responsible for these changes.

Behavioral relevance

At first glance, the observed ambiguity in neuronal coding of sound pattern depending on sound location seems to be enigmatic. Indeed, one psychoacoustic experiment shows that the extent of lateralization of a SAM sound depends on its modulation frequency (Bernstein and Trahiotis 1985).

However, spatial cross-correlation models suggest a different interpretation for this phenomenon. In these models, processing of sound location using binaural information is coupled to the analysis of sound pattern such as pitch or periodicity (Loeb et al. 1983; Shamma et al. 1989). A similar dependency of spectral tuning of neurons on IIDs or ITDs can be seen in the “stereausis” model, proposed by Shamma. In this model, the change in the spectral tuning of neurons is supposed to provide additional information for sound localization (Shamma et al. 1989). Moreover, these models have properties that might account for certain complex binaural, psychophysical observations such as the cocktail party effect.

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REFERENCES


