Physiological Studies of the Precedence Effect in the Inferior Colliculus of the Cat. II. Neural Mechanisms

RUTH Y. LITOVSKY AND TOM C. T. YIN
Department of Neurophysiology, University of Wisconsin, Madison, Wisconsin 53706

Litovsky, Ruth Y. and Tom C. T. Yin. Physiological studies of the precedence effect in the inferior colliculus of the cat. II. Neural mechanisms. *J. Neurophysiol.* 80: 1302–1316, 1998. We studied the responses of neurons in the inferior colliculus (IC) of cats to stimuli known to evoke the precedence effect (PE). This paper focuses on stimulus conditions that probe the neural mechanisms underlying the PE but that are not usually encountered in a natural situation. Experiments were conducted under both free-field (anechoic chamber) and dichotic (headphones) conditions. We found that in free field the amount of suppression of the lagging response depended on the location of the leading source. With stimuli in the azimuthal plane, the majority (84%) of units showed stronger suppression of the lagging response for a leading stimulus placed in the cell's responsive area as compared with a lead in the unresponsive field. A smaller number of units showed stronger suppression for a lead placed in the unresponsive field, and a few showed little effect of the lead location. In the elevational plane, there was less sensitivity of the leading source to changes in location, but for those cells in which there was sensitivity, suppression was always stronger when the lead was in the cell's responsive area. Studies on stimulus locations also were conducted under dichotic conditions by varying the interaural differences in time (ITD) of the leading source. Results were consistent with those obtained in free field, suggesting that ITDs play an important role in determining the amount of suppression that was observed as a function of leading stimulus location. In addition to location and ITD, we also studied the effect of varying the relative levels of the lead and lag as well as stimulus duration. For all units studied, increasing the level of the leading stimulus while holding the lagging stimulus constant resulted in increased suppression. Similar effects of leading source level were observed in azimuth and elevation. The effect of varying the duration of the leading source also showed that longer duration stimuli produce stronger suppression; this finding was observed both in azimuth and elevation. We also compared the suppression observed under binaural and monaural contralateral conditions and found a mixed effect: some neurons show stronger suppression under binaural conditions, others to monaural contralateral conditions, and still others show no effect. The results presented here support the hypothesis that the PE reflects a long-lasting inhibition evoked by the leading stimulus. Five possible sources for the inhibition are considered: the auditory nerve, intrinsic circuits in the cochlear nucleus, medial and lateral nuclei of the trapezoid body inhibition to the medial superior olive, dorsal nucleus of the lateral lemniscus (DNLL) inhibition to the ICC, and intrinsic circuits in the ICC itself.

INTRODUCTION

The precedence effect (PE), also known as the law of the first wave-front or the Haas effect, is a perceptual phenomenon that is thought to enhance our ability to localize sounds in a reverberant environment. Most of what is known about the PE comes from psychophysical studies, which are reviewed briefly in the preceding paper (Litovsky and Yin 1998) and more extensively elsewhere (Blauert 1983; Zurek 1987). The PE is experienced when two sounds are presented from different locations with a brief delay between them. When the delay is short enough, rather than localizing each sound at its respective position, the listener perceives one ''fused'' sound, the apparent location of which is dominated by the leading source. Although spatial information of the echo apparently is suppressed by the PE, its presence nonetheless affects other aspects of the perceived sound, such as its pitch, loudness, and timbre.

In this study, we present data on physiological responses to stimuli that are designed to probe the neural mechanisms of the PE. Although we did not study perceptual effects of the PE in the cat, we find it useful to relate our physiological responses to known psychophysical effects. This, of course, presumes that the PE in the cat is similar to that in humans, an assumption that has some experimental support (Populin and Yin 1998). For the purposes of relating our physiological results to psychophysics, it is convenient to identify physiological correlates of two commonly used psychophysical terms (echo suppression and echo threshold). *Echo suppression* is the range of interstimulus delays (ISDs) at which the PE is active and only one sound is heard (~1–5 ms for clicks) (Freyman et al. 1991; Wallach et al. 1949; Zurek 1980). *Echo threshold* is the ISD at which echo suppression breaks down and the lagging sound is perceived and localized at its respective position (Freyman et al. 1991). An apparent correlate of echo suppression has been described in physiological studies of the inferior colliculus (Fitzpatrick et al. 1995; Litovsky et al. 1997b; Litovsky and Yin 1998; Yin 1994): when a pair of transient stimuli are delivered in quick succession, the response to the lagging stimulus is suppressed for short, but not long, ISDs. For convenience, the ISD at which the lagging response is suppressed to 50% of its response in the absence of the leading stimulus is called the *half-maximal ISD* and is hypothesized to be related to the psychophysical echo threshold. Psychophysically, echo thresholds vary widely with stimulus characteristics (Blauert 1983), and physiologically half-maximal ISDs vary considerably with different cells (Fitzpatrick et al. 1995; Litovsky and Yin 1998; Yin 1994).

In the preceding paper (Litovsky and Yin 1998), we studied the suppression of the lagging responses in the inferior colliculus (IC) of cats to PE stimuli for a variety of stimulus parameters, all of which are likely to occur in a natural listening environment. In the present paper, our aim is to explore the neural mechanisms responsible for the suppression by using stimuli similar to those that elicit the PE, but designed to evaluate how changes in the stimulus parameters

of the leading sound affect the suppression of the lagging sound. We hypothesize that the neural mechanism underlying the suppression of the lagging stimulus is a long-lasting inhibition evoked by the leading stimulus. In most of the manipulations reported here, we used a general paradigm whereby we compared the changes in half-maximal ISD for various leading stimuli exerted on the same lagging sound. For example, we varied the level, duration, and location of the leading sound while holding the lagging sound constant to quantify the suppressive effect of these parameters. Our results support a model in which the central nucleus of the IC (ICC) receives excitation from the ipsilateral medial superior olive (MSO) and contralateral lateral superior olive (LSO), which represent cells sensitive to interaural time delays (ITDs) and interaural level differences (ILD), respectively, with peak responses in the contralateral sound field, and a parallel inhibitory pathway through the dorsal nucleus of the lateral lemniscus of both sides.

METHODS

The general experimental methods are described in more detail in the preceding paper (Litovsky and Yin 1998). Briefly, cats with no sign of middle ear infection were anesthetized with pentobarbital sodium. The dorsal surface of the inferior colliculus (IC) was exposed by a craniotomy and aspiration of the overlying cortex. Extracellular recordings were made in the ICC using tungsten microelectrodes. A hydraulic microdrive was used to move the electrode remotely. The times of occurrence of spikes from well-isolated single units were measured by a unit-event timer and saved in computer files. Physiological criteria were used to identify cells within the ICC (Carney and Yin 1989).

Free-field experiments were conducted in a double-walled, sound-insulated room (IAC) with all surfaces lined with 4-in reticulated foam wedges (Sonex) to reduce acoustic reflections. After the IC was exposed, a steel rod was secured to the skull to position the head in an approximate stereotaxic orientation and in the center of a circle of 90-cm radius that defined the loudspeaker array. Loudspeakers were positioned at 15° intervals along the horizontal and vertical axes in the frontal hemifield (Fig. 1*A* of Litovsky and Yin 1998). In our coordinate system, the point directly in front is (0°,0°), and sounds in the contralateral hemifield or above the animal are positive. Azimuthal and elevational response curves were obtained by presenting either clicks or noise from each loudspeaker at 5–20 dB above threshold. The PE was simulated by presenting two sounds from different loudspeakers with one sound lagging relative to the other. Because of hardware limitations, the two stimuli could not be placed at the same location.

For dichotic experiments, the cat also was placed in a double-walled IAC chamber. Both pinnae were dissected away and the external ear canals were transected transversely so that acoustic stimuli could be delivered to each ear through hollow ear-pieces. Acoustic stimuli were generated by a digital sound system, which was calibrated from 0.1 to 42 kHz for each ear. The characteristic frequency (CF) of each cell was defined as the frequency with the lowest threshold for the contralateral ear or under binaural stimulation if the contralateral ear was not effective. For cells with low CF (<3 kHz), we measured their sensitivity to ITDs using clicks or noise bursts and identified the ITDs at which the cell was most (at the peak) and least (at the trough) sensitive. By convention, positive ITDs refer to the contralateral ear leading. Thresholds were estimated for clicks and noise by varying the level to either the contralateral ear alone or with binaural stimuli with an ITD of 0. Stimuli with a PE configuration were simulated by presenting two dichotic pairs of clicks or noise separated by an ISD; ITDs were imposed separately for each stimulus pair. The ISD was defined as the time difference between the onset of the two stimuli delivered to the contralateral ear. In dichotic experiments, the sound pressure levels (SPLs) of tones were referenced to 20 μPa. The levels of noise and click stimuli were computed as the effective SPL by summing the total energy in the waveform from convoluting the spectrum of the signal with the transfer characteristics of the earphone.

Stimuli were either click (100 μs) or noise (usually 5 ms duration) usually delivered every 300 ms and repeated 50 times. Narrow band-pass noises were usually 0.2 kHz wide, digitally filtered from broadband (0.1–30 kHz) noises with steep slopes (1,000 dB/octave), and centered on the CF of the cell.

RESULTS

The database consists of the same 178 units in the ICC. described in the companion paper (Litovsky and Yin 1998).

Effects of lead stimulus position or ITD on suppression

One of the most obvious features of sounds in a normal listening environment is that they appear from many different locations. Because a well-known feature of ICC neurons is their selectivity for direction along the azimuth, a natural question is how the variability in response with direction of the leading sound influences the degree of suppression of the lagging sound. This manipulation is important because, if the suppression is sensitive to stimulus location, it places constraints on the origin of the suppression. In our experimental setup, the locations of the leading or lagging source could be varied independently in free field, and the corresponding manipulation was accomplished under dichotic conditions by varying the relative ITDs of the leading and lagging stimulus pairs. We varied the location of the leading stimulus while holding constant that of the lagging sound. In this way, we could compare the amount of suppression that leading stimuli from different locations or with different ITDs exerted on the same lagging response.

Figure 1, *A* and *B*, shows responses to click stimuli in the form of dot rasters of a representative ICC cell in which the ISDs were 20 and 10 ms, respectively. In both cases, the leading stimulus was varied along the azimuth from −90 to +90° while the lagging stimulus was held constant at +30° (Fig. 1*B*, →). At any given ISD, the amount of suppression of the lagging response depended on the stimulus location of the leading source as well as on the time delay. At 20 ms (Fig. 1*A*), the lagging response, which occurred at ~34–36 ms, was somewhat suppressed at +15 and +45°, with relatively little effect at the other locations, where the response to the leading sound was weak. Where there was a weak suppressive effect on the lagging click at +15 and +45°, the latency of the response was also increased. At a shorter delay of 10 ms (Fig. 1*B*), the amount of suppression increased and spread out, eliminating responses at 0, +15, and +45° and reducing the lagging response at most of the other locations as well.

A striking feature of Fig. 1*B* is the complete suppression of the lagging response when the leading stimulus was at 0°, where there was practically no response to the lead, as well as at +45°, where the leading response was greatest. It is important to note, however, that there was weak or no

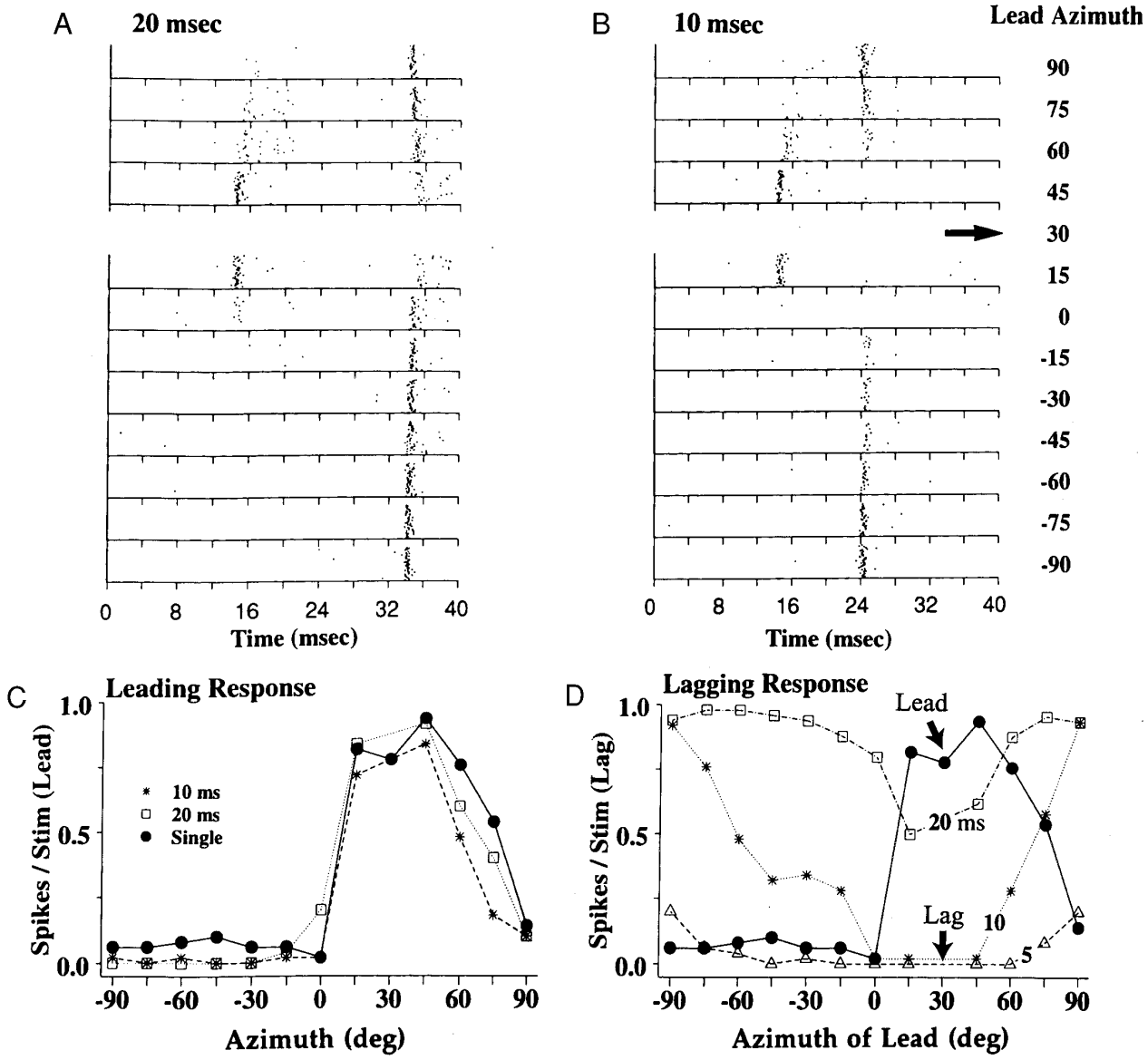

FIG. 1. Modulation of echo suppression by azimuthal location of the leading stimulus in response to clicks [characteristic frequency (CF) = 3 kHz]. *A* and *B*: dot rasters with an interstimulus delay (ISD) of 20 ms (*A*) and 10 ms (*B*). Responses to the leading stimuli occur near 14–18 ms, changing as a function of location from +90° (*top*) to −90° (*bottom*). Responses to the lagging stimulus at +30° are suppressed or occur later in time as summarized in *C* and *D*. *C*: responses to the leading stimulus from *A* and *B* (□ and ∗), as computed from counting spikes in the interval between 12 and 22 ms, and to single clicks (●) as a function of azimuth. *D*: responses to the lagging stimulus from *A* and *B* as a function of the azimuthal location of the leading stimulus. Responses to single clicks from *C* are shown again (●). →, location of the lagging source (+30°); if no suppression occurs, then the lagging response should equal the response of the neuron to a single click at 30°. Responses to the lagging clicks at ISDs of 5, 10, and 20 ms are shown.

suppression of the lagging click when the leading stimulus was at other locations in the ipsilateral field (negative azimuths) where there was no response to the lead. Apparently it is the proximity to the excitatory response area when the leading stimulus was at 0°, rather than the strength of the response to the leading stimulus per se that was critical.

At both 10 and 20 ms delays, the response to the leading sound, which occurred at a latency of ~14–16 ms, was similar, being strongest on the contralateral side between 15 and 45°; no response was observed at the negative azimuth values on the ipsilateral side (Fig. 1, *A* and *B*). These responses of the leading stimulus are plotted as a function of azimuth in Fig. 1*C* along with the response to a single click with no lagging stimulus. The similarity of the three curves in Fig. 1*C* indicates that the response to the leading click was not affected by the presence of the lagging click.

The sensitivity of the suppression to the location of the leading click is summarized by plotting separately the responses to the lagging click (Fig. 1*D*) at 5, 10, and 20 ms as a function of the location of the leading sound as well as the response to single clicks (●). For all delay conditions, the lagging sound was placed at 30° (→), a location at which the neuron responded near maximally. Any decrease in the response below that indicated by the response at 30° reflects

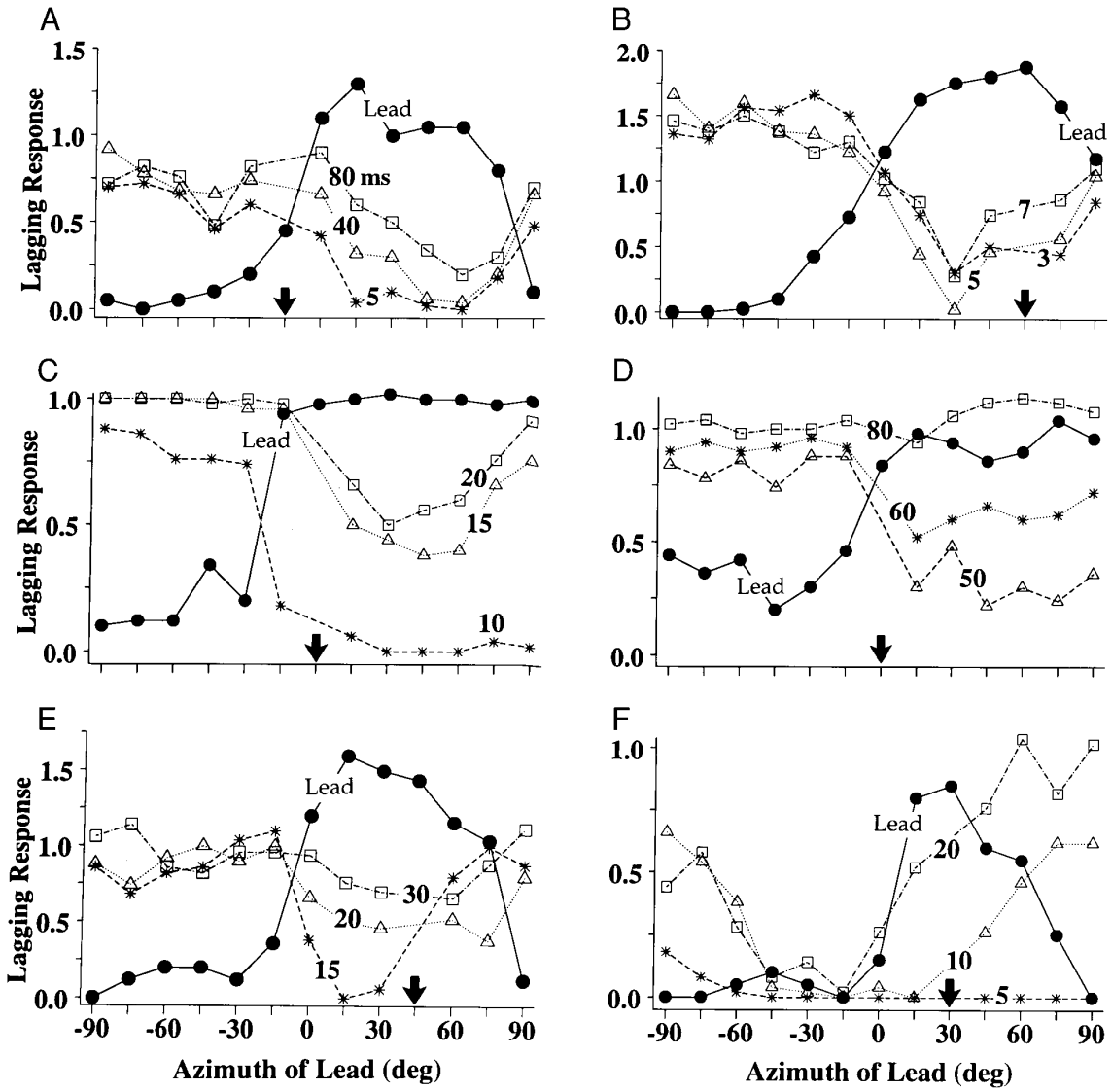

FIG. 2. Responses to the lagging stimulus at various ISDs for 6 neurons as a function of the location of the leading stimulus in the same format as Fig. 1*D*. In *A*–*D* are examples of neurons the ''preferred'' locations of which exert strong suppression with click stimuli. *E*: same effect with noise (5-ms duration, 200-Hz bandwidth, centered at 5.5 kHz). *F*: opposite effect to that seen in *A*–*D*, also with click stimuli; suppression is strongest at locations that are least excitatory for the neuron. CFs of the neurons, from *A* to *F*, were 0.85, 5.9, 6.9, 5.5, 5.5, and 1.6 kHz, respectively.

the suppressive effect of the presence of the leading stimulus. At 20 ms there is a small dip in the response at 15–45°, where the leading stimuli exerts maximal excitation. At 10 ms there is a larger dip, which spreads out so that the response is suppressed even at positions where the neuron does not respond to the leading stimulus at all. Finally, at 5 ms the response is suppressed completely at nearly all positions of the leading sound.

In Fig. 1*D*, the troughs of the lagging responses, which indicate its suppression, occur near the same location as the peak of the leading and single-click response. This shows that the suppression was greatest when the leading sound was located near the point at which the cell responded maximally for single clicks. Most cells in our sample responded similarly, as illustrated for a sample of six cells in Fig. 2. For five of these cells (Fig. 2, *A*–*E*), the suppression is strongest when the leading response is strong, whereas the cell shown in Fig. 2*F* is different in that the suppression is strongest at a point where there is no response to the lead. From our results in the companion paper and those shown in Fig. 1, it is clear that for most units there will be no suppression of the lagging response at any location of the leading stimulus if the ISD is long enough. Likewise if the ISD is small enough, the lagging response may be suppressed at all positions (e.g., 5 ms in Fig. 1). Between these two extremes, we found a variety of suppressive effects in different cells. We were interested particularly in the relationship between the azimuthal position of the lead (and its related response sensitivity) and strength of suppression. Therefore, we compared the suppression evoked when the leading click was located in the middle of the cell's azimuthal response area (usually in the contralateral field) with that evoked when it was in the middle of the unresponsive field (usually in the ipsilateral field). The *lead modulation index* (LMI)

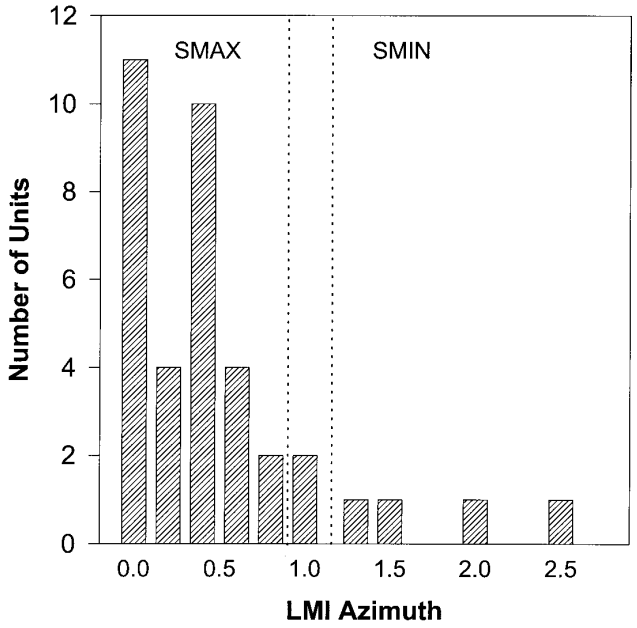

FIG. 3. Distribution of lead modulation index (LMI) for our sample of 37 neurons tested along the azimuth. We arbitrarily define values of LMI <0.8 to be suppression at maximum (SMAX) cells and values of LMI >1.2 to be suppression at minimum (SMIN; boundaries marked by dotted lines).

is the ratio of the lagging response when the lead is in the centroid of the azimuthal response area peak to that in the trough. If maximal suppression occurs when the leading stimulus is near the peak (as in Fig. 1), then the LMI will be small. Clearly, the choice of ISD will greatly affect the LMI: we chose the shortest ISD at which the peak of the lagging response versus azimuth of the lead function (Fig. 1*D*) was >75% of the lagging response by itself and the trough of this function was <50%. In Fig. 1*D* the ISD chosen would be 10 ms because at 20 ms the trough is not low enough and at 5 ms the peak is not high enough to meet the criteria.

The results shown in Fig. 2, *A*–*E*, are exemplary of cases in which the LMI <0.8 because the maximal suppression occurs at positions for which the leading sound elicits maximal response, which we will call suppression at maximum (SMAX). Neurons with LMI >1.2 have maximal suppression at positions for which the leading sound exerts minimal response, or suppression at minimum (SMIN). A typical example is shown in Fig. 2*F*. For single clicks presented in isolation, this unit responded maximally at +15 and +30° (●) but not at negative angles. The lagging sound in this case was placed at +30°, and maximal suppression occurred at −15, −30, and −45°.

Figure 3 shows a histogram of the distribution of LMI for 37 neurons. If there were no modulation of the lag by the azimuth of the lead, we would expect an LMI value of 1, indicating that the lagging response was suppressed to the same degree regardless of the location of the leading response. The majority of units (84%; 31/37) had an LMI <0.8, indicating strong suppression of the lag response for a lead placed in the cell's responsive area (e.g., Fig. 2, *A*–*E*); these are the SMAX units. The SMIN units (11%; 4/37) are ones with an LMI >1.2, where suppression is strongest for a lead placed in the unresponsive field (e.g., Fig. 2*F*). Finally, a small number of units (5%; 2/37) had LMI between 0.8 and 1.2, indicating little or no effect of the lead location on suppression.

There was no correlation between LMI and the ISD that was used to calculate the LMI ($r = 0.11$, $P > 0.5$, not shown). Thus variation of lag suppression with azimuth of the lead occurs in neurons that exhibit suppression at both long and short ISDs. In addition, there was only weak correlation between LMI and CF that was not significant ($r = 0.25$; $P > 0.5$, not shown). The latter insignificant correlation is consistent with results shown in our companion paper (Litovsky and Yin 1998) that suggest a lack of correlation between ISD and CF.

In the previous paper (Litovsky and Yin 1998), we showed that echo suppression is similar for stimuli along the azimuthal or elevational planes. We explored whether that similarity also pertained to the sensitivity of echo suppression to the location of the leading stimulus. In Figs. 4 and 5, we show that the effect of lead location on echo

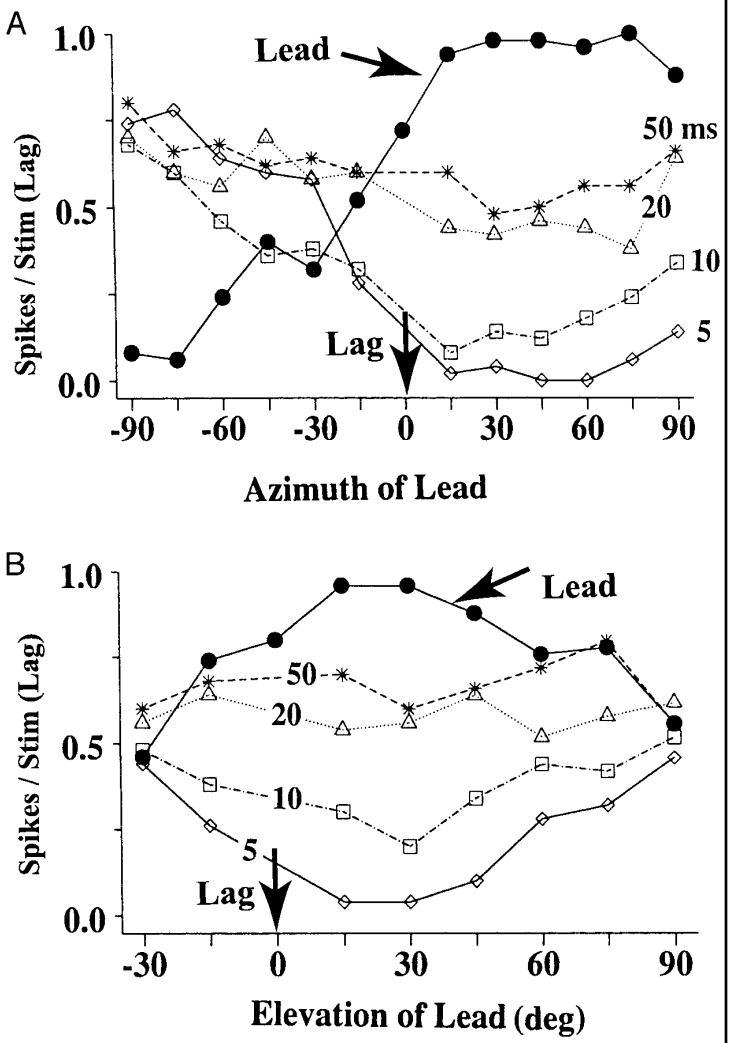

FIG. 4. Comparison of the effect of varying the leading stimulus along azimuth (*A*) or elevation (*B*) in 1 cell (CF = 10 kHz). Same format as Fig. 1*D* except that the leading click was varied along the azimuth (*A*) or elevation (*B*). In both cases, the lagging click was at the same location.

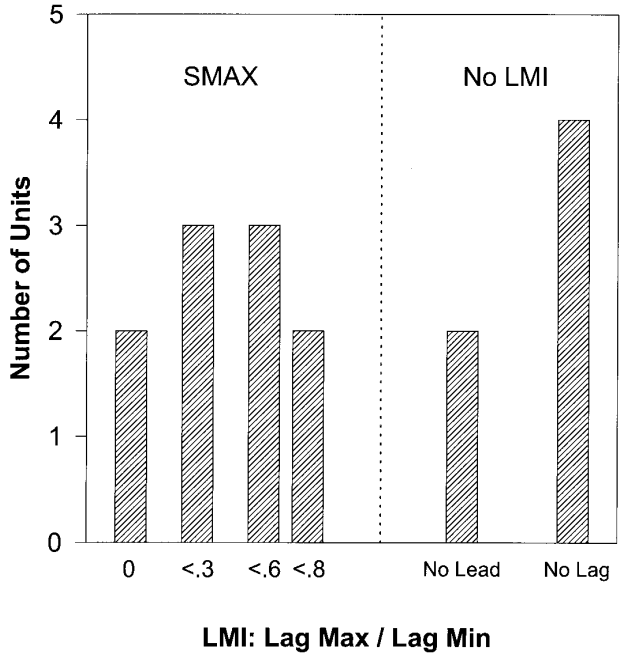

FIG. 5. Distribution of LMI for our sample of 16 neurons tested in elevation. As in the azimuth (Fig. 3), we arbitrarily define values of LMI <0.8 to be SMAX cells and values of LMI >1.2 to be SMIN. In elevation, all neurons fell into the SMAX category. Dotted line separates SMAX neurons and those for which LMI was not measurable due to lack of modulation in either the leading response (No Lead) or lagging response (No Lag).

suppression is similar in elevation and in azimuth. In Fig. 4 we compare the effect of varying the leading stimulus along either the azimuth (*top*) or elevation (*bottom*) in the same cell, while the lagging sound was at (0°,0°), which is common to both axes. Along the azimuth this unit shows clear preference for stimuli presented in the contralateral hemifield, whereas there is a mild sensitivity in elevation, with preferences for locations −15 to +75° and maximal responses at 15 and +30°. In response to sounds that simulate the PE, this unit behaves similarly to the SMAX units shown in Fig. 2 for both azimuthal and elevational pairs: there is more suppression of the lagging response when the leading sound is placed where excitation is strong.

Sixteen neurons were studied for the effect of lead location on suppression of the lagging response in elevation. A histogram of LMI values in elevation is shown in Fig. 5. In 37.5% (6/16) of neurons studied, the LMI was not measurable (indicated as No LMI in Fig. 5): in two neurons, suppression was always either below or above 50% of the maximum response at all delays, and in the other four neurons there was no modulation in the leading response. The remaining 62.5% (10/16) of neurons were all categorized as SMAX, indicating strong suppression of the lag response for a lead placed in the cell's responsive area (e.g., Fig. 4, *bottom*).

Effect of lead location can be studied either by holding the delay constant while many different lead locations are tested, as was done to generate the data for Figs. 1–5, or by holding the lead location constant while testing many different delays. In Fig. 6 we show the effect of lead location on strength of echo suppression as a function of ISD, comparing azimuth and elevation. Figure 6*B* shows rate-azimuth functions, and Fig. 6*D* shows rate-elevation functions for single clicks. For each axis, the lag was placed at −15°, and we ran four conditions that varied in the location of the lead with ISDs from 1 to 101 ms. As expected, lagging responses were influenced strongly by lead location, usually with maximal suppression exerted by lead stimuli that were near the peak of rate functions on the right, as in the cases shown earlier (Figs. 1 and 2). Similarly, at locations below (−30°) and above (+75°) in elevation, where there was only a weak response to single clicks (Fig. 6*D*), the cell exerted only weak suppression; however when the lead was near front at +15° and +30°, where the unit responded strongly to the lead, there was also strong suppression (Fig. 6*C*).

Studies on the effect of stimulus location on half-maximal ISD described thus far were all conducted in free field where spatial selectivity is based on the natural interaural disparities in time and level and on spectral cues (Hebrank and Wright 1974; Middlebrooks and Green 1991; Searle et al. 1975). Fitzpatrick et al. (1995) also studied the effect of varying the spatial cues in the leading stimulus under dichotic conditions in ICC of the awake rabbit by varying the interaural time difference (ITD) in the leading click while holding the lagging click constant. In contrast to our findings of a large majority (84%) of SMAX cells, Fitzpatrick et al. (1995) found about an equal number of SMAX and SMIN cells. To see whether the presence of the other localization cues might account for this difference, we also studied cells under dichotic conditions and varied ITD. The PE was simulated under dichotic conditions by presenting pairs of clicks that varied in ISD and had ITDs imposed separately for each click pair (Fig. 1*B* of Litovsky and Yin 1998). In this manner, the leading and lagging click pairs could simulate independently a lateralized location along the azimuth. Plotted in Fig. 7*A* is an ITD function for one cell, with a maximum at +200 μs and a weaker response at −200 μs. The paradigm here was to hold the ITD of the lagging click pair at the ITD of maximal response (+200 μs), while the lead ITD was set to either the maximal (+/+) or the minimal (−/+) condition. Compared in Fig. 7*B* are the lagging responses, normalized under both conditions by the response to the click presented at +200 μs in isolation. Stronger suppression was exerted when the leading sound was at the peak (+/+) than when it was at the trough (−/+) (Fig. 7*B*). For that reason, this response type was analogous to the SMAX units described in preceding text, with a difference of 15 ms between half-maximal delays in the +/+ (39 ms) and −/+ (24 ms) conditions.

In Fig. 8*A* we show two additional units. In one (△, ▲), the suppression is stronger in the +/+ condition (half-maximal delay of 14 ms) than in the −/+ condition (half-maximal delay $<$ 1 ms). Thus, this cell also would be comparable to an SMAX unit using free-field stimuli, though it had a much lower half-maximal delay than the one shown in Fig. 7. The second unit (○, ●) exemplifies a cell type for which the amount of suppression did not vary with ITD of the leading click pair. Nineteen units were studied under these conditions, and the population data are summarized in Fig. 8*B* as a correlation plot of half-maximal delays for −/+ and +/+ conditions. The majority of units (74%; 14/19) fell into the SMAX category, with +/+ thresholds exceeding those of −/+ by $>$10%. One neuron (5%) showed

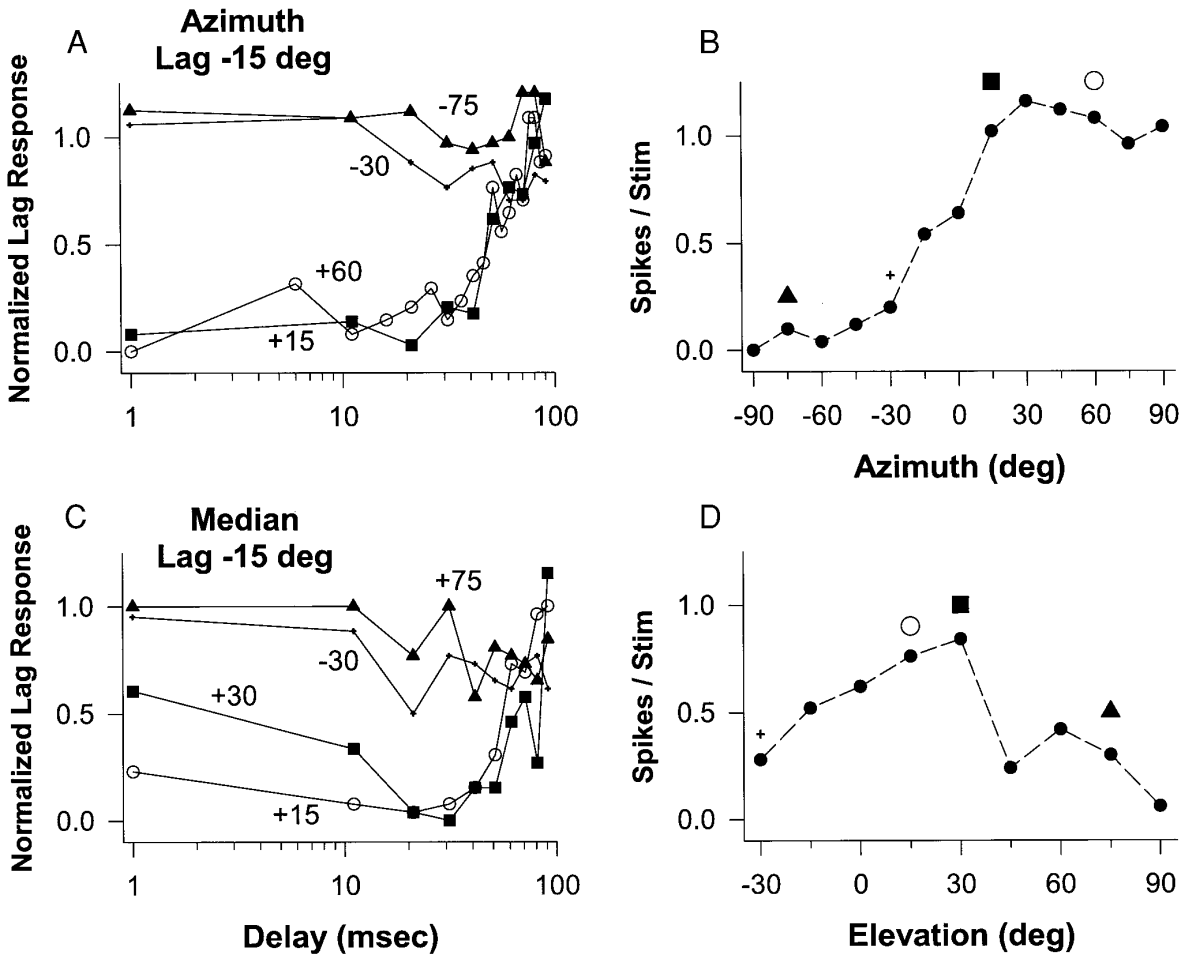

FIG. 6. Recovery curves (*left*) and response areas (*right*) for 1 cell at different leading locations along the azimuth (*top*) or median sagittal plane (*bottom*). Stimulus was a 5-ms noise burst with a 200-Hz bandwidth centered at the cell's CF of 3 kHz. The lagging stimulus was held at (−15°,0°) (*top*) or (0°,−15°) (*bottom*). *Left*: recovery curves for precedence stimuli with 4 different leading speakers and the same lagging speaker. *Right*: neuron's responses to single clicks varying in azimuth (*top*) or elevation (*bottom*). Locations of the 4 different leading speakers are indicated by the corresponding symbols on the *right.*

the opposite effect of suppression with −/+ being 2.6 times stronger than that for the +/+ condition. A third group of units (21%; 4/19), such as the unit in Fig. 8*A* (○, ●), showed no effect (i.e., differences <10%). These data suggest that modulation in effectiveness of the leading stimulus as a function of ITD is similar to that as a function of location of the leading stimulus. However, ITD is not necessary for this modulation because similar effects are seen in elevation in the absence of ITDs (Figs. 4 and 5).

Effect of relative stimulus level

To study the effect of varying the relative levels of the lead and lag, one could either maintain the level of the lag constant and vary the leading level or vice versa. In Fig. 9 we show results from one unit using the first manipulation in which the level of the lagging click was held constant at 40 dB and the lead level varied from 30 dB (below threshold) to 60 dB in 5-dB steps. This manipulation was repeated at delays of 10, 20, and 30 ms. The response to the leading click, which occurs at a latency of ~12 ms, is very similar for all three ISD conditions: there is little or no response at 30 and 35 dB with progressively stronger responses as the lead level is increased. The effect of the leading click on the lagging response, which occurs at a time of about (ISD + 12) ms, is most apparent at high levels: there is complete suppression at ISD of 10 ms, only weak suppression at 30 ms, and an intermediate response at 20 ms. In this cell, there is little suppression seen when the leading response is at or below threshold (30–40 dB). Hence, we see a strong trade-off between level and delay, a phenomenon that has long been documented in psychophysics of the PE (Blauert 1983; Wallach et al. 1949; Yost and Soderquist 1984).

Figure 10, *A* and *B,* presents summary data from Fig. 9 and from the same unit for stimuli in the median plane, respectively. In both cases, at the shortest delay tested (10 ms) where suppression is maximal, the lagging response recovers to 0.5 when the lead is ~45 dB. In addition, on both planes, there is a clear trade-off between delay and level, with suppression weakening at the longest delays or at lower stimulus levels for the lead. The effect of varying lead level also is found in cells with much shorter echo thresholds, such as the cell shown in Fig. 10*C* where the echo threshold lies between 4 and 6 ms when both lead and

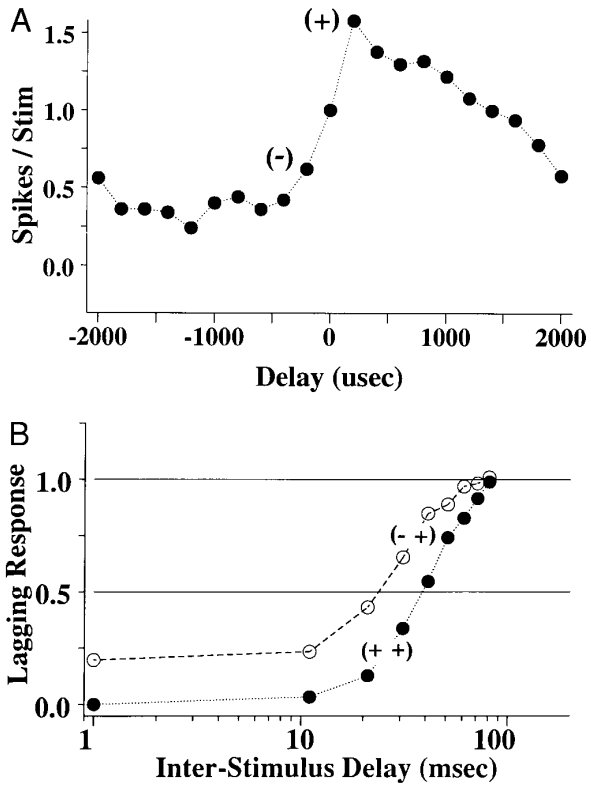

FIG. 7. Lagging responses of 1 neuron (CF = 1 kHz) under dichotic conditions depend on the ITD of the lead. *A*: discharge rate as a function of ITD. This neuron shows a peak at +200 μms with a decreased response at negative ITDs. *B*: lagging response is plotted as a function of ISD. Lagging stimulus was held constant at +200 μm, and the leading stimulus was set to either +200 (+/+) or −200 (−/+) μm.

lag are at 60 dB. With ISD = 8 ms, there is virtually no suppression until the leading click is raised to 80 dB.

For all units studied (n = 17), increasing the level of the leading stimulus while holding the lagging stimulus constant had the effect of increasing suppression. The same result can be obtained by varying the level of the lagging stimulus for a constant lead as shown in Fig. 10*D*, this time as a function of ISD. For this unit, we held the leading click at 70 dB, ~15–20 dB above threshold, and set the lagging level to either 55, 57, or 60 dB. As expected, the lowest level lagging click is easiest to suppress, and the amount of suppression decreases accordingly as the lag level is increased from 55 to 60 dB, but this effect was only studied in a few cells. Similar results have been presented by Yin (1994).

Effects of lead duration

Thus far, we have considered the effect of the position and level of the leading stimulus on the degree of suppression of the lagging stimulus. For both position and level, the amount of suppression was correlated with the response to the leading sound: the stronger response, the more suppression. Another parameter we tested was the effect of varying the duration of the leading stimulus. If the same principles hold for duration as for position and level, we would expect more suppression with longer duration leading stimuli.

The protocol again was to change the leading sound while holding the lagging sound constant. This experiment was only conducted in free field, and in 86% (12/14) of neurons studied, increasing duration of the leading sound produced increased suppression. Responses from two units are shown in Fig. 11. In both cases, the lagging stimulus duration was set constant at 5 ms and the leading durations were varied between 5 and 40 ms. Figure 11*C* plots the half-maximal ISD as a function of the duration of the lead: for both cells, suppression was stronger for the longer duration leading stimuli. In two other units, there was no clear trend of the effect of increasing the lead duration on suppression for the durations tested; from 5 to 15 ms in one case and from 15 to 20 ms in the other. Finally, the effect of changing stimulus duration for the leading source also was observed when the manipulations were conducted in elevation. Figure 12 shows responses with the lagging source at 0° for both azimuth and elevation for the same unit. The leading sources on the

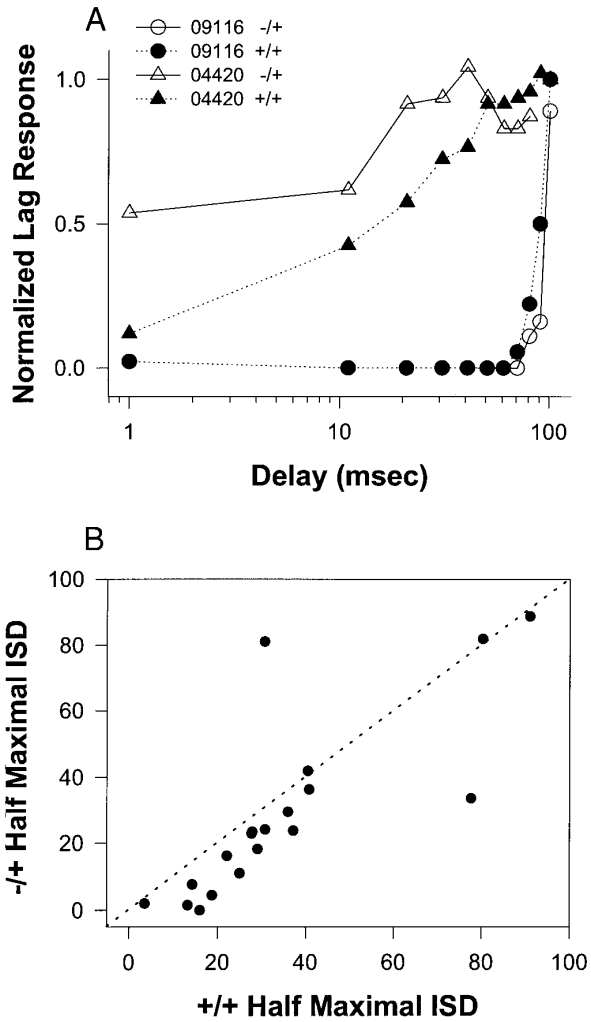

FIG. 8. Effect of ITD on echo suppression. *A*: responses of 2 neurons comparing the effect of 2 different values of ITD in the leading click pair. Format is same as in Fig. 7*B*. ● and ▲, represent the +/+ condition, in which the leading stimulus is at the ''preferred'' ITD; ○ and △, −/+ condition. For 1 neuron (△ and ▲; CF = 18 kHz), stronger suppression is observed in the +/+ condition, whereas for the 2nd neuron (● and ○; CF = 2.7 kHz), there is little difference. *B*: comparison of *echo thresholds* under the +/+ and −/+ conditions for the population of neurons (n = 19).

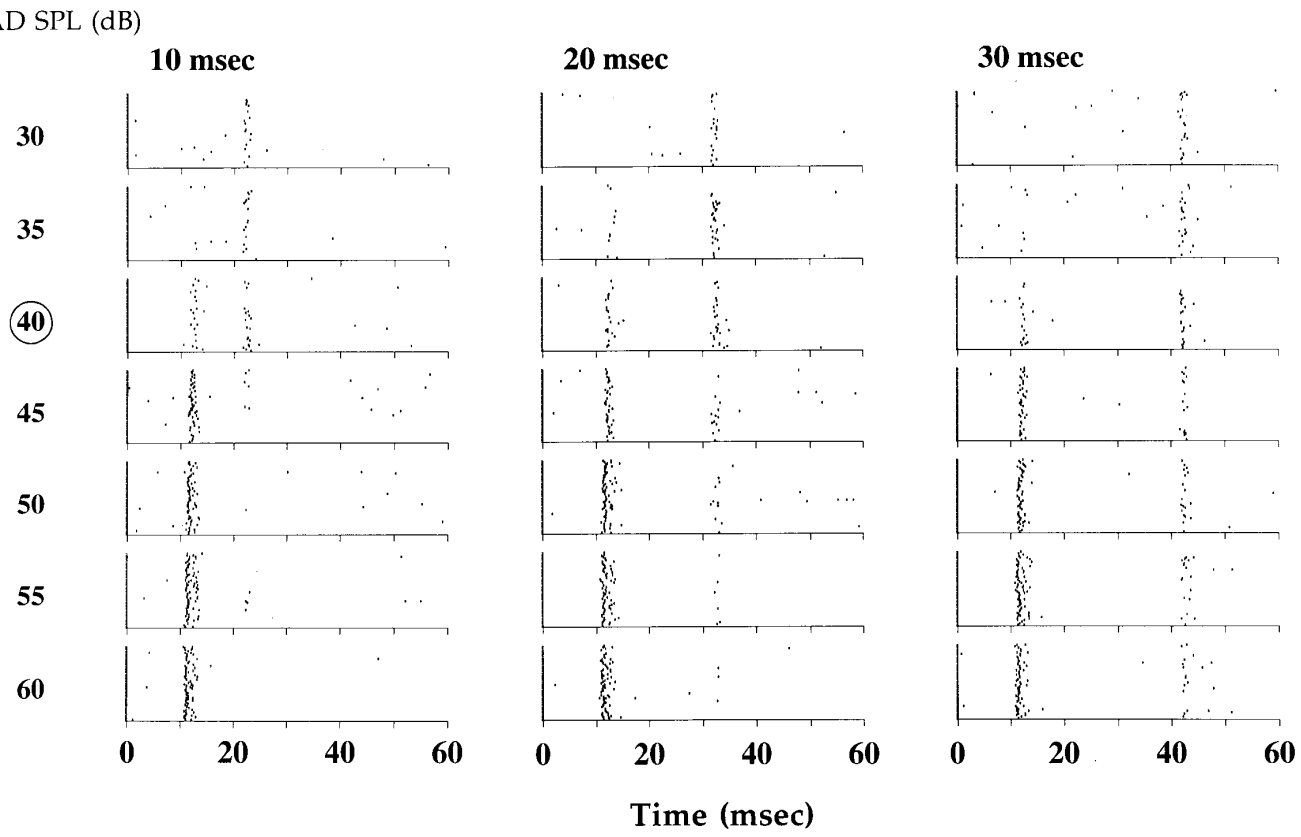

FIG. 9. Effect of the sound pressure level (SPL) of the lead. Leading click SPL was varied from 30 to 60 dB in 5-dB steps, whereas the SPL of lagging click was held constant at 40 dB at ISDs of 10, 20, and 30 ms. Leading click was at (+90°,0°) while lagging click was at (0°,0°). CF of the cell was 2.7 kHz.

azimuth (+90°) and elevation (+90°) were chosen so that the responses exhibited similar discharge rates. In both cases, there is an increase in the strength of suppression as the duration of the leading stimulus was increased, with remarkable similarity in the shapes of the functions along azimuth and elevation.

Binaural versus monaural stimulation

In a small number of neurons ($n = 9$), we compared the suppression observed under binaural and monaural contralateral conditions. We did not study the monaural ipsilateral condition because in most cases stimulation to the ipsilateral ear alone did not evoke a lagging response that was robust enough to study. Figure 13 shows three examples of binaural and monaural recovery curves that correspond to three classes of responses seen: neurons in which suppression under binaural conditions is stronger than under monaural contralateral conditions by ≥10% ($n = 3$; Fig. 13*A*), neurons with a difference <10% between the two conditions ($n = 4$; Fig. 13*B*), and neurons in which suppression under monaural conditions is stronger than under binaural conditions by ≥10% ($n = 2$; e.g., Fig. 13*C*). Figure 14 shows a correlation plot of half-maximal ISD for binaural/monaural and CF. The correlation of 0.75 was significant ($P < 0.05$), suggesting a tendency for neurons with higher CFs to display stronger suppression under binaural conditions than under contralateral conditions.

DISCUSSION

In this paper, we have examined the effect of different parameters of a leading stimulus on suppression of a lagging one in the context of the PE, using the general paradigm of varying the leading stimulus while holding the lagging one constant. The aim was to probe the neural mechanisms of the suppression by determining which characteristics of the leading sound influence it. In general, we found that for most but not all cells, whatever stimulus parameter led to a stronger response to the leading stimulus also proved to be a more effective suppressor. The parameters we explored included stimulus location, ITD, duration, and SPL.

Effect of stimulus location and ITD

The IC is thought to be important in encoding the auditory cues that facilitate sound localization because individual neurons in the IC are sensitive to ITDs and ILDs, which presumably dictates their selectivity for certain azimuthal locations in space. In this paper, we exploited this feature of IC neurons to study the importance of stimulus location for physiological correlates of the PE. We found that for most units (84%), stronger suppression occurs when the leading stimulus is presented from locations that are most excitatory for the neuron. A simple explanation of this phenomenon would be to assume that once a neuron has been excited maximally, it is rendered incapable of responding to the lagging sound for a certain time period. However, this

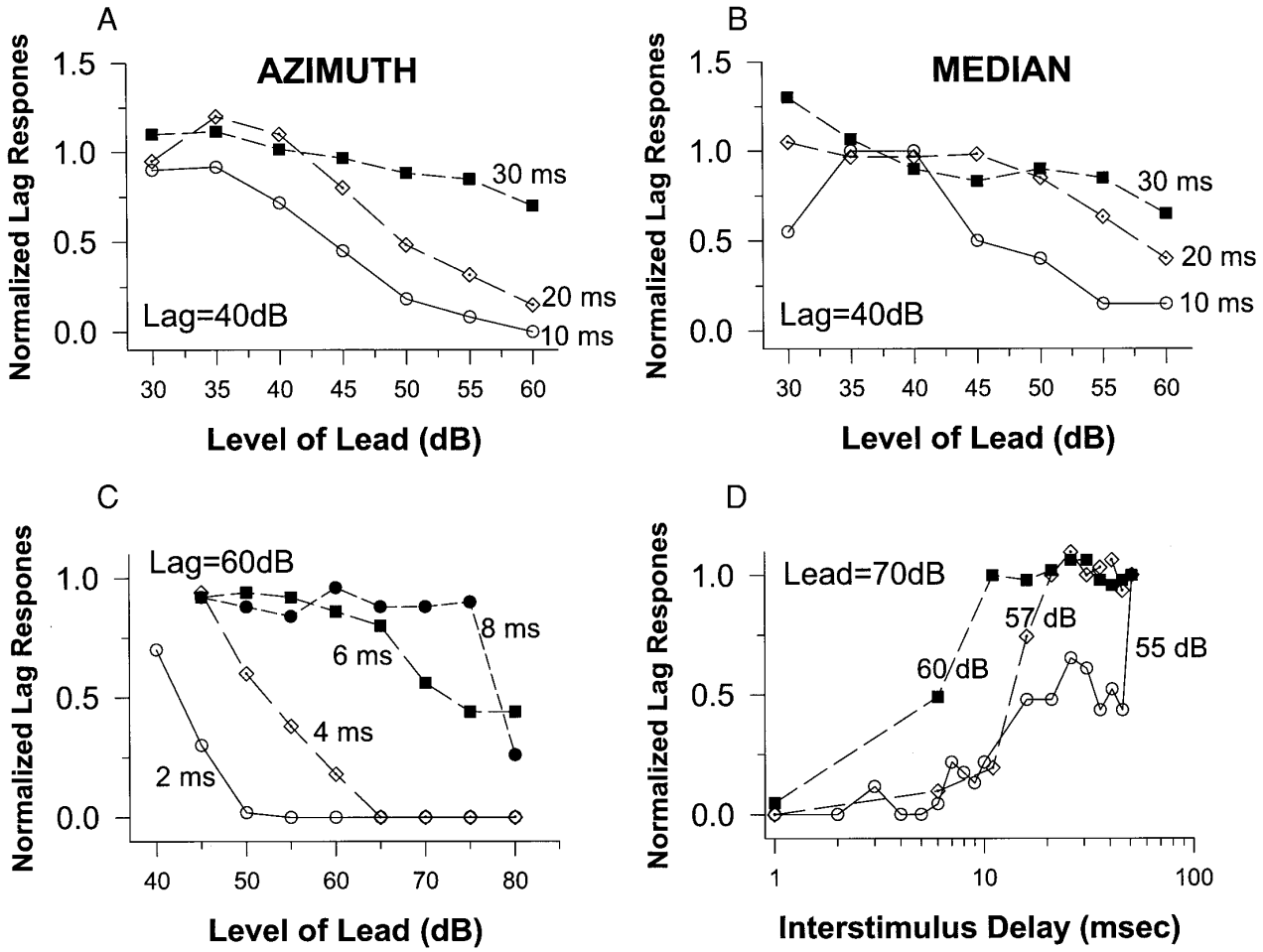

FIG. 10. Effect of the SPL of leading (*A–C*) or lagging (*D*) clicks on suppression in the azimuthal and elevational planes. *A*: lagging responses of the data in Fig. 7. Each curve represents the lagging response at 1 ISD plotted as a function of the SPL of the leading stimulus. *B*: for the same neuron shown in *A*, the leading SPL also was varied along the elevation. In both *A* and *B*, the lagging click was positioned at (0°,0°), and the leading stimuli at locations that elicited similar discharge rates when presented alone (CF = 2.7 kHz). *C*: lagging responses of another neuron, plotted as a function of lead SPL at ISDs between 2 and 8 ms. The lagging source was located at −45° at 60 dB SPL, and the leading source was at +45° and SPL varied from 35 to 75 dB (CF = 2.5 kHz). *D*: recovery curves for a cell (CF = 9.3 kHz) at 3 different SPLs of the lagging click. Leading stimulus at +75° was held constant at 70 dB, whereas the lagging stimulus at +30° was set to either 55 (○), 57 (◇), or 60 dB (■).

explanation is not convincing for several reasons. First, the refractory period of IC neurons is much shorter than the suppression, which lasted up to tens of milliseconds and sometimes >100 ms. Second, for many neurons, suppression of the lagging response could occur even when the neuron did not respond to the leading source, e.g., Fig. 1*B* at 0° azimuth. Third, a small sample of our cells, the SMIN cells, showed more suppression of the lagging stimulus when the response to the leading stimulus was minimal (Fig. 2*F*).

We found comparable suppression sensitivity with dichotic stimulation, where maximal suppression was usually found in the +/+, rather than the −/+, condition, that is, greater suppression when the leading stimulus was set at a favorable, rather than unfavorable, ITD (Figs. 7 and 8). However, Fitzpatrick et al. (1995) in the awake rabbit ICC using dichotic stimulation reported that the incidence of SMIN responses was about equal to that of the SMAX type, whereas we found 84% SMAX units using free-field location and 74% +/+ units using dichotic stimuli. The explanation for these differences is not clear, although two obvious differences in preparation stand out as likely candidates: the difference in species and in anesthetic state.

Our underlying hypothesis is that the suppression is caused by a long-lasting inhibition evoked by the leading stimulus. The modulation of suppression with the location or ITD in most ICC cells of our sample places constraints on the source of the inhibition to cells that are themselves sensitive to stimulus location or ITD. This eliminates monaural nuclei, such as the cochlear nucleus (Wickesberg and Oertel 1990) or certain nuclei in the superior olive, as a possible source of inhibition at least for SMAX and SMIN cells.

Psychophysical data comparing the relative locations of the leading and lagging sources are limited and conflicting. Some studies have found that the PE is stronger when the difference between the leading and lagging ITDs or spatial locations is larger (Boerger 1965; Shinn-Cunningham et al. 1993). However, those studies did not measure echo thresh-

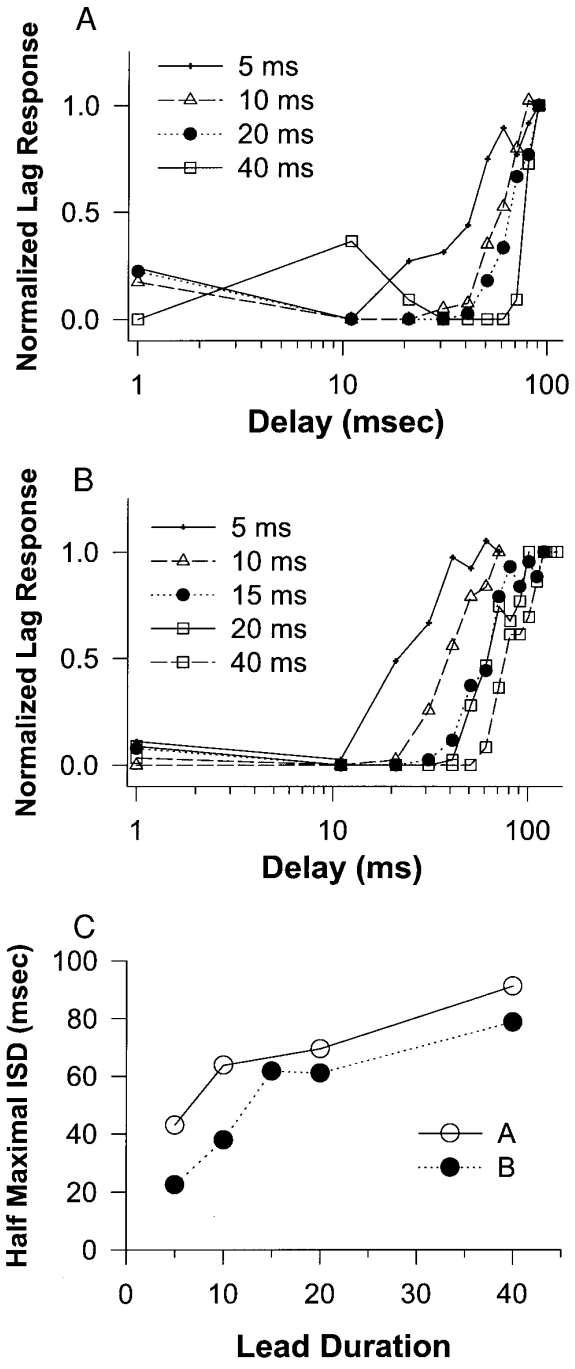

FIG. 11. Responses of 2 different neurons (*A* and *B*) to variations in the duration of the leading stimulus. Both neurons were tested with a noise of 200-Hz bandwidth, centered at CF (3 kHz in *A* and 10 kHz in *B*). In both cases, the lagging source had a constant duration of 5 ms but the duration of the leading source was varied. Respective leading and lagging source locations were +60 and −15° in *A*, and 45 and 30° in *B* along the azimuth. *C*: half-maximal ISDs are plotted as a function of lead duration for the neurons in *A* (○) and *B* (●).

olds but rather other aspects of the PE. Recent work by Litovsky and colleagues (Hawley et al. 1997; Litovsky and Colburn 1998) in which echo suppression was measured suggests that the PE is strongest when the lead and lag arise from the same location and weakens as the physical separation between the sources increases. These findings suggest that SMAX units should be more prevalent in the auditory pathway, a condition we found to be true in this study.

Results comparing the effect of lead location in azimuth and elevation suggest a weaker modulation effect in elevation. Whereas modulation was measurable using our LMI measure in all neurons studied in the azimuth ($n = 37$), in 37.5% (6/16) of neurons, modulation was not measurable in elevation because the elevational modulation was too weak. Because for most cells the amount of suppression was dependent on the strength of response to the leading stimulus, the effectiveness of location to modulate the suppression will depend on the degree to which the cell is sensitive to or modulated by stimulus location. Moreover, because most cells in the IC are more sensitive to variations in azimuth than to elevation, it is not surprising that the modulatory effect of lead location on suppression of the lag is more pronounced in azimuth than elevation. In addition, the average LMI was somewhat higher (indicating weaker modulation) in elevation (0.43) than in the azimuth (0.23), although the difference was not statistically significant ($P > 0.05$). A more striking difference between azimuth and elevation is the absence of SMIN responses in elevation, although this result was based on a small sample ($n = 16$).

Effect of lead level and duration

Our findings on the effect of varying the leading source level are consonant with psychophysical results, which show

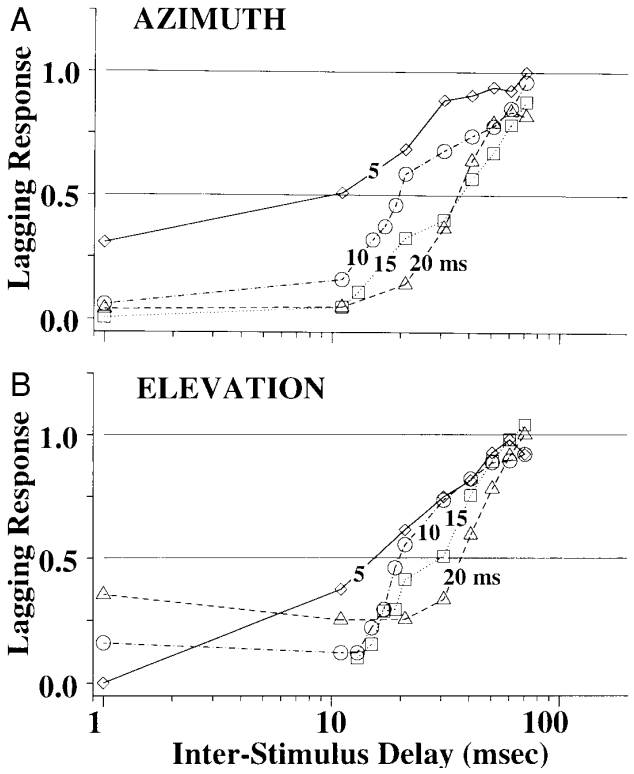

FIG. 12. Responses of 1 neuron to variation in duration of the leading stimulus on azimuth or elevation. Stimuli were noise bursts with bandwidth of 200 Hz centered at CF (2.4 kHz). For both *A* and *B*, the lagging stimulus was at 0°, and the leading stimuli were at 90° on either the azimuth (*A*) or elevation (*B*); at these 2 locations, the lead elicited similar discharge rates. Durations of the leading stimuli are marked with the same symbols in the 2 graphs, at 5 (◇), 10 (○), 15 (□), and 20 (△) ms.

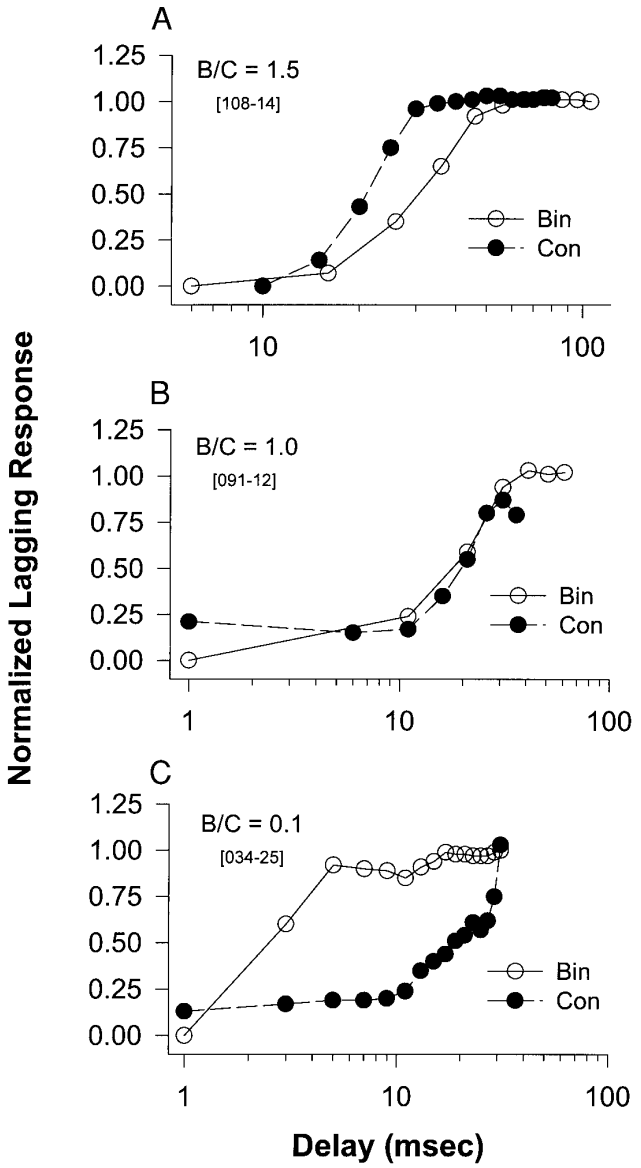

FIG. 13. Monaural contributions to the precedence effect (PE) under dichotic conditions. In all 3 panels, stimulation was either binaural (Bin) or to the contralateral ear alone (Con). Lagging responses were standardized for each condition with its own lag response at the maximum ISD. The panels illustrate neurons that show stronger suppression under binaural conditions (*A*), no difference between the 2 conditions (*B*), and stronger suppression under the contralateral condition (*C*). Ratios of binaural/contra half-maximal ISDs are marked in each plot

that increases in the level of the lagging stimulus reduce echo thresholds, and an opposite effect occurs when the lag level is decreased (Babkoff and Sutton 1966; Blodgett et al. 1956; Thurlow and Parks 1961). Yin (1994) also has reported similar results in studies on PE in the IC. At this point, we must note that the standard manner in which the PE is studied (including our own work) does not actually simulate ''realistic'' reverberations. In a normal reverberant environment, reflections are filtered and attenuated depending on the reflective surface. Because a reduction in the lagging stimulus level results in stronger suppression (Fig. 12), our studies and those of others on the PE are most likely underestimating the strength of echo suppression that occurs in normal listening environments. Finally, our results are not surprising when incorporated into a conceptual network of binaural mechanisms. In a model of PE in the IC, Cai et al. (1998a,b) found that the effect of leading level on suppression is easy to generate. By increasing the amount of excitation in the contralateral MSO, the resulting effect in the IC is that of increased inhibition through the contralateral dorsal nucleus of the lateral lemniscus (DNLL).

Monaural responses

Our preliminary results (Fig. 14) and similar findings by Yin (1994) show that there is little difference in the echo suppression under binaural or monaural conditions. A preliminary interpretation of these data might suggest that the PE is mediated by monaural circuits such as those reported in the cochlear nucleus. However, one must bear in mind that the IC receives bilateral inputs, thus presenting stimuli that are monaural does not mean that one is studying a monaural circuit directly. Most IC neurons are responsive to monaural stimuli, but any of the suppression in the circuit could be mediated in lower binaural structures but still measured with a monaural stimulus. A more direct measure of monaural echo suppression would be to record from peripheral neurons in the auditory system before the site of primary binaural interaction, such as the auditory nerve and cochlear nucleus (see next section).

Neural mechanisms that might be involved in the PE

Experiments discussed in the present paper and in the preceding one (Litovsky and Yin 1998) were aimed partially at comparing the activity of single neurons in the IC with known psychophysical phenomena. A second aim, and perhaps a more challenging one, is that of providing information that would help to identify the neural circuits responsible for mediating the suppressive effects. It must be noted that although we found correlates of precedence in responses of cells in the IC, the initial site generating these effects may be in its inputs. The IC holds an integral place in the central auditory system because a substantial number of inputs from

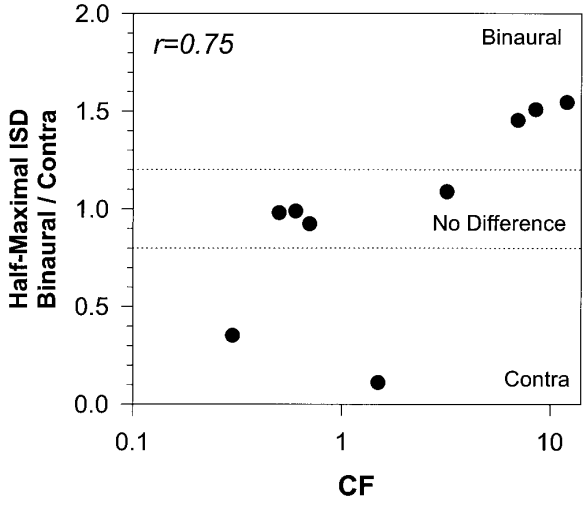

FIG. 14. Correlation plot of ratio of half-maximal ISD binaural/contralateral and CF ($r = 0.75$).

lower structures converge in the IC, and many of them contribute significantly to the response properties of IC neurons (Cant and Hyson 1992).

Several findings reported here suggest that inhibitory mechanisms might be involved in processing PE stimuli. At long ISDs, all neurons responded to both leading and lagging sources as if they were delivered alone. As the ISDs were shortened, the lagging response became suppressed, although the ISD of half-maximal suppression varied considerably within the population, ranging from 2 to 100 ms. Under many conditions, the leading stimulus need not have elicited a response for the suppression to occur.

Yin (1994) proposed five possible sources for the inhibition that is thought to underlie suppression of the lagging response: the auditory nerve, intrinsic circuits in the cochlear nucleus, medial nucleus of the trapezoid body (MNTB) and lateral nucleus of the trapezoid body (LNTB) inhibition to the MSO, DNLL inhibition to the ICC, and intrinsic circuits in the ICC itself. First, auditory nerve fibers have been shown to exhibit a form of forward masking (e.g., Harris and Dallos 1979; Smith 1979). Recently, using a two-click paradigm, Parham et al. (1996) observed suppression of a lagging click in most auditory-nerve fibers studied. However, the maximal ISD at which suppression was observed ($<$10 ms) is much shorter than the values we have observed in the IC. Second, Wickesberg and Oertel (1990) described, at the level of the cochlear nucleus, an anatomic circuit, which they proposed to provide inhibition at short ISDs. However, our finding that the modulatory effect is ITD dependent, as well as recent physiological data (Wickesberg 1996), does not support the presence of additional suppression in the ventral cochlear nucleus beyond that which is found in the auditory nerve. Suppression at this level, for neurons that recover at short ISDs, might be involved in the non-ITD-dependent suppression, such as that observed in the median plane.

Third, anatomic evidence suggests that the MSO receives inputs from the lateral and medial nuclei of the trapezoid body (Cant and Hyson 1992; Kuwubara and Zook 1991; Smith et al. 1989) that are thought to be glycinergic and therefore inhibitory (Helfert et al. 1989; Wenthold et al. 1987). Intracellular recordings made in the MSO of the guinea pig have revealed that electrical stimulation in the trapezoid body produces large inhibitory postsynaptic potentials (Grothe and Sanes 1993; Smith 1995). Although stimuli with a precedence configuration have not been studied in the superior olivary complex, studies on ITD sensitivity with delayed stimulation in one ear relative to the other have shown that cells in the MSO display long-lasting suppression (Moushegian et al. 1967; Rupert et al. 1966) similar to that observed in the IC by Carney and Yin (1989). Inputs from the MSO to the IC are therefore possible candidates for mediating some of the inhibition observed at the level of the IC, but the MNTB and LNTB, like the cochlear nuclei, are probably both primarily monaural nuclei and therefore cannot mediate any ITD- or azimuth-sensitive inhibition.

Fourth, as suggested by Yin (1994) and Fitzpatrick et al. (1995), inhibitory inputs from both the ipsilateral and contralateral DNLL to the IC (Oliver and Schneiderman 1991; Schneiderman et al. 1988) are the most likely candidates for suppression. Because DNLL cells, like MSO cells (Yin and Chan 1990), are sensitive to ITDs (and therefore presumably also to azimuth in free field), they could mediate either stronger suppression by a leading source placed in the peak of the cells' azimuthal response area (SMAX) or stronger suppression by a leading source placed in the trough of the response area (SMIN). In this model, the SMAX cells in the IC presumably would receive more inhibition from the ipsilateral DNLL than from the contralateral DNLL. Likewise, the SMIN cells in the IC would receive stronger inhibition from contralateral DNLL than from the ipsilateral DNLL. Physiological experiments in which the DNLL has been inactivated support this hypothesis (Yang and Pollack 1994).

Finally, a fifth possible source of suppression is the inhibition that is generated within the IC by collateral circuits (Oliver et al. 1994). As Yin (1994) points out, the finding that suppression often occurs in the absence of a response to the leading source suggests that our results cannot be accounted for entirely by this recurrent inhibitory circuit. However, because some degree of suppression is observed even when the leading stimulus does not activate the cell, these are not likely collaterals from the same cell.

Thus the location and ITD sensitivity of the suppression point to the ipsilateral and contralateral DNLL as the likely source for the long-lasting inhibition in the ICC. This suggests that most ICC cells receive predominant inhibitory input from the ipsilateral DNLL because most are SMAX, whereas the SMIN cells receive predominant contralateral DNLL inhibition. The excitatory input is presumed to project to the ICC in parallel pathways through the ipsilateral MSO and contralateral LSO for low and high CF neurons that are sensitive to ITDs and ILDs, respectively. A simplified model of a typical low-frequency SMAX cell is that it receives excitatory input from the ipsilateral MSO and inhibitory input from the ipsilateral DNLL. Likewise, a high-frequency SMAX cell receives its predominant excitatory inputs from the contralateral LSO. All of these inputs are azimuth sensitive, either through ITD or ILD sensitivity. The degree to which the peaks of the azimuthal response areas and the troughs of the lagging responses (when plotted as a function of azimuth location) in Figs. 1*D* and 2 line up is a measure of the congruence of the peaks of the excitatory and inhibitory response areas.

Possible relation to psychophysics

The precedence effect actually refers to several perceptual phenomena that are experienced when listeners are presented with stimuli that are similar to those used here (e.g., Litovsky et al. 1997a,b). *Fusion,* which refers to the perceptual absence of the lag as an independent auditory event (Blauert 1983), is most analogous to the neural responses measured in the present study in which the response to the lag is measured. Several lines of evidence suggest that at least some aspects of fusion may be achieved by the monaural system. First, fusion is most robust for clicks at ISDs of 1–8 ms, the same ISDs at which suppression occurs in the monaural circuits (see *Binaural versus monaural stimulation*). Second, fusion is experienced at similar delays by listeners with profound monaural deafness and listeners with normal binaural hearing (Litovsky et al. 1997a). Third, fusion is experienced at similar delays in the azimuthal and median planes, where binaural and monaural spectral cues, respectively, dominate localization.

Two lines of evidence suggest that fusion cannot be accounted for entirely by the monaural system. First, the suppression seen in IC extends out to much longer delays (>100 ms) than that seen in the auditory nerve or cochlear nucleus (<10 ms). Second, because the evidence for suppression at the level of the auditory nerve and cochlear nucleus represent neural responses under monaural conditions, it cannot account for the dependence of suppression on the azimuth or ITD of the lead observed in most neurons (e.g., Figs. 1 and 2, and 7 and 8 for azimuth and ITD, respectively). Although these arguments have been made by Yin (1994), the present paper provides more definitive evidence for the sensitivity to azimuth effect, thereby making the monaural effects less probable.

Finally, other than fusion, perceptual aspects of precedence such as the dominant effect of the leading source on the perceived location of the fused image and the inability of listeners to discriminate changes in the locations of the lag, appear to be more robust under binaural than monaural conditions (Litovsky et al. 1997b; R. Y. Litovsky, R. M. Dizon, and H. S. Colburn, unpublished data). Investigations of neural correlates of these effects may help to further elucidate the roles that various levels of the auditory circuit mediate in the precedence effect.

The authors are grateful to the staff of the Dept. of Neurophysiology for technical support, in particular to R. Kochhar and J. Sekulski (software); I. Siggelkow, J. Ekleberry, and J. Meister (histology); T. Stewart (photography); C. Dizak (illustrations); and R. Olson (hardware). We thank D. Fitzpatrick, D.R.F. Irvine, S. Kuwada, and L. Carney for comments on previous versions of this manuscript.

This work was supported by National Institute of Deafness and Other Communicative Disorders Grants DC-00116 and DC-00078.

Present address and address for reprint requests: R. Litovsky, Dept. of Biomedical Engineering, Boston University, 44 Cummington St., Boston MA 02215. LITOVSKY@ENGA.BU.EDU.

Received 26 August 1997; accepted in final form 29 May 1998.

REFERENCES

BABKOFF, H. AND SUTTON, S. End point of lateralization for dichotic clicks. *J. Acoust. Soc. Am.* 39: 87–102, 1966.

BLAUERT, J. *Spatial Hearing*. Cambridge, MA: MIT Press, 1983.

BOERGER, G. On the persistence of the directional sensation in hearing, *Proc. 5th Int. Congr. Acoustics*, LiJge, 1965, B27.

BLODGETT, H. C., WILBANKS, W. A., AND JEFFRESS, L. A. Effect of large interaural time differences upon the judgment of sideness. *J. Acoust. Soc. Am.* 28: 639–643, 1956.

CAI, H., CARNEY, L. H., AND COLBURN, H. S. A model for binaural response properties of inferior colliculus neurons. I. A model with ITD-sensitive excitatory and inhibitory inputs. *J. Acoust. Soc. Am.* 103: 475–493, 1998a.

CAI, H., CARNEY, L. H., AND COLBURN, H. S. A model for binaural response properties of inferior colliculus neurons. II. A model with ITD-sensitive excitatory and inhibitory inputs and an adaptation mechanism. *J. Acoust. Soc. Am.* 103: 494–506, 1998b.

CANT, N. B. AND HYSON, R. L. Projections from the lateral nucleus of the trapezoid body to the medial superior olivary nucleus in the gerbil. *Hear. Res.* 58: 26–34, 1992.

CARNEY, L. H. AND YIN, T.C.T. Responses of low-frequency cells in the inferior colliculus to interaural time differences of clicks: excitatory and inhibitory components. *J. Neurophysiol.* 62: 144–161, 1989.

FITZPATRICK, D. C., KUWADA, S., BATRA, R., AND TRAHIOTIS, C. Neural responses to simple, simulated echoes in the auditory brainstem of the unanesthetized rabbit, *J. Neurophysiol*. 74: 2469–2486, 1995.

FREYMAN, R. L., CLIFTON, R. K., AND LITOVSKY, R. Y. Dynamic processes in the precedence effect. *J. Acoust. Soc. Am*. 90: 874–884, 1991.

GROTHE, B. AND SANES, D. H. Synaptic inhibition influences the temporal coding properties of medial superior olivary neurons: an in vitro study. *J. Neurosci.* 14: 1701–1709, 1993.

HARRIS, D. M. AND DALLOS, P. Forward masking of auditory nerve fiber responses. *J. Neurophysiol.* 42: 1083–1107, 1979.

HAWLEY, M. L., LITOVSKY, R. Y., AND COLBURN, H. S. Precedence effect in normal-hearing and hearing-impaired listeners. *Assoc. Res. Otolaryngol.* 1997.

HEBRANK, J. H. AND WRIGHT, D. Spectral cues used in the localization of sound sources on the median plane. *J. Acoust. Soc. Am*. 56: 1829–1834, 1974.

HELFERT, R. H., BONNEAU, J. M., WENTHOLD, R. J., AND ALTSCHULER, R. A. GABA and glycine immunoreactivity in the guinea pig superior olivary complex. *Brain Res.* 501: 269–286, 1989.

KUWABARA, N. AND ZOOK, J. M. Classification of the prinicpal cells of the medial nucleus of the trapezoid body. *J. Comp. Neurol.* 314: 707–720, 1991.

LITOVSKY, R. Y. Physiological studies of the precedence effect in the inferior colliculus of the kitten. *J. Acoust. Soc. Am.* 103: 3139–3152, 1998.

LITOVSKY, R. Y. AND COLBURN, H. S. Precedence effects under binaural and monaural conditions (Abstract). *Assoc. Res. Otolaryngol.* 1998.

LITOVSKY, R. Y., HAWLEY, M. L., DIZON, R., AND COLBURN, H. S. Measurements of precedence in binaural and monaural conditions. *J. Acoust. Soc. Am*. 101: S3083, 1997a.

LITOVSKY, R. Y., RAKERD, B., YIN, T.C.T., AND HARTMANN, W. M. Psychophysical and physiological evidence for a precedence effect in the median sagittal plane. *J. Neurophysiol.* 77: 2224–2226, 1997b.

LITOVSKY, R. Y. AND YIN, T.C.T. Physiological studies of the precedence effect in the inferior colliculus of the cat. I. Correlates of psychophysics. *J. Neurophysiol.* 80: 1285–1301, 1998.

MIDDLEBROOKS, J. C. AND GREEN, D. M. Sound localization by human listeners. *Annu. Rev. Psych.* 42: 135–159, 1991.

MOUSHEGIAN, G., RUPERT, A. L., AND LANGFORD, T. L. Stimulus coding by medial superior olivary nucleus. *J. Neurophysiol.* 30: 1239–1261, 1967.

OLIVER, D. L. AND SCHNEIDERMAN, A. The anatomy of the inferior colliculus: a cellular basis for integration of monaural and binaural information. In: *Neurobiology of Hearing: The Central Auditory System*, edited by R. A. Altschuler, R. P. Bobbin, B. M. Clopton, and D. W. Hoffman. New York: Raven, 1991, p. 195–222.

OLIVER, D. L., BECKIUS, G. E., AND OSTAPOFF, E. M. Connectivity of neurons in identified auditory circuits studied with transport of dextran and microspheres plus intracellular injection of Lucifer Yellow. *J. Neurosci. Methods* 53: 23–27, 1994.

PARHAM, K., ZHAO, H. B., AND KIM, D. O. Response of auditory nerve fibers of the unanesthetized decerebrate cat to click pairs as simulated echoes. *J. Neurophysiol.* 76: 17–29, 1996.

POPULIN, L. C. AND YIN, T.C.T. Behavioral studies of sound localization in the cat. *J. Neurosci.* 18: 2147–2160, 1998.

RUPERT, A., MOUSHEGIAN, G., AND WHITCOMB, M. A. Superior-olivary response patterns to monaural and binaural clicks. *J. Acoust. Soc. Am.* 39: 1069–1076, 1966.

SCHNEIDERMAN, A., OLIVER, D. L., AND HENKEL, C. G. Connections of the dorsal nucleus of the lateral lemniscus: an inhibitory parallel pathway in the ascending auditory system? *J. Comp. Neurol.* 276: 188–208, 1988.

SEARLE, C. L., BRAIDA, L. D., CUDDY, D. R., AND DAVIS, M. F. Binaural pinna disparity: another auditory localization cue. *J. Acoust. Soc. Am*. 57: 448–455, 1975.

SHINN-CUNNINGHAM, B. G., ZUREK, P. M., AND DURLACH, N. I. Adjustment and discrimination measurements of the precedence effect. *J. Acoust. Soc. Am*. 93: 2923–2932, 1993.

SMITH, P. H. Structural and functional differences distinguish principal from nonprincipal cells in the guinea pig MSO slice. *J. Neurophysiol.* 73: 1653–1666, 1995.

SMITH, P. H., JORIS, P. X., BANKS, M. I., AND YIN, T.C.T. Physiology and anatomy of principal cells in the cat MNTB. *Soc. Neurosci. Abstr*. 15: 746, 1989.

SMITH, R. L. Adaptation, saturation, and physiological masking in single auditory-nerve fibers. *J. Acoust. Soc. Am.* 65: 166–178, 1979.

THURLOW, W. R. AND PARKS, T. E. Precedence-suppression effects for two click sources. *Percept. Mot. Skills* 13: 7–12, 1961.

WALLACH, H., NEWMAN, E. B., AND ROSENZWEIG, M. R. The precedence effect in sound localization. *J. Am. Psychol.* 57: 315–336, 1949.

WENTHOLD, R. J., HUIE, D., ALTSCHULER, R. A., AND REEKS, K. A. Glycine

immunoreactivity localized in the cochlear nucleus and superior olivary complex. *Neuroscience* 22: 897–912, 1987.

WICKESBERG, R. E. Rapid inhibition in the cochlear nucleus complex of the chinchilla. *J. Acoust. Soc. Am*. 100: 1691–1702, 1996.

WICKESBERG, R. E. AND OERTEL, D. Delayed frequency-specific inhibition in the cochlear nuclei of mice: a mechanism for monaural echo suppression. *J. Neurosci.* 10: 1762–1768, 1990.

YANG, L. AND POLLAK, G. D. The role of GABAergic and glycenergic inhibition on binaural processing in the dorsal nucleus of the lateral lemniscus of the mustache bat. *J. Neurophysiol.* 71: 1999–2013, 1994.

YIN, T.C.T. Physiological correlates of the precedence effect and summing localization in the inferior colliculus of the cat. *J. Neurosci.* 14: 5170–5186, 1994.

YIN, T.C.T. AND CHAN, J.C.K. Interaural time sensitivity in medial superior olive of the cat. *J. Neurophysiol.* 64: 465–488, 1990.

YOST, W. A. AND SODERQUIST, D. R. The precedence effect: revisited. *J. Acoust. Soc. Am*. 76: 1377–1383, 1984.

ZUREK, P. M. The precedence effect. In: *Directional Hearing*, edited by W. A. Yost and G. Gourevitch. Berlin: Springer-Verlag, 1987, p. 85–105.

ZUREK, P. M. The precedence effect and its possible role in the avoidance of interaural ambiguities. *J. Acoust. Soc. Am*. 67: 952–964, 1980.