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Relations among early postexposure noise-induced threshold shifts and permanent threshold shifts in the chinchilla

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Threshold shifts (TS) were measured at various times following a wide variety of noise exposures on over 900 chinchillas. An analysis of postexposure TS measures and noise-induced permanent threshold shift (PTS) showed that, across audiometric test frequency, there was a consistent relation between these variables of the form $PTS \text{ (dB)} = \alpha(e^{TS/\beta} - 1)$, where, for a given test frequency, α (dB) and β (dB) are constants. TSs were measured immediately following exposure (TS_0), 24 h after exposure (TS_{24}), and at several intermediate times in order to estimate the maximum TS (TS_{max}). Correlation between TS and PTS at the various test frequencies was highest for TS_{24} . An analysis of the 90th-percentile PTS showed a linear growth of PTS with TS_{24} of approximately 0.7 dB PTS/dB TS_{24} . These data provide some support, in the chinchilla model, for a variation of the three postulates originally presented by Kryter *et al.* [J. Acoust. Soc. Am. **39**, 451 (1966)]. Specifically: (i) TS_{24} is a consistent measure of the effects of a traumatic noise exposure. (ii) All exposures that produce a given TS_{24} will be equally hazardous. (iii) Noise-induced PTS in the most susceptible animals, following many years of exposure, is approximately equal to $(0.7)TS_{24}$ measured after an 8-h exposure to the same noise. © 2002 Acoustical Society of America. [DOI: 10.1121/1.1428545]

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I. INTRODUCTION

Temporary threshold shift (TTS) and compound threshold shift (CTS) measured on subjects following exposure to noise have been fundamental measures of the effects of a noise exposure on hearing in laboratory experiments using human and other mammalian species for more than 50 years. CTS differs from TTS in that the postexposure-shifted threshold recovers toward the preexposure levels but the recovery is not complete, leaving the subject with a permanent threshold shift (PTS). CTS is associated with a damaged sensory epithelium. Unlike the TTS experiments, which often used human subjects, experimentation that produced a CTS was invariably conducted on various nonhuman species.

Since it seemed reasonable to assume that temporary losses of hearing were somehow related to permanent losses (Reger and Lierle, 1954), the former simply being a milder manifestation of the latter, TTS experiments became very popular. While a considerable amount has been learned about the behavior of TTS and its relation to exposure parameters, the results have arguably had a modest impact on our knowledge of how noise-induced permanent threshold shift (NIPTS) accumulates over a working lifetime.

Data on TTS ultimately found their greatest practical application in noise-exposure criteria (e.g., Kryter *et al.*, 1966). Implicit in the development of the Kryter *et al.* document was the acceptance of three postulates: (a) TTS measured 2 min after an exposure (TTS_2) is a consistent measure of the effects of a single day's exposure to noise. (b) All

exposures that produce a given TTS_2 will be equally hazardous; and (c) NIPTS following 10 years of exposure, 8 h/day is approximately equal to the TTS_2 measured after an 8-h exposure to the same noise. At the time these three postulates were published, their insecure foundations were clearly recognized. There is still not a sufficient database available from which the validity of these postulates can be assessed for industrial workers.

Auditory threshold shifts (TS) following noise exposure represent a complex response whose biophysical substrata are still not completely understood. The magnitude of the shift, whether a TTS or a CTS (Miller *et al.*, 1963), its frequency specificity, and its postexposure time course, which is dependent upon the magnitude of the TS, vary in a complex manner with the exposure stimulus parameters. The early stages of fatigue described by Hirsh and Ward (1952) and by Hirsh and Bilger (1955), in which TS was shown to have a diphasic profile during the first two minutes (TTS_2) postexposure, led to the adoption of TTS_2 as an index of the effects of an exposure, i.e., Kryter's postulate (a). As stimulus levels increased it became clear that complex TS dynamics was not just limited to the early postexposure period, but could also be found in the steady growth of TS over 8 to 12 h following a high-level exposure (Luz and Hodge, 1971; Hamernik *et al.*, 1988; Dancer *et al.*, 1991). This growth of TS has been associated with mechanical disruption of the structural integrity of the organ of Corti, and in animal models has been shown to be associated with sensory cell loss and NIPTS (Hamernik *et al.*, 1988).

An underlying rationale that pervades many of the TS studies is the desire to estimate PTS based upon some measure of TS. This goal has remained elusive despite some

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novel attempts such as the use of time-integrated TS as an index of PTS (Sitler, 1972; Kraak, 1973). Thorough reviews of TS phenomena can be found in the literature (e.g., Ward, 1973; Kraak, 1981; Mills, 1986). This paper presents an analysis of the relation between TS measured at various postexposure times and the resulting PTS using a database obtained from over 900 chinchillas exposed to various noises.

II. METHODS

All data were obtained from chinchillas that were used in various noise-exposure experiments over a period of approximately 7 years in two different laboratories using different experimental protocols. All animals were made monaural by the surgical destruction of the left cochlea. Pure-tone thresholds were measured in each animal using either a behavioral avoidance-conditioning technique (Patterson *et al.*, 1993) or evoked-response audiometry (Ahroon *et al.*, 1996). The electrode for recording the auditory-evoked potentials (AEP) was implanted into the left inferior colliculus during the monauralizing surgery. Following surgery all animals were allowed to recover for 2 weeks before any preexposure testing began. All animals were awake during threshold testing. The average of at least three separate threshold determinations at each frequency obtained on different days was used to define the preexposure audiogram. Following a 30-day postexposure recovery period, thresholds were measured again on 3 different days and averaged for each animal to establish PTS. PTS was defined as the difference between the mean 30-day post- and preexposure audiograms.

The TS data obtained from the 936 chinchillas that were used in this analysis were separated into the following three data sets based on the type of noise exposure that was used.

Data set I ($N=192$): Acute exposures to broadband or narrow-band impacts having peak SPLs in the range 129 through 147 dB. All exposures lasted for 5 min. Thresholds were measured at 2 min, 1 h, 3 h, 6h, and 24 h postexposure at a number of frequencies using a behavioral avoidance-conditioning paradigm. Only thresholds at the octave intervals of 0.125, 0.250, 0.5, 1.0, 2.0, 4.0, and 8.0 kHz were used in the following analysis. Details of exposure and threshold testing procedures can be found in Patterson *et al.* (1993).

Data set II ($N=423$): Acute exposures to high-level, broadband impulses having peak SPLs in the range 150 through 160 dB. Exposures lasted from a fraction of a second (e.g., a single impulse) to 16.5 hours (e.g., 100 impulses; 1 impulse every 10 min). Thresholds were measured using evoked-response audiometry recorded from the inferior colliculus. TS measures were obtained 15 min, 2 h, 8 h, and 24 h postexposure at 0.5, 2.0, and 8.0 kHz. Details of the exposure and threshold testing protocols can be found in Ahroon *et al.* (1996).

Data set III ($N=321$): Five-day uninterrupted exposures to broadband impacts, octave bands of noise, or combinations of these two classes of noise. These exposures produced an asymptotic threshold shift (ATS) (Blakeslee *et al.*, 1978). Peak SPLs of the impacts ranged from 113 through 125 dB and rms levels of the octave band noises varied between 86 and 95 dB. Threshold shifts were obtained at 15

min, 2 h, 8 h, and 24 h postexposure at 0.5, 2.0, and 8.0 kHz. Details of the exposures and threshold testing protocols can be found in Ahroon *et al.* (1993).

Correlations between TSs and PTS, over a broad range of audiometric test frequencies, were possible only for data set I. Data from the three test frequencies measured in data sets II and III were used to verify and expand the observations made from data set I.

From the postexposure threshold recovery function for each animal, the following three TS measures were obtained for correlation with PTS at the corresponding frequency:

- (1) TS_0 : The first TS measured between 0 and approximately 20 min postexposure;
- (2) TS_{max} : The maximum TS measured in the 0- to 24-h postexposure period (Hamernik *et al.*, 1988).
- (3) TS_{24} : The TS measured 24 h following removal from the noise.

III. RESULTS AND DISCUSSION

The analysis presented below treats all TSs as equivalent, regardless of the type of noise exposure (continuous octave band, continuous non-Gaussian, impact or impulse) or frequency spectrum that produced the TS.

A. Scatter plots

Some perspective on the relation between TS and PTS can be obtained by plotting the PTS for each test frequency from each of the three data sets (together or separately) as a function of each of the three TS measures. An example of the resulting scatter plots for the 0.5-, 2.0-, and 8.0-kHz test frequencies for the entire data pool is shown in Fig. 1. The data at these frequencies represent the largest pool available for analysis ($n=936$). There is considerable variability in the data. For example, during the early postexposure period (TS_0) there are large numbers of animals that show $0 < TS < 80$ dB. After a 30-day recovery period, these same animals show $0 < PTS < 10$ dB. Similarly, animals with, for example, $60 < TS < 70$ dB can show $0 < PTS < 60$ dB. While some relatively small part of this variability is inherent in the experimental methods, the largest component most likely reflects variability in susceptibility (Ward, 1968) to noise, as has been often reported in the literature especially following impulse/impact noise exposures. For those animals with no PTS (i.e., $-5 < PTS < 5$ dB) the postexposure TSs can be considered TTSSs. Also seen in Fig. 1 is a number of animals with $PTS < -5$ dB despite having a broad range of TSs, reflecting either inadequately defined pre- or postexposure thresholds or a "real" improvement in thresholds following noise exposure. The animals presented in this analysis had preexposure thresholds that were typically within ± 1 s.d. of the laboratory norms (Hamernik and Qiu, 2000) with typical test/retest reliability of ± 5 dB.

Because the data shown in Fig. 1 suggest both linear and nonlinear relations among the TS/PTS variables, a function that would allow nonlinear and (nearly) linear descriptions of the data of the form $PTS = \alpha(e^{TS/\beta} - 1)$ was chosen to describe the results of the three data sets. This relation allows PTS to be zero with zero TS; it is nonlinear for small values

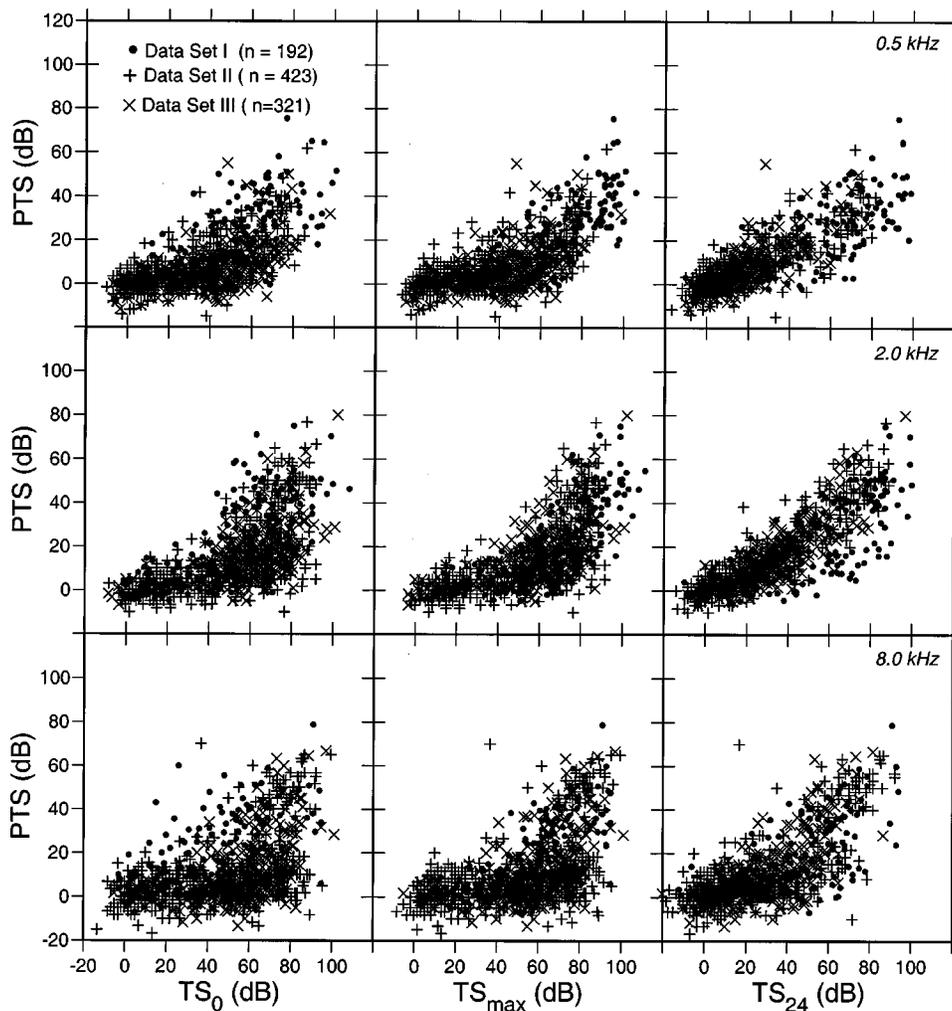


FIG. 1. Scatter graphs displaying threshold shift immediately following noise exposure (TS_0), maximum threshold shift (TS_{max}), and threshold shift 24 h following exposure (TS_{24}) with the corresponding permanent threshold shifts at the 0.5-, 2.0-, and 8.0-kHz test frequencies for data sets I, II, and III.

of the variable β and approaches linearity for larger values of β . A power series expansion of this function shows that the exponential becomes linear of the form $PTS = (\alpha/\beta)TS$, for large values of β , with a slope of α/β and a zero intercept. All bivariate regression and correlation analyses were computed using DELTAGRAPH PROFESSIONAL on a Macintosh computer. The constants α , β , and coefficients of determinance r^2 , which were obtained following a nonlinear regression analysis, for each frequency and data set are shown in Table I. In general, the highest correlations were found for the TS_{24}/PTS relation. This was expected for at least two reasons. (i) Since many of the severe exposure conditions produced a growth of TS (Hamernik *et al.*, 1988) TS_0 will underestimate the PTS and (ii) a large part of the TTS component of CTS, which is arguably the most labile part, has recovered during the 24-h postexposure period (see also Pfander *et al.*, 1980). Also evident in this table are the typically smaller values of the constant β for the TS_{max} data compared to the TS_0 and TS_{24} data. This can be explained by noting that TS_{max} is equal to TS_0 for smaller (<30 dB) values of TS. At these levels of TS NIPTS is small but increases rapidly when there is a postexposure growth of TS (i.e., when $TS_0 < TS_{max}$).

The trends in this data are more clearly seen when the predictor TS measurements are collapsed into 5-dB bins and the mean TS within the bin is plotted against the mean PTS

for that bin. Examples of such a data reduction at the 2-kHz test frequency for each of the data sets are shown in Fig. 2. [This statistical manipulation (or "pretreatment") has the added benefit of eliminating skewness in the predictor vari-

TABLE I. Coefficients of determinance (r^2) and the constants α (dB) and β (dB) for the exponential curve fit for the relation between PTS and TS_0 , TS_{max} , and TS_{24} for all three data sets.

| kHz | r^2 | TS_0 | | TS_{max} | | TS_{24} | | r^2 | α | β |
|--------------|-------|----------|---------|------------|----------|-----------|-------|-------|----------|---------|
| | | α | β | r^2 | α | β | r^2 | | | |
| Data set I | | | | | | | | | | |
| 0.125 | 0.47 | 23.8 | 90.0 | 0.54 | 3.9 | 35.4 | 0.58 | 17.2 | 69.5 | |
| 0.25 | 0.57 | 28.0 | 93.2 | 0.59 | 3.2 | 34.3 | 0.62 | 19.8 | 77.1 | |
| 0.5 | 0.57 | 48.4 | 140.6 | 0.65 | 5.5 | 44.3 | 0.66 | 64.7 | 183.2 | |
| 1.0 | 0.55 | 61.4 | 163.0 | 0.66 | 7.8 | 50.4 | 0.67 | 48.3 | 139.2 | |
| 2.0 | 0.58 | 40.7 | 118.0 | 0.63 | 5.1 | 42.1 | 0.64 | 17.5 | 69.4 | |
| 4.0 | 0.50 | 128.1 | 310.0 | 0.53 | 7.4 | 50.7 | 0.52 | 33.1 | 106.1 | |
| 8.0 | 0.45 | 209.9 | 480.2 | 0.51 | 6.7 | 47.0 | 0.53 | 26.5 | 88.5 | |
| Data set II | | | | | | | | | | |
| 0.5 | 0.49 | 6.1 | 46 | 0.54 | 8.4 | 58.5 | 0.66 | 64.7 | 183.2 | |
| 2.0 | 0.54 | 7.2 | 46.6 | 0.59 | 1.7 | 29.1 | 0.85 | 39.2 | 96.0 | |
| 8.0 | 0.33 | 6.4 | 49.6 | 0.32 | 3.5 | 36.9 | 0.64 | 9.9 | 45.1 | |
| Data set III | | | | | | | | | | |
| 0.5 | 0.34 | 2.3 | 34 | 0.34 | 2.3 | 34.4 | 0.58 | 42.1 | 119.0 | |
| 2.0 | 0.31 | 4.9 | 43.9 | 0.32 | 10.1 | 66.4 | 0.65 | 24.8 | 72.4 | |
| 8.0 | 0.26 | 7.5 | 60.1 | 0.27 | 7.0 | 57.6 | 0.50 | 6.9 | 36.0 | |

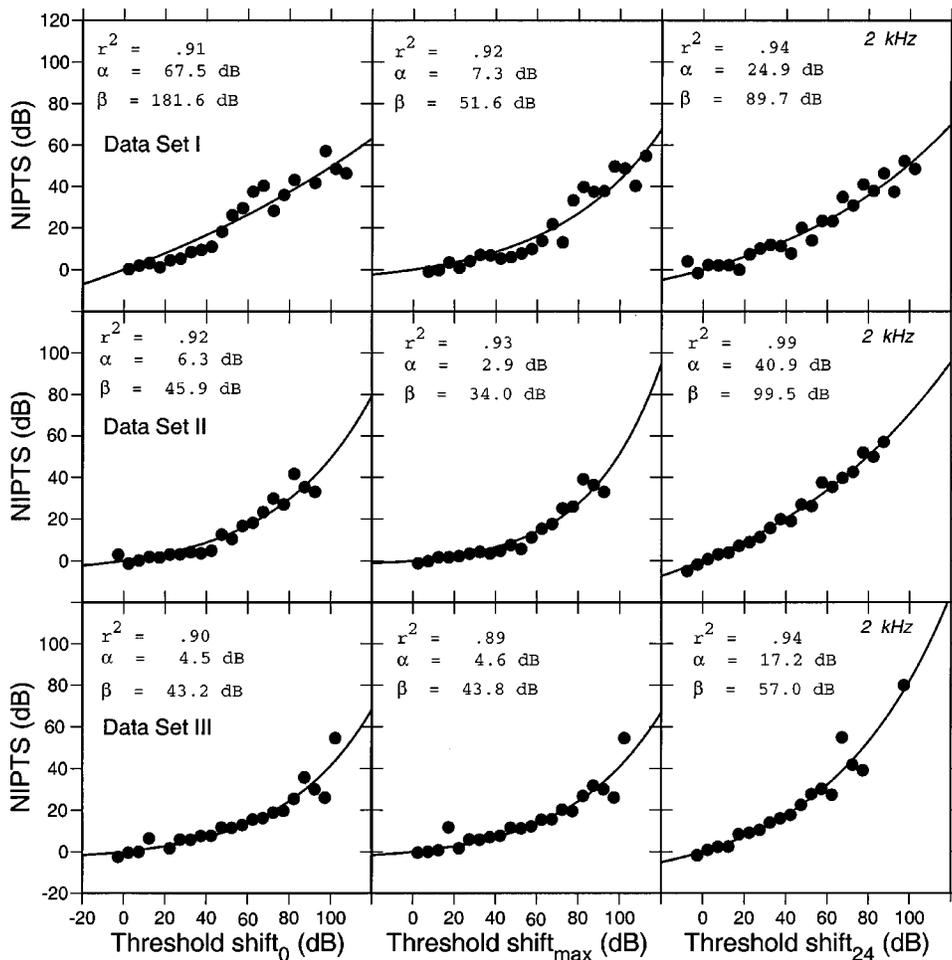


FIG. 2. The 5-dB bin reduction of the scatter plot data displaying threshold shifts immediately following noise exposure (TS_0), maximum threshold shift (TS_{max}), and threshold shift 24 h following exposure (TS_{24}) with the corresponding permanent threshold shifts at the 2.0-kHz test frequency for data sets I, II, and III. The solid curves represent a least-squares approximation to the exponential function $f(x) = \alpha(e^{TS/\beta} - 1)$.

ables.] In this figure, the abscissa represents the midpoint of a TS bin and the ordinate is the mean PTS for the subjects displaying the TS measure within the 5-dB bin. In general, the graphs for each data set and each frequency were similar and clearly show a positive relation between the TS variables and PTS. The 5-dB bin analysis, as expected, yields deceptively high correlation coefficients.

B. Percentile results

Noise-exposure criteria are typically designed to protect a certain percentile of the exposed population from an NIHL. Audiometric testing of employees in industrial settings is usually performed following a period of respite from the noise environment. With such considerations in mind the entire data set was analyzed using the same nonlinear function to relate TS_{24} to the median and 90th percentile PTS data. Figure 3 illustrates the exponential regression curves for the median (lower curve in each panel) and 90th percentile (upper curve) PTS within each 5-dB TS_{24} bin for the 0.5-, 2.0-, and 8.0-kHz test frequencies for each data set. Each median curve in Fig. 3 displays a nonlinear trend with increasing TS_{24} while the 90th percentile results generally show linear trends. Figure 4 presents the ratio of the α and β coefficients from the exponential least-squares analysis of percentile data from all three data sets. The slopes of these curves at $TS_{24}=0$ (i.e., ratio of α/β) for the median data are smaller than those of the 90th-percentile data, indicating a slow growth of

NIPTS for relatively small values of TS_{24} . Surprisingly, the slopes of the 90th-percentile data are similar across frequency with a value of approximately 0.7, with no consistent change in the rate of growth of PTS with frequency. The linear growth of NIPTS with increasing TS_{24} in the 90th-percentile analysis suggests that, in the chinchilla model, a modification of the Kryter *et al.* (1966) postulate (c) with a factor of something less than 1.0 may be useful in estimating the NIPTS in the most susceptible chinchillas.

C. Multiple linear regression

The exponential least-squares regression described above relates a single predictor variable to the criterion PTS variable. Multiple regression and correlation methods allow the association of more than one predictor variable to a single-criterion variable. Because of the limited frequencies represented in the TS data of sets II and III a multiple regression analysis was best limited to data set I. Since PTS typically occurs over several audiometric test frequencies, such an analysis seemed appropriate. Thus, three sets of multiple regression and correlation analyses were performed using the PTS as the criterion variable and one of three TS measures as the predictor variables using the SPSS (Release 4) statistical package.

There are a number of multivariate regression techniques used to make predictions or measures of relation between a criterion variable and a set of predictor variables

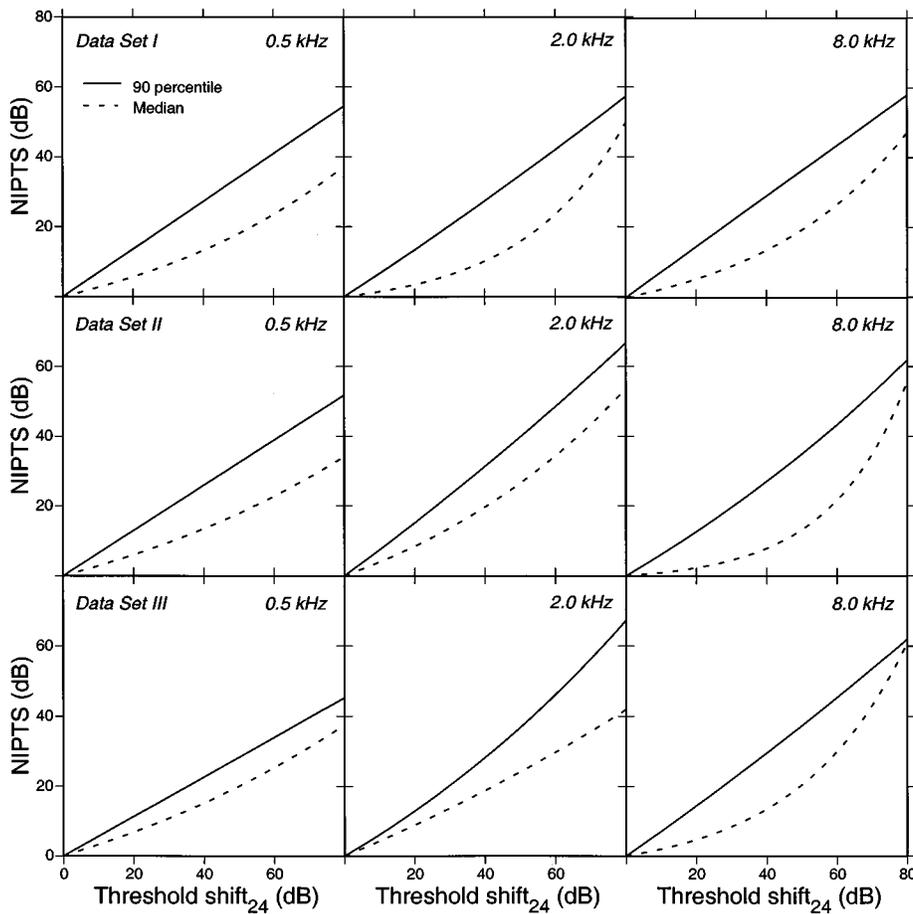


FIG. 3. Exponential least-squares regression lines showing the relation between TS_{24} and median PTS (lower curves) and 90th-percentile PTS (upper curves) at 0.5, 2.0, and 8.0 kHz for each of the three data sets.

(e.g., stepwise, forward entry, etc.). It seemed appropriate to reference any multiple correlations with the correlations between any of the TS measures and PTS at a single test frequency. Thus, the multiple regression/correlation model that was chosen for the analysis of the TS data performed separate bivariate regressions of the PTS (criterion variable) and the TS measure (predictor variable) at each test frequency. Following the calculation of the least-squares regression line and the associated r^2 , multiple correlations were computed by adding the TS measures at other test frequencies in descending order of importance. The addition of additional variables was stopped when the change in the r^2 was not significantly increased ($\alpha=0.05$). (That is, the analysis

model specified a forced entry of the first predictor variable and then forward entry of any additional predictor variables.) For example, the r^2 between PTS at 2.0 kHz and TS_{24} at the 2.0-kHz test frequency was approximately 0.64. Following this calculation, the TS_{24} measure at the 1.0-kHz test frequency was added and the r^2 increased to approximately 0.66. At this point, adding any of the eight other TS_{24} measures did not cause a statistically significant increase in r^2 and therefore the multiple regression procedure stopped. This analysis was performed for all seven test frequencies and three predictor variables for data set I.

Table II lists the r^2 values from the multiple regression and correlation analyses. Each row in the table represents a summary of one complete multiple-correlation analysis. The first set of columns lists the results from the bivariate correlation. A second or third set of columns is presented if adding another TS measure at a specified frequency significantly improved the r^2 value reported in the previous column. Two things are apparent from this table. First, as noted above, the linear correlations between PTS and the TS measures are all relatively high. Second, while the incorporation of additional variables increases the correlation between the criterion and predictor variables for most test frequencies and predictor variables, this increase is relatively modest, ranging from no increase (TS_{max} at 0.125 kHz and TS_{24} at 0.125, 1.0, and 4.0 kHz) to 0.07 (TS_0 at 8.0 kHz). This largest difference represents a total of 7% (45% to 52%) change in r^2 , reflecting a 7% increase in the amount of variability in PTS that could be explained based upon the variability of the TS_{24} variables.

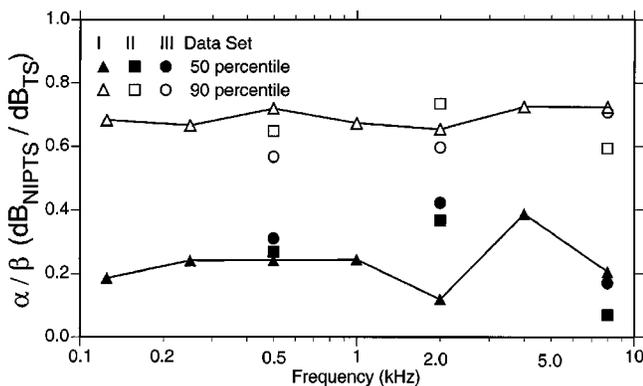


FIG. 4. The slope (α/β) of the regression line at $TS=0$ derived from the exponential least-squares regression equations between the median TS_{24} and the median and 90th-percentile PTS for all three data sets.

TABLE II. Summary of multiple correlation analyses for data set I.

| kHz | r^2 | kHz | r^2 | kHz | r^2 |
|-------------------|--------|-------|--------|-------|--------|
| TS ₀ | | | | | |
| 0.125 | 0.4661 | 1.000 | 0.5041 | | |
| 0.250 | 0.5675 | 1.000 | 0.6028 | | |
| 0.500 | 0.5687 | 0.125 | 0.6037 | 2.000 | 0.6182 |
| 1.000 | 0.5536 | 2.000 | 0.5950 | 0.125 | 0.6117 |
| 2.000 | 0.5794 | 0.250 | 0.6029 | 8.000 | 0.6141 |
| 4.000 | 0.4987 | 1.000 | 0.5375 | | |
| 8.000 | 0.4525 | 0.250 | 0.5163 | | |
| TS _{max} | | | | | |
| 0.125 | 0.5391 | | | | |
| 0.250 | 0.5872 | 1.000 | 0.6450 | 0.125 | 0.6557 |
| 0.500 | 0.6492 | 0.125 | 0.6708 | | |
| 1.000 | 0.6640 | 0.125 | 0.6763 | | |
| 2.000 | 0.6335 | 1.000 | 0.6653 | | |
| 4.000 | 0.5254 | 1.000 | 0.5651 | | |
| 8.000 | 0.5104 | 1.000 | 0.5601 | | |
| TS ₂₄ | | | | | |
| 0.125 | 0.5770 | | | | |
| 0.250 | 0.6170 | 0.125 | 0.6558 | 1.000 | 0.6726 |
| 0.500 | 0.6557 | 0.125 | 0.6888 | | |
| 1.000 | 0.6687 | | | | |
| 2.000 | 0.6432 | 1.000 | 0.6607 | | |
| 4.000 | 0.5171 | | | | |
| 8.000 | 0.5274 | 1.000 | 0.5606 | | |

Thus, based on the large linear correlation coefficients and relatively mild improvements in prediction based on the incorporation of additional criterion variables, a multiple-correlation approach to this data is probably not warranted due to the rather large increase in complexity of models to predict PTS from TS measures.

IV. CONCLUSIONS

- (1) The data presented in this report (Fig. 1) suggest that an exponential function of the form $PTS = \alpha(e^{TS/\beta} - 1)$ is adequate to describe the relation between threshold shifts following a noise exposure and the concomitant permanent changes in hearing in the chinchilla.
- (2) The correlations between TS and PTS were generally highest for the TS₂₄ variable and lowest for the TS₀/PTS relation.
- (3) The 90th-percentile NIHL is linearly related to TS₂₄ with a slope of approximately 0.7, independent of test frequency.

Considering the above, the results presented in this paper provide support, in the chinchilla model of NIHL, for a modified version of the three Kryter *et al.* (1966) postulates mentioned in the Introduction. Specifically, (a) TS₂₄ is a consistent measure of the effects of a single 8-h work-day exposure to noise. (b) All exposures that produce a given TS₂₄ will be equally hazardous. Finally, considering that the 90th-percentile data shown in Fig. 3 are roughly similar for all three data sets; that data set III is derived from various 5-day asymptotic TS exposure paradigms and that the suggestion has been made that ATS represents an upper bound to the NIPTS to be expected from many years of exposure, then postulate (c) becomes NIPTS, in the most susceptible 10% of

the chinchilla population, following 10 years of exposure, 8 h/day is approximately equal to (0.7) TS₂₄ measured after an 8-h exposure to the same noise.

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