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Binaural interaction of the auditory brain-stem potentials and middle latency auditory evoked potentials in infants and adults [1]

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Summary   Binaural interactions in brain-stem auditory evoked potentials and in middle latency auditory evoked potentials were studied in 18 normal hearing adults and 10 normal term infants. Binaural interactions at the times of ABR waves V and VI were comparable in term infants and adults. Binaural interaction during the time domain of the middle latency auditory evoked potentials was the greatest at N_{20} in term infants and at N_{40} in adults. Measurement of binaural interaction during maturation may be a useful tool in assessing neurologically affected infants.

Key words: Binaural interaction; Evoked potentials; Infants; Adults

Binaural processes such as localization of sound sources, detection of threshold signals (MLDs) and binaural beats may have correlates in auditory evoked potentials (AEPs). Binaural interaction is observed when the AEP to binaural stimulation is not equal to the sum of the monaural AEPs (Kemp and Robinson 1937; Rosenzweig and Amon 1955; Wernick and Starr 1968). Binaural interaction in the auditory brain-stem potentials (ABRs) occurs between 5 and 8 msec and approaches about 25% of the expected amplitude of the binaural potential in humans and as much as 50% in cats and guinea pigs (Dobie and Berlin 1979; Hosford-Dunn et al. 1981; Levine 1981; Wrege and Starr 1981; Wada and Starr 1983; Özdamar et al. 1986). Binaural interaction has also been observed in middle latency components (MLRs) of the AEP at a latency of about 20–40 msec (Anslie and Boston 1980; Dobie and Norton 1980; Berlin et al. 1984).

The auditory brain-stem pathway in humans is immature at birth but development is completed by about 1 year of age (Hecox and Galambos 1974; Salamy and McKean 1976; Starr et al. 1977; Rotteveel et al. 1985). This development is reflected in changes in AEP morphology, latency, and peak amplitude (Hecox and Galambos 1974; McPherson et al. 1985). In this study, we defined how maturation alters binaural interaction in the brain-stem and middle latency components of the AEP by studying this process in newborns and comparing the results with comparable measures in adults.

Methods

Subjects

Eight normal hearing adults (23–40 years of age) and 10 normal newborn infants (conceptional ages between 38 and 41 weeks) were studied. All subjects met the following requirements: (1) the lowest visual detection level of wave V of the auditory brain-stem response did not exceed 20 dB nHL for adults and 30 dB nHL for infants; (2) monaural threshold for ABR wave V from left and right ears was within 5 dB; and (3) the inter-ear

latency difference at wave V threshold was not greater than 0.25 msec. Adults had behavioral air conduction thresholds of 15 dB HL (ANSI-1970) or better at octave intervals from 0.25 kHz through 4 kHz, bilaterally. All testing was carried out in a quiet, darkened room with adults supine and the infants asleep in a bassinet.

Clicks were generated by passing 0.1 msec square pulses through an attenuator to a pair of matched earphones (Telephonics TDH-39) encased in cushions. These were modified for term infants to be circumaural for the neonatal ear. Stimulus presentation rate was 15.1/sec.

Electrical activity from the scalp was amplified 10^5 times and filtered between 10 and 3000 Hz (3 dB down, 12 dB/octave).

Amplified signals were digitized and averaged for a series of 2000 trials. A 50 msec post-stimulus sample was acquired using 1024 sampling bins. Artifact rejection level was set to prevent samples with portions of the signals exceeding 80% of the amplifier gain. Electrodes were placed along the midline of the scalp with the active electrode (positive) placed at the vertex (Cz), an inactive electrode (negative) placed at a non-cephalic site on the seventh cervical vertebra (C_{VII}), and a common (ground) electrode placed on the upper forehead (Fpz). This electrode montage and filter settings differ from routine clinical practice (Cz-mastoid and 100–3000 Hz). The effects on the ABR wave forms have been described earlier (Mc-Pherson et al. 1985). Interelectrode impedance was below 2000 Ω. All subjects were tested during a single session lasting approximately 2 h.

Auditory evoked potentials were obtained at 40 dB above threshold for wave V. The potentials to 2000 stimulus repetitions were averaged for each of 3 conditions: right monaural, left monaural, and binaural. Two replicable averages were recorded for each condition. The polarity of the click stimulus was then reversed, and the sequence was repeated.

The binaural interaction component (BIC) was determined by subtracting the binaurally evoked auditory potentials from the sum of the monaural auditory evoked potentials:

$$[\text{binaural} - (\text{left monaural} + \text{right monaural})]$$

Grand averaged wave forms were obtained by summation of individual wave forms and dividing the summed response by the number of subjects for each group. Both individual and grand average peak latencies were measured for waves III and V of the early auditory evoked potentials, N_{20}, P_{30}, and N_{40} of the middle auditory evoked potentials, and the peaks of the binaural interaction wave form. Baseline-to-peak amplitudes were measured for waves III and V. Measurements were made for the peaks of N_{20}, P_{30} and N_{40} relative to the prestimulus baseline. An upward deflection of the BIC wave form occurred when the sum of the monaural responses was greater than the binaural response. The converse was true for a downward peak. The terms used to describe the binaural interaction components are: D refers to the difference between the binaural and the sum of the monaural followed by the approximate timing of this difference as it relates to the monaural components (i.e., D_V is the binaural interaction occurring approximately at the time of wave V in the ABR; D_{30} refers to the binaural interaction occurring at approximately P_{30} of the MLR, etc.). Measures of binaural interaction were performed using results from rarefaction stimuli.

Means, standard deviations, and ranges for peak latency and amplitude values were obtained for the AEPs and BICs within each group. A multianalysis of variance (MANOVA) was completed prior to tests for repeated measures and yielded a significant F ratio. Post hoc, a 1-way analysis of variance (ANOVA), between-subjects design, was used to calculate significant differences in the AEPs and BICs among age groups. A 1-way ANOVA, within-subjects design, was used to calculate significant differences between the binaural and the sum of the monaural responses of the AEPs within each group studied. All statistical comparisons in this study were considered significant at the $P < 0.01$ level.

Results

Auditory brain-stem responses

Monaural stimulation. The latencies of the components of the ABR to monaural stimulation were significantly longer in term infants than in

TABLE I

Means and standard deviations of the latencies (msec) of the monaural, binaural, summed monaural responses and the binaural interaction component of the ABR and MLR for rarefaction and condensation click polarity stimuli in the adult and term infant groups. Numbers in parentheses are the standard deviation. RE = right ear response; LE = left ear response; BIN = binaural response; BIC = binaural interaction component; SUM = summed response of the RE + LE; ND = not detected.

Condition		Auditory evoked response wave form					
		III	V	VI	N_{20}	P_{30}	N_{40}
Adult	RE	4.3 (0.4)	6.1 (0.3)	7.8 (0.4)	14.1 (1.1)	25.0 (1.5)	37.5 (1.5)
rarefaction	LE	4.4 (0.4)	6.3 (0.2)	7.7 (0.3)	14.1 (1.6)	25.0 (1.0)	37.3 (2.4)
	BIN	4.3 (0.4)	6.2 (0.2)	7.7 (0.2)	13.9 (0.5)	25.7 (1.1)	37.3 (2.5)
	SUM	4.4 (0.4)	6.2 (0.3)	7.8 (0.2)	14.8 (1.2)	25.9 (1.5)	37.1 (1.4)
	BIC	ND	6.3 (0.5)	ND	14.9 (1.6)	26.1 (2.2)	37.0 (2.5)
Condensation	RE	4.3 (0.3)	6.3 (0.3)	7.9 (0.6)	13.5 (1.1)	26.0 (1.3)	38.0 (2.2)
	LE	4.4 (0.3)	6.3 (0.3)	7.9 (0.4)	13.0 (1.1)	26.3 (1.7)	37.7 (1.6)
	BIN	4.3 (0.3)	6.2 (0.3)	7.8 (0.3)	12.4 (0.9)	26.9 (1.5)	37.8 (2.4)
	SUM	4.3 (0.3)	6.3 (0.3)	7.7 (0.4)	13.0 (1.1)	26.3 (1.5)	38.2 (2.3)
	BIC	ND	6.9 (0.2)	ND	13.9 (1.9)	26.6 (2.0)	37.6 (2.4)
Term infant	RE	4.9 (0.3)	7.5 (0.4)	8.8 (0.6)	13.5 (0.7)	23.3 (2.3)	ND
rarefaction	LE	4.9 (0.3)	7.6 (0.4)	8.9 (0.4)	14.3 (0.1)	24.6 (2.6)	ND
	BIN	4.9 (0.3)	7.4 (0.3)	8.5 (0.2)	14.7 (1.0)	24.5 (2.4)	ND
	SUM	4.9 (0.2)	7.5 (0.4)	8.8 (0.5)	14.3 (0.2)	24.2 (2.0)	ND
	BIC	ND	7.3 (0.7)	ND	18.8 (1.6)	ND	ND
Condensation	RE	4.9 (0.3)	7.6 (0.4)	8.9 (0.4)	14.3 (0.3)	24.6 (2.6)	ND
	LE	5.1 (0.6)	7.6 (0.5)	8.7 (0.5)	13.5 (0.5)	25.2 (2.2)	ND
	BIN	4.8 (0.2)	7.4 (0.3)	8.7 (0.4)	14.0 (1.7)	24.3 (3.3)	ND
	SUM	4.8 (0.2)	7.5 (0.4)	8.7 (0.5)	13.6 (0.5)	25.6 (1.9)	ND
	BIC	ND	7.4 (0.9)	ND	20.6 (3.6)	25.4 (3.4)	ND

adults using rarefaction and condensation stimuli (Table I). Within each age group there were significant differences in the latencies of wave V as a function of click polarity, with condensation being longer. Mean baseline-to-peak amplitude of waves III and V was significantly larger for the adults

TABLE II

Means and standard deviations of the amplitude (nanovolts) of the monaural, binaural, summed monaural responses and percent binaural interaction (i.e., {[sum monaurals − binaural]/sum monaurals} × 100) of the ABR and MLR for rarefaction click polarity stimuli in the adult and term infant groups. Numbers in parentheses are the standard deviation. Abbreviations as in Table I.

Condition		Auditory evoked response wave form				
		III	V	N_{20}	P_{30}	N_{40}
Adult	RE	261 (68)	562 (89)	416 (77)	420 (127)	507 (100)
rarefaction	LE	195 (81)	604 (107)	387 (86)	402 (55)	448 (99)
	BIN	299 (70)	783 (62)	716 (73)	402 (77)	609 (84)
	SUM	344 (79)	960 (80)	802 (103)	862 (80)	873 (118)
	BIC %		16 (5)	31 (8)	49 (16)	52 (11)
Term infant	RE	25 (12) *	87 (10) *	313 (38)	122 (17) *	ND
rarefaction	LE	35 (12) *	104 (16) *	286 (51)	138 (58) *	ND
	BIN	126 (62) *	175 (49) *	200 (60) *	194 (43) *	ND
	SUM	196 (36) *	243 (54) *	382 (63) *	270 (71) *	ND
	BIC %	ND	17 (9)	62 (18) *	35 (13)	ND

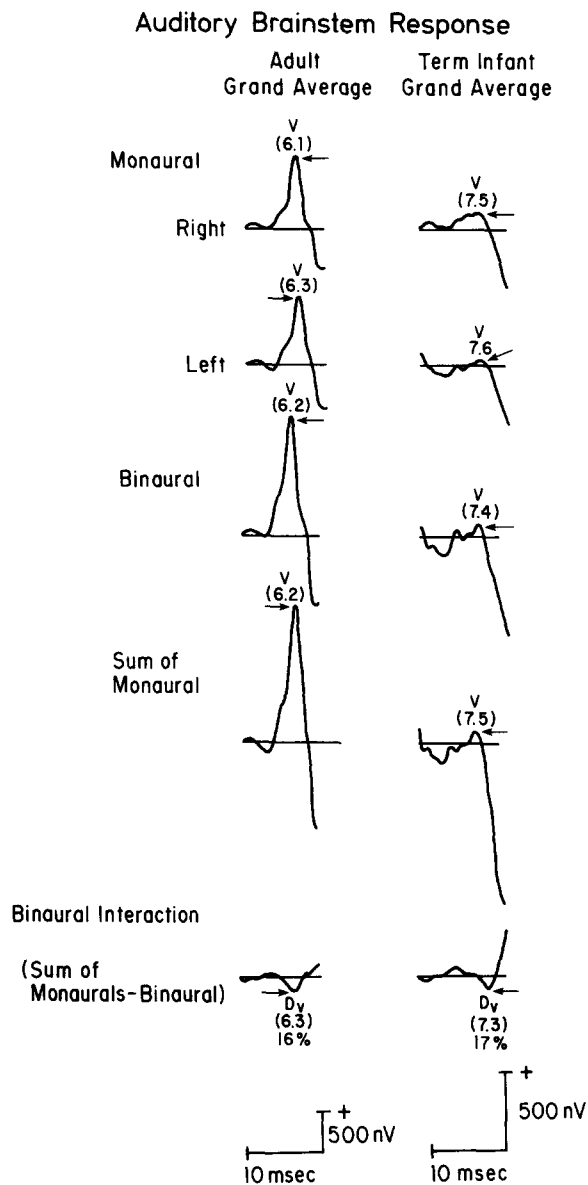* $P < 0.005$.

Auditory Brainstem Response

Fig. 1. This shows the grand average of auditory brain-stem potentials in adults and term infants. The potentials differ in appearance from the customary clinical records because the recording derivation was vertex to non-cephalic reference with relatively wideband filtering (10–3000 Hz) at a click intensity of 40 dB above threshold for wave V. Wave V is prominent with these parameters and is identified on the tracing with its latency noted in parentheses. Note that the amplification scale in term infants is twice that of adults. A binaural interaction component can be identified at the time of waves IV and V and is of similar appearance in the two age groups. The latency in msec of the components is noted in parentheses below each component. The '%' notation below the components of binaural interaction reflects their percentage as a function of the sum of the monaural responses. The relative percentage of binaural interaction as a function of the sum of the monaural responses is equivalent in the two age groups.

than for term infants (approximately 228 nV vs. 30 nV for wave III and approximately 583 nV vs. 95 nV for wave V (Table II). When peak to following trough (i.e., peak-to-peak) measures of these components are made in conjunction with a more standard clinical protocol (i.e., Cz-mastoid and 100–300 Hz), the amplitudes between infants and adults are more comparable (e.g., for wave V: 823 nV in adults, and 762 nV in infants).

Binaural interaction. Binaural interaction occurred at the time of wave V and is labeled D_V in Fig. 1. The absolute amplitude of D_V differed between term infants and adults due to amplitude differences of the monaural ABRs at this latency. When amplitude differences were adjusted by normalization (e.g., making the sum of the monaural ABRs to be 100%), binaural interaction at the time of wave V was comparable in term infants and adults, equal to about 16% of the sum of the monaural ABRs (Table II).

Middle latency responses

Monaural stimulation. There were striking differences in the morphology and amplitudes of the middle latency components between adults and term infants (Fig. 2). The N_{20} component in term infants was narrow and peaked at about 13 msec. In contrast, this component was broader in adults making a flat trough extending from 10 to 18 msec. The amplitudes of this initial negative component were not significantly different between adults and term infants (412 nV vs. 300 nV, respectively). The P_{30} component was significantly larger in adults (408 nV) than in term infants (130 nV). The N_{40} component was large in adults (465 nV) and could not be detected consistently in term infants. The absence of a negative response at N_{40} in term infants masked to some extent the immediately preceding P_{30} component. Tables I and II contain measures of the latencies and amplitudes of the middle latency components in the two age groups.

Binaural interaction. The distribution of binaural interaction in the middle latency range differed in infants and adults (Fig. 2 and Table I). Binaural interaction was of a relatively greater magnitude at the time of the N_{20} component in the term infant (approximately 62% of the expected sum of the monaural potentials) and sig-
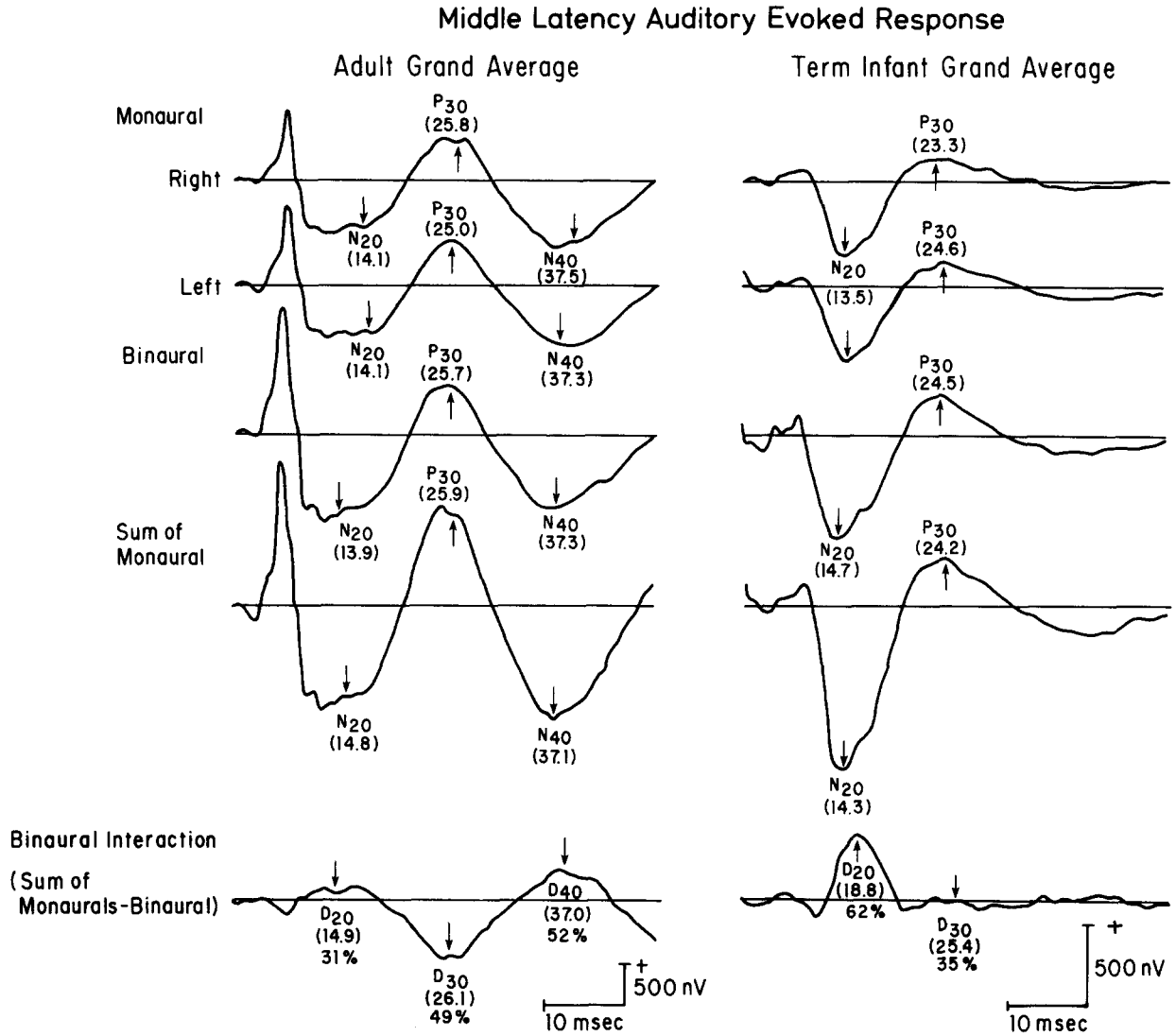
Middle Latency Auditory Evoked Response

Fig. 2. This figure shows the grand average of the middle latency auditory evoked potentials in adults and term infants. The potentials differ in appearance from the customary clinical records because the recording derivation was vertex to non-cephalic reference with relatively wideband filtering (10–3000 Hz) at a click intensity of 40 dB above threshold for wave V. There are clear differences between the two age groups with N_{20} being broadened in adults compared to term infants but of equivalent amplitude. Note that the amplification scale in term infants is twice that of adults. P_{30} is smaller in term infants than in adults and N_{40}, which is present in adults, is absent in the term infants. The binaural interaction components differ between the two age groups. The latency in msec of the components is noted in parentheses below each component. The '%' notation below the components of binaural interaction reflects their percentage as a function of the sum of the monaural responses.

nificantly smaller in the adult (approximately 31% of the expected sum of the monaural potentials). Conversely, binaural interaction in the P_{30} component was greater in adults (binaural interaction accounting for approximately 49% of this component) compared to 35% in the term infant ($P = 0.005$). Finally, binaural interaction at the time of N_{40} occurred in the adults and was approximately

52% of the sum of the monaural responses. There was no BIC at the time of N_{40} since this component was not seen in infants.

Discussion

Our results confirm observations of significant differences in middle latency responses in term infants compared to adults (Rotteveel et al. 1985). In our study, component N_{20} was of shorter duration in newborns than in adults, but N_{40}, clearly defined in adults, was absent in newborns. The broadness of the adult N_{20} cannot be accounted for by large variations since the standard deviation is relatively small (less than 10% of the mean). Absence of the N_{40} component in newborns may reflect immaturity of generators of the middle latency components such that those contributing to N_{20} are relatively mature at birth (in the term infant the amplitude of this component is comparable in newborns and adults); those contributing to P_{30} are relatively immature (the amplitude of this component in infants is approximately 1/3 of the adult) and those contributing to N_{40} are undeveloped (the component is absent). By 3 months of age the generators of P_{30} and N_{40} components are mature and these components reach adult form (Rotteveel et al. 1985). Our results show that the N_{20} component, although of similar amplitude in infants and adults, differs in appearance in the two age groups. The broadness of the initial negativity following waves VI and VII of the ABR in adults may reflect the interaction of several subcomponents in this time domain (Picton et al. 1974) (i.e., N_o occurring at 10 msec, P_o occurring at 13 msec, and N_a or N_{20} occurring at 20 msec). In infants, some of these subcomponents may not be fully developed, and thus the initial negativity is narrow compared to adults.

Binaural interaction is comparable in newborns and adults in the time domain of the ABR, equal to approximately 16% of the sum of the monaural responses. A binaural interaction component was detected in the time domain of waves IV, V and VI. The finding of binaural interaction in the newborn indicates that certain binaural processes intrinsic to the brain-stem are present at birth.

However, this information is apparently not utilized in the newborn for auditory stimulus localization since directional head and eye turning to a sound source does not appear until about 3 months of age (Northern and Downs 1978).

We were surprised at the magnitude of binaural interaction that occurred at the time of the middle latency components compared to the ABR components. Binaural interaction in middle latency components could amount to almost 50% of the sum of the monaural responses, a value significantly greater than the 16% reported for the ABR. This result suggests that binaural processes constitute a major function of the auditory pathway rostral to the pons. Certainly the inferior colliculus which does not contribute to generation of components of the ABR is involved to a significant degree in binaural processing of inputs from the two ears (Rose et al. 1966; Semple and Kitzes 1985). Pathways connecting auditory cortices in each hemisphere in primates and humans (Pandya et al. 1969) may be involved in binaural processing above the brain-stem.

The extent of binaural processing in middle latency components as reflected in the amplitude of binaural interaction is different in newborns and adults. State of arousal may have influenced our results since infants were studied while asleep and adults were studied awake. The effect of arousal is seen probably on the amplitude of the middle latency components evoked at or near threshold (Linden et al. 1985) and not at suprathreshold (Picton et al. 1974). Since the intensity used in the present study was suprathreshold (40 dB above detection of wave V of the ABR) this is not considered to be a significant influence on our results.

The N_{20} component in newborns has a much greater proportion of its amplitude devoted to binaural interaction than the adult (62% vs. 31%, respectively). The significance of this finding is difficult to assess considering that binaural interaction at the time of the next middle latency component, P_{30}, is greater in the adults than in the newborns. It may be that maturational factors have differential effects on monaural and binaural systems as a function of age.

AEPs are eminently suitable for investigating

binaural processes during maturation. The results of the present study show differences in binaural interaction between term infants and adults particularly in the range of the N_{20}, P_{30} and N_{40} components. The time course of binaural processing of AEPs following birth needs further study. It will also be important to obtain other measures of binaural processing maturation using behavioral parameters such as head and eye turning or middle ear muscle responses to lateralized signals.

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