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I am submitting herewith a thesis written by Stacy S. McDaniel entitled "Human Frequency Following Response Correlates of Interaural-Intensity Differences." I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Arts, with a major in Audiology.

Dr. A. Krishnan, Major Professor

We have read this thesis
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HUMAN FREQUENCY FOLLOWING RESPONSE CORRELATES OF INTERAURAL-INTENSITY DIFFERENCES

A Thesis Presented for the Master of Arts Degree
The University of Tennessee, Knoxville

Stacy S. McDaniel
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DEDICATION

This thesis is dedicated with much love to Bill, Doris, Lori, and Alan.

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I personally wish to thank my friends for their constant support. To Alan, I offer a very warm thanks for always providing a smile. And to my parents and sister, for their faith in me and their love for me, I am forever grateful.

ABSTRACT

The binaural interaction component (BIC) represents the difference between the sum of two independent monaural responses and the binaural response. The existence of an electrophysiologic correlate of lateralization as exhibited in BIC of the human frequency-following response (FFR) evoked by 500 Hz tone bursts and the alterations of the BIC as a function of interaural-intensity differences (IID) were investigated. The FFR BIC was demonstrated and was shown to systematically decrease with increasing IID, much like the summed monaural response. The binaural FFR response showed a smaller decrease in amplitude as a function of IID. These results indicate that an excitation-inhibitory mechanism is the basis for binaural interaction and that the BIC represents a decrease in the firing rate of neurons as a 500 Hz tone burst lateralizes from a midline position to one side. The change in the BIC with IID, and therefore with lateralization of the fused image of the 500 Hz tone burst from midline to one ear, is taken to reflect the electrophysiologic correlate of lateralization.

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CHAPTER I

RATIONALE

The identification of the location of a sound source extracranially (referred to as localization) or intracranially (referred to as lateralization) is mediated by two binaural cues (references). One is the interaural-time difference (ITD) which refers to the difference in the time of arrival of the sound at the two ears, and the other is the interaural-intensity difference (IID) which refers to the difference in intensity of the sound at the two ears.

While the neurophysiological bases for sound localization or lateralization is not yet well understood, it has been clearly demonstrated that neural elements exist in the mammalian auditory brainstem that are systematically influenced by either ITD or IID presented in binaural stimulation (Hall 1965; Goldberg and Brown 1969; Stillman 1972; Moushegian, Rupert, and Gidda 1975). Based on these results, it has been proposed that sound localization is mediated by a complex binaural interaction mechanism involving neural excitation and inhibition. The existence of this binaural interaction in the brainstem nuclei of animals has been convincingly documented (Rosenzweig and Wyers 1955; Hall 1965; Rose et al. 1966; Boudreau and Tsuchitani 1967; Wernick and Starr 1968; Starr and Don 1972; Guinan, Jr., Guinan, and Norris 1972).

Binaural interaction has also been demonstrated in the

scalp recorded auditory brainstem evoked responses (ABR) suggesting that these responses contain information about the binaural processing (Dobie and Berlin 1979; Dobie and Norton 1980; Wrege and Starr 1981). Like wave V of the ABR, the human frequency following response (FFR) reflecting phase-locked neural activity is derived from neural activity within the rostral brainstem (proximal to ABR wave V generator site) where binaural interaction is known to occur. Given this, it was reasoned that the FFR may also provide information regarding binaural processing mediating sound lateralization/localization. The objective of this study was to describe the nature of the alterations of both the binaural FFR and the derived binaural interaction FFR component as the IID is varied. Consistent with this objective, the specific aims of this study were: (1) to determine behaviorally the IID range required to produce complete lateralization from midline of a 500 Hz tone burst; (2) to determine if a binaural interaction component (BIC) exists for the midline condition; and (3) to evaluate the alterations of the binaural FFR component and the derived interaction component as a function of IID.

CHAPTER II

REVIEW OF LITERATURE

Introduction

Sound lateralization is the ability to identify the position of a sound intracranially and by definition involves the presentation of binaural signals through earphones (Shackelton, Bowsher, and Meddis 1991). The term lateralization will be used throughout this study and will be used to mean lateralization/localization. Lateralization is accomplished through binaural information being processed by structures in the auditory pathway of the brainstem (Dobie and Berlin 1979; Hink et al. 1980). The superior olive complex (SOC) contains bilaterally innervated neurons (Rasmussen 1946; Stotler 1953; Rose et al. 1966; Dobie and Berlin 1979) and is the initial region at which input from both ears converge; it is the first structure in the brainstem to process binaural information (Wernick and Starr, 1968; Guinan, Jr., Guinan, and Norris 1972; Moushegian, Rupert, and Gidda 1975).

Cues that govern lateralization, ITDs dominating the lower frequencies and IIDs dominating the higher frequencies (Woodworth 1938; Sandel et al. 1955; Mills 1958; Moushegian and Jeffress 1959), are both processed at the SOC. Specifically, ITDs and IIDs are believed to be mediated in the medial superior olives and the lateral superior olives,

respectively (Durrant and Lovrinic 1984). Under earphones, an IID of 15-20 dB is sufficient for a sound to lateralize from the midline to one ear regardless of frequency (Deutsch and Richards 1985).

Neural Basis of Lateralization

The underlying process of lateralization is an excitation-inhibition (E-I) effect. The E-I effect may also be referred to as the occlusive phenomenon. Stillman (1972) observed E-I effects with neural responses of the kangaroo rats and determined that the maximum output was limited by the excitatory input. Starr and Don (1972) observed a general E-I effect in evoked responses of the squirrel monkey. With contralateral input, excitation of monaural responses occurred, and monaural responses were suppressed (inhibited) by ipsilateral input. Ozdamar, Kraus, and Grossman (1986) also observed an inhibitory effect with ipsilateral input evoking neural responses of guinea pigs.

Binaural Interaction Component

BIC is derived by a process first described by Kemp and Robinson (1937) which involves subtracting the summed monaural response from the binaural response. The basis of BIC is that if the ears are represented by independent, non-interactive neural populations, the sum of the monaural left and monaural right response should equal the response to

binaural stimulation. However, if there is any deviation from this linear model, an interaction component exists. BIC represents the difference between the summation of the independent monaural responses and the binaural response (Kemp and Robinson 1937; Rosenzweig and Wyers 1955; Wernick and Starr 1968; Dobie and Berlin 1979).

Characteristics of BIC

BIC has been clearly identified in single-unit and near-field response studies, the ABR of animals and humans, and the human FFR. Characteristics of BIC include the following: (1) the region of generation of BIC is the rostral brainstem, specifically the SOC and/or the inferior colliculus (IC) (Rosenzweig and Wyers 1955; Guinan, Jr., Guinan, and Norris 1972; Dobie and Berlin 1979; Ozdamar, Kraus, and Grossman 1986); (2) the binaural response is smaller than the sum of the monaural responses (Rosenzweig and Wyers 1955; Hink et al. 1980; Dobie and Norton 1980; Wrege and Starr 1981; Kelly-Ballweber and Dobie 1984; Dobie and Wilson 1985; Ozdamar, Kraus, and Grossman 1986; McPherson and Starr 1993; Parthasarathy and Moushegian 1993); (3) the BIC is best observed in the IV through VI components of the human ABR (Kevanishvilli and Aphonchenko 1979; Ainslie and Boston 1980; Dobie and Norton 1980; Wrege and Starr 1981); (4) the amplitude of the IV-V BIC complex decreases as the IID increases (Wrege and Starr 1981);

(5) the underlying process of binaural interaction is an E-I effect (Boudreau and Tsuchitani 1968; Stillman 1972; Moushegian, Rupert, and Gidda 1975; Dobie and Berlin 1979; Hink et al. 1980; Ozdamar, Kraus, and Grossman 1986; McPherson and Starr 1993); and (6) low-frequency components are involved in the interaction process, i.e. low frequencies influence the BIC (Whitworth and Jeffress 1961; Wrege and Starr 1981; Fowler and Leonards 1985; Fowler and Broadard 1988).

The amplitude of the BIC decreases as the IID is increased and/or the signal intensity is decreased. Wrege and Starr (1981) demonstrated that as signal intensity is decreased, the amplitude of the BIC is decreased. They indicated that the BIC amplitude was attenuated more than that of the monaural summed and binaural evoked potentials.

Low-frequency components are more involved with the binaural interaction as opposed to higher frequencies. Kevanishvilli and Aphonchenko (1979) concluded that the binaural interaction of the human ABR was associated with the IV through VI complex and that the frequencies involved with these components were the 100-500 Hz frequency range. Subsequent studies support these results. Wrege and Starr (1981) indicated that the most effective stimulating frequency for interaction centered around 500-550 Hz. This was supported by the finding that an interaction component was elicited from individuals with high-frequency hearing

losses and that their interaction did not significantly differ from that elicited from normal hearing individuals. A similar study investigated the influence of low-frequency activity of the BIC and found that a 1000 Hz stimulus produced more and larger potentials of the interaction component as compared to a 4000 Hz stimulus (Fowler and Leonards 1985).

Neural Basis of the Evoked Potential BIC

Like the phenomena of lateralization, the BIC is believed to be governed by an occlusive effect. By studying human FFRs elicited by monaural and binaural low-frequency beats, Hink et al. (1980) concluded that the occlusive phenomenon was the underlying mechanism of binaural interaction. The site of generation of the FFR is the IC, and by this point, binaural interaction could have occurred at several lower levels (Hink et al. 1980), i.e., the SOC, the dorsal nuclei of the lateral lemniscus, and the IC itself (Rosenzweig and Wyers 1955; Rose et al. 1966; Wernick and Starr 1968; Brugge, Anderson, and Aitken 1970). They noted that this effect was an indication of input convergence due to overlapping neural populations, thus the decrease in activity with binaural stimulation. Wrege and Starr (1981) concluded that some type of E-I effect was the neural basis of the BIC by observing a reduction of the BIC of the human ABR during the presentation of binaural

stimuli. McPherson and Starr (1993) studied auditory evoked potentials to monaural and binaural click stimuli, and the binaural interaction reflected a relative decrease in activity with binaural stimuli; therefore, they noted that inhibition may be a major mechanism of binaural processing.

Conclusion

It has been established that the BIC can be demonstrated by using the human FFR. The general purpose of this study is to determine if there is an electrophysiologic correlate of lateralization as reflected in the human FFR. Specifically, this study is designed to determine if there is a systematic alteration of the BIC with lateralization resulting from IIDs. The FFR is particularly suitable to measure this phenomenon partially because the FFR is a sustained neural response with a waveform that practically mimics the acoustic stimulus (Marsh and Worden 1968). Also, the FFR is believed to originate at the level of the IC, at which point there have been several occasions for binaural interaction to occur at lower levels (Hink et al. 1980). Furthermore, the FFR is best elicited by low-frequency stimuli which is more effective in producing an optimal interaction component (Gerken et al. 1975; Glaser et al. 1976; Huis in't veld, Osterhammel, and Terkildsen 1977; Wrege and Starr 1981; Fowler and Leonards 1985).

CHAPTER III

METHOD

Subjects

Ten adult human subjects, ranging in age from 18 to 28 years, participated in this study. The subjects were volunteers, and each received a standard clinical hearing test as a qualifying procedure. Only those subjects with hearing sensitivity 15 dB HL or better for octave frequencies from 500 to 8000 Hz were included in the study.

Stimulus

Stimuli used in this study were two independently generated 500 Hz tone bursts. Each tone burst was 60 msec overall duration, including 5 cycles of rise and fall times and 20 cycles of plateau duration. A cosine envelope was utilized to limit spectral splatter of the tone burst stimulus. These tone bursts were generated and controlled by an auditory stimulus generation and data acquisition system [Modular Instruments (MI), M100] interfaced to a microcomputer (Everex, 386/25). The stimulus generation modules (MI, M308) were triggered by a pulse delivered by the I/O module of the system. The outputs of the stimulus generators were then routed to the stimulus control module (MI, M300). The stimulus control module provided for amplification, attenuation, and mixing of the tone burst

stimuli before being delivered to the earphone(s). A timer module (MI, M214) controlled the timing of the stimuli and provided the synchronous trigger pulse for the onset of digitization. Signal parameters, such as intensity, waveform shaping, and routing of signals to the appropriate earphone(s), were controlled by the microcomputer using menu-driven stimulus generation and control software (WAV). The tone bursts were finally presented either monaurally or binaurally through magnetically shielded TDH-49 earphone(s) encased in μ-metal.

Recording System

Subjects sat comfortably in a reclining chair in an acoustically and electrically shielded booth. Evoked response potentials were recorded differentially between scalp electrodes placed on the midline of the forehead at the hairline and the 7th cervical vertebrae. Another electrode placed on the left mastoid served as common ground. The interelectrode impedances were maintained below 3000 ohms. The EEG inputs were amplified 200,000 times and band-pass filtered (Grass,P511k) from 100 to 3000 Hz (6 dB/octave roll-off, RC response characteristics) before being routed to the Analog-to-Digital conversion module (M202a) for digitization. Each evoked potential reflected the response to 2000 stimulus presentations averaged over 80 msec at a sampling frequency of 25 kHz. The signal

averaging program of the M100 system was used for response averaging; display of ongoing averaging and averaged data; and manipulation of recorded data.

Response Evaluation

Evaluation of the FFRs to monaural and binaural stimulus presentation included derivation of the BIC and Fast Fourier Transform (FFT) of the summed monaural responses, binaural responses, and BIC derived for all experimental conditions. The BIC was derived by first summing the monaural right and the monaural left responses and then subtracting the binaural response from the summed monaural response. The FFT yielded both the magnitude and the phase spectrum of the FFR. However, only the magnitude spectrum was used to measure the amplitude of the FFR for each condition (i.e., the amplitude in volts of the FFR spectral peak at 500 Hz). Using this measure of amplitude, the change in the BIC as a function of IID was evaluated. In addition, the FFRs obtained for the binaural condition which produced the midline image of the tone burst served as reference for comparing with FFRs obtained from binaural conditions that shifted the image of the tone burst away from the midline. The signal processing software of the M100 system enabled waveform additions, subtractions, spectrum analysis, and plotting of the waveforms on the plotter (HP,7475A).

Experimental Protocol

FFRs were obtained under the following experimental conditions:

1. FFR to monaural stimulation of the right ear - MON(R) at a stimulus level of 65 dB HL.

2. FFR to monaural stimulation of the left ear - MON(L) at stimulus levels of 65, 60, 55, 50, 45, 40, and 35 dB HL.

3. FFR to binaural stimulation with the following seven IID:

   RE: 65 dB HL; LE: 65 dB HL (MIDLINE)
   RE: 65 dB HL; LE: 60 dB HL
   RE: 65 dB HL; LE: 55 dB HL
   RE: 65 dB HL; LE: 50 dB HL
   RE: 65 dB HL; LE: 45 dB HL
   RE: 65 dB HL; LE: 40 dB HL
   RE: 65 dB HL; LE: 35 dB HL (RIGHT EAR)

Figure 1 shows the IID paradigm.

The tone burst was presented at a rate of 6.1/sec using rarefaction polarity. The experimental conditions were randomized within and across subjects. The 30 dB attenuation range was selected for the IID because lateralization of the tone burst from the midline to one ear was complete within this intensity range as determined behaviorally from pilot study subjects.

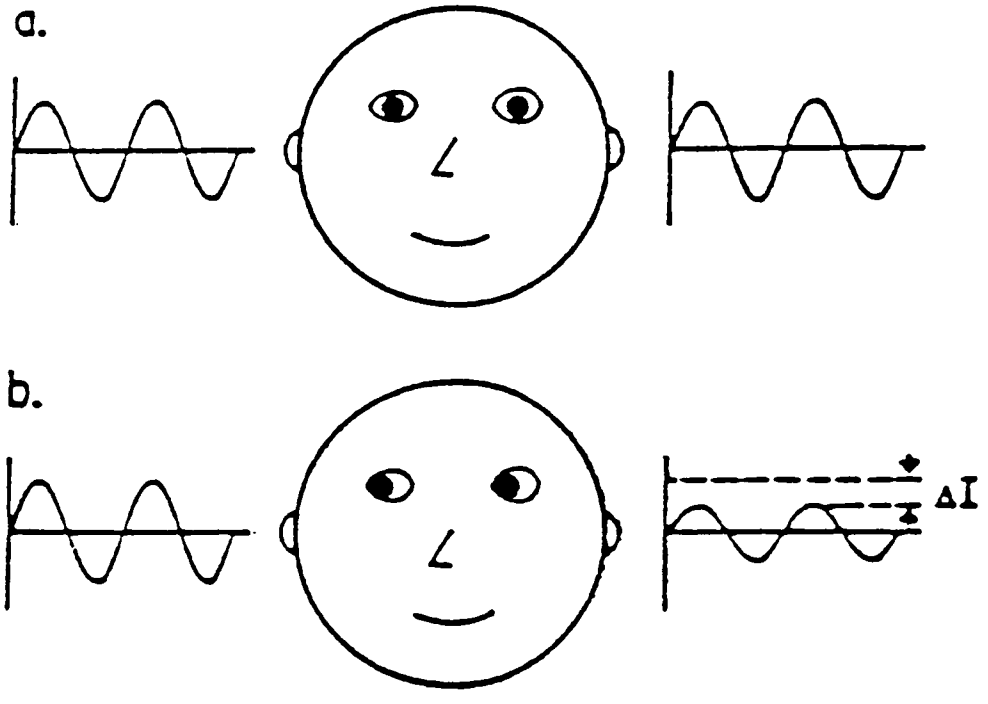

Figure 1. Illustration of the lateralization paradigm used in this study. The cue is the interaural-intensity difference.

CHAPTER IV

RESULTS

Demonstration of the FFR Binaural Interaction Component

Since one of the specific aims of this study is to describe the behavior of the BIC as a function of IID, it is necessary to first, clearly demonstrate the existence of the FFR BIC. To this end, the BIC was derived by subtracting the binaural FFR from the summed monaural FFRs obtained with an IID of 0 dB. Shown in Figure 2 are waveforms from one subject representing the summed monaural FFR (TOP TRACE), the binaural FFR (MIDDLE TRACE), and the difference FFR representing the BIC (BOTTOM TRACE). It can be seen that the amplitude of the summed monaural FFRs is almost twice as large as the binaural response. The consequence is the rather robust BIC reflected in the difference trace shown at the bottom. A closer examination of the waveform data does not reveal any latency/phase difference between the monaural summed and the binaural response that could potentially contaminate the derivation of the BIC. The magnitude of the spectral peak at 500 Hz, derived from FFT on these response waveforms, was used to express amplitude of the FFR. The results of FFT shown in Figure 3 are consistent with the waveform data and clearly demonstrate the presence of a robust FFR BIC. It should be noted that not all subjects presented an additional FFR component at 1000 Hz as is the

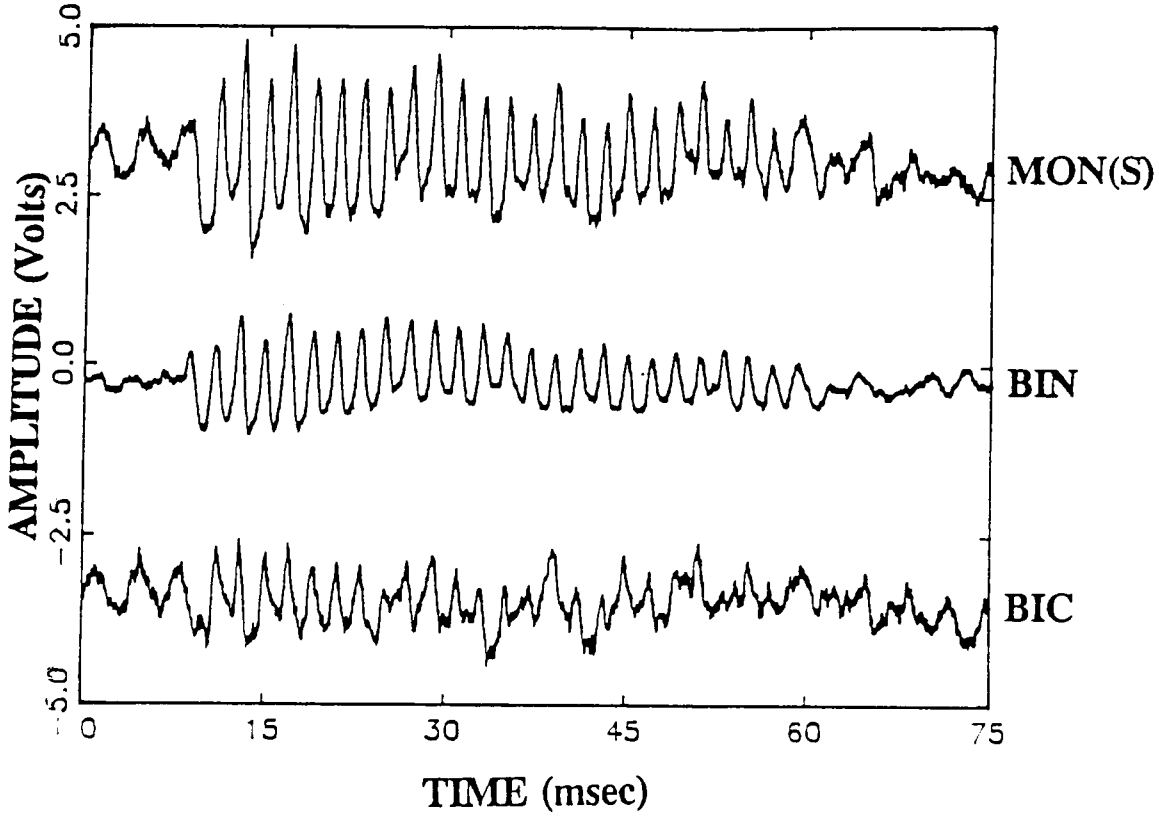

Figure 2. Evoked response waveforms from one subject in response to 500 Hz tone bursts at 65 dB HL. The three recording conditions are identified at the right of each waveform trace.

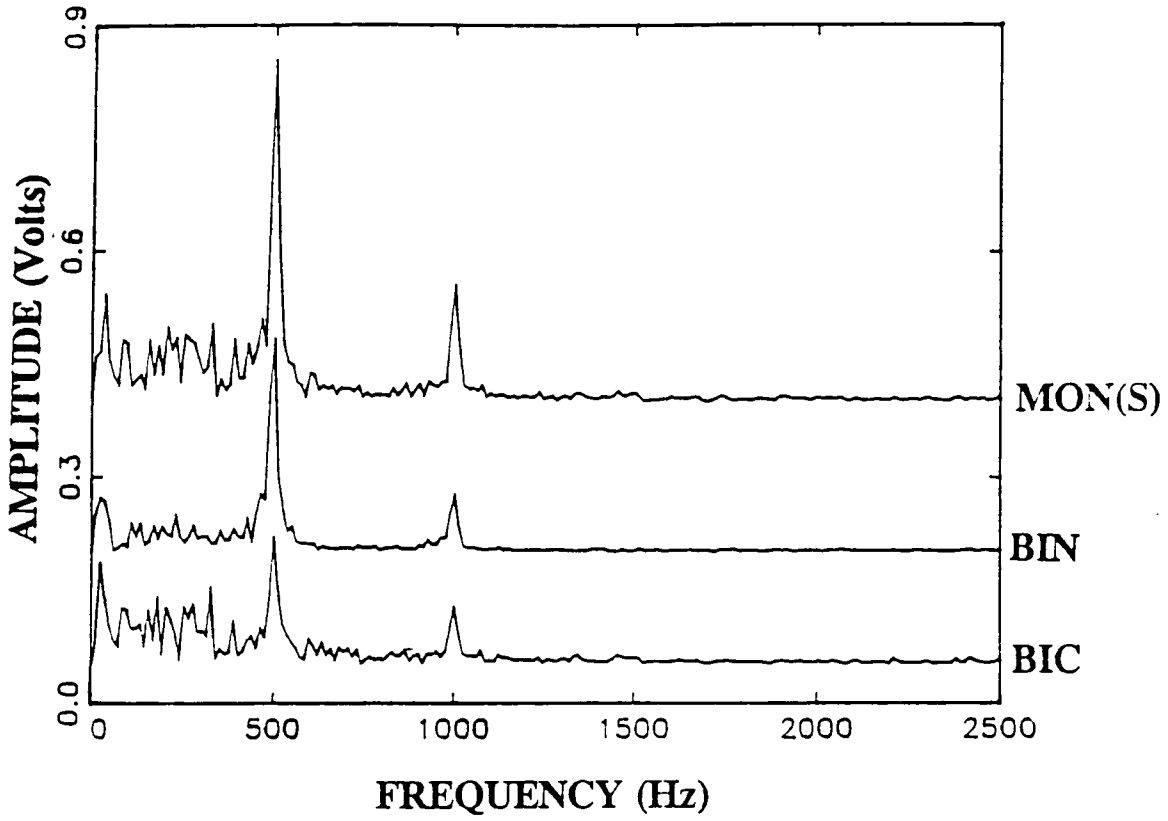

Figure 3. Spectrum analysis of waveforms from one subject in response to 500 Hz tone bursts at 65 dB HL. The three recording conditions are identified at the right of each spectrum.

case with this subject.

Binaural FFR/FFR BIC versus the Summed Monaural FFR: Effects of IID

The effects of IID on the summed monaural and the binaural FFRs were compared to determine if IID altered the binaural and the summed monaural responses differently. The FFRs from one subject representing the summed monaural response (LEFT PANEL), the binaural response (CENTER PANEL), and the BIC (RIGHT PANEL) as a function of IID are shown in Figure 4. Upon comparison of the waveform data in the left and the center panels, it is apparent that the amplitude of the summed monaural response decreases as the IID is increased, particularly for IID values greater than 10-15 dB. In contrast, the binaural response appears to show a slight reduction in amplitude at an IID of 30 dB with no visible change in amplitude for IIDs below 30 dB. The mean amplitude change as a function of increasing IID for the summed monaural, binaural, and the BIC responses are plotted in Figure 5. The solid lines in the figure are fit to data with a simple linear function of the form y=a+bx. The relatively steeper amplitude functions for the summed monaural and the BIC exhibiting a clear reduction in amplitude with increasing IID (as reflected in the strong correlation coefficients of 0.906 and 0.924 respectively, for these two functions) is in sharp contrast with the almost horizontal binaural amplitude function showing a much

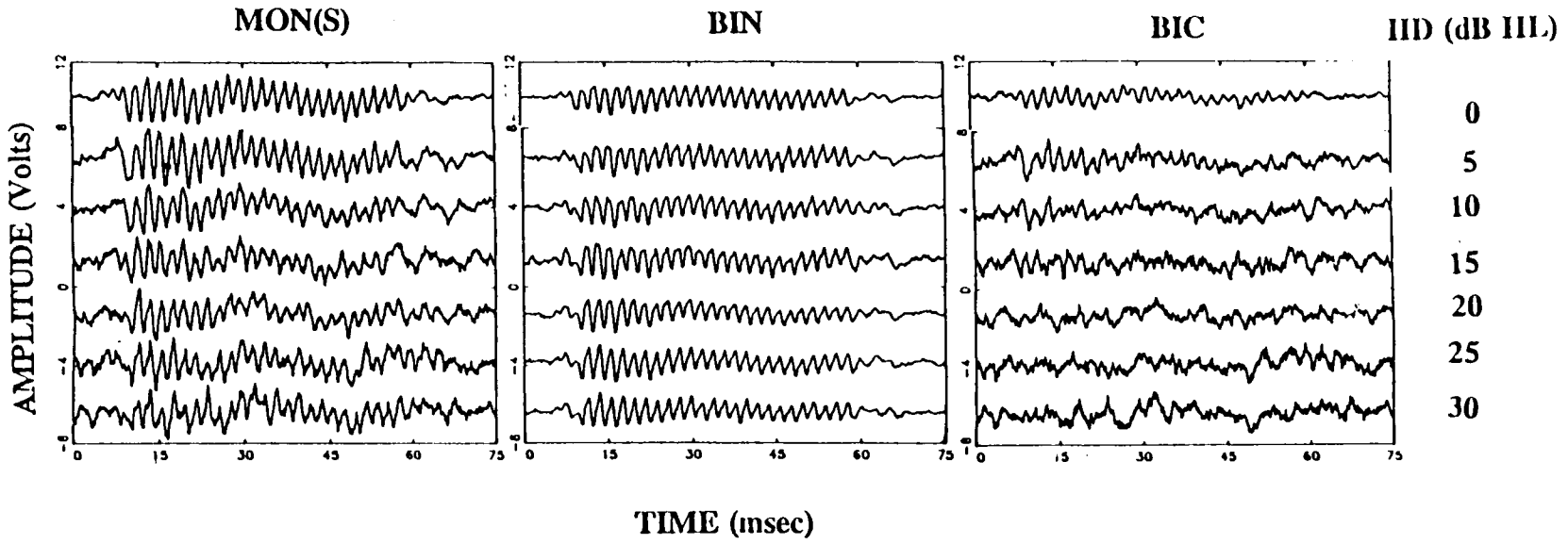

Figure 4. Evoked response waveforms from one subject representing activity of MON(S) (left panel), BIN (center panel), and BIC (right panel) as a function of IID. IIDs are identified at the right of the three sets of traces.

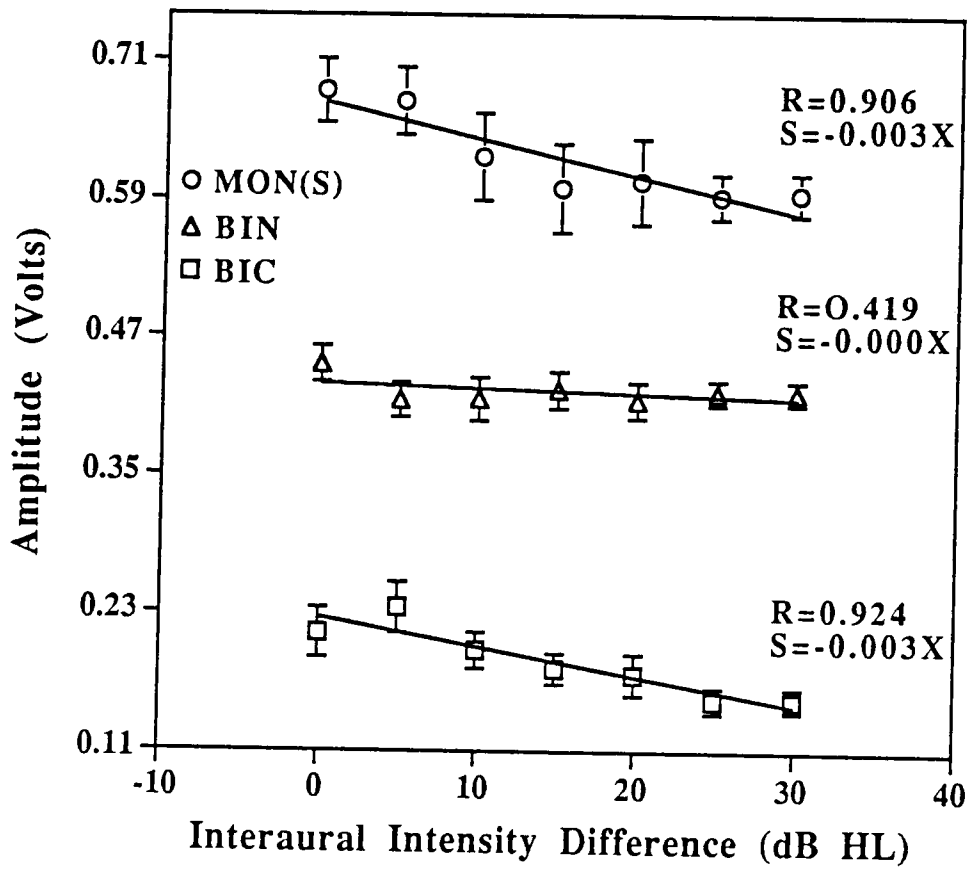

Figure 5. Mean amplitude of the FFRs, MON(S) (○), BIN (△), and BIC (□), plotted as a function of IID.

smaller reduction than the BIC amplitude as the IID was increased. These results demonstrate that increasing IID produces essentially similar amplitude changes for the summed monaural and the BIC, on one hand, and clearly different amplitude effects on the binaural response, on the other hand.

CHAPTER V

DISCUSSION

The results of this study can be summarized by the following three observations: (1) the presence of a robust FFR BIC; (2) the amplitude of this BIC decreases systematically as a function of increasing IID; and (3) the amplitude of the binaural FFR exhibits appreciably smaller reduction in amplitude as a function of increasing IID compared to both the summed monaural FFR and the BIC. These findings seem to support the notion that the 500 Hz FFR to binaural stimulation reflects the output of non-linear neural interactive processes within the rostral brainstem and not simply a reflection of a passive linear sum of neural activity produced by two independent generators. We will first consider the neural basis of this interaction component and then discuss the effects of varying the IID on both the BIC and the binaural FFR and its implication on sound lateralization.

The FFR Binaural Interaction Component

Consistent with the robust BIC demonstrated in our study, the presence of a BIC in surface recorded evoked potentials, suggesting binaural interaction within the brainstem, has been well documented for both the auditory brainstem evoked response (Dobie and Norton 1980; Kelly-

Ballweber and Dobie 1984; Dobie and Wilson 1985; Parthasarathy and Moushegian 1993; McPherson and Starr 1993) and relatively recently for the 500 Hz FFR (Hink et al. 1980; Parthasarathy and Moushegian 1993). In most cases, the BIC component was derived by subtracting the smaller binaural response from the larger summed monaural response. The reduced amplitude of the binaural response compared to the summed monaural response is taken to reflect the result of a complex neural interaction among binaurally sensitive neurons; specifically, binaurally innervated neurons in the SOC (Rasmussen 1946; Stotler 1953; Boudreau and Tsuchitani 1968; Dobie and Berlin 1979) and the IC (Rose et al. 1966; Stillman 1972; Semple and Aitkin 1979) can be classified as E-I (excited by ipsilateral stimulation and inhibited by contralateral stimulation) and less commonly as E-E (binaurally excitatory). Thus with the binaural stimulation, the E-I interaction would produce a decrease in firing rate due to the inhibition provided by the contralateral input (relative to the firing that occurs when only the ipsilateral ear is stimulated) (Stillman 1972; Moushegian, Rupert, and Gidda 1975). The smaller amplitude of the binaural FFR response compared to the summed monaural in our study presumably reflects such a binaural interaction. This type of binaural interaction can be altered by interaural-time and intensity differences. The next section will focus on the effects of IID on this BIC as

well as the binaural response.

Effects of IID on the BIC and the Binaural Response

Results of our study showed that the amplitude of the BIC and the binaural response decreased as the IID was increased over a range of 30 dB. Similar findings have been reported for the ABR BIC using click stimuli (Dobie and Berlin 1979; Prasher, Sainz, and Gibson 1981; Furst, Levine, and McGaffin 1985). Evoked potential binaural interaction, like neural interaction in single units, is commonly explained using models of binaural interaction. Models of binaural interaction based on psychoacoustics and physiology (Colburn and Durlach 1978) assume that sounds are presented to a central binaural interaction processor following acts either as a correlation device or as a coincident counter.

In order to explain the decrease in the BIC as a function of increasing ITD and IID, Furst, Levine, and McGaffin (1985) used a binaural interaction processor model with the following specifications: (1) the processor produces an output only when the inputs from the two sides arrive within about 1.0 sec; and (2) the output level of this processor is proportional to its average input level from the two ears. This model can be readily used to explain the results of this study. The first specification, while primarily used to explain their ITD data, may also account for our observation that BIC was almost difficult to

discern at an IID of 30 dB, because an IID of 30 dB corresponds to an ITD of about 1.0 sec, the limit where this processor would fail to produce an output. More directly relevant to our data is the second specification which can clearly explain our observation that the BIC amplitude decreased as a function of increasing IID, suggesting that the output of the processor is proportional to its average input. While the anatomical locus of this processor is not certain, it would appear that this interaction phenomenon reflects events proximal to the neural elements generating the human FFR, presumably the IC; however, BIC could originate at levels below the IC. There is evidence to support not only the presence of binaurally sensitive neurons in the IC but also the possibility that the human FFR is generated at this level.

Another aspect of interest to us was the relationship between the electrophysiologic FFR BIC measure and the perceived location of the fused image as the IID was varied. Similar to our observation, Furst, Levine, and McGaffin (1985) observed that for increasing IIDs, the BIC amplitude decreased as the fused image of the sound moved toward the ear receiving the louder click. Furthermore, they observed that whenever a BIC was present, the binaural click stimuli was always perceived as a fused image and whenever the image was not fused, the BIC was not present. Based on these observations, these authors concluded that the BIC and

binaural fusion are related and that the BIC was sufficient to code for binaural fusion. Although we did not evaluate the BIC and the perception of binaural stimuli beyond an IID of 30 dB, it is very likely that we would have obtained similar results.

Potential Limitations of this Study

Two potential limitations that might account for the binaural interaction are acoustic crosstalk and monaural response asymmetry. Acoustic crosstalk occurs when the monaural stimulation presented to the ipsilateral ear is intense enough to stimulate the contralateral ear. As a result, the binaural condition cannot be accurately predicted because the monaural response would actually be the sum of the ipsilateral ear and a small input from the contralateral ear. In turn, the interaction component would be a product of an acoustic crosstalk response even if no actual binaural interaction existed (Ainslie and Boston 1980). The effects of acoustic crosstalk were not investigated in the present study; however, evidence has been established that rules out the possibility of binaural interaction simply being the case of acoustic crosstalk (Dobie and Berlin 1979; Dobie and Norton 1980; Dobie and Wilson 1985). The use of masking may be used to eliminate the effects of acoustic crosstalk. If BIC is a product of acoustic crosstalk, then the interaction component recorded

in the presence of noise should differ from the one elicited by stimuli without noise. Dobie and Wilson (1985) recorded auditory brainstem potentials with and without noise. They presented contralateral noise at a level just at or below the threshold of audibility (73 dB SPL) and demonstrated that the effects of masking did not alter the ABR BIC; therefore, they concluded that the BIC was not simply a product of acoustic crosstalk. The second limitation is that of monaural response asymmetry as a source of BIC. Asymmetry results when the monaural left and monaural right ear responses differ. It is assumed that if the two independent monaural responses are symmetrical, then a flat line (no difference between responses) will result if one is subtracted from the other (Spivak and Seitz 1988). However, it has been shown that asymmetries do exist in the lower brainstem (Ballachanda, Rupert, and Moushegian 1994) and that these differences effect the BIC (Decker and Howe 1981; Spivak and Seitz 1988). Decker and Howe (1981) concluded that binaural stimulation was not processed symmetrically along the auditory pathway of the brainstem; in turn, they questioned whether the binaural interaction was really an indicator of neural processing or whether it was the product of asymmetrical processing of binaural stimuli. Spivak and Seitz (1988) noted that the BIC was a product of binaural processing; however, they determined that the interaction component was influenced by other factors, i.e., interear

asymmetries, other than those related to binaural processing. In the present study, asymmetry was identified and was derived by the process described by Spivak and Seitz (1988) in which the left monaural response is subtracted from the right monaural response. The midline conditions of two subjects were sampled. The result showed that the amplitude of the BIC differed from that of the difference trace representing the monaural conditions. It was assumed that the BIC was not influenced by asymmetry; if asymmetrical responses contaminated the results, it would seem that the binaural response would reflect these differences. Instead, the binaural response remained relatively stable as a function of IID and did not reflect the product of asymmetry.

Implications

If BIC and its behavior as a function of IID does reflect brainstem mechanisms related to lateralization/ localization, then this measure can be used as a clinical tool to assess functional integrity of this brainstem mechanism. Furthermore, the midline condition (0 dB HL IID) and the lateralized condition (30 dB HL IID) would be sufficient to use since this difference achieves lateralization. In this sense, it could be added to the test battery evaluating central auditory processing disorders (CAPD). The pathway of the central auditory

system extends from the pontomedullary junction of the brainstem to auditory projections throughout various areas of the hemispheres of the brain (Musiek 1985). Along this pathway exists the structures which process binaural information, i.e., the IC, the dorsal nucleus of the lateral lemniscus, and the SOC (Rosenzweig and Wyers 1955; Rose et al. 1966; Wernick and Starr 1968; Brugge, Anderson, and Aitken 1970). The possibility of this clinical application for CAPD warrants further research. Also, since the BIC is related to binaural fusion, it might be used to assess binaural fusion in a clinical setting. Theoretically, this FFR paradigm might serve as an analytical tool to evaluate certain binaural phenomena in the brainstem.

The investigation of asymmetry as a function of IID requires the attention of further research. In this study, only the midline condition, RE 65 dB HL and LE 65 dB HL, could be used to determine the presence of asymmetrical responses. At the other stimulus conditions, asymmetry would exist merely as a result of different intensity levels presented to each ear.

Conclusion

The general purpose of this study was to determine if there was an electrophysiologic correlate of lateralization as reflected in the human FFR. More specifically, this study questioned whether there was a systematic alteration

of the BIC as a function of lateralization resulting from IIDs. BIC was determined by presenting monaural stimuli to the left and right ear, summing the responses, and then subtracting the binaural response from the summed monaural. The difference between the two responses was referred to as the BIC. The BIC is a result of overlapping neural populations. If some type of neural interaction did not occur with the presentation of binaural stimuli, then the product of the two monaural responses added together should equal the binaural response. This was not demonstrated in our study. Rather, it was demonstrated that the BIC not only represented the difference between the summed monaural and the binaural responses, but that it also represented an electrophysiologic correlate of lateralization reflected in the human FFR. The BIC decreased systematically as the IID between ears was increased. Therefore, the relationship between the BIC and lateralization was characterized by the decrease in the firing rate of the neurons elicited by 500 Hz tone bursts lateralizing to the right side as a function of increasing IIDs.

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APPENDICES

APPENDIX A
SUBJECT CONSENT FORM

INFORMED CONSENT FORM FOR STUDY

Title: **Human Frequency Following Response Correlates of Interaural-Intensity Differences**

I. DESCRIPTION

You are being asked to participate in an experimental study of the frequency following response to determine how differences in the loudness of sounds at the two ears are represented in these responses. Should you agree to participate, your hearing sensitivity will be determined initially using a routine clinical test. In this basic test of hearing sensitivity, tones of different pitches will be presented to you through headphones, and you will be instructed to respond when you hear them. Next, your eardrum and middle ear system will be tested for mobility. This test requires the insertion of a small ear-plug-like probe and the variation of pressure in your ear canal.

Following completion of the above tests, the frequency following responses (FFR) will be recorded using the proposed stimulus paradigm in which a 20 msec tone burst is presented to one ear and/or to both ears. The FFR involves measuring brain waves using small metal discs applied to your scalp with a paste and held in place with plastic tape. This test requires you to relax and remain still while reclining and listening to the repetitive sounds through earphones. The FFR test session will not exceed two hours.

The above tests and procedures are routine clinical procedures which offer no known health risks. However, every effort will be made to minimize any potential risk or discomfort. Although you may not obtain direct benefit from this study, you will have contributed to our understanding of our ability to detect the direction of sounds.

II. CONFIDENTIALITY

Any information obtained about you for this study will be kept strictly confidential. Information carrying personal identifying material will be kept in locked files. Research records, just like hospital records, may be subpoenaed by court order. Your identity will not be revealed in any description or publication of this research.

III. RIGHT TO REFUSE OR TO END PARTICIPATION

You are free to refuse to participate in this study or to withdraw at any time without having it affect your care in any of the University clinics and without any loss of benefits to which you might otherwise be entitled.

IV. VOLUNTARY CONSENT

I have read the above materials, and they have been explained to me by the investigator. My questions have been answered, and I understand what will take place during the experiment. It has been explained to me that my identity will not be revealed in any description or publication of this research. Therefore, I consent to such publication for scientific purposes.

Any questions I have concerning my rights as a research subject will be answered by Stacy McDaniel, the principal investigator, or Dr. A. Krishnan, the co-principal investigator, at 547 S. Stadium Hall.
Telephone (615) 974-1811

A copy of this consent form will be given to me.

My signature below means that I have freely agreed to participate in this experimental study.

_____

signature of subject date

_____

signature of witness date

V. INVESTIGATOR'S CERTIFICATION

I certify that I have explained to the above individual the nature and purpose, the potential benefits, and the possible risks associated with participating in this research study. I have answered any questions that have been raised, and have witnessed the above signature.

_____

signature of investigator date

APPENDIX B
INDIVIDUAL AMPLITUDE DATA (IN VOLTS) FOR SUMMED MONAURAL RESPONSES EVOKED BY 500 HZ TONE BURSTS

INDIVIDUAL AMPLITUDE DATA (IN VOLTS) FOR SUMMED MONAURAL RESPONSES EVOKED BY 500 HZ TONE BURSTS

	Interaural Intensity Difference (dB HL)						
Subject	0	5	10	15	20	25	30
1	0.796	0.721	0.592	0.573	0.570	0.586	0.601
2	0.638	0.658	0.651	0.560	0.548	0.528	0.532
3	0.775	0.682	0.675	0.634	0.619	0.575	0.550
4	0.718	0.729	0.629	0.631	0.637	0.622	0.670
5	0.728	0.716	0.732	0.759	0.751	0.663	0.648
6	0.713	0.611	0.494	0.525	0.520	0.531	0.546
7	0.657	0.757	0.766	0.719	0.749	0.674	0.582
8	0.722	0.726	0.544	0.434	0.455	0.557	0.618
9	0.628	0.707	0.774	0.751	0.759	0.673	0.679
10	0.487	0.440	0.416	0.415	0.449	0.519	0.527

APPENDIX C
INDIVIDUAL AMPLITUDE DATA (IN VOLTS) FOR BINAURAL RESPONSES EVOKED BY 500 HZ TONE BURSTS

INDIVIDUAL AMPLITUDE DATA (IN VOLTS) FOR BINAURAL RESPONSES EVOKED BY 500 HZ TONE BURSTS

	Interaural Intensity Difference (dB HL)						
Subject	0	5	10	15	20	25	30
1	0.488	0.461	0.433	0.468	0.447	0.480	0.465
2	0.455	0.396	0.375	0.372	0.397	0.381	0.383
3	0.460	0.464	0.434	0.423	0.385	0.401	0.402
4	0.445	0.366	0.360	0.403	0.445	0.426	0.424
5	0.487	0.450	0.510	0.474	0.471	0.446	0.419
6	0.460	0.392	0.373	0.423	0.413	0.432	0.472
7	0.407	0.428	0.434	0.478	0.431	0.402	0.404
8	0.407	0.392	0.365	0.341	0.317	0.397	0.413
9	0.508	0.470	0.513	0.477	0.475	0.461	0.453
10	0.344	0.333	0.367	0.379	0.369	0.394	0.388

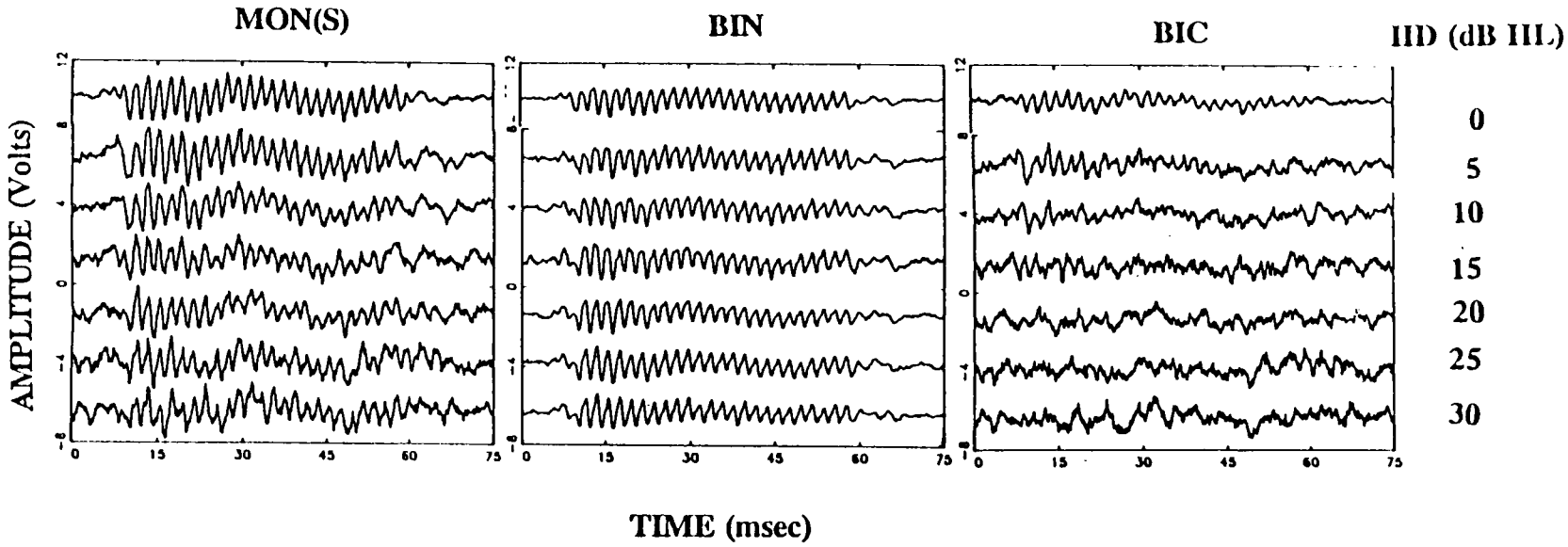
APPENDIX D
INDIVIDUAL AMPLITUDE DATA (IN VOLTS) FOR BINAURAL INTERACTION COMPONENT

INDIVIDUAL AMPLITUDE DATA (IN VOLTS) FOR BINAURAL INTERACTION COMPONENT

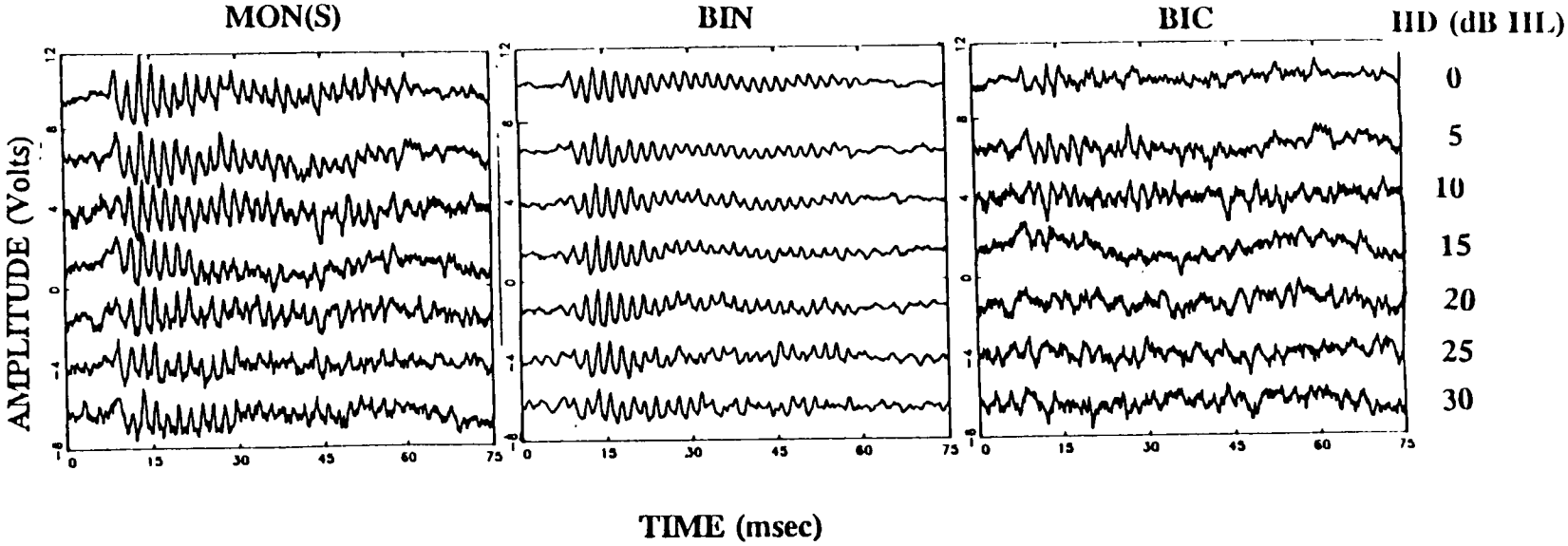
	Interaural Intensity Difference (dB HL)						
Subject	0	5	10	15	20	25	30
1	0.270	0.221	0.163	0.186	0.111	0.097	0.120
2	0.142	0.216	0.230	0.140	0.136	0.132	0.115
3	0.246	0.172	0.194	0.173	0.186	0.136	0.129
4	0.310	0.354	0.227	0.177	0.182	0.175	0.210
5	0.223	0.280	0.233	0.258	0.238	0.167	0.180
6	0.218	0.214	0.119	0.119	0.115	0.122	0.136
7	0.220	0.292	0.285	0.192	0.273	0.223	0.138
8	0.266	0.292	0.155	0.169	0.132	0.182	0.192
9	0.123	0.195	0.218	0.239	0.236	0.162	0.181
10	0.107	0.112	0.160	0.174	0.164	0.149	0.148

APPENDIX E
WAVEFORMS REPRESENTING ACTIVITY OF MONAURAL SUMMED, BINAURAL, AND BINAURAL INTERACTION COMPONENT AS A FUNCTION OF INTERAURAL-INTENSITY DIFFERENCES FOR EACH SUBJECT (E-1 - E-10)

APPENDIX E-1
SUBJECT 1



APPENDIX E-2
SUBJECT 2



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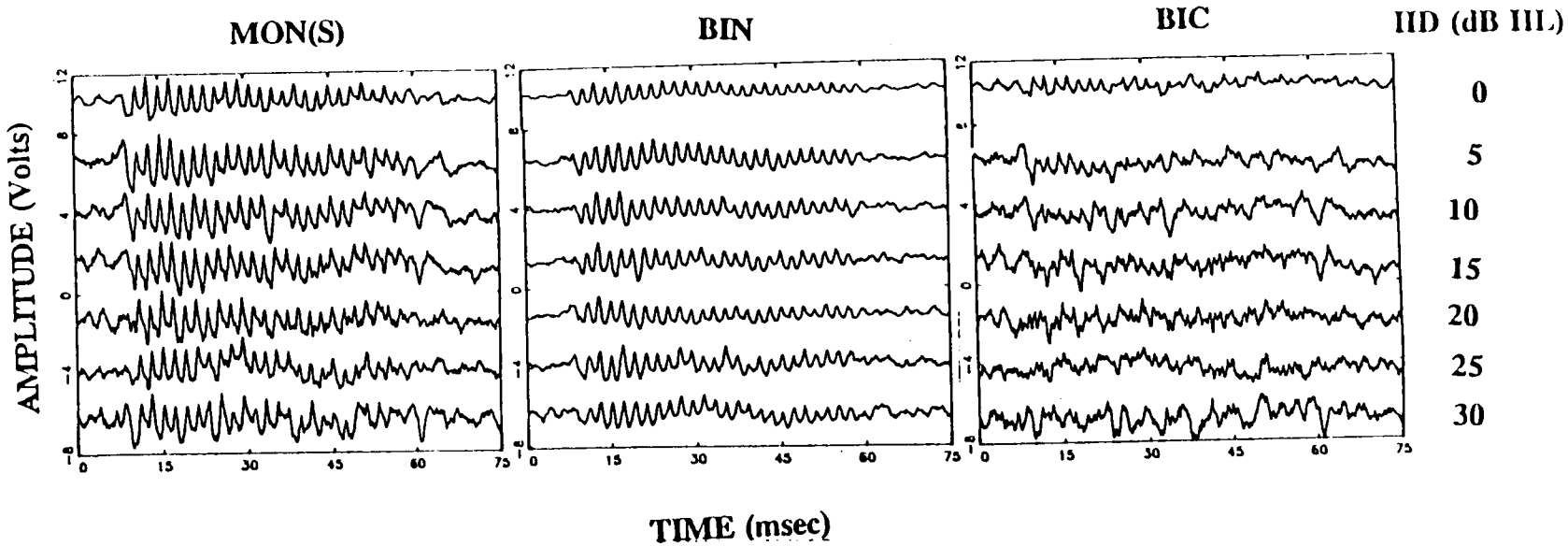
SUBJECT 3



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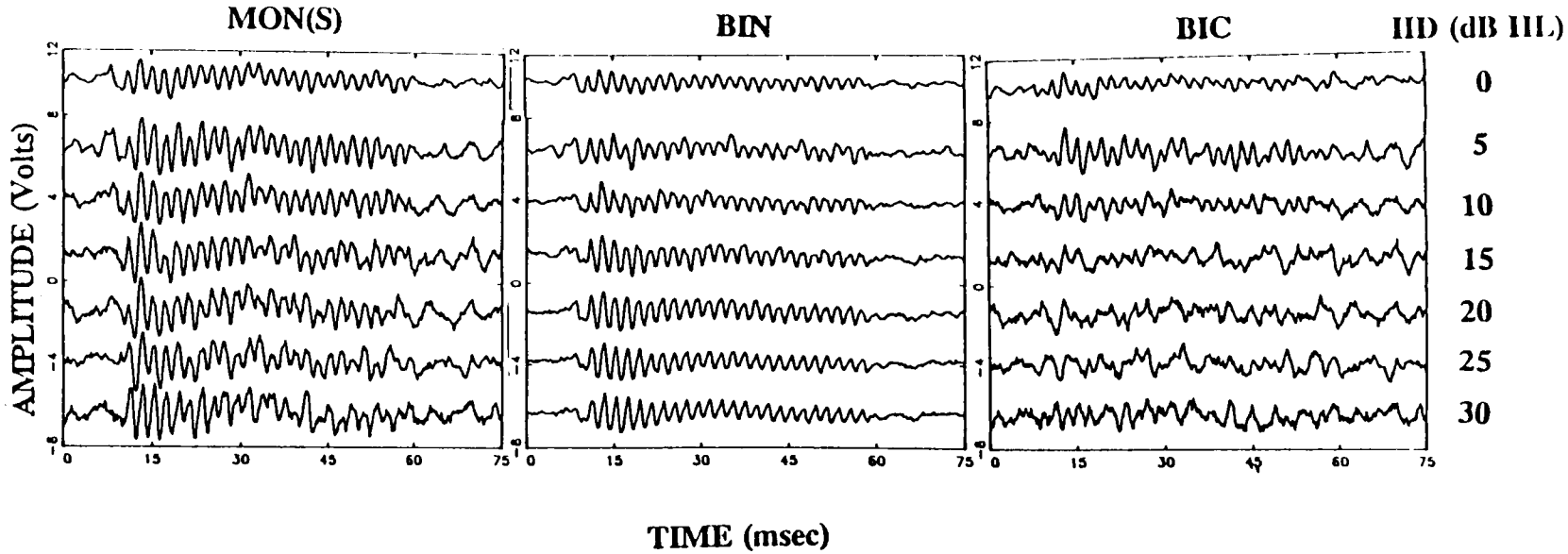
SUBJECT 4



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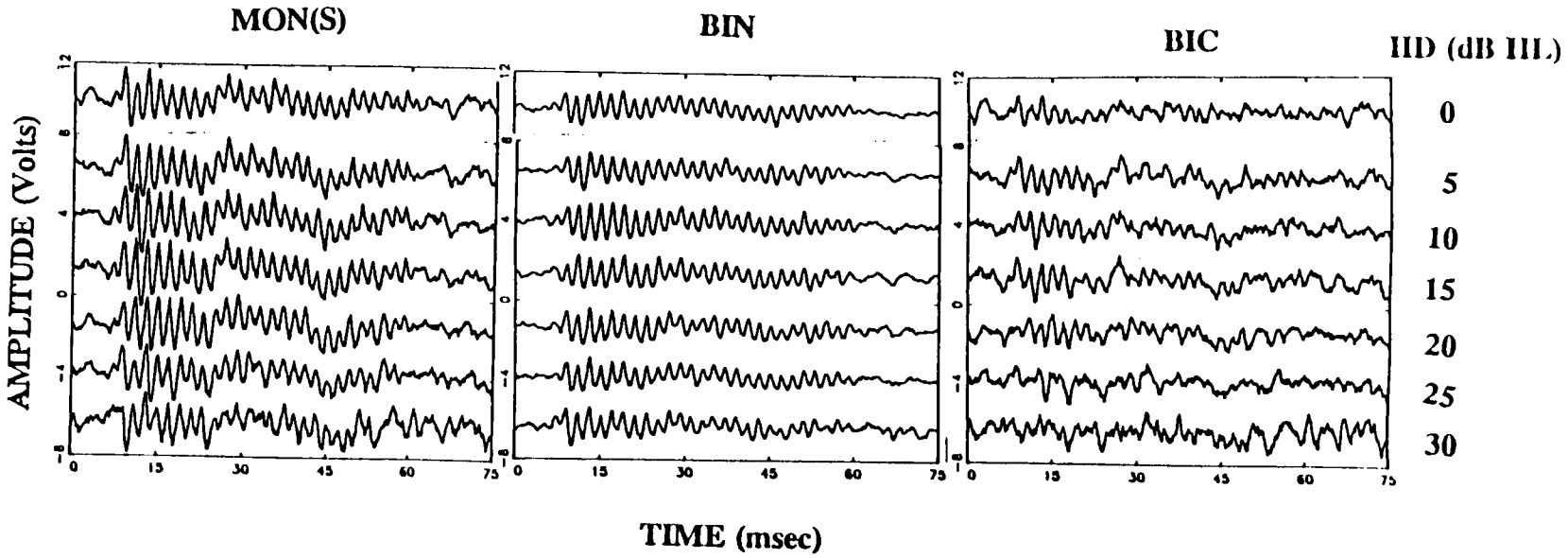
SUBJECT 5



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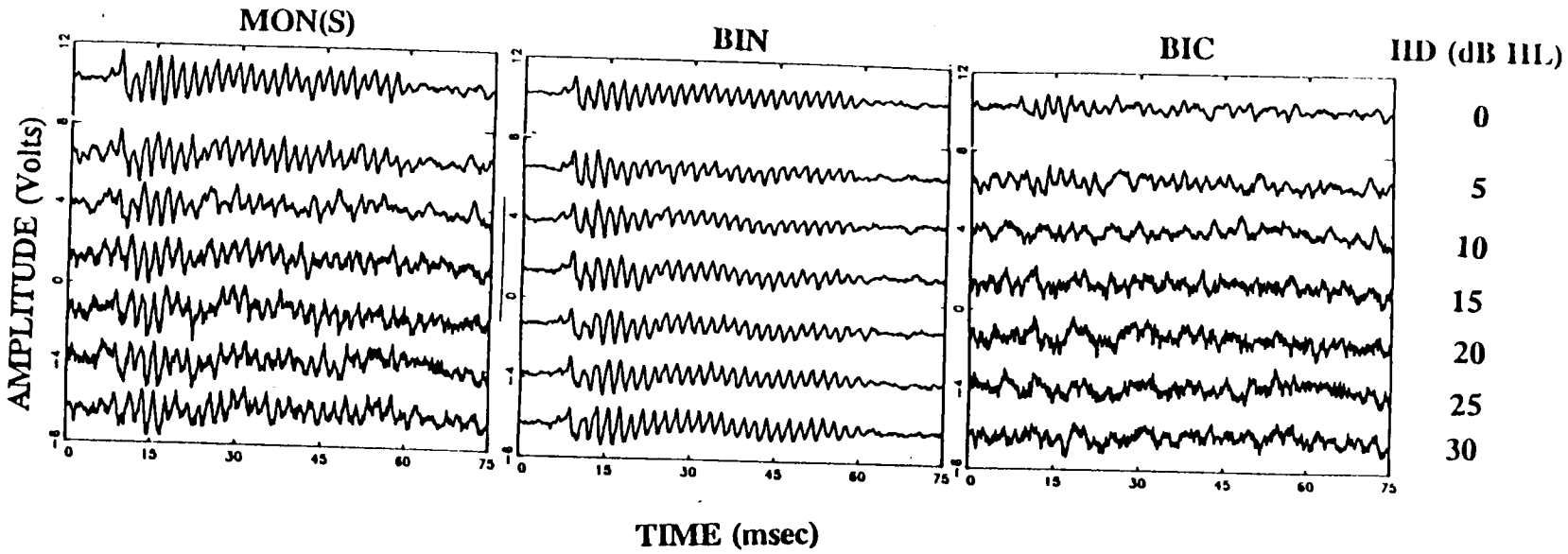
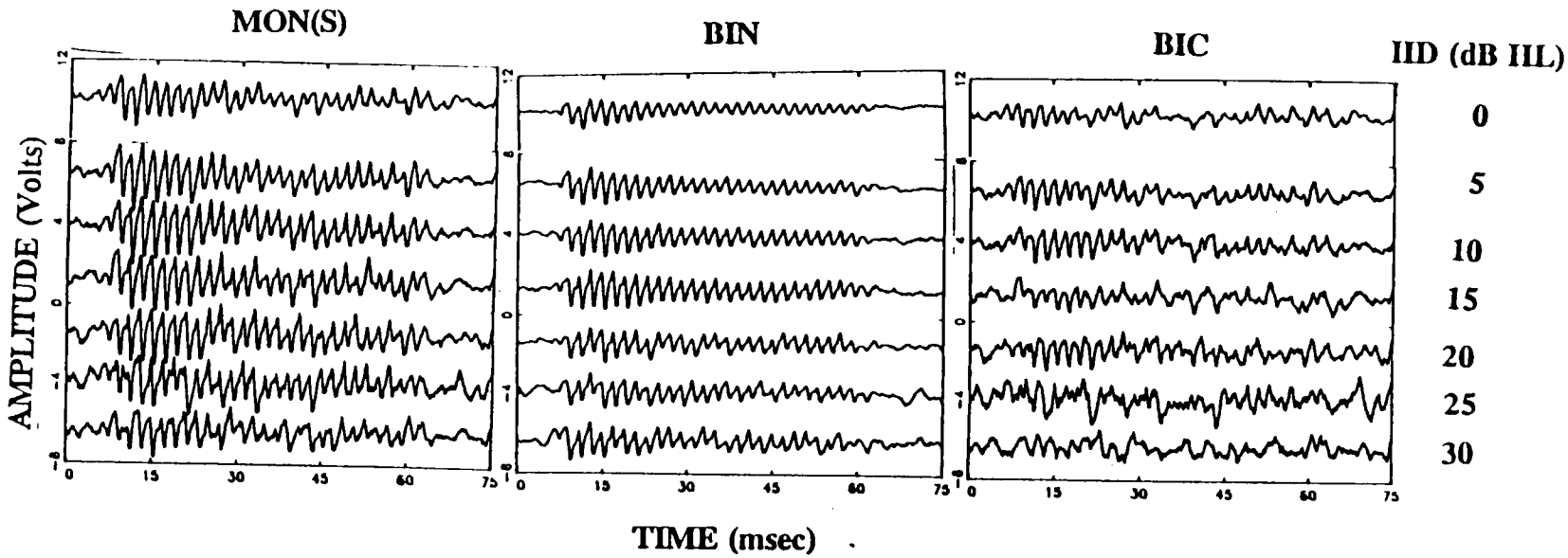
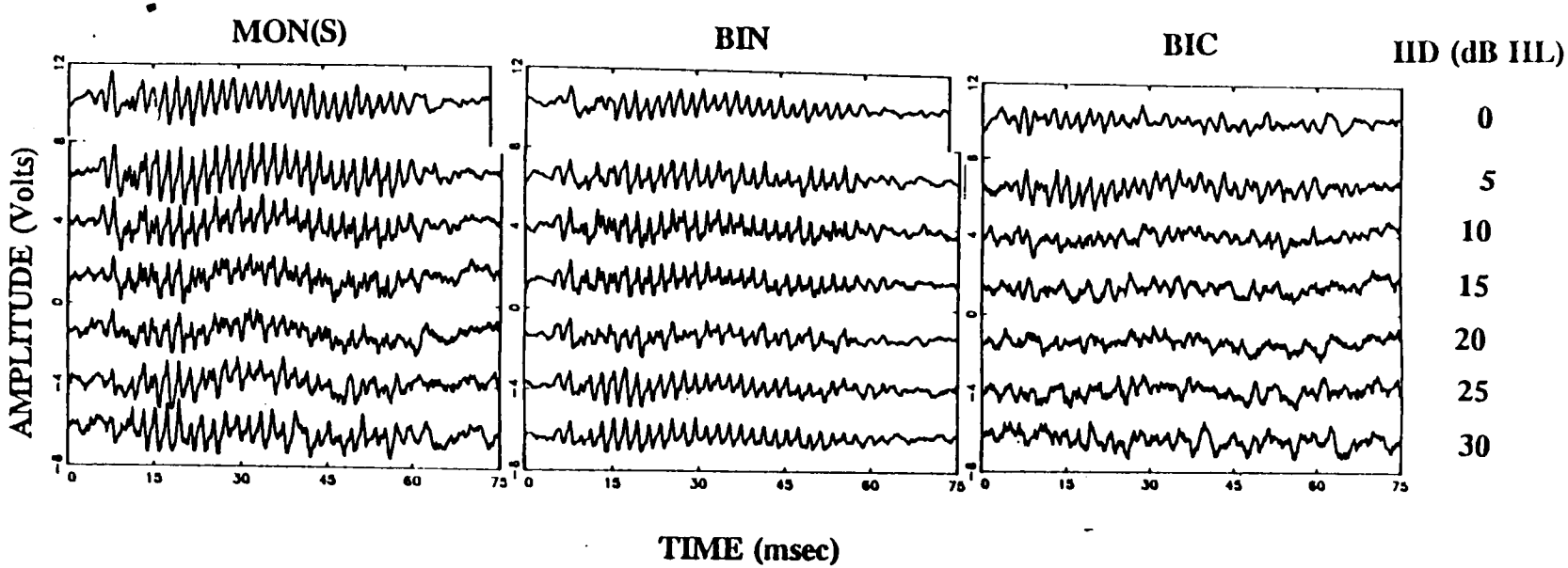


APPENDIX E-7
SUBJECT 7



APPENDIX E-8
SUBJECT 8



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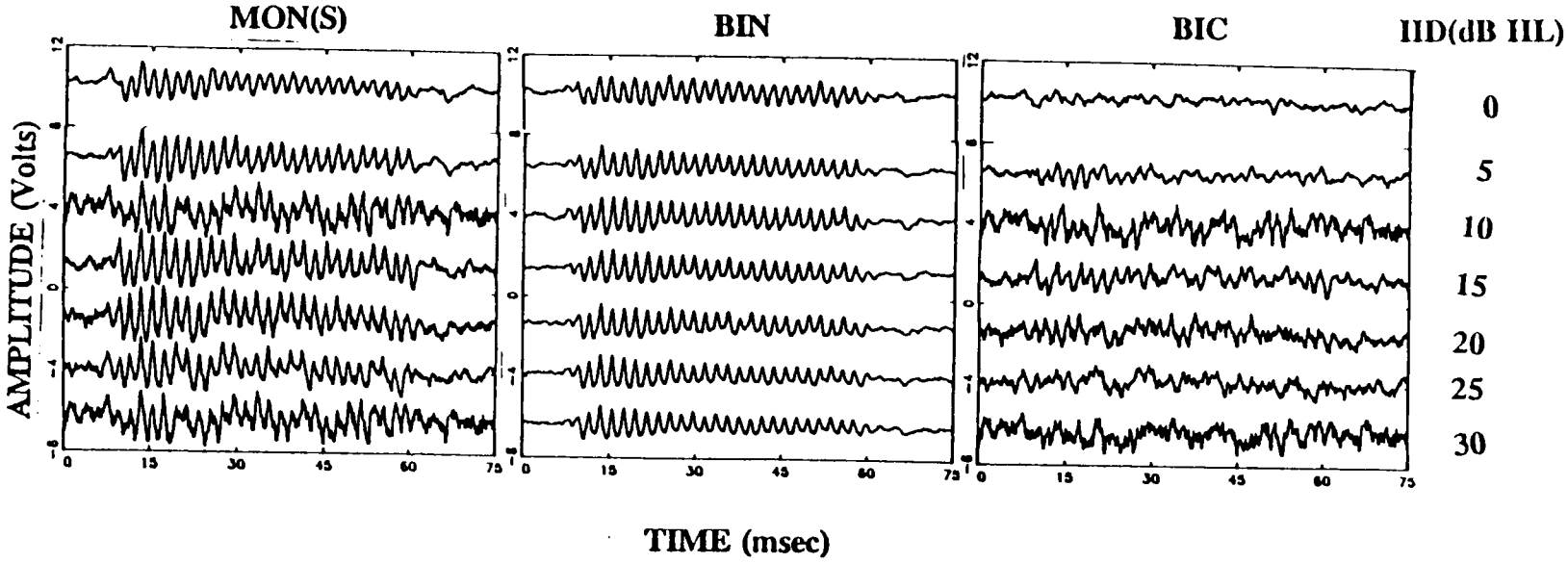
SUBJECT 9



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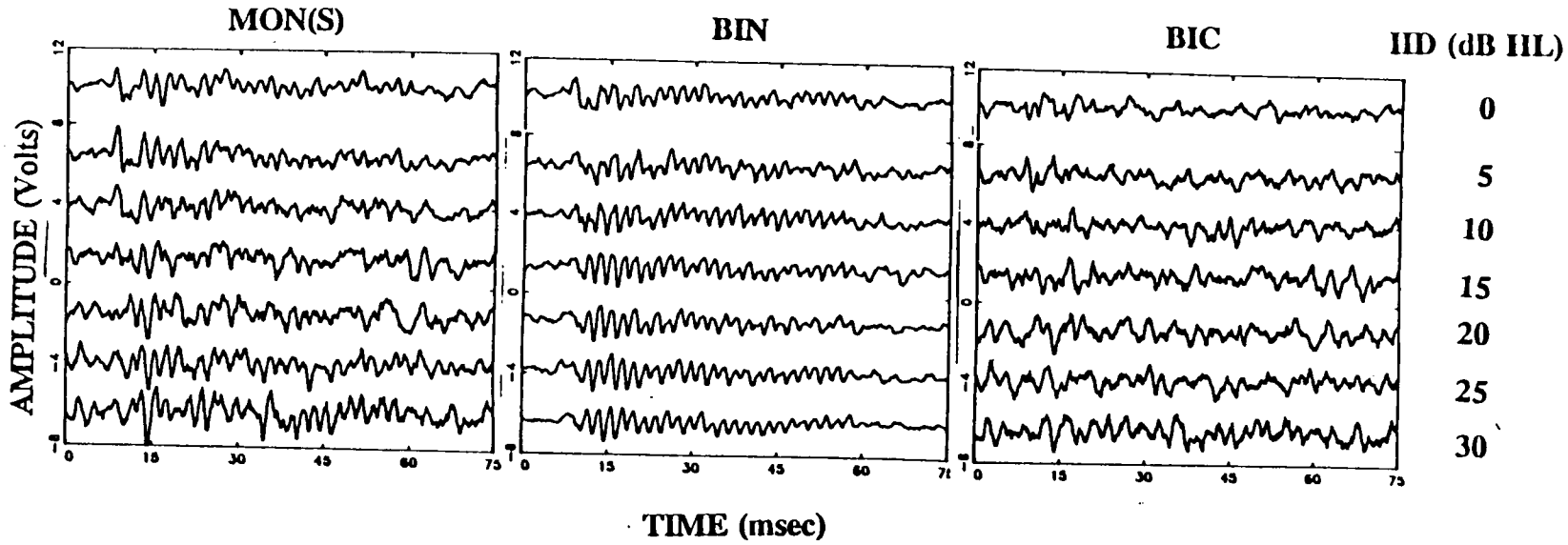
SUBJECT 10



VITA

Stacy S. McDaniel was born in Jackson, Tennessee on April 14, 1970. She received her Bachelor of Arts in Hearing and Speech from the University of Tennessee, Knoxville, in August of 1992. Future plans include completing a Clinical Fellowship Year in Audiology and pursuing a Doctoral degree.