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The relationship between auditory brainstem response latencies and behavioral thresholds in normal hearing infants and adults

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Abstract

The relationship between behavioral thresholds and auditory brainstem response (ABR) latencies for 4 and 8 kHz tone pips were examined in normal-hearing 3-month-olds, 6-month-olds and adults. The latencies of waves I and V and the I-V interval of the ABR were analyzed. A linear latency-intensity function was also fit to each subject's latencies for each wave at several levels. The y-intercept of the latency-intensity function was used as a summary measure of latency to examine behavior-ABR correlations. The pattern of age-related change in behavioral threshold was not closely matched by age-related latency reduction for Wave I, Wave V or the I-V interval. However, 3-month-olds with higher behavioral thresholds had longer Wave V latencies and longer I-V intervals than 3-month-olds with lower behavioral thresholds. There was no significant difference in latency between 6-month-olds or adults with higher thresholds and 6-month-olds or adults with lower thresholds. There was also a significant correlation between the Wave V - Wave I latency-intensity intercept difference and behavioral threshold at both 4 and 8 kHz among 3-month-olds. The correlation was not significant among 6-month-olds or adults. These findings suggest that one of the factors responsible for immature behavioral thresholds at 3 months is related to transmission through the auditory brainstem. Because variability in hearing threshold among normal-hearing adults is low, it is not surprising that behavioral threshold is unrelated to ABR latency in this group. However, the lack of such a relationship among 6-month-olds implies that structures central to the auditory brainstem, either sensory or nonsensory, or both, must be responsible for immature behavioral thresholds after 6 months of age.

Key words: Hearing; Development; Human; Evoked potentials; Psychophysics

1. Introduction

There is a general consensus that the sound intensity required to elicit a behavioral response declines progressively with age between infancy and late childhood (Berg and Smith, 1983; Nozza and Wilson, 1984; Olsho et al., 1988; Schneider et al., 1986; Trehub et al., 1980; Trehub et al., 1988). The sources of this age-related change in hearing are less clear. While some investigators believe that properties of the primary auditory system are largely responsible (e.g., Schneider and Trehub, 1992), others hold that central factors such as attention are also important (e.g., Werner, 1992; Wightman and Allen, 1992). In support of the role of primary auditory system maturation it has been noted that behavioral threshold development follows a time course similar to that reported for some evoked potential measures (e.g., Eggermont, 1985; Schneider et al., 1989).

The aspects of primary auditory system maturation that could be involved in both threshold and evoked potential development are not well established. The available data suggest that the cochlea is close to maturity in newborns (e.g., Pujol and Lavigne-Rebillard, 1992; Bargones and Burns, 1988), but conductive immaturities have been reported to persist into childhood (Keefe et al., 1993, 1994; Okabe et al., 1988). Maturation of the primary auditory nervous system could conceivably play a part: For example, synaptic immaturity could lead to a loss of information along the neural pathway which would, in turn, lead to reduced sensitivity, prolonged evoked potential latency and reduced evoked potential amplitude in young hu-

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mans. The data bearing on the structural development of the human auditory nervous system is, however, quite limited (e.g., Perazzo and Moore, 1991; Perazzo et al., 1992; Ponton et al., 1994; Yakovlev and Lecours, 1967).

In a previous paper (Werner et al., 1993), we developed a simple model of how the relationship between behavioral and evoked potential measures could be used to address the sources of developmental change, and we used this model in assessing the relationship between behavioral threshold and auditory brainstem response (ABR) threshold among human infants. The model holds that there are three ways that behavioral and evoked potential measures could be related which would suggest a common underlying mechanism of maturation.

First, the relative average values of the measures could remain constant during development. For example, adults' behavioral thresholds average 10–15 dB lower than their ABR thresholds (e.g., Gorga et al., 1988); if infants' behavioral and ABR thresholds were similarly related, it would suggest that the sensory system constrains the behavioral response in a similar way in infants and adults. In fact, Werner et al. (1993) reported that the relative average values of behavioral and ABR thresholds changed between infancy and adulthood.

Second, the two measures could show similar developmental gradients. For example, high-frequency behavioral thresholds tend to become adultlike earlier than low-frequency behavioral thresholds (e.g., Olsho et al., 1988; Schneider and Trehub, 1992); common sensory mechanisms would be suggested if evoked-potential measures develop along the same frequency gradient. However, Werner et al. (1993) found that behavioral and ABR thresholds followed different frequency gradients during development.

Third, the two measures taken in the same individuals could be correlated. For example, normal-hearing infants with higher behavioral thresholds could have higher ABR thresholds, and those with more adultlike behavioral thresholds could have more adultlike ABR thresholds. It should be noted that such correlations may be more evident during development than they are in the mature listener: The range of variation among normal-hearing adults may not be sufficient to support a correlation, but during development variability in the status of the auditory system may be great enough to support a correlation (see discussion by Gottlieb, 1971). In other words, it is possible that one would find a significant correlation among normal-hearing infants, even when the correlation among normal-hearing adults was not significant. Werner et al. (1993) reported a significant correlation between behavioral and ABR thresholds at 4 kHz, but not at 1 or 8 kHz, among 3-month-olds. No behavioral-ABR correlations were significant among 6-month-olds or adults. Thus, in general, the results from Werner et al. provide scant evidence for a common source of behavioral and ABR maturation.

Before rejecting the possibility that the maturation of behavioral sensitivity and the maturation of the ABR have a common source, however, it seemed appropriate to examine other ABR measures. It is generally recognized that amplitude-based ABR measures, such as response threshold, can be highly variable (discussed, e.g., by Hall, 1992). In examining our own ABR data, in fact, we found that as a proportion of the mean of each measure, the variability in ABR threshold tended to be higher than the variability in ABR latency. To the extent that the additional variability in ABR threshold is not related to auditory sensitivity, it would make it more difficult to find significant correlations with behavioral sensitivity [1]. Conversely, if these additional sources of variability do not contribute to ABR latency, it should be easier to find relationships between ABR latency and behavioral threshold, if such relationships are present. Of course, latency measures have the disadvantage that they may be influenced by factors (e.g., myelination) that do not affect behavioral sensitivity (e.g., Hendler et al., 1990).

In the present paper, we compare the development of behavioral tone-pip thresholds to that of tone-pip-evoked ABR Waves I and V latencies. The behavioral thresholds are those described in Werner et al. (1993). The latencies were calculated from the ABR recordings used to estimate thresholds in that study. Only responses to 4 and 8 kHz tone pips are described here; Wave I latencies proved extremely difficult to estimate at 1 kHz, especially for adults.

2. Method

Subjects

The subjects were: 96 three-month-olds; 89 six-month-olds and 76 adults, all of whom provided a behavioral threshold at either 4 or 8 kHz. All subjects met the following criteria for inclusion:
1) no family history of congenital hearing loss or other risk factors for hearing loss
2) normal developmental course, including term birth
3) healthy on test date
4) normal tympanometry results on test date
5) no more than two prior episodes of ear infection and at least one week since treatment for last ear infection was completed

[1] The variability in behavioral threshold that is not related to auditory sensitivity also makes it difficult to identify relationships with ABR measures. Unfortunately, we know of no ready, less variable alternative to threshold in the case of behavior.

6) identifiable click-evoked ABR at 20 dB nHL.

Of these subjects, 72 three-month-olds, 70 six-month-olds, and 65 adults also provided latency estimates for at least one of ABR Waves I or V at one or more sound pressure levels.

Stimuli and apparatus

Details of the spectra of the stimuli, the calibration procedure, and ABR recording are given in Werner et al. (1993). A brief summary is given here. The stimuli were digitally generated 4 and 8 kHz tone pips, with 3-cycle rise, 1-cycle plateau, and 3-cycle fall. This meant that the rise time of the 4-kHz tone pip was longer than that of the 8-kHz tone pip. Although ABR latency is affected by stimulus rise time, infants' latencies are not differentially affected by this stimulus variable (Folsom and Aurich, 1987). Thus, the difference between 4-kHz and 8-kHz latencies may be slightly exaggerated by this procedure, but differences between infant latencies and adult latencies would not be affected.

The tone pips were presented at a rate of 13.3/s and presented through Etymotic ER-1 insert phones with foam ear tips. Peak SPL was measured at the output of the Etymotic sound delivery tube with a Zwislocki coupler fit with a commercially available adaptor and a sound level meter set to 'peak hold'. The insert phone was used for both ABR and behavioral testing; only the right ear of each subject was tested. Both the behavioral and ABR experiments were under computer control. The ABRs were averaged over 2048 stimulus presentations.

In order to optimize the respective response, it is common practice to use long-duration tones to elicit behavioral responses and short-duration tones to elicit the ABR. For the purposes of identifying common sources of variability in behavior and ABR, however, it is not clear that this is appropriate. While using long-duration tones might reduce the contributions of processes such as attention to the behavioral threshold, it will increase the contributions of processes such as temporal integration to that measure. Using short-duration tones should do the reverse. Neither attention nor temporal integration should affect the ABR. Thus, no matter which stimulus we choose to elicit behavioral responses, we will add a source of variance that is not common to the two measures, making it more difficult to identify correlations. In the present study we chose to use short-duration tone pips to elicit both responses. However, whether long-duration tone behavioral thresholds would be more strongly correlated with ABR measures is an interesting question deserving additional attention.

Absolute latencies were scored off-line on the microcomputer using locally developed software. Latency of Wave I was taken at the positive-going peak. Latency of Wave V was taken at the farthest point (in time) prior to the precipitous drop to the negative trough following the positive-going Wave-V peak (see Fig. 1). Each waveform was given an arbitrary code number at the time of data collection, to ensure that scorers were blind to stimulus condition and subject age at the time of scoring. Coded waveforms were scored on separate occasions by two individuals experienced in response identification. Disparities greater than 0.1 ms were arbitrated by a third scorer. The latency for each peak was averaged over replicated waveforms.

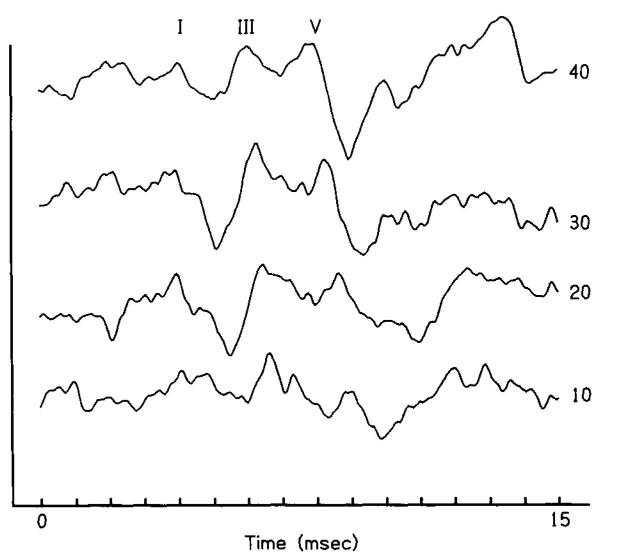

Fig. 1. Examples of auditory brainstem response waveforms of a 3-month-old infant. The stimulus was an 8-kHz tone pip. Level in dB HL is shown to the right of each waveform; the wave number is centered above the point chosen as the latency for each wave.

Procedure

Behavioral thresholds were estimated using the observer-based psychoacoustic procedure (OPP; Olsho et al., 1987). OPP is a discrimination learning paradigm: An observer uses the infant's behavior to judge whether a sound has been presented on a given trial, and the infant's responses to the sound are visually reinforced. Following training to an 80% correct criterion, thresholds were estimated using a one-up, two-down adaptive algorithm. Adult thresholds were estimated using essentially the same procedure. For additional details, see Werner et al. (1993).

For ABR recordings, both infants and adults were tested in natural sleep; EEG and EMG activity was monitored during each session and recordings were not made during periods of excessive EEG or EMG activity. In an earlier study (Werner et al., 1993), ABR thresholds were estimated using a modified method of limits algorithm; the level of the tone pip was set at 20 dB above the expected threshold on the first run, reduced in 10 dB steps until the response could not be identified, then increased in 2 dB steps to establish threshold. Because of differences among subjects in threshold, the levels at which responses were recorded differed across subjects. In addition, because threshold was defined as the lowest level at which Wave V could be identified, Wave I was frequently not identifiable near threshold. Insufficient data were available at any single level to make analysis at a single level meaningful. In two of the analyses reported here, all of the available latencies were analyzed and level was used as a covariate to make sure that any age or threshold effects were not due to differences in the levels presented to different subjects.

Analyzing latency with level as a covariate is not a completely satisfactory statistical solution where the correlation between threshold and ABR latency is of interest: For example, individuals who provided latencies at several levels would contribute more to such an analysis than individuals who provided a single latency. To get around such difficulties, we also analyzed the intercept of the latency-intensity function for each subject. This analysis included 64, 3-month-olds, 60, 6-month-olds, and 55 adults. If a subject had responses for at least two levels, ranging from 0 to 40 dB nHL in 10 dB steps, a line was fit, by least-squares criterion, to the data points describing latency as a function of level. Separate fits were used for Waves I and V for each subject. We will refer to this line as the latency-intensity function. The y-intercept, or 'latency intercept', of this line reflects its position along the latency axis. The latency intercept was taken as a measure of latency, allowing the available data to be summarized in an equivalent fashion for each subject. The reader should keep in mind that the values of the latency intercept need not correspond to any measured response latency; it is simply taken as a convenient summary statistic. To make this distinction clear, the term 'latency intercept' will be differentiated from the term 'latency' throughout the remainder of the paper.

Examples of latency-intensity functions obtained from one subject at each age are shown in Fig. 2. These data are typical of those obtained. The data were generally well characterized by single linear functions. For the vast majority of subjects (obviously excluding those who had only two latencies for a given wave), the linear fit accounted for more than 90% of the variance, and in all cases more than 70% of the variance was accounted for. There was no difference between infants and adults in goodness of fit to the data. There was no evidence that the range of intensities used to estimate the latency-intensity function affected the goodness of fit to the data or the slope and intercept of the function. There were two subjects, one 3-month-old and one adult, whose latency-intensity functions had slopes and intercepts that were more than 4 standard deviations from the mean at their respective frequencies; these subjects were not included in the analyses.

3. Results

Relationship between latency and behavioral threshold

Of the three approaches to describing the relationship between evoked potential and behavioral measures described in the Introduction, two are appropriate to relating latency measures to behavioral threshold: comparing the time course of development, or developmental gradients, of the two measures and assessing correlations between the two measures.

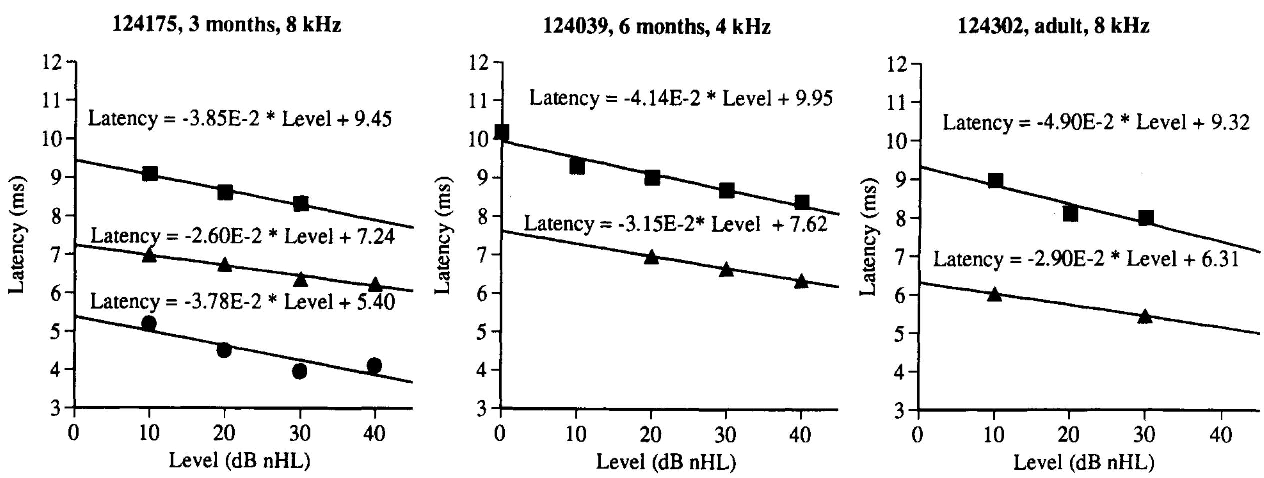

Fig. 2. Examples of latency-intensity function data and linear fits for three subjects, as indicated above each panel. In each panel, latencies for Wave I (●), Wave III (▲), and Wave V (■) are shown as a function of level. The equation of the best-fitting line is given above the corresponding function.

Developmental time course comparison. Average behavioral threshold is plotted as a function of age in Fig. 3. Threshold improved between 3 and 6 months at 8 kHz, but only slightly, if at all, at 4 kHz. Threshold improved at both 4 and 8 kHz between 6 months and adulthood. Analysis of variance (ANOVA) with Tukey HSD post-hoc, pairwise comparisons confirmed that the threshold difference between 3- and 6-month-olds was significant at 8 kHz ($P < 0.001$), but not at 4 kHz ($P < 0.06$). The differences between infants and adults was significant at both frequencies ($Ps < 0.001$).

The question is whether ABR latencies followed a similar developmental pattern to behavioral thresholds. The average latencies of Waves I and V and the I-V interval are plotted as a function of level for each age group in Fig. 4. To test for significant age effects, multiple regression was used; age, level, frequency and their interactions were entered as predictors of latency. Where specific pairwise age differences were of interest, ANOVA with Tukey HSD comparisons was used, although some of these comparisons included only a few subjects. Within each regression analysis (Wave I, Wave V, I-V interval), an alpha level of 0.007 was required for significance in order to maintain an overall Type I error rate for that regression analysis of 0.05 (Wilcox, 1987). In the case of follow-up analyses, an alpha level of 0.05 was used. If an effect is not mentioned, it was not statistically significant.

For Wave I, no systematic change in latency was evident between 3 and 6 months, although it appears that infants had longer latencies than adults in some conditions (Fig. 4a). Significant effects of age, frequency and level were identified (all $Ps < 0.001$). Follow-up comparisons between means confirmed that only the difference between infants and adults was significant ($P < 0.001$).

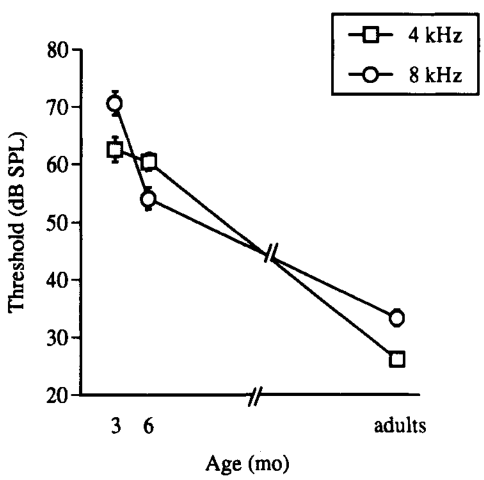

Fig. 3. Developmental time course of behavioral threshold. Error bars are ±1 standard error.

For Wave V, a progressive decrease in latency with age was observed in most conditions, a small decrease between 3 and 6 months and then a larger decrease between 6 months and adulthood (Fig. 4b). The exceptions were at 10 and 20 dB HL at 4 kHz, where 6-month-olds have latencies quite close to those of adults. The regression analyses indicated a significant age × frequency interaction ($P < 0.001$), a significant frequency × level interaction ($P < 0.003$), and significant main effects of frequency and level ($Ps < 0.001$). A separate regression showed significant age and level effects at 8 kHz, and pairwise comparisons showed significant differences between infants and adults ($Ps < 0.001$), but only a marginal difference between 3- and 6-month-olds ($P < 0.07$). At 4 kHz, the age × level interaction was significant ($P < 0.003$); follow-ups indicated a marginal age effect at 10 dB HL ($P < 0.07$), a significant difference between 3-month-olds and older listeners ($P < 0.002$) at 20 dB HL, and significant differences between infants and adults ($P < 0.007$) at 30 and 40 dB HL.

For the I-V interval, a progressive decrease with age was also observed in most conditions, although variability in this measure tended to be high (Fig. 4c). Here there was a larger decrease between 3 and 6 months than between 6 months and adulthood at both 4 and 8 kHz. The regression analysis indicated a significant age × frequency × level interaction ($P < 0.001$). At 4 kHz separately, only the age effect was significant: 3-month-olds had longer I-V intervals than 6-month-olds who had longer I-V intervals than adults ($P < 0.001$). At 8 kHz, the age × level interaction was significant ($P < 0.001$), and one-way ANOVAs showed significant age effects at 20, 30 and 40 dB HL ($Ps < 0.03$), but not at 10 dB HL ($P = 0.28$) where variability was highest. At 20 dB HL, 3-month-olds had longer I-V intervals than adults ($P < 0.02$), but 6-month-olds did not differ from either of the other age groups ($Ps > 0.10$). At 30 and 40 dB HL, 3-month-olds had significantly longer I-V intervals than either 6-month-olds ($Ps < 0.04$) or adults ($Ps < 0.05$), who did not differ from each other ($Ps > 0.8$). In all cases, however, the mean I-V interval of 6-month-olds was higher than that of adults, although the variability inherent in a difference measure may have prevented the mean difference from achieving significance.

In summary, none of the ABR latency measures showed a developmental pattern that exactly matched that seen in behavioral thresholds. Both Wave V latency and the I-V interval tended to decrease between 3 and 6 months, as behavioral thresholds do. However, the decrease tended to be about the same at 4 and 8 kHz, while behavioral thresholds improve more at 8 kHz than at 4 kHz for these stimuli. All of the ABR latencies decreased between infancy and adulthood, and, of course, behavioral thresholds improve between infancy and adulthood as well. Given the failure to find a correspondence at younger ages, the long time span involved, and the large number of factors that could contribute to behavior and the ABR independently, this 'correspondence' in developmental course is not impressive.

Correlations between behavioral threshold and ABR latency intercepts. We examined the correlations between behavioral threshold and three latency measures: latency intercepts for Waves I and V and the Wave V-Wave I latency intercept difference. Because the numbers of subjects in each age × frequency condition was relatively small, we applied multiple regression to assess the relationship between behavioral threshold and latency intercept in each age group. Frequency and latency intercept were entered as predictor variables in each regression. This procedure would allow us to assess the independent contributions of frequency and latency intercept to the behavioral threshold. Thus, the final regression analysis consisted of 3 regressions (one for each latency intercept) at each age, with latency intercept and frequency the predictor variables and behavioral threshold the dependent variable. More than 20 subjects (n = 20–46) were included in each regression, with two exceptions: only 12 adult subjects provided data in the analyses for Wave I latency intercept and for Wave V-Wave I latency intercept difference. A Bonferroni adjustment was used to hold the Type I error rate for the entire regression analysis to 0.05; thus, a result had to be significant at

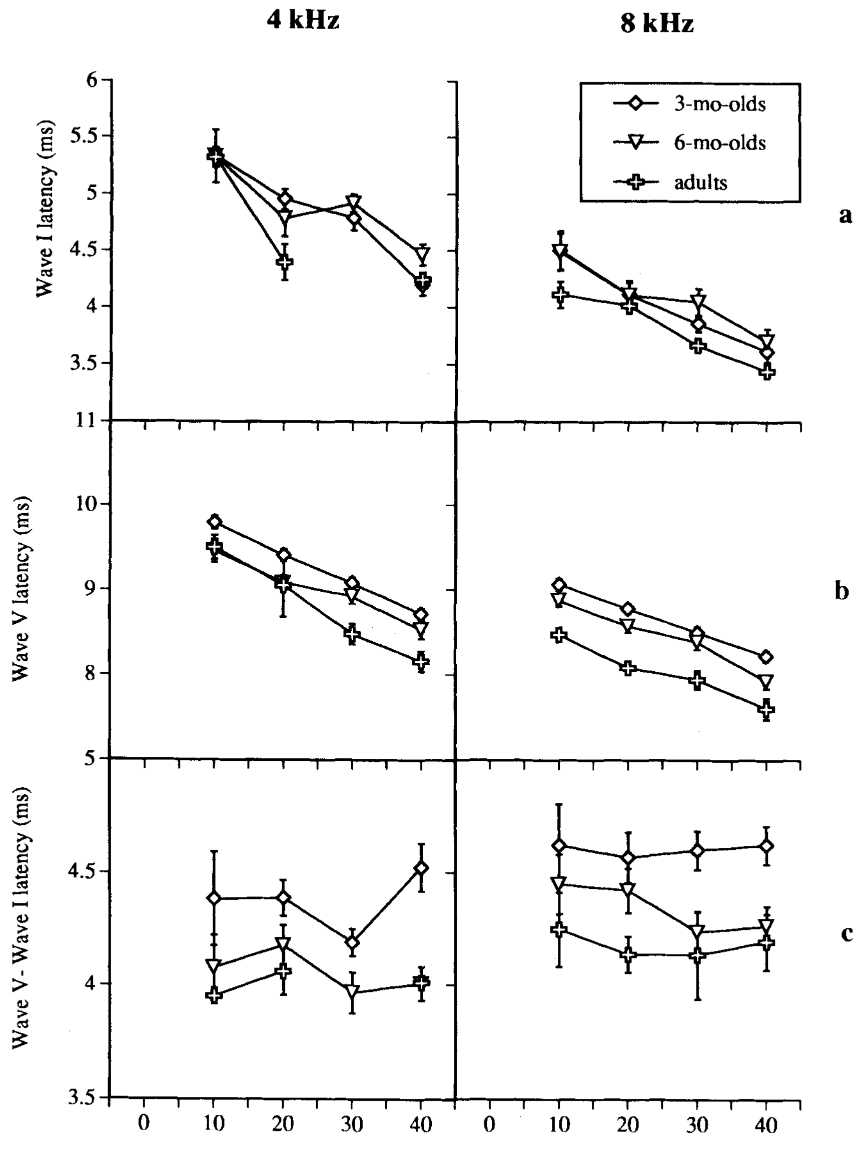

Fig. 4. ABR latencies as a function of level for three latency measures and three ages. Top panel (a) shows Wave I latency; middle panel (b) shows Wave V latency; bottom panel (c) shows the I–V interval. Error bars are ±1 standard error.

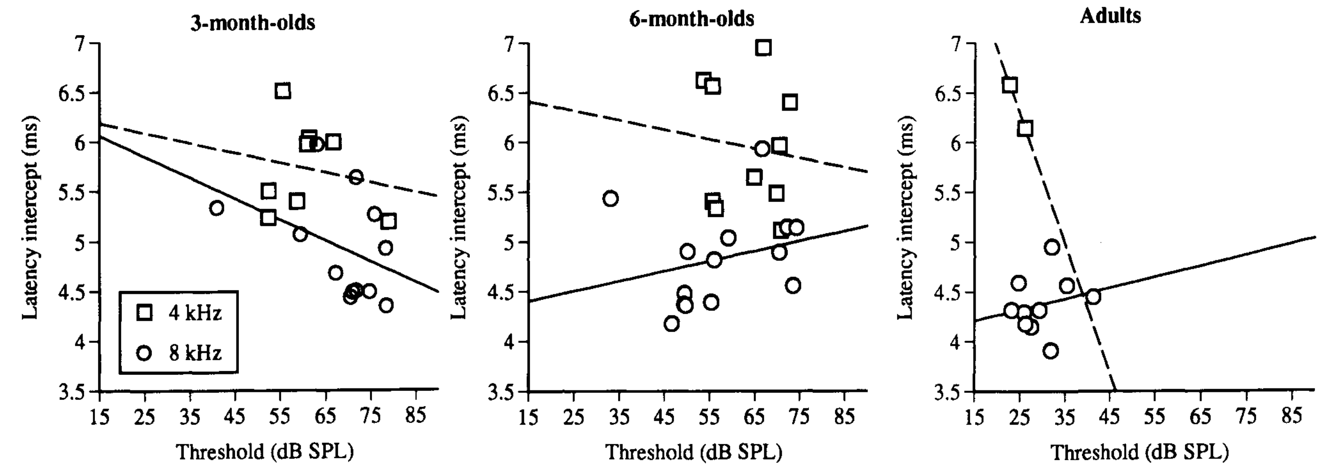

Fig. 5. Latency-intensity intercept of Wave I as a function of behavioral threshold at 4 kHz and 8 kHz for individual 3-month-olds, 6-month-olds and adults. The dashed lines indicate the linear relationship between threshold and latency intercept at 4 kHz. The solid lines indicate the linear relationship between threshold and latency intercept at 8 kHz.

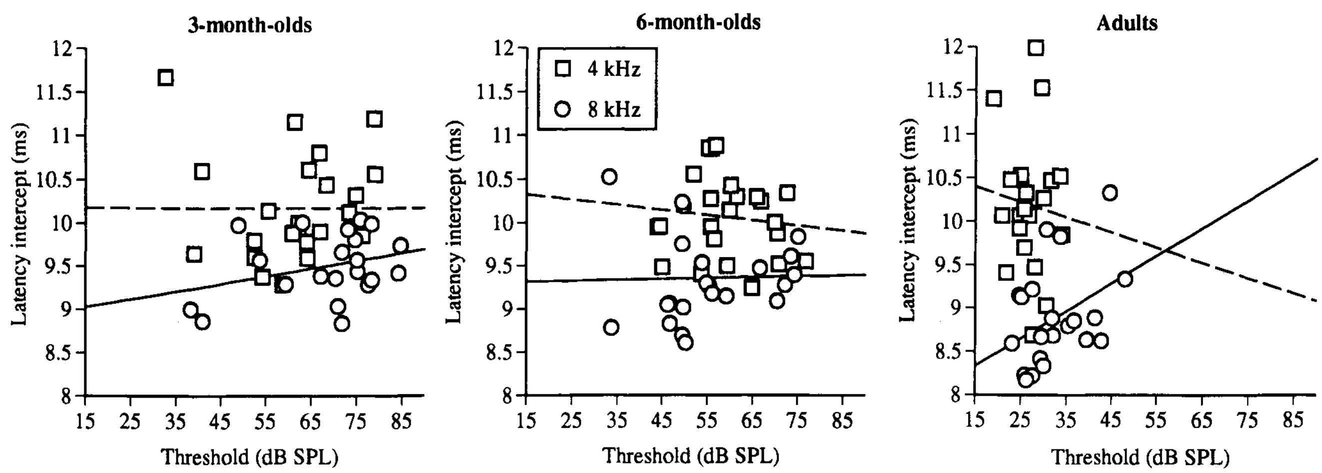

Fig. 6. Latency-intensity intercept of Wave V as a function of behavioral threshold at 4 kHz and 8 kHz for individual 3-month-olds, 6-month-olds and adults. The dashed lines indicate the linear relationship between threshold and latency intercept at 4 kHz. The solid lines indicate the linear relationship between threshold and latency intercept at 8 kHz.

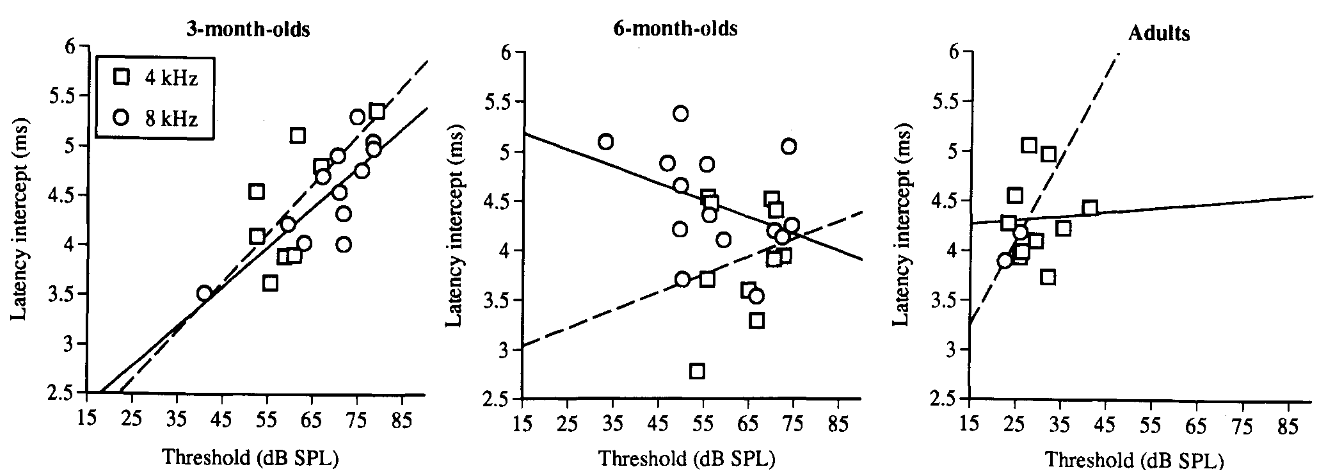

Fig. 7. Wave V–Wave I latency intercept difference as a function of behavioral threshold at 4 kHz and 8 kHz for individual 3-month-olds, 6-month-olds and adults. The dashed lines indicate the linear relationship between threshold and latency intercept at 4 kHz. The solid lines indicate the linear relationship between threshold and latency intercept at 8 kHz.

the 0.004 level to be considered statistically significant (Wilcox, 1987).

Scatterplots of the latency intercepts as a function of threshold are shown for each age group in Figs. 5 and 6. The regression lines are the simple regressions of threshold on latency intercept at each frequency. For Wave I (Fig. 5), the regression analysis indicated that the latency intercept did not significantly predict threshold in any age group (all $Ps > 0.15$). Similarly, Wave V latency intercept did not predict behavioral threshold for any age group (all $Ps > 0.28$; Fig. 6).

However, consider the relationship between Wave V-Wave I latency intercept difference and behavioral threshold illustrated in Fig. 7. As was the case for the absolute latency intercepts, the regression analyses showed no significant relationship between latency intercept difference for 6-month-olds ($P > 0.39$) or for adults ($P > 0.83$). However, there was a rather strong positive relationship between latency intercept difference and behavioral threshold among 3-month-olds ($P < 0.001$). The simple correlation between Wave V-Wave I latency intercept was 0.68 at 4 kHz and 0.80 at 8 kHz among 3-month-olds, indicating that latency intercept difference accounts for between 45 and 64% of the variance in behavioral threshold.

To summarize, Wave I and V latency intercepts do not reliably predict behavioral threshold at any of the ages tested. However, the Wave V-Wave I latency intercept difference is a strong predictor of behavioral threshold at 3 months at both 4 and 8 kHz. The Wave V-Wave I latency intercept difference does not predict behavioral threshold among 6-month-olds or adults.

Median-split analysis. Because latency intercepts are not commonly used to summarize ABR data, it would be natural to wonder if the correlation between the 3-month-olds' Wave V-Wave I latency intercept and behavioral threshold is an artifact associated with the latency intercept measure. To try to approach this problem from a slightly different angle, we performed an additional analysis of the original latencies. For each age and frequency, median threshold was calculated. Each subject was then classified according to whether his threshold fell above or below the median for his age and frequency. In other words, a 'median split' was performed on the behavioral thresholds. Then for each latency measure (Wave I, Wave V and I-V interval) and age group, an analysis of covariance was performed with the factors high v. low threshold, frequency, and their interaction; level was used as a covariate. Thus, in this analysis a significant high v. low threshold effect would indicate that subjects with high behavioral thresholds tended to have different latencies from subjects with low behavioral thresholds. An alpha level of.004 was used to hold the Type I error rate to 0.05 for the analysis of each latency measure.

Table 1
Average latencies (in ms, standard error in parentheses) of Wave I, Wave V, and the I-V interval for infants and adults with thresholds above ('high') and below ('low') median threshold

Age	Threshold	Wave I	Wave V	I–V interval
3 months	High	4.33	9.15 *	4.72 *
		(0.12)	(0.08)	(0.07)
	Low	4.39	8.99	4.37
		(0.11)	(0.07)	(0.06)
6 months	High	4.48	8.86	4.27
		(0.09)	(0.06)	(0.06)
	Low	4.31	8.82	4.25
		(0.11)	(0.07)	(0.07)
Adults	High	3.92	8.54	4.14
		(0.12)	(0.11)	(0.05)
	Low	4.00	8.43	4.26
		(0.11)	(0.08)	(0.10)

High threshold latencies which were significantly higher than the low threshold latency for that age and wave are marked with an asterisk (*).

Table 1 shows the mean and standard error of each latency for each age; the latencies have been averaged across frequency since the frequency × high v. low threshold interaction was not significant in any analysis (all $Ps > 0.3$). The difference between high-threshold subjects and low-threshold subjects in Wave I latency was not significant for any age group ($Ps > 0.10$). The differences between high-threshold and low-threshold 3-month-olds in both Wave V latency and the I-V interval were significant ($Ps < 0.004$). The high v. low threshold difference was not significant in either Wave V latency or the I-V interval for either 6-month-olds or adults ($Ps > 0.4$). Thus, the median-split analysis confirms the results of the correlational analysis: 3-month-olds with higher behavioral thresholds tend to have longer I-V intervals. It also indicates a relationship between Wave V latency and threshold among 3-month-olds, which while not unexpected given the I-V interval/threshold correlation, was not apparent in the correlational analysis.

Other observations

Latencies. The average latencies shown in Fig. 3 demonstrate frequency and level effects consistent with expectations. For both Waves I and V, the latency at 8 kHz was shorter than that at 4 kHz ($Ps < 0.001$ in 'developmental time course' regression analyses). That result is consistent in size and direction with many earlier reports (e.g., Klein and Teas, 1978) and is readily accounted for in terms of cochlear travel time. The effect of level was also highly significant for both Waves I and V ($Ps < 0.002$ in 'developmental time course' regression analyses). The average I-V interval was unexpectedly greater at 8 kHz than at 4 kHz at all ages, and the regression analysis indicated a significant effect of frequency ($P < 0.001$). Although it is generally held that the ABR I-V interval is independent of frequency, in fact, a similar tendency for higher frequencies to have longer interpeak latencies is evident in the data of Klein and Teas (1978), Teas et al. (1982), and Fabiani et al. (1979). Since the effects of frequency were controlled in the analyses addressing the relationship between behavioral threshold and ABR latencies, this unexpected frequency effect would not have affected the evaluation of that relationship.

Relationship between ABR Wave V threshold and ABR latency intercept. Although the focus of this paper has been on using ABR latencies to predict behavioral thresholds, the relationship between ABR threshold and ABR latencies may be of some interest. A larger number of subjects were available for these comparisons than for the behavior-latency comparisons, thus simple correlations at each age and frequency were sufficient to document the ABR threshold-latency relationships. The only latency measure that was related to ABR threshold among infants was the Wave V latency intercept. For 3-month-olds this correlation was only significant at 8 kHz (4 kHz: $r = 0.20$, $P > 0.65$; 8 kHz: $r = 0.41$, $P < 0.05$). For 6-month-olds, the correlations were significant at both frequencies (4 kHz: $r = 0.62$, $P < 0.005$; 8 kHz: $r = 0.43$, $P < 0.01$). Among adults, none of the latency measures were significant predictors of ABR threshold at either 4 or 8 kHz. Thus, the relationship between ABR threshold and latency and the relationship between behavioral threshold and latency are quite different.

4. Discussion

The major finding of this study is that the Wave V - Wave I latency difference is a strong predictor of a normal-hearing 3-month-old's behavioral threshold. No ABR measure predicts the behavioral threshold of normal-hearing 6-month-olds or adults. This pattern of results suggests that some factor related to the transmission of information through the auditory brainstem undergoes development during the first 6 months of human postnatal life. This factor influences both the detection of sound and the latency of the ABR. During the period of development, variability in this factor among individuals is high; as a consequence, correlations between behavioral threshold and brainstem transmission measures can be observed. Once a mature state has been achieved, however, the variability in this factor among individuals is much lower. Thus, although brainstem transmission obviously still influences both the evoked potential and behavioral threshold, the variability among normal-hearing, mature listeners is too small to support a significant correlation.

What sort of factor could influence both brainstem transmission time and auditory sensitivity during development? The development of evoked potential latencies is usually explained in terms of the progressive myelination of the auditory pathways during development (e.g., Yakovlev and Lecours, 1967), and this process is generally not expected to influence auditory sensitivity (e.g., Hendler et al., 1990). However, other factors could well affect evoked potential latencies during development. For example, it is widely documented in nonhumans that besides having prolonged response latencies, immature auditory neurons have reduced spontaneous and driven firing rates compared to mature auditory neurons (reviewed by, e.g., Brugge, 1988; Sanes, 1992). Both the prolonged response latency and the reduced firing rates could well result from synaptic immaturity: An immature synapse may transmit information at a slower rate and it may be less likely to reliably transmit information than a mature one (see discussion by Banks, 1992). Moreover, one would expect both prolonged evoked potential latencies and reduced sensitivity as a result. The functional properties of central auditory synapses during development are only beginning to be explored, but it is clear that synaptic maturation plays an important role in the development of auditory coding in nonhumans (e.g., Sanes, 1993). How and when the functional properties of central auditory synapses mature in humans is unknown. However, the present results are consistent with persistence of brainstem synaptic immaturity to at least 3 months postnatal age in humans.

By this line of reasoning, factors other than brainstem transmission must be responsible for immature sensitivity among infants and children older than 6 months of age. There are several likely possibilities. First, the properties of the external and middle ear are not adultlike until well into childhood (Keefe et al., 1993, 1994; Okabe et al., 1988). Second, the primary auditory pathway central to the brainstem may continue to mature beyond 6 months (e.g., Perazzo et al., 1992). Third, the development of auditory attention may prove to be a major factor (e.g., Bargones, 1992; Werner and Bargones, 1991). Of these variables, only middle ear immaturity could contribute to both behavioral threshold and ABR latency (at least when these are measured with insert earphones), and it may well be that the magnitude and variance of the immaturity are too small to be detected with the measurement and correlational techniques employed here (Keefe et al., 1993).

It may seem counterintuitive that the correlational analyses indicate a common source of variance for behavioral thresholds and brainstem transmission among 3-month-olds, when the developmental course of average threshold and average latency measures are different. It is important to keep in mind in this regard that the brainstem transmission measure can account for about 50% of the variance in behavioral threshold; other factors account for the remaining 50% of the variance. If these other factors (e.g., conductive mechanisms, more central sensory mechanisms, cognitive mechanisms) mature at different rates and at different times, they may make it difficult to isolate the changes that are occurring in average threshold as a result of brainstem maturation. It should also be noted that of the latency measures examined in the present study, the average brainstem transmission measure was the one that improved between 3 and 6 months in a way that was most similar to the change seen in behavioral thresholds during that age period.

The pattern of ABR latency development observed here is qualitatively similar to that reported by other laboratories. While the size of the age differences we report for Wave V and the I-V interval tend to be somewhat smaller than previously reported, we find as others have, that Wave V and the I-V interval tend to be more adultlike at 4 kHz than at 8 kHz (e.g., Teas et al., 1982; Ponton et al., 1992; Eggermont, 1991). Teas et al. (1982), on the other hand, report that Wave I latency is quite close, within 0.1 ms, to adult values at these frequencies for both 12.5- and 24.5-week-old infants, while we find a significant difference between infants and adults in Wave I latency, on the order of 0.2–0.3 ms. The reason for this difference is not clear. An obvious difference between this study and that of Teas et al., however, is that while an insert transducer was used here, TDH-39 earphones were used in the Teas et al. study. By using the insert earphone, the contribution of the ear canal to the auditory response is effectively eliminated: The volume of the ear canal beyond the sound delivery tube is quite small for both infants and adults, and its resonant frequency will be shifted to a very high value. Thus, whatever advantage infants may normally have in sound level delivered to the eardrum as a consequence of a small ear canal volume is more or less eliminated by the insert earphone. In addition, because age-related change in the shape of the ear canal transfer function undoubtedly contributes to frequency gradients in the development of sensitivity, it may not be surprising that the details of these gradients are somewhat different when this contribution is eliminated. For example, Keefe et al. (1993) have reported that impedance looking into the middle ear is higher among infants than among adults, particularly for frequencies above 2 kHz; Keefe et al. (1994), however, have shown that the higher impedance of the middle ear is partially compensated for by the fact that the infant's ear canal resonance is shifted toward higher frequencies. Thus, if the resonance effect is eliminated, the differences between infants and adults in middle ear function may well be reflected in Wave I latency at 4 or 8 kHz. A direct comparison of infant auditory sensitivity measured with different transducers would be needed, though, to establish whether ear canal effects can account for the differences between studies.

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