Medial efferent inhibition produces the largest equivalent attenuations at moderate to high sound levels in cat auditory-nerve fibers

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Previous work has shown that medial efferents can inhibit responses of auditory-nerve fibers to high-level sounds and that fibers with low spontaneous rates (SRs) are inhibited most. However, quantitative interpretation of these data is made difficult by effects of adaptation. To minimize systematic differences in adaptation, efferent inhibition was measured with a randomized presentation of both sound level and efferent stimulation. In anesthetized cats, efferents were stimulated with 200/s shocks and auditory-nerve-fiber responses were recorded for tone bursts (0–100 dB SPL, 5-dB steps) at their characteristic frequencies. Below 50 dB SPL, efferent inhibition (measured as equivalent attenuation) was similar for all fibers with similar CFs in the same cat. At 45–75 dB SPL, low-SR and medium-SR fibers often showed much larger inhibition, and substantial inhibition even at 100 dB SPL. Expressed as a fractional decrease in rate, at 90–100 dB SPL the inhibition was 0%, 6%, and 13% for high-, medium-, and low-SR fibers (differences statistically significant). Finding the largest equivalent attenuations at 45–75 dB SPL does not fit with the hypothesis that medial-efferent inhibition is due solely to a reduction of basilar-membrane motion. The large attenuations, some over 50 dB, indicate that medial efferent inhibition is more potent than previously reported. © 1996 Acoustical Society of America.

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INTRODUCTION

The earliest work on the effects of efferents left a lasting impression that efferent inhibition is large only at low sound levels (Galambos, 1956; Desmedt, 1962; Weiderhold, 1970; Teas et al., 1972). This impression has been reinforced by more recent work showing that efferent inhibition of evoked otoacoustic emissions (OAEs) and reduction of basilar-membrane motion is largest at low sound levels (Mountain, 1980; Moulin et al., 1993; Dolan and Nuttall, 1994). Furthermore, efferent inhibition being largest at low sound levels is consistent with the hypothesis that efferent inhibition is due to medial efferents acting on outer hair cells (OHCs) to reduce basilar-membrane motion.

However, medial efferents can produce substantial inhibition at high sound levels in responses of single auditory-nerve fibers (Guinan and Gifford, 1988a; see also Gifford and Guinan, 1983). This inhibition is largest for auditory-nerve fibers with low and medium spontaneous rates (SRs), the fibers which are probably most important in carrying information at high sound levels (Vieheimer, 1983; Young and Barta, 1986).

Although this single-fiber work showed that efferent inhibition is present at high sound levels, the methods were not adequate for comparing the strength of efferent inhibition at low and high sound levels. Guinan and Gifford (1988a) used level functions run in sequence from low to high sound levels with efferent stimulation alternating with no efferent stimulation at each level. In such sequential level functions, adaptation increases as sound level goes up and can distort the shape of the level function (Sachs and Abbas, 1974). In many low-SR and medium-SR auditory-nerve fibers, strong saturation of the firing rate (i.e. a “plateau”) is seen at high sound levels in sequential level functions, but continued growth with a lower slope at high sound levels (“sloping saturation”) is seen in randomized level functions (Sachs and Abbas, 1974). Thus the efferent-induced reduction of plateau rate observed in sequential level functions by Guinan and Gifford (1988a) may actually be due to an efferent-induced attenuation of effective sound level, because adaptation turned a sloping saturation into a plateau. Such possibilities make it impossible to accurately compare efferent effects across sound levels using sequential level functions.

The primary goal of the present work is to measure ef-
different effects in a way that will allow valid comparisons across sound levels. To do this we have minimized the influence of adaptation by using randomized level functions. We simultaneously randomized sound level and the presence of efferent shocks to allow comparison of firing rates at different sound levels both with and without efferent stimulation.

A second goal of the present work is to compare efferent effects across auditory-nerve fibers grouped according to their spontaneous rates. Guinan and Gifford (1988a, 1988c) reported that low-SR fibers showed substantially larger efferent inhibitions than high-SR fibers, both in threshold shift and plateau inhibition. Since differences in medial-efferent effects across SR groups would have important implications for the mechanisms involved [auditory-nerve fibers in each of the three SR classes can synapse with the same inner hair cell (IHC)], this issue is worthy of re-examination using data that are not strongly influenced by adaptation, i.e., with the randomized level functions.

Our results show that the largest efferent-induced effective attenuations occur in low-SR and medium-SR auditory-nerve fibers at moderate to high sound levels (45–75 dB SPL) with substantial efferent inhibition present even at 100 dB SPL. These data do not fit with the hypothesis that medial-efferent inhibition is due solely to a reduction of basilar-membrane motion. The very large efferent-induced attenuations we have found, some over 50 dB, indicate that medial efferent inhibition is considerably more potent than previously reported.

I. METHOD

A. Surgical preparation

Anesthesia was induced in adult cats by intraperitoneal injection of 0.15 ml/kg Dial in urethane (100 mg/ml diallyl barbiturate, 400 mg/ml monotheyeurea, and 400 mg/ml urethane) and maintained with injections of 1/10 of the original dose, as needed. Treatment of experimental animals was in accordance with protocols approved by the Committees on Animal Care at the Massachusetts Institute of Technology and the Massachusetts Eye and Ear Infirmary.

Most aspects of the surgery, acoustic stimulation and recording from auditory-nerve fibers are similar to those used earlier (Gifford and Guinan, 1987; Guinan and Gifford, 1988a). Important points and differences are noted here. The ear canals were surgically exposed and the auditory bullae were opened. The bony septum between the bulla and middle ear was removed and the tendons of the middle-ear muscles were cut. After a posterior craniectomy, both the lateral and medial parts of the cerebellum were aspirated to expose the floor of the fourth ventricle and the exit of the auditory nerve.

Auditory-nerve compound action potentials (CAPs) were monitored with an electrode on, or near, the round window (RW). An automated tone-pip audiogram determined the sound level at 0.5, 1, 2, 4, 8, 16, 23, and 32 kHz which evoked CAPs of 5 μV (electrode near the RW or 10 μV (electrode on the RW). Single fiber recordings began ten or more hours after cutting the middle-ear-muscle tendons so that the CAP audiograms were within the normal range during the period over which the data reported here were obtained.

B. Stimulation and recording

Efferents were stimulated with a multiprong electrode along the midline of the floor of the fourth ventricle [midline olivocochlear bundle (OCB) stimulation] (Gifford and Guinan, 1987). Shocks were delivered through the pair of adjacent prongs which yielded the greatest inhibition of the CAP response without evoking movement. Shock pulses were 0.3 ms at 200/s and coupled by a transformer so that no net charge was delivered. The efferent inhibition of the CAP response was equivalent to decreasing the sound level by amounts ranging from 9 to 19 dB during the period over which the data reported here were obtained.

Single auditory-nerve fibers were recorded (as in Kiang et al., 1965) using broadband noise bursts as a search stimulus. Fibers of all SRs were studied but we were biased toward low-SR fibers to provide adequate numbers to contrast with the more numerous high-SR fibers. We were also biased toward studying fibers with characteristic frequencies (CFs) within a narrow range in the same cat, so that inhibition of high-SR and low-SR fibers of similar CFs could be examined. Because of this, comparison of the overall data set across frequency may be biased. After making contact with a fiber, the data gathering sequence was: (1) to obtain enough of a tuning curve to determine the CF of the fiber, (2) to record the spontaneous firing for 20 s and calculate the SR of the fiber, (3) to run level functions. On most animals, we ran only randomized level functions, however in some cases (most fibers on cat 20) we ran both sequential and randomized level functions for comparison. Fibers were put into SR groups using the categories of Liberman (1978): low is SR < = 0.5, medium is 0.5 < SR < 18, high is SR = 18.

We were careful to insure that each spike triggered a time marker. One important potential problem is spurious spike triggering caused by electronic artifacts at the recording electrode produced by the efferent shocks. For each data set, we examined peri-stimulus-time histograms locked to the shock times. We rejected those data which showed either extra time markers caused by the positive phase of the shock artifact triggering the spike detector, or a period of reduced time markers caused by the negative phase of the shock artifact reducing the number of triggers from the spikes. We also rejected data when spike interval histograms revealed that short-interval spikes were missed.

C. The level-function paradigm

Level functions were simultaneously randomized across sound levels and the presence or absence of efferent stimulation. In the initial exploratory experiments, the range of sound levels was set separately for each fiber. In the final experimental series, all randomized level functions went from 0–100 dB SPL in 5-dB steps. Thus with 21 sound levels and two shock conditions, there were 42 randomized trials in a set. If the unit spikes remained high enough in amplitude, multiple sets of randomized level functions were...
obtained for a fiber, each randomized independently. The results were then combined by averaging the rates for each sound-level and shock condition.

All tone bursts were at the fiber CF, 50 ms on, 50 ms off, with 2.5-ms rise/fall times. At each level-function trial, the firing rates in response to ten tone bursts were averaged. For each tone burst, the time window for counting spikes began 2 ms after the beginning of the rise of the tone burst and ended 3 ms after the end of the fall of the tone burst. If the trial was “with efferent shocks,” the shocks began 100 ms before the beginning of the first tone burst and lasted 1.1 s (i.e., until the end of the 10th tone-burst period). Individual trials were every 3 s in the final animals (every 2.5 s in some earlier animals). In some cases, 15 tone bursts were given in each trial (only the first ten were averaged) so that there would be five tone bursts after the shocks for looking at the time course of efferent effects.

Sequential level series had the same timing within a trial as the randomized series. However, in the sequential level series, the sound levels increased monotonically from low to high, and at each level shocks/no-shock trials were alternated. At every sound level, a fixed number (1 to 4, usually 2) of shock/no-shocks trials were alternated with the same condition always presented first throughout the level function (arbitrarily chosen at the beginning of the series).

Randomized data were gathered on eight cats. The data reported here are from 99 auditory-nerve fibers from the last four cats in which all of the runs were randomized over 0–100 dB SPL. The data from the earlier animals are consistent with these results.

II. RESULTS

A. Sequential versus randomized data

As expected from previous reports (Sachs and Abbas, 1974), randomization changed the shapes of many level functions. In particular, many medium-SR and low-SR auditory-nerve fibers which showed plateaus in sequential level series showed sloping saturations in randomized level series [Fig. 1(a), (b)]. Some sequential level functions without efferent stimulation had their largest rate just above the rising phase [e.g., at * in Fig. 1(c)]; the corresponding randomized level functions had plateaus or sloping saturations without this rate bulge [e.g., Fig. 1(d)]. There were also many cases where randomization had little effect on the shapes of the level functions but increased the rates at high sound levels. This was the pattern for some very low-SR auditory-nerve fibers [e.g., Fig. 1(e), (f)] and for almost all high-SR auditory-nerve fibers (not illustrated).

Since a single randomized run usually produced a very “noisy” level function, multiple randomized runs had to be averaged to obtain a smooth level function. When multiple randomized runs were obtained from the same fiber, the overall shapes of the level functions, although noisy, were always similar (Figs. 2–4).

B. Level shifts

The standard way to measure efferent effects has been the efferent-induced attenuation, or level shift, \( \Delta L \). This is the amount by which the sound level must be increased (i.e., shifted) with efferent stimulation to produce the same response as that obtained without efferent stimulation [see Fig. 2(b)]. One advantage of measuring \( \Delta L \) is that it is an equal response measure and is not changed by any nonlinear transformations which might occur functionally after the site of efferent action. Thus if medial-efferent inhibition is produced solely by a reduction of basilar-membrane motion, then the \( \Delta L \) measured from auditory-nerve responses would equal the \( \Delta L \) measured from basilar-membrane motion.

Although the level shift, \( \Delta L \), is conceptually simple, calculating it from a pair of noisy level functions can be complicated. Furthermore, in some fibers, \( \Delta L \) cannot be calculated at high sound levels because the firing rate without efferent stimulation is higher than the highest rate obtained with efferent stimulation (e.g., the no-efferent-stimulation points at, and above, 50 dB SPL in Fig. 3). Nonetheless, an automated procedure has been developed [see caption for Fig. 2(c)] which calculated \( \Delta L \) in the fast rising phase of the level functions (large points in plots of \( \Delta L \)), in noisy sloping regions (smaller points in plots of \( \Delta L \)), and at 100 dB SPL by extrapolating the with-shocks data to sound levels above 100 dB SPL [points at 100 dB SPL, see Fig. 2(b)]. This procedure provided calculations of \( \Delta L \) over the range from threshold to 100 dB SPL for low-SR and medium-SR fibers and in the rising phase for high-SR auditory-nerve fibers.

The efferent induced level shift, \( \Delta L \), showed a variety of patterns across auditory-nerve fibers (Figs. 1–4). In some fibers, \( \Delta L \) was relatively constant in the fast rising phase [Fig. 1(a), (b)]. In many fibers with sloping saturations, the level function without efferent shocks had a sloping saturation but the level function with efferent shocks was relatively straight (Fig. 2). With this pattern, the resulting \( \Delta L \) is greatest at sound levels near the bend in the sloping saturation [Fig. 2(c)]. In a few cases, the level function with efferent stimulation appeared to plateau producing what might be called an efferent depression of plateau rate (Fig. 3).

High-SR auditory-nerve fibers often had level functions in which the fast rising phase with efferent stimulation had a higher slope than the fast rising phase without efferent stimulation (Fig. 4). This produced a \( \Delta L \) which decreased as sound level increased [Fig. 4(c)]. We hypothesized that this difference in slopes might be due to differences in adaptation caused by the efferent stimulation inhibiting the spontaneous activity which was present in the 50 ms between the tone bursts [somewhat like the process which produced the “bulge” in Fig. 1(c)]. To test this hypothesis, on a sampling of fibers which showed large changes in \( \Delta L \) with sound level, we reprocessed the spike-time data to include in the response window used to calculate the rate all spike times from both during the tone bursts and the time between the tone bursts. The resulting rate-level functions showed average rates of approximately half the previous values, but the \( \Delta L \)’s calculated from these [e.g., the open diamonds in Fig. 4(c)] were little different from those calculated just from the period during the tone bursts [e.g., the filled diamonds in Fig. 4(c)]. Thus the decrease in \( \Delta L \) with sound level in high-SR fibers does not appear to be caused by efferent inhibition of spontaneous activity changing the adaptation level.
C. Averaged level functions

In order to get an overall picture of the effects of efferent stimulation on the responses of auditory-nerve fibers, we averaged randomized level functions from many auditory-nerve fibers. For fibers in each SR class, we averaged the data from all fibers with CFs in octave bands centered at approximately 2, 4, 8, 16, and 32 kHz. To make the curves smoother, we weighted data from each fiber by the number of runs done on that fiber. This is equivalent to averaging all of the runs from the fibers with CF’s in the octave band. The resulting smoothness allows more accurate determinations of $\Delta L$, particularly in regions of low slope. The $\Delta L$’s calculated from these average level functions are shown in Fig. 6.

Figure 5 shows that the shapes of the level functions and the pattern of efferent inhibition varied systematically with fiber SR and CF. The rates of high-SR fibers rise sharply with sound level and form clear plateaus with little efferent inhibition at high sound levels. In contrast, the medium-SR and low-SR fibers show less sharp plateaus and definite efferent inhibition at high sound levels. Across frequency, the pattern of efferent inhibition is similar to that found before (Wiederhold, 1970; Guinan and Gifford, 1988c). The greatest inhibition was in the 6- to 12-kHz band and there was less inhibition at higher and lower frequencies (Figs. 5 and 6).

Despite averaging level functions from many fibers, the plots in Figs. 5 and 6 are still inadequate to accurately define $\Delta L$ for high-SR fibers at high sound levels. In an attempt to provide a better estimate of this $\Delta L$, an overall average of the data for the frequency region in which efferent inhibition was large (6–24 kHz) is given in Fig. 7, along with the calculated $\Delta L$’s. It should be kept in mind that the plots in Fig. 7 are still somewhat inadequate to accurately define $\Delta L$ for high-SR fibers at high sound levels.

FIG. 1. Examples of level series obtained sequentially (left) and randomized (right) from the same auditory-nerve fiber. Each row is from a different fiber. Top: fiber 20–65, characteristic frequency (CF) = 18.62 kHz, spontaneous rate (SR) = 0.1 sp/s. Middle: fiber 20–57, CF = 23.44 kHz, SR = 2.0 sp/s. Bottom: fiber 20–52, CF = 28.84 kHz, SR = 0.0 sp/s. The number of trials of each condition averaged for each panel, in sequence, are 2, 2, 2, 4, 4.
Fig. 7 average across frequency regions in which the strength of the efferent effect varied substantially. Figures 6 and 7 show that within a given frequency band, the average $D_L$'s for high-, medium-, and low-SR fibers are similar, usually within 5 dB for sounds below 50 dB SPL. At levels near 50 dB SPL, $D_L$ rises with sound level so that the highest $D_L$'s are at 45–75 dB SPL, at least for low-SR and medium-SR fibers. At sound levels above 75 dB SPL, $D_L$ decreases, but there are few $D_L$ points, principally because at these high levels the rates without efferent stimulation often exceed the highest rate with efferent stimulation. Finally, extrapolation of the level functions with efferent stimulation past 100 dB SPL indicates that $D_L$ at 100 dB SPL is usually considerably below the peak $D_L$. The data also show a relatively consistent pattern for the high-SR fibers.

FIG. 2. Randomized level series from a single auditory-nerve fiber. (a) Five measurement sets (coded by different symbols) of the firing rate, each with a randomized presentation of sound level and efferent stimulation, illustrating the reproducibility of the randomized level functions. (b) The level functions derived by averaging the rates obtained at each sound level and efferent stimulation condition. The inset shows the computation of the efferent-induced level shift, $\Delta L$, at 100 dB SPL (see below). (c) $\Delta L$ calculated from the data in panel (b). For each no-shocks point, $\Delta L$ was the amount the sound level had to be raised to reach the same rate on the with-shocks level function [$\Delta L$ in panel(b)]. $\Delta L$ was calculated for every no-shocks point clearly in the rising phase (i.e., no point at a higher sound level had a lower rate and no point at lower sound level had a higher rate) and is shown with large symbols. $\Delta L$ was also calculated, for low-SR and medium-SR fibers as follows: (1) for points at higher sound levels (small symbols) until their rates exceeded the maximum rate with efferent shocks, (2) from the no-shocks response curve to the with-shocks point at 100 dB SPL, whenever this point had the highest with-shocks rate (rotated small symbol), and (3) for 100 dB SPL, by extrapolating the with-shocks rates to sound levels above 100 dB SPL using a line through the 90- and 100-dB SPL points [see inset in panel (b)] (small symbol at 100 dB SPL). Since this last point is based on extrapolated data, it is connected by a dotted line. Fiber 20–47, CF = 3.55 kHz, SR = 0.05 sp/s.

FIG. 3. Randomized level series and the resulting level shifts from a single auditory-nerve fiber. Layout as in Fig. 2. Fiber 21–80, CF = 6.31 kHz, SR = 0.2 sp/s.

Fig. 7 average across frequency regions in which the strength of the efferent effect varied substantially.

Figures 6 and 7 show that within a given frequency band, the average $\Delta L$'s for high-, medium-, and low-SR fibers are similar, usually within 5 dB for sounds below 50 dB SPL. At levels near 50 dB SPL, $\Delta L$ rises with sound level so that the highest $\Delta L$'s are at 45–75 dB SPL, at least for low-SR and medium-SR fibers. At sound levels above 75 dB SPL, $\Delta L$ decreases, but there are few $\Delta L$ points, principally because at these high levels the rates without efferent stimulation often exceed the highest rate with efferent stimulation. Finally, extrapolation of the level functions with efferent stimulation past 100 dB SPL indicates that $\Delta L$ at 100 dB SPL is usually considerably below the peak $\Delta L$. The data also show a relatively consistent pattern for the high-SR fibers.
group at very low sound levels. In all frequency bands except one, $\Delta L$ was biggest at the lowest sound level and decreased as level increased up to about 40 dB SPL. This is the pattern shown by the fiber in Fig. 4.

D. Comparison of individual level functions in narrow CF bands

It is useful to look at level functions from fibers with a wide range of spontaneous rates but within a narrow range of CF’s. The averaged level functions, and the $\Delta L$’s calculated from them, are useful for getting an overview of the data, but they may mask patterns which are present in some level functions but not in others. In addition, Gifford and Guinan (1988a, 1988c), using averaged data, reported that efferent-induced level shifts and threshold shifts were greater for low-SR fibers than for high-SR fibers. To help discern whether this is due to pooling data across cats and CF’s, we wanted to compare $\Delta L$’s from fibers with similar CF’s obtained in the same cat.

To compare fibers with similar CF’s, we included each case in the four final cats for which there was at least one high-SR and one low-SR fiber in the same cat with CF’s within 10%. We included all fibers with nearby CF’s, as long as the frequency band was not made greater than 10%. All of

FIG. 4. Randomized level series and the resulting level shifts from a single auditory-nerve fiber. Layout as in Fig. 2. In panel (c), the closed symbols were obtained using a response window which just included the spikes during the tone bursts. The open symbols were obtained using a response window which included spikes both during the tone bursts and during the times between tone bursts (see text). Fiber 21–86, CF=14.79 kHz, SR =33.3 sp/s.

FIG. 5. Average level functions from all of the auditory-nerve fibers in a SR category which have CF’s in adjacent octave bands. Solid lines are level functions without efferent stimulation, dashed lines are level functions with efferent stimulation. The highest “octave” had no fiber CF’s>31 kHz. Averages were obtained by (1) normalizing the data from each fiber so that the rates equaled 100 averaged over the 90–100 dB SPL points with no efferent stimulation, and (2) at each level and efferent stimulation condition, averaging the normalized rates with the data from each fiber weighted by the number of randomized runs for that fiber. In each panel, the number of fibers and the total number of runs included are

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the cases are from two cats because the CF’s were too spread out on the other cats. The data obtained from earlier cats in which randomized level functions were done over ranges less than 0–100 dB SPL are similar to those shown here.

The efferent-induced shift, $D_L$, as a function of sound level for fibers with CF’s in narrow frequency bands are shown in Fig. 8. At low sound levels there was usually a tight distribution of $D_L$ values at each sound level, but at moderate to high sound levels there was sometimes considerable spread. The interpretation of these data is made difficult by the fact that noise in individual level functions can sometimes produce large differences, particularly at the end points of the fast rising phase and in sloping saturations. Within the level of accuracy of the data, Fig. 8 indicates that $D_L$ from high-, medium-, and low-SR fibers are about the same at low sound levels, although the data do not rule out small differences. In particular, the largest difference reported by Guinan and Gifford (1988c) was that $D_L$ for low-SR fibers exceeded $D_L$ for high-SR fibers by more than a factor of 2 for the octave centered at 16 kHz. The data of Fig. 8 do not show any difference close to this for sounds less than 50 dB SPL. However, at the highest sound levels, some of the differences in Fig. 8 appear to be too large to attribute to random errors [e.g., Fig. 8(f)].

E. Efferent inhibition at high sound levels

The efferent-induced level shift, $D_L$, may not be the best way of looking at efferent inhibition at high sound levels, in part because the value of $D_L$ can be affected greatly by small changes in rate when the slope of the level function is very low. An alternate way of looking at this inhibition is the efferent-induced change in rate. The change in rate can be calculated for fibers which span the entire range of SRs and for any level-function shape.

We calculated the efferent-induced change in rate, $D_R$, from the rates with and without efferent stimulation, each averaged over the responses from 90 to 100 dB SPL. The resulting $D_R$’s are plotted versus fiber spontaneous rate in Fig. 9. To include as many fibers as possible, but only fibers on which the efferent effect was large, we included only fibers with CF’s from 3–24 kHz.

Figure 9 shows that the efferent inhibition of firing rate at high sound levels depends strongly on spontaneous rate. Efferent stimulation did not produce a significant change in rate for high-SR fibers (ave. $\Delta R = +0.4\%$). However, $\Delta R$ from the medium-SR fibers (ave. $\Delta R = -6.5\%$) was significantly less ($t = 4.34, p = 0.00009$ by a Student’s $t$ test) than $\Delta R$ from the high-SR fibers, and $\Delta R$ from the low-SR fibers (ave. $\Delta R = -12.7\%$) was significantly less ($t = 2.29, p = 0.028$) than $\Delta R$ from the medium SR fibers. If the one fiber with a very low $\Delta R$ is dropped from the low-SR group

FIG. 6. Level shifts of the high-SR (circles), medium-SR (×’s) and low-SR (triangles) auditory-nerve fibers in octave bands, calculated from the data in Fig. 5. Symbol size and orientation indicate the method used to obtain the $\Delta L$ (see Fig. 2 caption).

FIG. 7. Level functions (left) and level shifts (right) averaged from all auditory-nerve fibers with CF’s from 3–24 kHz. Fibers were separated into groups according to spontaneous rate: high-SR (circles), medium-SR (×’s) and low-SR (triangles). Symbol size and orientation indicate the method used to obtain the $\Delta L$ (see Fig. 2 caption).
(see Fig. 8), the $\Delta R$ from low-SR fibers is still significantly less than the $\Delta R$ from medium-SR fibers ($t = 2.34, p = 0.025$). Although these data show that at high sound levels efferent inhibition is significantly different across SR groups, they do not separate whether this inhibition is due to a level shift or a plateau depression.

### III. DISCUSSION

#### A. Efferent inhibition as a function of sound level

Our data provide a distinctly different picture of efferent inhibition than that obtained from previous work. Although it had been thought that medial efferents produce the largest level shifts at low sound levels, our data show that the largest level shifts are actually at moderate to high sound levels (Figs. 2, 3, 6, 7, 8). Furthermore, we have found level shifts which are much greater than any previously reported. In the 6–12 kHz band, the average $\Delta L$ in the low-SR fibers was over 40 dB, and in individual fibers $\Delta L$ was over 50 dB (Fig. 3). Thus medial efferents can have a much more powerful influence on auditory-nerve responses than was indicated by previous evidence.

It seems worth noting, that even though high-SR fibers are the most common, medium-SR and especially low-SR fibers are probably more important carriers of information at high sound levels (Viemeister, 1983; Young and Barta, 1986). Thus at high sound levels efferent effects on low-SR and medium-SR fibers are likely to be more important than efferent effects on high-SR auditory-nerve fibers.

The impression that efferent inhibition is largest at low sound levels was due mostly to measurements which do not give a full picture of how efferents affect auditory-nerve fibers. The original reports were for efferent inhibition of CAP responses. CAPs are dominated by responses of high-SR fibers and are strongly influenced by responses fibers responding to sound energy which is not at their CF (efferent inhibition is strongest at CF; Wiederhold, 1970; Brown and Nuttall, 1984; Guinan and Gifford, 1988c). Thus CAP responses do not reveal efferent effects on low-SR fibers, even though these may be the largest effects. Furthermore, reports of efferent inhibition of OAEs and basilar-membrane motion provide measures of efferent effects on cochlear mechanics (Mountain, 1980; Moulin et al., 1993; Dolan and Nuttall, 1994), but these do not reflect any influence of medial-efferents which takes place functionally after basilar-membrane motion. Finally, none of the previous reports of efferent effects on single auditory-nerve fibers revealed the inhibitory ability of medial efferents at moderate to high sound levels because they did not randomize the presentation of level functions and efferent stimulation, or because they focused on other issues (Fex, 1962; Wiederhold and Kiang, 1970; Wiederhold, 1970; Teas et al., 1972; Gifford and Guinan, 1983; Winslow and Sachs, 1987; Guinan and Gifford, 1988a, b, c; Kawase et al., 1993). Winslow and Sachs (1987) used randomized level functions, but they randomized sound levels in the shocks and no-shocks level-functions separately, so that a comparison of these does not accurately show the efferent inhibition at high sound levels. This emphasizes the importance of simultaneously randomizing both sound level and the presence of efferent stimulation so that the expected amount of prior adaptation is simi-
lar for all points on the two resulting level functions. In addition, this procedure should equalize the influence of "slow" efferent effects similar to those reported by Sridhar et al. (1995). Finally, we note that even though most previous reports focused on efferent effects at low sound levels, there was clear evidence that some auditory-nerve fibers showed substantial inhibitions at high sound levels (Wiederhold, 1970; Gifford and Guinan, 1983; Guinan and Gifford, 1988a).

Although previous reports did not use randomized paradigms, they provide some evidence relevant to the patterns of \( \Delta L \) in the fast rising phases of level functions. Wiederhold (1970) found, in cats, that \( \Delta L \) was relatively constant in the rising phases of most fibers, but Teas et al. (1972) found, in guinea pigs, that \( \Delta L \) was greatest near threshold and decreased as sound level increased (the pattern we found for most high-SR fibers). One difficulty in interpreting results from these early reports is that they did not segregate fibers by spontaneous rate. Guinan and Gifford (1988a) measured the overall slopes of the rising phases of level functions and found that efferent stimulation increased the slope by 14.3% (on the average) in high-SR fibers and decreased the slope by 10.5% in medium-SR fibers and by 14.3% in low-SR fibers. These trends are consistent with our newer data from different SR groups (e.g., Fig. 7) considering that the sound-level ranges over which the fast rising phases occur increase as fiber SR decreases.

B. Is efferent inhibition different across SR groups?

Our data suggest that low-SR fibers are inhibited more by efferent stimulation than high-SR fibers, but these data do not completely settle the issue of whether efferent inhibition is different across SR groups. The level functions from fibers with CF’s within 10% frequency bands (Fig. 8) indicate that there are not large systematic discrepancies in \( \Delta L \) across SR groups at low-sound levels, but the noisiness of these data prevents stronger conclusions from being drawn. The overall average level functions (Fig. 7) provide a strong indication that \( \Delta L \) is larger, on the average, in low-SR fibers than in high-SR or medium-SR fibers. However, this conclusion is tempered by the octave-band averages (Figs. 5, 6) in which the pattern is not so clear cut. Finally, there are statistically significant differences across SR groups in the efferent inhibition of firing rate at high levels (Fig. 9). If efferent inhibition at high sound levels were due solely to a process which produces a level shift, then this difference across SR groups might then account for the different plateau inhibitions found by Guinan and Gifford (1988a). Although these suggestions may not fully account for the differences across SR groups found by Guinan and Gifford (1988a, 1988c), it seems likely that they at least account for some part of the difference.

C. The mechanisms by which medial efferents inhibit auditory-nerve fibers

All of the efferent effects reported here are likely to be due to medial efferents with little or no effect from lateral efferents. We have stimulated efferents with electric shocks at 200/s. Such shocks are much more effective at stimulating the myelinated medial efferents than the unmyelinated lateral efferents (Gifford and Guinan, 1987). If any lateral efferents were stimulated, the most likely would be the crossed lateral efferents; these mostly innervate the apex of the cochlea but the pattern of effects we found was strongly biased toward the base, with a maximum near the location with the greatest medial-efferent innervation (Guinan et al., 1984). In addition, the effects we report here are similar in most basic respects to those reported by Guinan and Gifford (1988a) who used focal stimulation at the brain-stem origin of medial-efferents, a technique which should not excite any lateral efferents. Finally, any hypothesis which would account for the depression of responses at high levels by lateral efferent synapses on auditory-nerve-fiber dendrites must account for the fact that, on the average, there was no inhibition at 90–100 dB SPL in high-SR fibers even though they receive lateral efferent synapses. All considered, it seems unlikely that lateral efferents had a major role in producing the efferent effects reported here.

A considerable body of evidence indicates that medial efferents inhibit auditory-nerve fibers mechanically through a depression of basilar-membrane motion. With this hypothesis, efferents act on OHCs to reduce basilar-membrane motion thereby reducing the sound drive to IHCs and inhibiting the responses of auditory-nerve fibers. Supporting this "mechanical hypothesis" are direct measurements showing effer-
ent inhibition of basilar-membrane motion (Dolan and Nuttall, 1994) and indirect evidence from the efferent inhibition of OAEs (Mountain, 1980; Siegel and Kim, 1982). This mechanism also fits with the hypothesis that the high sensitivity and frequency selectivity of the cochlea is brought about by the fast motility of OHCs acting to amplify basilar-membrane motion, and the fact that medial efferents synapse directly on OHCs. Medial efferents are well placed to regulate the action of OHCs.

Our data on the efferent inhibition of auditory-nerve fibers as a function of sound level do not fit with the hypothesis that this inhibition is caused solely by a reduction of basilar-membrane motion. The one report on efferent inhibition of basilar-membrane motion found that the biggest inhibitions were at low levels and the inhibition decreased as sound level increased (Dolan and Nuttall, 1994). A similar picture can be derived from many other measurements of basilar-membrane motion which show that near the best frequency, basilar-membrane motion is compressively nonlinear. Factors that reduce basilar-membrane motion do so by making the compressive nonlinearity more linear so that the greatest reductions of basilar-membrane motion are at low sound levels (e.g., Rhode, 1973; Sellick et al., 1982; Ruggiero and Rich, 1991).

The $\Delta L$’s from high-SR auditory-nerve fibers are largest at the lowest sound levels (ignoring the large $\Delta L$’s sometimes found just below a plateau), so they appear to match the expected change in basilar-membrane motion. In contrast, the $\Delta L$’s from low-SR and medium-SR auditory-nerve fibers (and from high-SR fibers if we consider the large $\Delta L$’s sometimes found just below a plateau) peak at moderate to high sound levels, a pattern which does not fit with the reported pattern (Dolan and Nuttall, 1994) of efferent inhibition of basilar-membrane motion. This discrepancy indicates that some mechanism, in addition to depression of basilar-membrane motion, also acts to provide efferent inhibition of auditory-nerve fibers, with the two mechanisms adding in some way.

In addition to the inhibition of basilar-membrane motion, there are several possible mechanisms by which medial efferents might suppress responses of auditory-nerve fibers. One possibility is that efferents produce a mechanical change (e.g., a distortion of the organ of Corti) that reduces the mechanical coupling of basilar-membrane motion to sound-frequency bending of IHC stereocilia (de Boer, 1990). However, if the efferent inhibition of basilar-membrane motion fully accounts for the efferent inhibition of auditory-nerve CAP responses at low sound levels (as indicated by Dolan and Nuttall, 1994), then there would be little room for an additional reduction due to another mechanism which acts at low sound levels. The distortion in the organ of Corti would have to have little or no effect at low sound levels, an effect up to 50 dB at moderate to high sound levels, and a lesser effect at 100 dB SPL. Such a pattern seems very unlikely.

Another possibility is that mechanical rectification in OHCs leads to a slow bending of IHC stereocilia (this might be the main method of exciting auditory-nerve fibers for high-frequency sounds; Evans et al., 1991), and efferent activity may inhibit by reducing the OHC rectification or the coupling of the resulting motion to IHCs. This hypothesis suffers from the same drawbacks as the previous possibility. It seems unlikely that such a mechanism would have little or no effect at low sound levels and very large effects at moderate to high sound levels.

A third possibility is that medial efferents change the firing of auditory-nerve fibers by an electrical effect (Geisler, 1974; Guinan and Gifford, 1988b). Activation of medial efferents produces a potential (the MOC potential) which is positive within the organ of Corti and negative in the endocochlear potential space (i.e., is a reduction of endocochlear potential) (Fex, 1967; Brown and Nuttall, 1984; Gifford and Guinan, 1987). The MOC potential might lead to less transmitter being released by IHCs (by increasing the transmembrane potential, i.e., slightly hyperpolarizing the IHC; Brown and Nuttall, 1984). Alternately, the MOC potential in the region of the dendrites of radial auditory-nerve fibers may reduce the probability of action potentials in response to a given transmitter release. As with the previous possible mechanisms, an efferent electrical effect would have to produce almost no level shift at low sound levels and a very large level shift at moderate to high sound levels. However, these electrical mechanisms would act at or after IHC synapses and are thus more likely to be exerting an effect best understood as a change along the rate dimension than along the level dimension. For instance, an action on the dendrites of auditory-nerve fibers might reduce the firing a fixed percentage no matter what the sound level. Such an action would produce an effect which is equivalent to a much larger level shift at high sound levels when the slope of the rate-level function is low, than in the fast rising phase of the level function. This action might also have effects of different magnitudes in fibers of different SR groups because these fibers synapse on opposite sides of IHCs, and are therefore at different distances from OHCs, the source of the MOC potential. Furthermore, the amplitude of the MOC potential varies as a function of sound level (Fex, 1967) which provides yet another way in which electrical effects can vary with sound level.

Important information about the site of efferent action has been provided by recordings of IHC receptor potentials with and without efferent stimulation (Brown and Nuttall, 1984). Considering four pairs of level functions, with and without efferent stimulation, from IHC receptor potentials (Fig. 3 of Brown and Nuttall, 1984), three appear to have $\Delta L$’s which decrease approximately monotonically as sound level is increased, and one has a $\Delta L$ which is constant at low sound levels and increases dramatically at 50 dB SPL, similar to the pattern we have often seen in auditory-nerve fibers. This suggests that at least some of the factors which cause the increase in $\Delta L$ at moderate to high sound levels are present at the level of IHC receptor potentials. Further experimental results are required to determine the actual combination of factors by which medial-efferents change auditory-nerve responses to high-level sounds.

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1Preliminary results were previously presented (Guinan and Stankovic, 1996).

2This difference supports the hypothesis of Guinan and Gifford (1988a) that the bulge is due to adaptation interacting with the alternating shocks/no-shocks paradigm. At the sound level of the bulge, the fiber was alternating between a high firing rate when there was no efferent stimulation and a much lower rate when there was efferent stimulation. Presumably, the low rate during the efferent stimulation produced little adaptation and allowed subsequent no-efferent-stimulation responses to be large. At higher sound levels, the firing rate is high during efferent stimulation, presumably producing considerable adaptation and lowering subsequent no-efferent-stimulation responses.


