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FREQUENCY ANALYSIS AS A METHOD OF SIGNAL DETECTION FOR THE BRAINSTSEM AUDITORY EVOKED RESPONSE

by

Steven Kaye

A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

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Abstract

Frequency Analysis as a Method of Signal Detection for the Brainstem Auditory Evoked Response

by

Steven Kaye

Advisor: Edward Greenblatt

The brainstem auditory evoked response (BAER) is a widely used clinical and research tool. Analysis of the BAER typically involves the measurement of the latency of its peaks. This type of analysis yields a limited amount of information from each BAER. Often, in clinical situations, patient's pathologies result in distorted or missing peaks. Recordings are often made under less than ideal conditions and false peaks are introduced. In these cases it may be impossible to make a quantitative statement about the waveform or in the case of a very degraded BAER it may be impossible to make any useful statement at all.

In this paper, a method of increasing the signal to noise ratio of the BAER through the use of frequency analysis was examined. The BAER was systematically degraded
by increasing the rate of stimulus presentation. Several measures derived from the frequency analysis based on

spectral magnitudes and phases were quantitatively compared with several traditional time-domain measures (inter-peak latencies and waveform morphology). The goal was to determine which measure or group of measures best predict or correlate with, signal presence (or overall quality of the BAER).

A measure derived from frequency analysis was found to be a better predictor of BAER quality than any of the traditional time-domain measures.

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Introduction

The Brainstem Auditory Evoked Response

The brainstem auditory evoked response (BAER) is the electrical response of the brainstem to an auditory stimulus (see figure 1). It may be recorded from any point in or on the brain as well as on the scalp. The signal energy of the BAER (approximately .5 microvolts peak to peak) is approximately one hundred times less than the background EEG (see appendix 1). Therefore unlike the EEG, the BAER can only be recorded using averaging techniques. In adults, the BAER is usually considered to be completed within 12 ms. following the onset of an auditory stimulus. Typical recordings are made with an "active" electrode on top of the head (vertex) referenced to an electrode on the side of the head, typically on the earlobe. The stimulus is often a brief (100 microsecond), broad spectrum white noise burst (click). A plot of voltage over time shows a series of vertex positive and vertex negative waves. In a normal adult human, between five and seven positive and five to seven negative waves occur within the first ten milliseconds. These waves are electrical potentials induced by activity in dendritic fields of the eighth nerve and nuclei of the medulla, pons, and midbrain (Stockard, Stockard, Westmoreland, and Corfits, 1979).

Most studies of the BAER have focused on the first five vertex positive waves (given the Roman numeral designations I through V). The exact anatomical locus of the generator(s) of each of the peaks is still a subject of controversy. With some reservations, Stockard et al. (1979) support a serial model of brainstem conduction with a one-to-one correspondence between waves and anatomical sites. Their research, based on clinical observations, suggests that wave I, II, III, IV, and V are generated by the auditory nerve, cochlear nuclei, superior olives, lateral lemnisci, and inferior coliculi respectively. Using intraoperative recordings on patients undergoing facial nerve surgery, Moller, Jannetta, and Moller (1981) conclude that the first two waves are generated by the eighth nerve. On the basis of lesion studies and intracranial as well as extracranial recording in cats, Achor and Starr (1979) conclude that only wave I has a clear correspondence to a single structure, the auditory nerve. All other waves are generated by two or more different structures. Regardless of their origin these waves are the most likely to be present and are also the most reproducible. In fact, an extremely high degree of reproducibility of these waves, both between and within normal subjects can be obtained when measuring latencies, and to a lesser extent amplitudes (Starr and Squires, 1982). However, to replicate the BAER all stimulus parameters must be held constant, any manipulation of the stimulus characteristics can change peak latencies.

Stimulus intensity, rate, polarity (phase), and frequency (spectral content) have all been shown to influence peak amplitudes and latencies of the BAER, each in their own systematic way (Stockard et al., 1979).

These properties of high within-subject replicability and low intersubject variance make the BAER a useful research as well as clinical tool. The BAER has been used as an aid to diagnosis in a variety of medical conditions that affect the peripheral auditory apparatus, the auditory nerve, or the brainstem. These conditions range from physical compression eg. posterior fossa tumors (Zappulla, Karmel, and Greenblatt, 1981), to nerve conduction defects eg. demyelinating diseases (Robinson and Rudge, 1977), to neurochemical changes eg. environmental toxin exposure (Jerger & Jerger, 1981), and to peripheral hearing loss as in middle ear infection or other otological conditions (Suzuki, Kodera, and Kaga, 1982). These pathological conditions influence the BAER in a variety of ways that can include missing peaks, diminished peak amplitudes, increased absolute peak latencies, increased inter-peak latencies (IPLs), and decreased reproducibility.

In the clinical setting judgments of BAER quality are usually based on overall waveform morphology as well as measurements of IPLs. There is some variation between clinicians as to which parameters of BAER measurement are most heavily weighted when making a clinical diagnosis. Attempts have been made however, to make clinical judgments more systematic. Zappulla et al. (1981) applied an objective measure based on a discriminant analysis of IPLs to a group of patients with posterior fossa tumors. The regression equation generated by the analysis correctly classified 35 out of 39 patients and 20 out of 21 normals. This study demonstrates that good clinical accuracy can be obtained measuring only IPLs, yet much more information is available from each waveform. Several other quantitative methods of BAER analysis were explored by Arnold (1985), using three different quantitative methods. The methods, correlation, variance ratio, and multiple pre-post Z tests were compared with the performance of experienced clinicians in classification of waveforms as signal or noise. The waveforms to be classified were recorded at stimulation levels of 40 dB SL, 25 dB SL, 10 dB SL, or no stimulus. Waveforms were recorded as pairs (no stimulus for 20 milliseconds followed by stimulus and a 20 millisecond recording). The correlation procedure produced a Pearson r for two successive groups of 2000 sweeps (see appendix 1). The variance ratio was the ratio of the variance of all points of a BAER to the variance of all points of its paired no-stimulus waveform. Higher variance indicated peaks and troughs in the waveform which were assumed to be signal related. The pre-post Z test took each digitized point in the signal waveform and subtracted from it the corresponding point in the no-stimulus waveform with which it was paired. Each difference was converted to a Z score by dividing it by the square root of the variance of the signal waveform plus the variance of the no-stimulus waveform divided by the number of sweeps. In this manner a group of 90 Z scores was obtained (corresponding to 90 samples from 1 to 10 milliseconds), for each waveform pair. An alpha level was selected and the number of Z scores (from 0 to 90) in each waveform pair exceeding that alpha level was used as the dependent measure.

The results of the above three analyses were submitted to a signal detection analysis and receiver operating characteristic (ROC) curves were generated. Four experienced clinicians also attempted to correctly classify each of the waveforms into the correct stimulus level category and a signal detection analysis was also performed on their results, generating ROC curves. ROC curves were compaired for the three "objective" analyses and the clinical ratings and an ANOVA was performed. Overall results showed a small non-significant advantage for the clinicians' ratings, but there was no significant difference between any of the four measures (three objective measures plus clinicians ratings). In fact, at low stimulation levels (10 dB) the correlation method was slightly superior to the clinicians' ratings. Arnold also noted that the clinicians' inter-rater reliability was poor (Kappa > .10).

These studies employed detailed analyses of the BAER in an attempt to objectify and refine the ability of the

BAER to discriminate groups. While Zappulla et. al.'s method was highly successful in discriminating a pathology group from normals, the study did not compare the discriminant equation's performance with the performance of clinicians. As of yet, a study has not been done using a discriminant equation to make more subtle discriminations such as levels of a stimulus variable such as stimulus rate or intensity. Arnold's "objective" methods discriminated no better than clinician's judgments. Therefore an objective waveform measure that can classify BAERs more accurately than clinicians has not been demonstrated.

Frequency analysis provides a novel perspective for BAER analysis. The procedure lends itself well to objective quantification of signal as well as straightfoward removal of noise.

Frequency Analysis and the BAER

The use of frequency analysis in electrophysiology is widespread. Frequency analysis of the EEG is now common in clinical practice as well as research (Bergland, 1969). Frequency analysis is also often used in the analysis of action potential responses in single unit studies (Allen, 1983). Frequency analysis of cortical visual and auditory evoked potentials is used for a variety of purposes from determining quality of signal (Beagley et al., 1979) to refining audiometric testing (Sayers et al., 1979) to basic neurophysiological investigations (Davis, 1973).

Frequency or spectral analysis can be accomplished by a variety of procedures. These include hardware and software implementations. In a hardware implementation, a biological signal is amplified and fed into a spectrum analyzer. Typically this device consists of a bank of band pass filters working in parallel. Each filter has a characteristic center frequency and bandwidth. Any energy from the original signal which oscillates outside the range of the specific filter is attenuated. The portion of the signal which does pass through the filter is measured and recorded (integrated in some capacitive circuitry) or displayed via a meter or light emitting diodes (LEDs). With a group of these filters working together any complex signal can be filtered and properly sorted into its component frequencies. The hardware spectrum analyser serves as a good model of the software implementation. Here too, a complex signal is filtered, in this case mathematically, and sorted into component frequencies.

There are several software implementations of spectral analysis. Typically, an amplified biological signal is sampled by a computer. The computer first digitizes the signal (the analog signal is converted to a series of numbers), then a procedure known as the Fast Fourier Transform (FFT) is performed (Bergland, 1969).

The basic assumption behind the FFT is that any complex time-domain waveform (a waveform plotted with time on the X-axis), such as a BAER or an EEG is composed of a group of sine waves each having their own characteristic frequency, phase (starting point of the sine wave in relation to the origin), and amplitude. The FFT simply decomposes a complex time-domain waveform into its component sine waves. For each sine wave frequency or spectral component the FFT produces a magnitude (see appendix 1), and a phase angle value (the angle that a line tangent to the sine wave at the Y-intercept forms with the X-axis). For more information see appendix 1.

Frequency analysis has not been widely used in the analysis of the BAER. A recent survey of the literature found only nine studies that were directly concerned with frequency analysis of the BAER; (Eberling, 1979; Fridman, John, Bergelson, Kaiser, and Baird, 1982; Fridman, Zappulla, Bergelson, Malis, Greenblatt, Hoepner, and Morrell, 1984; Greenblatt, Zappulla, Kaye, and Fridman, 1985; Kevanishvili and Aphonchenko, 1979; Laukli and Mair, 1981; Linden, Cambell, Hamel, and Picton, 1985; Stapells, Linden, Suffield, Hamel, and Picton, 1984; Zappulla, Greenblatt, Kaye, and Malis, 1984).

The studies by Stapells et al. and Linden et al. focused on steady state evoked potentials (see appendix 1). Using a hardware spectrum analyzer they studied rate of auditory stimulation and its effect on amplitude of the fundamental frequency of the steady state evoked potential in sleeping and waking subjects. The maximum amplitude of the major component of the evoked potential occurred at a stimulation rate of approximately 40 Hz. and significantly diminished during sleep. A steady state auditory evoked potential with a stimulation rate of 40 Hz. is made up of middle latency (see appendix 1) components as well as BAER components. The fact that the response diminishes during sleep suggests that most of the energy in the response is contributed by the middle latency components because the BAER amplitude does not diminish during sleep (Stockard et. al., 1979). Therefore these studies are not useful in studying the signal quality of the BAER.

The studies by Eberling (1979), Kevanishvilli and Aphonchenko (1979), and Laukli and Mair (1981), looked only at the distribution of power in the magnitude spectra (see appendix 1) derived from a Fourier transform. These three studies were primarily concerned with an analysis of high pass filtering techniques as well as the spectral composition of certain peaks. None addressed the assessment of signal quality. Kevanishvili & Aphonchenko presented binaural click stimuli at 10 clicks per second, at several intensities. An analysis epoch of 9 ms. after click presentation, was used. Their spectral analysis showed the greatest magnitudes centered around 150, 500, and 900 hertz. At lower stimulus intensities the higher frequencies drop out and the power present in the low frequencies shifts to still lower frequencies.

Eberling (1979) criticized the study by Kevanishvili & Aphonchenko because their analysis epoch was too short and the spectral transform was performed so as not to allow enough resolution in the individual frequency components. Eberling stated that a 9 ms. analysis epoch excluded important stimulus related activity, especially at low stimulus intensity levels where peak latencies increase and time-domain analysis shows the negative drop after peak V is often not complete after 9 ms. Eberling therefore, used a 16 ms. analysis epoch. Furthermore, he employed a technique of increasing frequency-domain (see appendix 1) resolution by adding zeros to the end of his time-domain data ("padding") before doing the Fourier transform. This procedure will not alter the overall shape of the frequency spectrum but because more time-domain points (with a frequency of zero) are included in the transformation, more frequency-domain points are produced by the transformation. The effect is increased frequency resolution. This technique increased the frequency resolution to 16 hertz which he stated was sufficient for his analysis. His results show the main spectral power always concentrated below 250 hertz. His other principal finding was a shift toward lower dominant frequencies with lower stimulus intensities.

Laukli & Mair (1981) presented short, fixed-phase tone bursts (sine waves at identical points in their cycle at onset time), of several different frequencies, to both humans and cats. They looked at analysis epochs of 20 ms. and 80 ms. both before and after the stimulus was presented. Therefore they had an epoch of spontaneous brain activity to compare with each post stimulus epoch. When examining post stimulus activity they found results similar to those of Eberling (1979). However, they took their analysis a step further. By subtracting the spontaneous brain activity spectrum from their frequency analysis, this technique allowed them to analyze signal related frequency spectra. The results changed dramatically. They now found that the dominant frequency of the spectral analysis was in the 500-2500 hertz range. The dominant low frequency activity was primarily related to spontaneous brain activity. Unfortunately this study did not make any attempt to relate any of the stimulus parameters i.e. variations in tone frequencies, in any systematic way to the resulting spectra.

Fridman et al. (1982) were the first to use spectral analysis of the BAER as a means of improving signal quality. Fridman's paper focused on an automated technique for peak detection in the time-domain representation of the BAER. The purpose of the investigation was to find a way to increase signal to noise ratio (see appendix 1) of the BAER so that a computer algorithm could be developed that would consistently, and reliably identify peaks I-V. The problem was the inherently low signal to noise ratio (about 2.5:1). With so much noise in the system many false peaks exist in the BAER. The trained human can usually determine which peaks are of biological significance, but a machine can not. Fridman applied a digital filter to the BAER. A digital filter is a noise removal technique that relies on spectral analysis. The BAER is transformed to the frequency-domain using an FFT, then frequency components outside a specified range are multiplied by zero. An inverse FFT (see appendix 1) is done to convert the frequency-domain waveform back into a time-domain waveform (ie. a BAER). The BAER now has much of the noise (extraneous peaks) removed and now simply by taking the first derivative of the waveform, peaks become evident (first derivative equals zero at a peak).

One problem Fridman et. al. faced was the determination of which frequencies should be digitally filtered. They had to determine which frequencies were time locked to the click and therefore should be considered signal and which were not time locked and should be considered noise. They chose to determine signal presence for a given frequency component by looking at its reproducibility.

First they analyzed magnitude spectra (see appendix 1) derived from the FFT. They collected ten groups of 200 sweeps each (see appendix 1). An FFT was done on each of the ten groups and then an FFT was performed on the time-domain (see appendix 1) composite of 2000 sweeps. For each spectral component a mean magnitude of the ten groups was calculated. These numbers were plotted as ratios of the magnitudes of the composite waveform. A low ratio (approaching one) indicated that 200 sweeps produced the same spectral component magnitude as 2000 sweeps, indicating that the spectral component was highly reproducible. A high ratio meant that the group mean was very different than composite magnitude and there was very low replication. Fridman et. al. used no inferential statistics but graphically showed the greatest stimulus-related signal (i.e. lowest ratios) to lie between 400 Hz. and 2000 Hz.

Fridman et. al. then did a second, parallel analysis of the variability of phase angles derived from the FFT. Like the above analysis, data were collected in ten groups of 200 sweeps. An FFT was done on each group but instead of examining the magnitude spectra, as in the above analysis, the phase angle spectra were examined. For each of the ten transformed BAERs, for each frequency component, an angle between 0 and 360 degrees was derived. This phase angle represents the angle that the component sine wave forms with the origin. Fridman et. al. reasoned that if each sweep of the BAER was identical all phase angles would be identical. Therefore, low variance in the phase angles across the ten groups would indicate signal presence in the frequency being examined. Fridman et. al. found phase angle variance to be the lowest in the frequency band between 450 Hz. and 1400 Hz.

On the basis of this empirical determination they set the digital filters to eliminate any activity outside of the 450-1400 Hz. range and was able to record reliable BAERs, in normal subjects, after only 400 sweeps with accurate automatic detection of peaks I-V.

Fridman's next study (Fridman et al., 1984), also focused on signal quality of the BAER. Here he elaborated on the concept of phase variance that was introduced in his previous study. The goal of this paper was to develop a measure that would reduce the BAER waveform to one objectively derived number, that would characterize signal quality. This number was called synchrony measure. Fridman et. al. state, "The proposed criterion of BAEP [brain stem auditory evoked potential] response detection based on the synchrony measure does not require visual inspection of the BAEP wave shape. It becomes possible to make objective and reliable statement about BAEP presence without intervention of a qualified neurophysiologist."

Synchrony measure (SM) was derived from the phase variance measure. BAERs, with and without an auditory stimulus were recorded using 100 normal subjects. In the "no-stimulus" conditions, recording procedures were identical to the "stimulus" conditions, but no click was delivered to the subject. FFTs were done on both the stimulus and no-stimulus condition. A phase variance was computed for each spectral component (see appendix 1). Composite phase variance spectra for both signal (the BAER) and no stimulus conditions were computed by averaging across all subjects. A Mann-Whitney U test was performed to find the spectral component frequencies that showed the least overlap between the stimulus and no-stimulus conditions. This non-parametric procedure was chosen because the distribution of phase variance values is non Gaussian (phase variance takes on values between 0, which is perfect synchrony, and 1, which is complete randomness). Six frequency values were chosen: 320 Hz., 480 Hz., 560 Hz., 880 Hz., 960 Hz., and 1040 Hz. Component synchrony measure (CSM) was defined as component phase variance subtracted from one, so that CSM would vary in a manner similar to the absolute value of a correlation coefficient i.e. values approaching zero would show low synchrony and values approaching one would show high synchrony. The overall SM for the BAER was an average of the six chosen CSM values.

Fridman et. al. stated that the theoretical probability of SM > 0.22 in the absence of signal is less than .001. Using this level as a cut-off for signal he showed that all of the BAERs collected on normals could be discriminated from the no-stimulus conditions with 100% accuracy. They then compared SMs of normal adults with the SMs of neurosurgical patients. Most patients had acoustic neuromas (a non-malignant tumor arising from the myelin sheath of the auditory nerve). Twenty-one out of 22 patients were correctly classified as abnormal using the

0.22 level as a cutoff for SM.

Zappulla et. al.'s (1984) paper extends the use of the synchrony measure as an objective measure for monitoring patients in the operating room by comparing the BAER with its associated CSM spectrum plot. BAERs have often been used to monitor auditory integrity in patients while undergoing surgery of the posterior fossa. Unfortunately, the intraoperative environment presents conditions of reduced signal and increased noise. The signal of the BAER is reduced because patients with pathology in or near the eighth nerve usually have a degraded BAER. In addition there is noise contamination from many electrical instruments used in operating rooms such as blood pressure transducers, bipolar coagulators, and various transformers and voltage regulators. For these reasons, time-domain representations of the BAER often show peaks when no signal is actually present or do not show peaks when there is signal. Although no overall SM was calculated and no inferential statistics were presented, Zappulla et. al. showed the clinical utility of monitoring a CSM spectrum concurrently with the time-domain plot. A group of case studies were presented which showed that the CSM spectrum was as good as and in some cases better than the BAER in evaluating signal presence. Since these measures are somewhat independent of each other, they can provide substantially more information about signal presence when used together. They allow the clinician to view the BAER from two partially independent perspectives.

Greenblatt et al. (1985) examined the utility of frequency-domain measures of the BAER with reduced stimulus intensity. They attempted to determine the lowest stimulus intensity, at which the frequency-domain measures would still detect signal. Both magnitude and CSM values were derived from BAERs recorded at 12 levels of stimulus intensity ranging from -5 dB SL to 55 dB SL, including a no-stimulus condition. As expected, magnitude and CSM values decreased with decreasing stimulus intensity. Higher frequency spectral components were the first to diminish. Mann-Whitney U tests were performed to compare each level of intensity to the no-stimulus condition for both magnitude and CSM spectra. Seven spectral components were selected as showing the least overlap between signal and noise conditions. There was sufficient similarity between magnitude and CSM spectra that the same spectral components were used for both analyses. The seven spectral components were averaged to form an overall SM and also a mean power value for each intensity, for each subject. A theoretical significance value was computed for SM and an empirical cut-off value was determined for mean power. The group data indicate that for SM, the observed signal can not be detected reliably when the stimulus intensity is somewhere between 5 dB and 10 dB. For the magnitude data, signal is lost at a stimulus intensity of between 15 dB and 20 dB. In comparing individual data to the group means it was also found that SM was consistently more sensitive than magnitude measures. These data corroborate Fridman et al's. (1984) finding that phase angle variance is a more sensitive measure of signal presence than magnitude variance.

It is clear from the above studies that spectral measures, specifically phase variance measures, are a useful adjunctive source of information about signal presence. In the typical time-domain analysis only five points are analyzed. The CSM spectrum represents information from all points in not only the 2000 sweep ensemble BAER, but all points in the 10 subgroups that make up that ensemble. Therefore the BAER, being an averaged waveform, collapses information across its acquisition time (typically, at 10 clicks per second, 4-5 minutes). The CSM spectrum however, subdivides that acquisition time to extract more information about signal quality than the BAER can.

None of the above studies have provided a systematic or quantitative comparison of time-domain versus frequency-domain measures in evaluating signal presence. Several of these studies have implied that a frequency-domain measure, specifically phase variance, might be a superior measure to time-domain analysis, but that assertion has only been supported anecdotally.

BAER Signal Degradation

As previously discussed, altering stimulus characteristics can produce changes in the BAER. Increasing stimulus rate or decreasing stimulus intensity will in systematic ways degrade the response (Stockard et. al., 1979). In the time-domain, increasing rate or decreasing intensity seem to have similar effects. Small alterations lead to small increases in IPLs. With greater stimulus change greater IPL changes are seen. With more change, peaks may diminish in amplitude then disappear. Finally with a low enough intensity or a fast enough stimulation rate no reproducible BAER may be present (Stockard et al., 1979). The effects on CSM, of decreasing the stimulus intensity and increasing the rate of stimulation may or may not be similar.

Rate of stimulation

The effects of rate of stimulation on the BAER are discussed in several studies (Gerling and Finitzo-Hiever, 1983; Stockard et al., 1979; Thornton and Coleman, 1975; Fujikawa and Weber, 1977; van Olphen, Rodenburg, and Verwey, 1979; Don, Allen, and Starr, 1977; Chiappa, Gladstone, and Young, 1979; Shanon, Gold and Himmelfarb, 1981).

The studies by van Olphen et al. (1979) and Chiappa et al. (1979) are typical of the larger group of rate studies. Both studies were done with normal adults and were largely descriptive. Neither study used inferential statistics. Only means and standard deviations of peak latencies and amplitudes were reported. van Olphen concluded that as click rate is increased from 2.5 hertz to 80 hertz there is a linear decrease in amplitude for waves II, III, and IV with the amplitude of wave V remaining constant. Wave I was not studied. The absolute latencies of waves II through V remain constant at stimulus rates of 2.5, 5, and 10 hertz but linearly increase between 10 and 80 hertz. Because all standard deviations were much larger (at least 2 to 1) than any mean difference and the author did not describe how missing peaks were dealt with, these results must be interpreted cautiously. Chiappa used rates of 10, 30, and 70 hertz. He also found a steady but non-linear decrease in amplitude for waves I, III, and a IV-V complex, with increasing rate. There was a much larger decrease in amplitude between 10 and 30 hertz than between 30 and 70 hertz. Between 10 and 70 hertz waves I and II did not show a latency shift. Waves III, IV, and V showed latency shifts of .3, .3, and .5 ms. respectively. Despite having high standard deviations, these latency shifts were almost identical to van Olphen's. Chiappa also acknowledged that not all peaks were recognizable in every subject. In general, more waves dropped out at the higher stimulus rates. Wave V was most resilient; it was present 97% of the time at 70 hertz. Waves II and IV were only recognizable 61% and 57% of the time at 70 hertz. Waves I and III were identified 76% and 85% of the time at 70 hertz.

In summary, increasing the rate of stimulation caused longer absolute peak latencies, longer inter-peak latencies (IPLs), decreased peak amplitudes, deteriorated peak morphology and missing peaks.

The present study compared traditional time-domain analysis of the BAER consisting of measurement of peak latency ie. inter-peak latency, and number of missing peaks, with measures of the CSM spectrum and the magnitude spectrum. The goal was to determine which of these quantitative measures of the BAER best characterizes signal quality.

It seems reasonable to employ systematic changes in rate as a technique of manipulating signal quality. The assumption being that manipulations of stimulus rate would produce changes in signal quality that would model "real world" variations in signal quality. Therefore whichever measures correlate best with rate or best discriminate levels of rate can be assumed to best predict signal quality.

Methods

Subjects

Subjects were thirteen normal adults ranging in age from 24 to 40. All subjects had normal hearing, by self report, in both ears. All had a negative history for any neurological disease, neurological trauma, or disease of or trauma to the auditory system, including frequent middle ear infections. Furthermore, subjects were screened with pure tone audiometry to insure normal hearing thresholds for frequencies between 250 and 8000 hertz. All subjects were volunteers, selected from among staff and students at The Mount Sinai Medical Center. After the entire procedure was explained, informed consent was obtained.

Recording Procedure

Grass, Gold plated, metal cup electrodes were placed on the vertex and both earlobes (Cz and A1, A2 respectively in the international 10-20 system). All inter-electrode impedances were kept under 3000 ohms at 40 hertz. The click stimuli were broad spectrum noise bursts with a very short rise-fall time and a plateau time of 100 microseconds. The click intensity was 60 decibels above the subject's hearing threshold (60 dB SL). Clicks were presented through a set of TDK-34 headphones, to one ear at a time. The ear contralateral to the ear receiving the click stimulation received a noise mask presented at 50 decibels sound pressure level (50 dB SPL) to prevent inadvertent stimulation of that ear.

Testing took place in a quiet room where the subjects reclined in a supine position. Data were collected on a Digital Equipment Corp. PDP-11-23 computer with a data acquisition front end designed by the Neurometrics Corporation. The amplifier gain was 100,000 with a noise level of three microvolts peak to peak and a common mode rejection of 100 decibels. Analog filters were set between 100 and 3000 hertz. The data were digitized at a rate of 10,000 hertz with a twelve bit analog to digital (A/D) resolution. Each evoked potential epoch (sweep) lasted 12.8 milliseconds (ms). Each sweep therefore, consisted of 128 digitized samples. Digitization began .5 ms. after the click onset and ended 12.8 ms later. Data were collected in groups of 128 sweeps. Artifacting (see appendix 1) occurred when voltage levels exceeded 12.5 microvolts. Artifacted sweeps were not added to the 128 sweep average. The computer performed an online 256-point Fast Fourier Transform (FFT) on each ensemble of 128 sweeps, as described under data analysis. Phase data were retained and magnitude data were discarded. Ten groups of

128 sweeps were collected for each evoked potential. For the time-domain data a straightforward average was computed of the 1280 sweeps. For the frequency-domain data, a phase angle variance spectrum was computed (see Data analysis). Each evoked potential with its phase angle variance spectrum was stored on the computer's hard disk and later downloaded to an IBM-PC for further analysis.

Design

A repeated-measures design was employed. All subjects received click stimulation at each of four stimulus rates. These were 10.1, 25.1, 40.1, and 55.1 hertz. Each of the thirteen subjects received the four stimulus rates in a different, randomly assigned order. Clicks were presented monaurally with the contralateral ear receiving a noise mask. Then the opposite ear was stimulated (using the same random order) so that recordings were made from both ears in all subjects. An ipsilateral channel was recorded between the vertex and the earlobe being stimulated. "No-stimulus" conditions were paired with the stimulus conditions. Recording from the same channels as the stimulus conditions, data were collected in the absence of any auditory stimulation. Digitization rate and number of sweeps collected was identical to the stimulus condition. In this way, for each stimulus condition (rate), for each ear, there were two waveforms recorded (stimulation and no-stimulation). The no-stimulus conditions served as a control for any synchronous electrical activity not directly related to the stimulus. This was especially valuable for frequency-domain analysis as in the method of Laukli & Mair (1981). Over the four stimulus rates, eight waveforms were collected for each ear or sixteen waveforms per subject.

Data Analysis

Eight measures were derived from each waveform. Four were derived from the time-domain representation of the BAER and four from the frequency-domain. The time-domain measures were I-III IPL, III-V IPL, I-V IPL, and the number of recognizable, positively deflected peaks. These measures were chosen because they are the ones most often used in the clinical setting (Stockard et. al., 1979). All peak measurements and judgments about peak presence were made by the author with a microcomputer program designed to display and measure evoked potentials. Four frequency-domain measures SM1, SM2, MM1, and MM2, were derived as described in the next section.

Online analysis

Online analysis consisted of ten 256 point FFTs for each evoked potential waveform. Although only 128 points were sampled per epoch a 256 point transform was performed to increase resolution in the frequency-domain. This effectively decreases the bandwidth of each spectral component. This was accomplished by first "baselining" the data (removing any DC component), then by "padding" (adding 128 zeros to the end of the waveform). By padding the waveform with zeros (a straight line made up of all zeros has a frequency of zero after it is transformed into the frequency-domain) the Fourier transform will produce more frequency-domain points. Because the time-domain sampling rate (or dwell time) remains the same, the maximum frequency component produced by the transform remains the same. With more frequency points and the same highest frequency the distance between frequency points decreases, giving increased resolution.

The ten FFTs were then used to compute a component synchrony measure spectrum. Recall that each FFT produces a set of spectral components from which a phase angle spectrum is derived (see appendix 1). Ten phase angle spectra were produced for each of the 128 spectral component frequencies over the 10 ensembles (each ensemble is a group of 128 averaged sweeps). The angular variance is defined as the length of the resultant vector (or sum) of the ten vectors each being a unit in magnitude and having a direction corresponding to the phase angle of the individual spectral component (Zappulla et al., 1984; Fridman et al., 1984; Mardia ,1972). Each spectral component or frequency band can be represented by an angle that expresses its phase relation to the origin. If for any one spectral component this phase relationship remains relatively constant across ten trials (or ten consecutive FFTs), then information at that frequency is time-locked to the stimulus. It exhibits low variance or high synchrony. The phase angle variance can be conceptualized by plotting each of the ten phase angles as vectors each with a magnitude of one unit and direction equal to the phase angle (some angle between 0 and 360 degrees). If these ten vectors are added a resultant vector is obtained. If all ten angles are identical the resultant vector will be a straight line ten units in length. If the ten angles are randomly distributed the resultant vector will approach a length of zero. The resultant vector's magnitude is then normalized (in this case, divided by 10) to compute a variance. A number between zero and one results. This number is defined as the component synchrony measure (CSM) and varies like the absolute value of a correlation coefficient such that when CSM=1 a perfect replication has occured and when CSM=0 complete randomness is present in the data.

The computational form for each spectral component is as follows:

CSM=R

Where:

$R=\sqrt{(C^2 + S^2)}$;

$C=1/n\ (\Sigma \cos(\theta))$;

$S=1/n\ (\Sigma \sin(\theta))$;

θ= The phase angle for the spectral component; and

n= Number of samples

Where n=10 for the ten subgroups. C and S represent the average cosine and sine components of the phase angle θ. The resultant, R is solved for by the Pythagorean theorem. In these equations R will be equal to the component synchrony measure for the spectral component.

Using the above computational procedure a spectrum of 128 CSMs was computed and stored with each BAER during data acquisition.

Offline analysis

After data collection, the BAERs and their associated CSM spectra were downloaded to an IBM-PC for offline analysis that proceeded as follows: First a time-domain analysis was done. The BAER waveforms were graphically displayed. All visually recognizable peaks I-V were identified and the absolute peak latencies, interpeak latencies, as well as percentages of identifiable peaks were calculated.

Frequency-domain analysis was then performed. All CSM spectra were averaged within a stimulation rate. A descriptive analysis determined which frequencies had the largest CSMs. An overall SM (designated SM1) was computed on the basis of an average of nine frequency components (CSMs). The nine CSMs were chosen by visual inspection of the mean CSM spectrum (figure 3). The curve of the mean CSM spectrum was found to be tri-modal and the three highest points of each of the modes were selected. This method is similar to the analyses of Fridman et. al. (1984) and Greenblatt et. al. (1985). A second SM (designated SM2) was computed by taking a mean of all CSMs within a frequency range of 300-1500 Hz. This range was also determined by visual inspection of the mean CSM spectrum.

Because magnitude spectra were not calculated in the online analysis a second set of FFTs were done on the BAERs offline. Before the transformation, linear trends were removed as described by Aubanel and Oldham (1985). This was necessary because the the Fourier transform assumes it is working on a continuous function with no beginning or end points in the time-domain. Because the BAER has a beginning and an end, false high frequency spectral components are introduced at the end points. Trend removal was done as an alternative to tapering the time-domain waveform to reduce these "end effects". Aubanel and

Oldham's method involves rotating the waveform so that the first and last points have the same Y-axis value. This is done by plotting a straight line between an average of the first five points and an average of the last five points of the waveform. The points comprising this line are then subtracted from the waveform. This has the effect of tilting the waveform so that the beginning and end have the same amplitude. The waveform then "appears" to the FFT as a continuous function.

Component magnitudes (CMs) were determined from the spectral components produced by the FFTs. Like the CSM analysis the largest CMs were found and a subset of eight were averaged to form an overall magnitude measure (MM1). Also like the CSM analysis, an overall MM (designated MM2) was formed by summing all CMs within an empirically predefined bandwidth of 300-1500 Hz.

Results

Figure 2A (on the left) superimposes ten subgroups of a BAER consisting of 128 sweeps each. It can be seen that the ten subgroups replicate well and therefore had a high synchrony measure (as seen on the right). Figure 2B (on the left) shows the ten subgroups that comprise a poor BAER. Replication is poor and this waveform had a low synchrony measure (right side).

Figure 3 shows the mean component synchrony measure spectrum for all four rates of stimulation. This figure represents the mean CSMs across all subjects at frequencies between 40 and 1560 Hz. with a resolution of 40 Hz. For all four rates, there seem to be three major peaks. These center around 160 Hz., 560 Hz., and 960 Hz. The nine frequency components which comprise SM1 were chosen using this plot. They are 120 Hz., 160 Hz., 200 Hz., 520 Hz., 560 Hz., 600 Hz., 920 Hz., 940 Hz., and 1000 Hz. SM2 was generated using all of the first 35 spectral components 40-1400 Hz.

Figure 4 shows the mean component magnitude spectrum. The mean values, across all subjects, of the magnitude spectrum generated by the FFTs are plotted. The results from all four rate conditions are presented. Frequencies of 80 to 1600 Hz. are presented in 80 Hz. increments. Figure 5 shows the same plot with the no-stimulus condition subtracted from each BAER. As in the method of Laukli and Mair (1982), a no-stimulus condition was collected with each stimulus condition. FFTs were done on both waveforms and the no-stimulus waveform's magnitudes were subtracted from those of the stimulus waveform. Figure 5 presents the spectrum of magnitude differences. Unlike Laukli and Mair's findings, uniformly lower magnitudes were the only difference between the stimulus and stimulus minus no-stimulus conditions. The relative shape of the two graphs was very similar. The magnitude measures (MM1 and MM2) were therefore derived from the unsubtracted magnitudes (figure 4). Eight component magnitudes were chosen for MM1. These components corresponded to the three major peaks seen in figure 4. The magnitude components chosen correspond to frequencies of 160 Hz., 240 Hz., 480 Hz., 560 Hz., 640 Hz., 880 Hz., 960 Hz., and 1040 Hz.

Table 1 presents the mean, standard deviation, and number of waveforms represented, for the I-III IPL, at the four rates of stimulation. Figure 6 is a plot of this data. It can be seen that the I-III IPL increases monotonically across the four stimulus rates. Table 2 and figure 7 show the III-V IPL. It can be seen that there is a slight decrease in inter-peak latency between the 10 and 25 CPS levels. The difference is very small compared to the standard deviation and probably does not represent any real difference. Table 3 and figure 8 show a monotonic and almost linear increase in I-V IPL across all stimulus rates. Table 4 and figure 9 show a linear decrease in the number of recognizable peaks (# peaks), with a large increase in the variance with increasing rate of stimulation. The standard deviation almost triples while the mean declines as the rate increases from 10 CPS to 55 CPS. This suggests much more homogeneity of waveform quality at the lower rates and a mix of very good and very bad waveforms at the higher stimulus rates. Tables 5 and 6, and figures 10 and 11 show synchrony measure 1 (SM1) and synchrony measure 2 (SM2) respectively. Both show parallel functions that decrease as rate increases. The means and standard deviations are uniformly higher for SM1. Tables 7 and 8, and figures 12 and 13 show magnitude measure 1 (MM1) and magnitude measure 2 (MM2) respectively. Both functions show a linear decrease with rate. They both also show a decreasing variance with increasing rate which is especially notable for MM2, whose variance at the 10 CPS level is quite large. The decreasing variance is probably due to the decrease in the mean and probably does not reflect any systematic phenomenon.

Repeated measures trial by subjects one way ANOVAs were done on each of the eight derived variables. Rate of stimulation was the repeated factor. Table 9 shows the F values for each of the eight measures in order highest to lowest relative probability value. All measures except I-III IPL were significant at least to the .01 alpha level and most at the .001 level. The actual probability values are not as important as is their order. The ANOVA was done primarily as a means of rank ordering the eight variables. SM2 is the most sensitive to changes in the stimulus rate. It's F value (20.06) is much larger than that of the next best measure, SM1 (F= 11.83). The ability of the two magnitude measures to discriminate different stimulus rates was somewhat worse than the abilities of the I-V and the III-V IPLs but better than the abilities of the number of peaks measure or the I-III IPL. This pattern indicates that after the synchrony measures the most information lies in the absolute latency of peak V. Previous research supports this assertion (Don et.al, 1977). The latency of peak III seems to be somewhat less important. The number of peaks measure did not discriminate well possibly due to large differences in variance at different levels of stimulus rate.

A zero order, pairwise, Pearson correlation matrix was generated to show the intercorrelations between all eight variables (sees table 10). The number in parentheses beside each Pearson r is the number of pairs used to generate each correlation coefficient. The coefficients for each of the eight variables with rate of stimulation are underlined. The relative sizes of the coefficients are generally similar to the results of the ANOVAs. SM2 is the largest, accounting for 16% of the variance. SM1 is the second largest coefficient accounting for 9% of the vaiance and I-III IPL is the smallest accounting for less than 2% of the variance. In this analysis however, the number of peaks measure is the third largest, almost as large as SM1. This is probably because a correlation is less sensitive to the between group variance then the ANOVA. Another notable change is that the two magnitude measures are now considerably larger than any of the IPL measures.

These eight coefficients are used in an inferential analysis. Hotelling's t-statistics (see appendix 2) were calculated to compare the correlation coefficients of the time-domain measures with the correlation coefficients of the frequency-domain variables so that inferential statements could be made as to the significance of differences found between pairs of correlation coefficients. For example the correlation coefficient of SM2 versus rate was -.398 and the correlation of I-V IPL versus rate was .227 (see table 10). The Hotelling's t for these two coefficients is 6.11 (see table 11). Therefore SM2 correlates significantly better ($p < .001$) with rate then does I-V IPL. Hotelling's ts for all contrasts between time and frequency-domain measures appear in table 11. Alpha levels were adjusted for the increased chance of making a type I error when t-tests are repeated 16 times. This was done by calculating the probability values and multiplying each of them by 16. Both SM2 and SM1 are significantly better correlated with rate of stimulation than any of the measures of interpeak latencies but not significantly better correlated with rate than the number of peaks measure. SM2 is better correlated with rate than any of the IPL measures (in no case is $p > .01$) and just misses significance when compared with the number of peaks measure. SM1 is also better correlated with rate than any of the measures of IPL (in no case is $p > .05$), but is not better correlated with rate than the number of peaks measure. The t values for SM2 are larger than those for SM1. MM1 and MM2 did have lower t values. MM1 is significantly better than III-V IPL and I-V IPL at predicting rate ($p < .05$) but MM1 is not significantly better then I-III IPL and is slightly worse (not significantly) then the number of peaks measure. MM2 was uniformly worse than MM1. MM2 was significantly better ($p < .05$) than I-V IPL only. It was slightly better than the other IPL measures and slightly worse than the number of peaks measure though none of the differences were significant.

All measures derived from the waveforms except I-V IPL (which contained information which was redundant with I-III IPL and III-V IPL), were then evaluated using a stepwise multiple regression with rate of stimulation serving as the predicted variable. Regression analyses were done to explore the possibility that some combination of measures would form a sensitive "meta-measure" that would be superior to any of the individual measures. This did not prove to be the case. This procedure was also performed to determine which variables were highly intercorrelated and therefore offer little additional information. The stepwise procedure was run in "automatic mode" with default settings of F >= 4 for a variable to enter the equation and F < 4 to remove. The procedure terminated after two steps and included only SM1 and SM2 in the final equation. A second stepwise multiple regression was run in "manual mode" in which all variables were entered one at a time. SM2 was entered first (see table 12). SM1 was entered second and increased the adjusted R squared. The number of peaks measure was entered third and further increased the adjusted R squared. The R squared decreased with each new entry until step six where MM1 increased it. The order in which the variables were entered was in descending order of their partial correlations, updated on each step. This means that their order entered was not only a function of their correlations with stimulus rate but also a reflection of their interdependence. The fact that SM1 increased the adjusted R squared after SM2 was entered despite their high inter-correlation indicates the strength of these measures.

One last series of exploratory regression analyses were done. Two equations were produced; one containing all time-domain variables, and the other, the frequency-domain variables. The equation of time-domain variables was set up as a model of the "typical" BAER analysis. This was an attempt to emulate as closely as possible, the situation that a clinician is faced with on an everyday basis.

Specifically, this is the need to make a judgment of waveform quality and signal presence based on IPLs and waveform morphology (which operationally often translates to, "How many peaks can be identified?").

The frequency-domain equation was more of the "kitchen sink" approach. A comparison of these two equations appears in table 13. The adjusted R squared produced by the frequency-domain equation (.186), is not much higher than the R squared for SM2 versus rate, alone (.152) (see table 12). Therefore not all that much is added by including the magnitude measures. Despite that, the frequency-domain measures produce a considerably higher adjusted, multiple R squared than the time-domain measures. Additionally, although no inferential statement can be made, it appears that SM2 alone provides considerably more information about signal presence than any or all of the time-domain measures.

A secondary analysis explored SM2 further. Since each BAER was collected with a paired no-stimulus condition it was possible to compute a SM2 for each of the 104 no-stimulus waveforms. A mean and standard deviation, collapsing across all stimulus rates, was computed for the no-stimulus distribution (see table 14). Setting a cut off at two standard deviations above the mean of the no-stimulus distribution (SM2=.109), all 208 waveforms (stimulus and no-stimulus), were classified. Two of the 104 no-stimulus waveforms were misclassified as being

BAERs. Six of the BAERs (one at 25 CPS, one at 41 CPS, and four at 55 CPS), were misclassified as being no-stimulus waveforms. All of the 10 CPS BAERs were correctly classified. This degree of accuracy in classification is similar to that reported by Fridman et. al (1984).

Discussion

These data suggest that the traditional measures of BAER waveform quality (i.e. peak latencies and waveform morphology) may not be the best available. Frequency-domain analysis has an advantage over time-domain analysis in that it allows information to be extracted from the entire waveform simultaneously. This information can be further refined by concentrating the analysis on the frequency components known to be relevant to the biological signal and discarding all information outside that range. This essentially provides a digital filter that effectively eliminates much of the noise associated with the waveform and increases signal to noise ratio. Such an analysis is not possible in the time-domain.

The synchrony measure, because it is a variance measure, allows more information to be extracted than measures simply based on means (such as the BAER). It relates information on changes over the time of the recording session more effectively than any of the time-domain measures or even the frequency-domain measure of magnitudes. The synchrony measure gives dynamic information on the state of the BAER over time, whereas the other measures represent a static picture analogous to a time exposure photograph. If the photographic subject moves over the time of the exposure all that remains is a blur.

The component synchrony measure spectrum is relatively stable. The two previous studies which reported on group-mean component synchrony measure spectra, like this study, found three major peaks in the spectrum (Fridman et al., 1984; Greenblatt et al., 1985). See figure 3. Despite differences in recording conditions, differences in subjects, and differences in the stimuli, the three studies produced very similar CSM spectra. Fridman found peaks at 320 Hz., 520 Hz., and 960 Hz. Greenblatt's peaks (55 dB condition) were at 200 Hz., 520 Hz., and 960 Hz. This study found peaks at 160 Hz., 560 Hz. and 960 Hz. Variations in the lowest frequency peak may be due to differences in high pass filter setting or effectiveness (eg. amplifier roll-off). The two higher frequency peaks are very replicable. This high degree of replicability applies only to group means. The fact that SM2 is a better predictor of rate than SM1 suggests that there is much individual variation from the mean spectra. This is the case because SM1 is a very specific measure drawing information from only nine specific points in the CSM spectrum. SM2 was designed to be an "all inclusive" measure drawing information from all points in the CSM spectrum that could possibly yield information. This study did not compare individual cases to group means but had this been done it is likely that the peaks in the CSM spectra of individuals would not all fall at the same three places as did the peaks of the mean CSM spectrum. Therefore for many individuals the specificity of SM1 weakened its predictive value whereas the more general measure SM2 was a better predictor when individual peaks did not fall on the same frequencies as the group mean.

The results of the three main analyses converge and show that the synchrony measure is a better predictor of rate of stimulation than any of the time-domain measures either singularly or in any combination. Since rate of stimulation is being used as an index of signal quality it can be inferred that synchrony measure is the best predictor of signal quality in the BAER. In each of the three analyses SM2 and SM1 consistantly performed better than any of the time-domain measures and as can be seen from table 13, the frequency-domain regression model accounts for more than twice as much variance in rate than the time-domain regression model (multiple R squared = .186 for the frequency-domain versus .087 for the time-domain). If it is in fact the case that the time-domain regression equation effectively represents the information on which a clinician makes a judgment (as was intended), then clearly the addition of frequency-domain measures will allow much more precise judgments to be made.

The ability of SM2 alone to correctly classify waveforms was also tested. While slightly less than 2% of the no-stimulus waveforms were misclassified as BAERS, slightly less than 6% of the BAERs were misclassified as no-stimulus waveforms. However, of the BAERs recorded to a 10 CPS stimulus rate, none were misclassified. This strongly endorses the value of SM2 as a "stand-alone", objective measure of waveform quality in the clinical setting. SM2 used as part of a multivariate equation in conjunction with other selected measures, would provide a very precise index of waveform quality.

Individual Cases

Below are several graphic examples that illustrate the usefulness of the component synchrony measure spectrum and SM2 in making determinations of signal presence in the BAER.

Figure 14A shows, on the left side, a BAER that would be considered to have "good waveform morphology", recorded at a stimulation rate of 10 CPS. On the right side is its component synchrony measure spectrum. Note the three prominent peaks in the CSM that seem to characterize a well formed BAER. The derived SM2 is .59 which is slightly more than one standard deviation above the mean for 10 CPS. In contrast, figure 14B shows, on the left, the above waveform's no-stimulus pair. On the right is its component synchrony measure spectrum. It is a typical CSM spectrum for a no-stimulus waveform.

Figure 15A-D shows BAERs (left) and their CSM spectra (right), from one subject, over four rates of stimulation.

Figure 15A is 10 CPS, 15B is 25 CPS, 15C is 41 CPS, and 15D is 55 CPS. A clinician would be hard pressed, solely on the basis of the BAERs, to order the four waveforms correctly. The BAER morphology is quite good even at the higher rates of stimulation. Peak latency changes are negligible. Wave IV disappears at higher rates but was not very prominent even at 10 CPS. Amplitudes of waves I and II decrease as rate increases but that type of change is idiosyncratic to this waveform set and is not necessarily typical. It is possible however, to order the waveforms correctly, on the basis of the appearance of their CSM spectra. The CSM spectra's peak amplitudes conspicuously decrease with each increase in rate of stimulation. The values of SM2 decrease monotonically from .45 to .16 as stimulation rate increases.

Figures 16a and 16b show, on the left, poor BAER responses (55 CPS) from one subject's left and right ears, respectively. On the right are the corresponding CSMs. Figures 16c and 16d are the no-stimulus waveforms that were recorded with 16a and 16b. On the right are their CSMs. Clearly all of the waveforms have very poor morphology. This example typifies the situation faced by a clinician who is recording in an electrically noisy environment or is dealing with a patient with extensive pathology. Figure 16a shows what appears to be a large IV-V complex but no recognizable peaks before it. Figure 16b shows two vertex positive waves, possibly waves III and V. Figure 16c is a no-stimulus waveform yet it has peaks which could easily be mistaken for waves IV and V. Figure 16d shows one prominent vertex positive wave and is similar in overall configuration to figure 16b. A clinician could easily misclassify any or all of these waveforms. A visual examination of the CSM spectra reveals a considerable difference between the BAERs and the no-stimulus conditions. The CSM spectra clearly show activity in the higher frequency components as well as higher synchronies in all spectral components of the BAERs. Using the criteria cited above (cutoff at two standard deviations above the mean of the noise distribution or SM2=.109), all four waveforms are correctly classified.

Each of the graphic examples presented above were chosen to make their respective points, but all are typical. Clinically, the use of the CSM spectrum for visual inspection or of SM2 when a quantitative statement need be made, would be very beneficial. A visual inspection of the CSM spectrum along with the BAER would make clinical judgments more reliable. The regression presented in table 12 suggests the use of SM2 in conjunction with quantitative time-domain variables would provide a better predictor of signal presence in a waveform than either variable alone.

Limitations of the experiment and future research

For the purposes of this experiment, rate of stimulation was chosen as the operational definition of signal presence. This seems to be a valid assumption but this experiment must be replicated using other methods of signal degradation. Decreased signal intensity, the use of pathological populations, introduction of external noise or alterations in the spectral content of the stimulus are all possible ways to accomplish this. The fact that rate of stimulation did not interact with component synchrony measure for any spectral component (see figure 3), ie. the curves are parallel, suggests that there was no confound with rate of stimulation and response frequency. If there was a confound between rate of stimulation and response frequency, it is probable that the curves in figure 3 would converge or cross in a systematic way. Although there is poor separation between the curves in the highest and the lowest frequencies, this does not seem to represent the kind of systematic effect that would be expected if an unknown confounding variable was present.

Another possible criticism of this study concerns the time-domain measures chosen for analysis as well as the method of analysis. Arnold's (1985) technique of using the judgments of experienced clinicians to determine whether a waveform was signal or noise is a technique that could have been adopted. The method used in the present study was really an attempt to model clinical judgments using quantitative measures but Arnold's study used the judgments themselves. Arnold reported poor inter-rater reliability but there is no judgment reliability problem in this study because results are far more objective. However, this study probably should be repeated using the judgments of experienced clinicians as a dependent measure.

The method of time domain analysis used in this study was less than ideal. Only one rater (the author) made all judgments and measurements of peak presence and latencies. The waveforms were not judged in a blind fashion which introduced the possibility of experimenter bias.

Another possible weakness in the design was the range of stimulus rates used. Due to equipment constraints, the highest rate of stimulation used was 55 CPS. Since previous research has recorded recognizable BAERs to stimulus rates in excess of 90 CPS, these results must be interpreted with the caution that they are only valid for relatively intact BAERs. Although there is no reason to doubt that the synchrony measure will continue to outperform time-domain analyses for more degraded signals, that was not demonstrated by this study.

Future research on the synchrony measure could take a number of different directions. Although one study demonstrating the clinical utility of the synchrony measure has already been done (Fridman et. al., 1984), clinical studies directly comparing the synchrony measure with traditional time-domain measures should be useful. A series of studies similar to Zappulla et. al.'s (1981) study in which a discriminant analysis was done demonstrating the ability of inter-peak latencies to discriminate normals from neurosurgical patients, could be constructed for several different clinical populations (eg. neurosurgical, multiple sclerosis, premature infants, auditory pathology). Discriminant equations could be generated for time domain measures and some combination of phase variance measures. In this way the two equations could be directly compared as to their abilities to discriminate pathology groups from normals.

Appendix I

A Glossary of Electrophysiological and Spectral Analysis Terminology

Artifact- As a noun, artifact is a transient high voltage disturbance in an electrophysiological recording. Its origin may either be biological or due to electrical noise but it is usually unwanted and attempts are made to eliminate it. As a verb, artifact is the process of eliminating transient high voltage disturbances usually by suspending recording.

EEG- The electroencephlograph is a recording of spontaneous electrical activity arising from the head.

FFT- The Fast Fourier Transform is a rapid, efficient algorithm implementing the Fourier transform. It was first published in 1965 by Cooley and Tukey and was designed specifically for digital computers.

Fourier Transform- This is a mathematical transformation which converts a time-domain waveform into the frequency-domain. A waveform plotted with time on the X-axis will be transformed into a waveform with frequency (cycles per second) on the X-axis. The Fourier transform produces two sets of numbers (or spectral components). These are the sine components and the cosine components. For each frequency one sine component and one cosine component are produced. The sine and cosine components can be combined to produce a magnitude spectrum or a phase angle spectrum.

Frequency Analysis- This is a general term for the decomposition of a time-domain waveform into its frequency components. This can be done mathematically as in Fourier transform or electronically using filters and electronic measurement devices. Used synonymously with Spectral Analysis.

Frequency-Domain- Any waveform plotted with frequency (cycles per second) on the X-axis.

Inverse FFT- A rapid, efficient computational algorithm for converting a frequency-domain waveform into the time-domain.

Magnitude Spectrum- A frequency-domain plot derived from the output of the FFT with frequency (cycles per second) on the X-axis and magnitude on the Y-axis. For each frequency magnitude is defined as the square root of the sine component squared plus the cosine component squared ($M = \sqrt{(S^2 + C^2)}$).

Middle Latency Evoked Potential- This is an auditory evoked response which occurs from 10 to 60 milliseconds after an auditory stimulus. It occurs after the BAER and before the cortical response. It has both neurogenic (originating in nerves) and myogenic (originating in muscle) components.

Phase Angle- This is an angle ranging between 0 and 360 degrees that is derived for each frequency, from the Fourier transform's spectral components. The phase angle is defined as the arctangent of the sine component divided by the cosine component (phase angle= Arctan (S ÷ C)).

Signal to Noise Ratio- This is an index of signal clarity or the amount of signal relative to the ambient interference.

Spectrum- A continuous sequence or range of frequencies.

Spectral Components- The sine and cosine components produced for each frequency, by the Fourier transform.

Steady State Evoked Potential- An evoked potential methodology involving continuous non-averaged recording. Stimuli are presented rapidly and often the response is not complete before the next stimulus is presented. The recording typically undergoes frequency analysis and the magnitudes of the fundamental frequency and its harmonics are examined.

Sweep- This is the time epoch within which a transient evoked potential is recorded. A typical BAER has a sweep time of 10-13 milliseconds and consists of 2000 averaged sweeps.

Transient Evoked Potential- This term is used synonymously with Averaged Evoked Potential. This methodology involves presenting a discrete stimulus, then recording until the response is over and then repeating the process many times, each time averaging the new waveform with the cumulative group.

Window effects- This term is used synonymously with the term "end effect" and refers to the introduction of spurious spectral components after performing a Fourier transform on any finite number of points. A basic assumption the Fourier transform makes is that the number of time-domain points is infinite. By introducing an abrupt begining and end to the time-domain waveform square waves are introduced which when transformed produce spectral components.

Appendix II

Hotelling's t-test

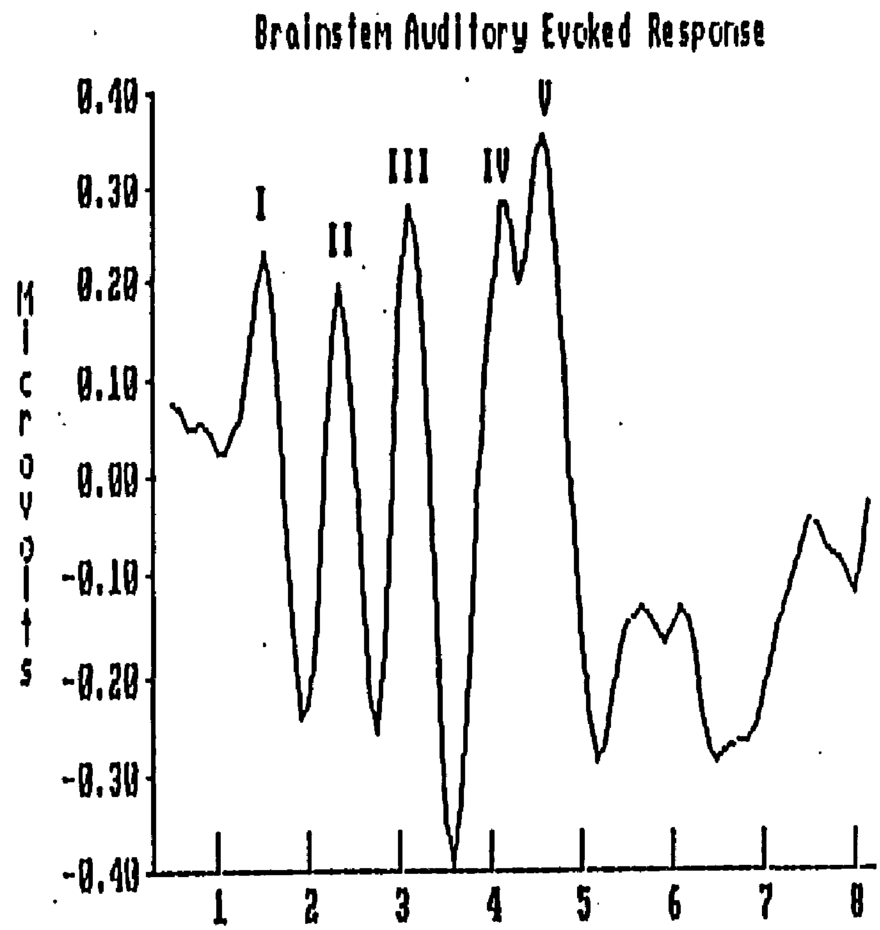
This statistic is used to determine the significance of differences between two correlation coefficients when the two coefficients share a common element and are intercorrelated. The form is:

$$t = (r12 - r13) \times$$

$$\sqrt{[((N - 3) \times (1 - r23)) \div (2 \times (1 - r23^2 - r12^2 - r13^2 + (2 \times r23 \times r12 \times r13)))]}$$

Where N is the number of pairs comprising each correlation coefficient. r12 is one correlation coefficient. r13 is the other correlation coefficient. r23 is the intercorrelation between the two coefficients.

Figure 1



Milliseconds

Figure 8

Ten Subgroups Which Combine to Form the BAER (A) with its Component Synchrony Measure Spectrum and Ten Subgroups of a No-Stimulus Waveform (B) with its CSM Spectrum

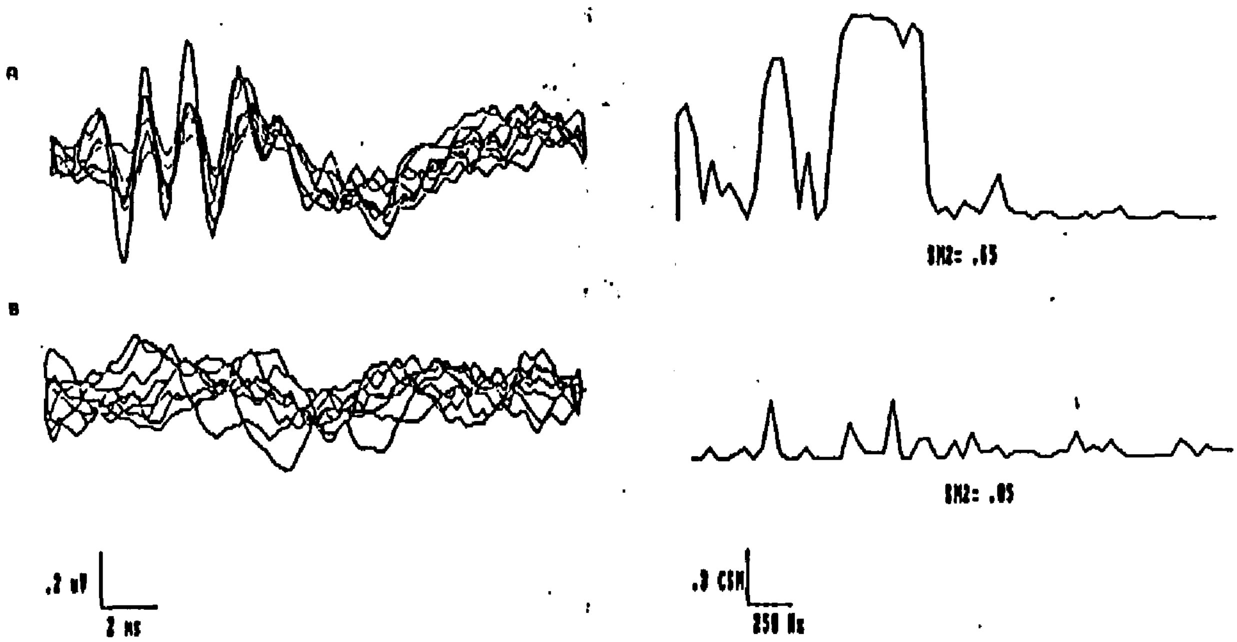


Figure 3
Mean Component Synchrony Measures

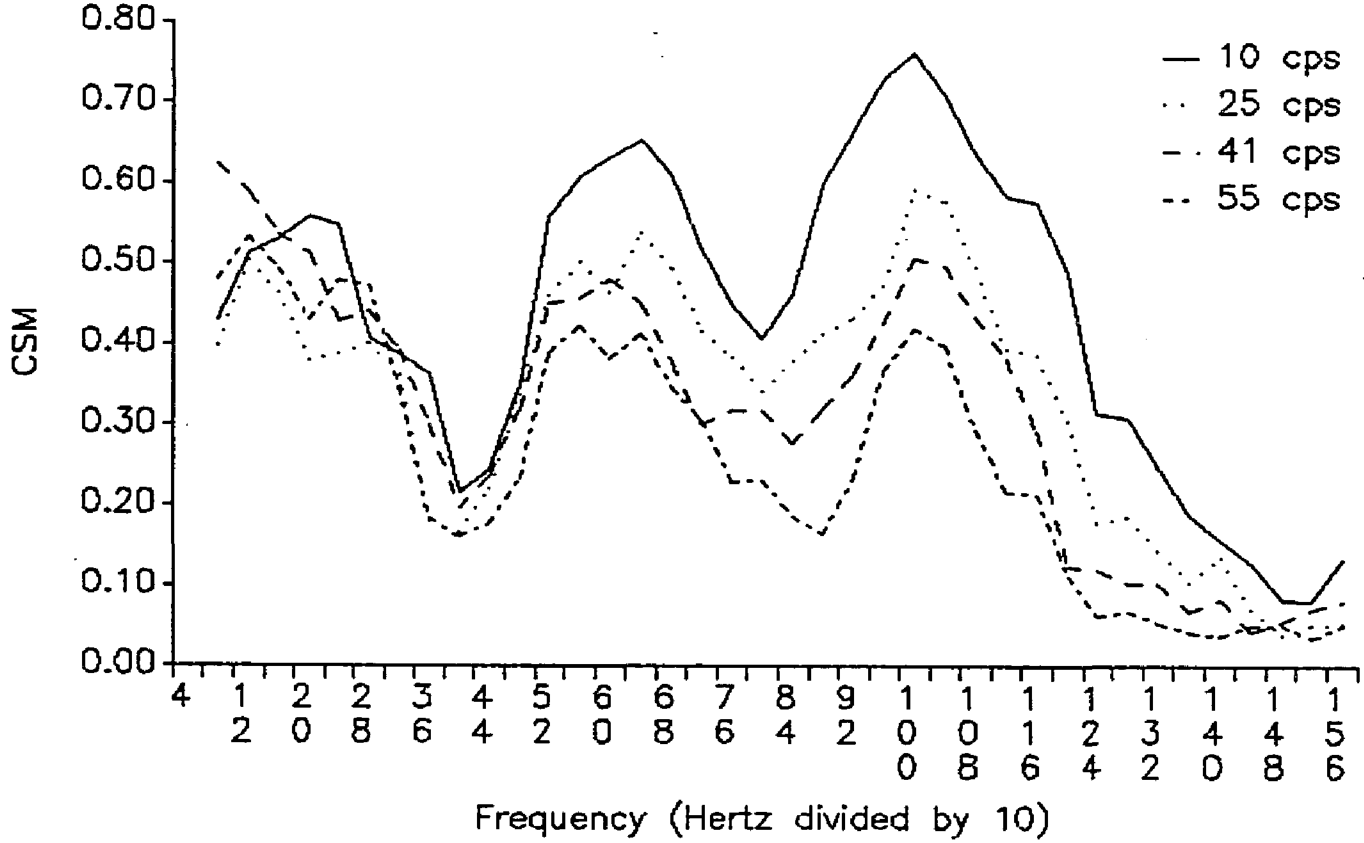


Figure 4
Magnitude Means

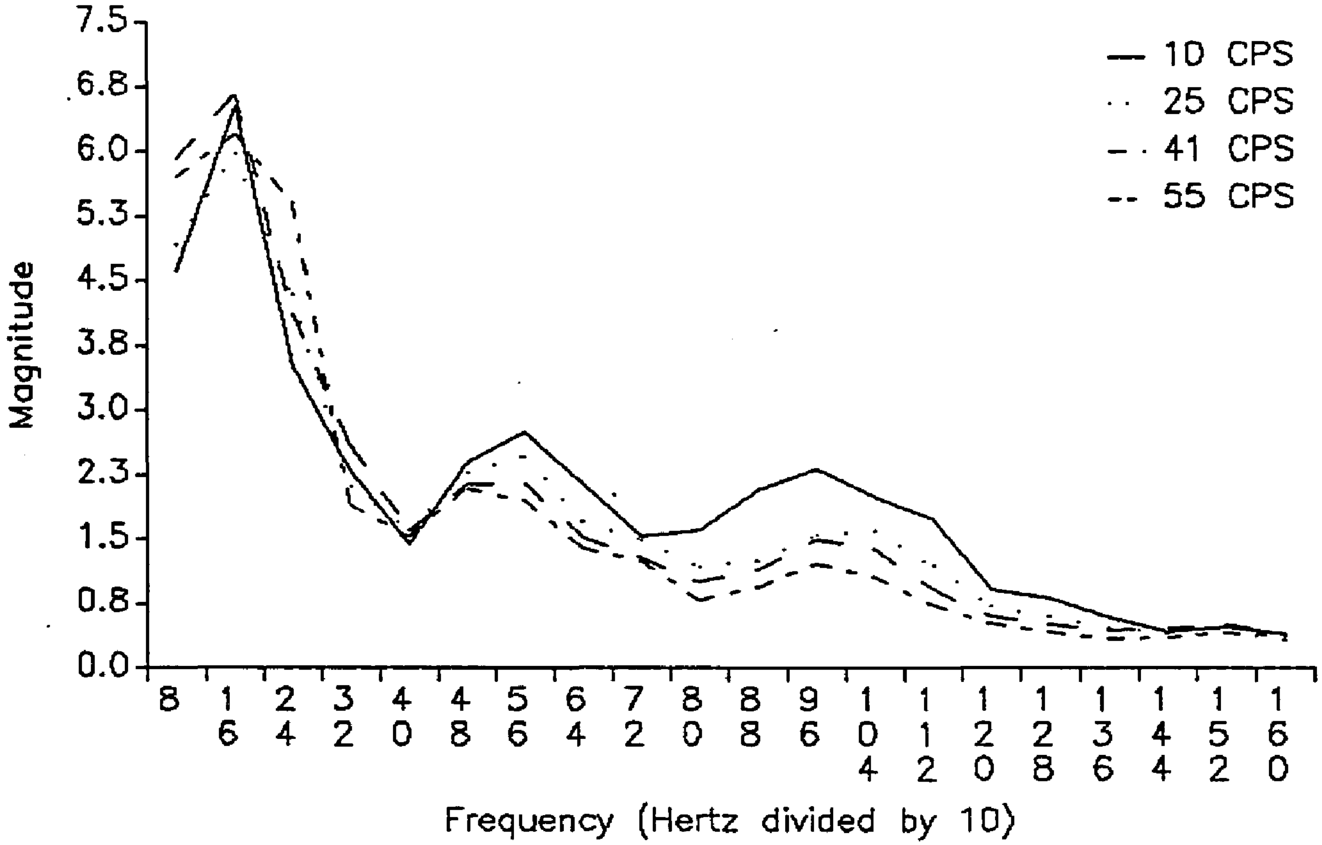


Figure 5
Stimulus minus No-Stimulus Magnitudes

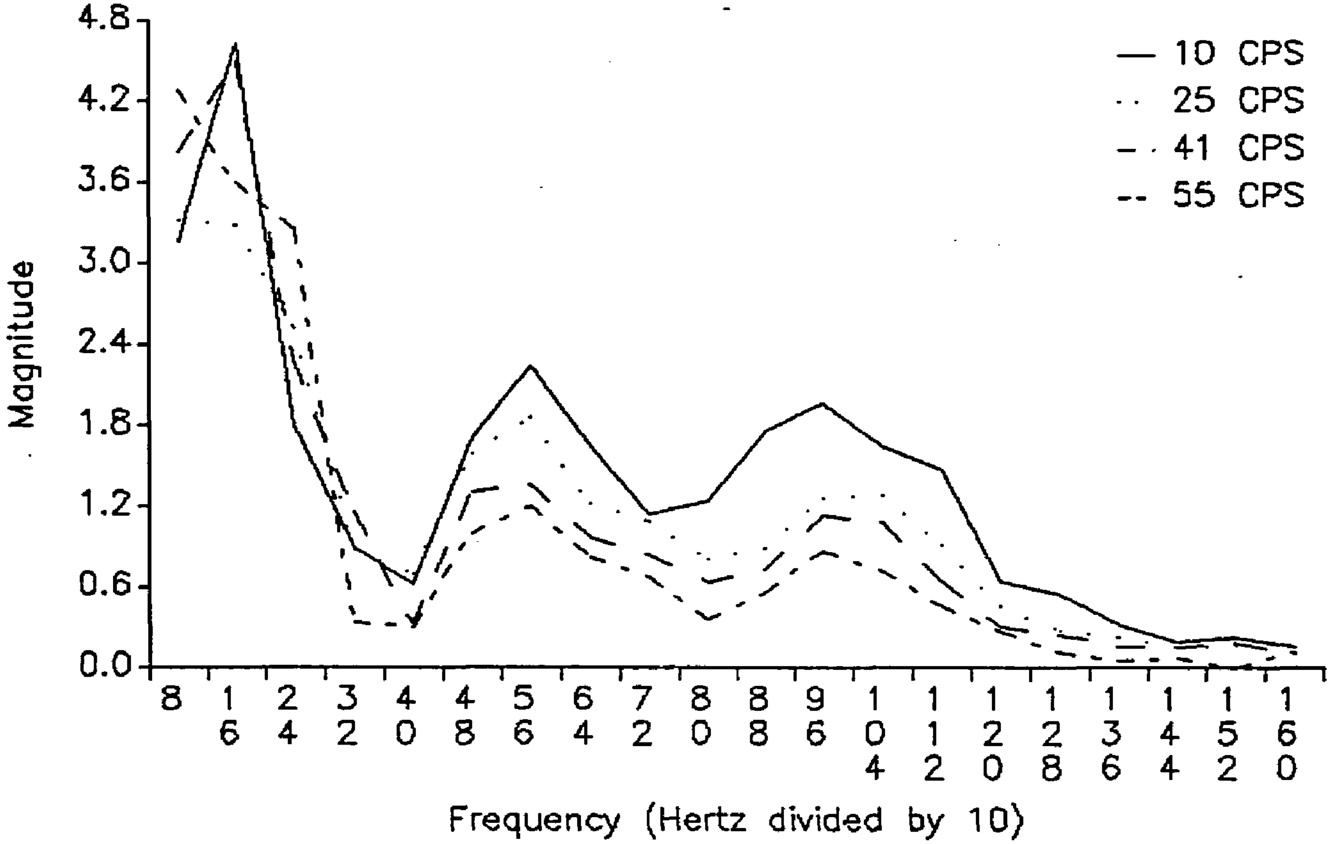


Figure 6
Means and Standard Deviations for
I-III IPL

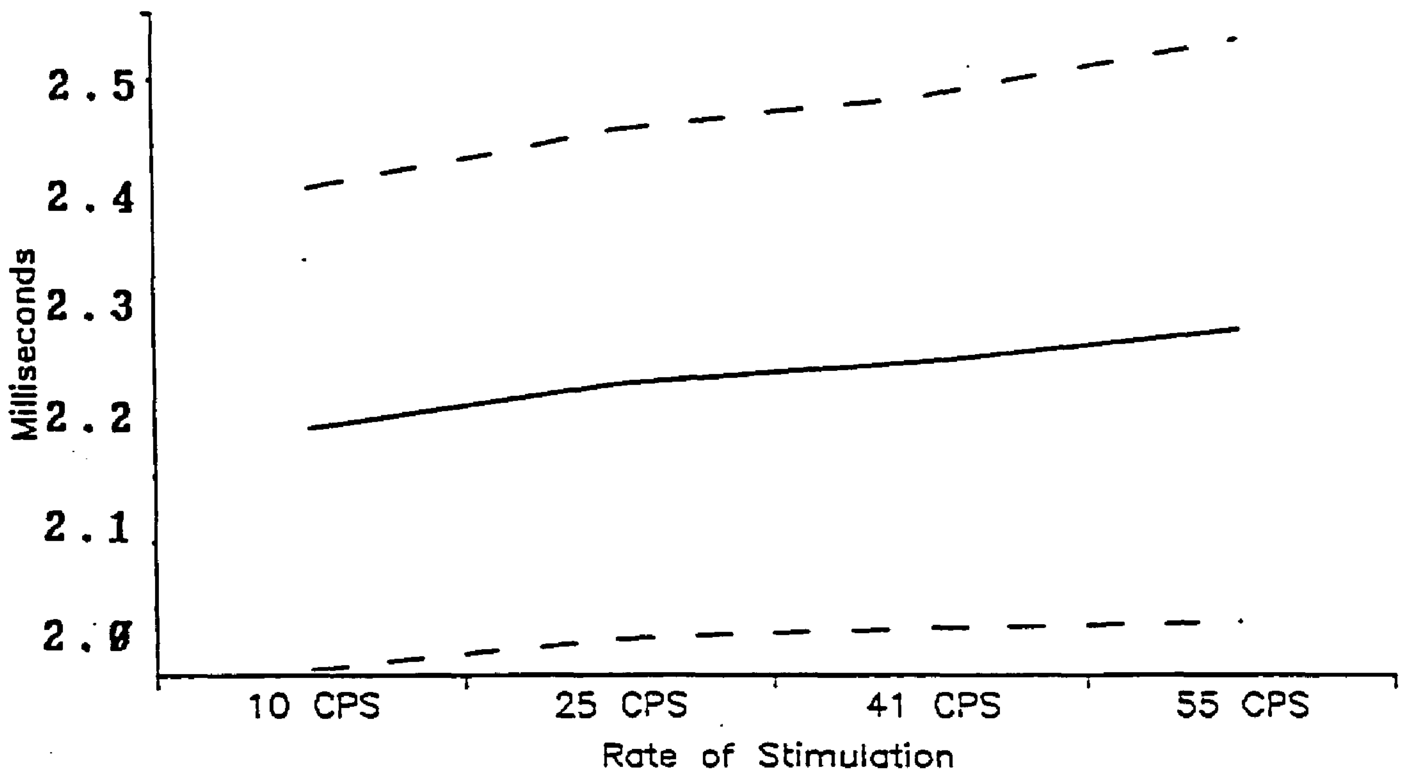


Figure 7
Means and Standard Deviations for
III–V IPL

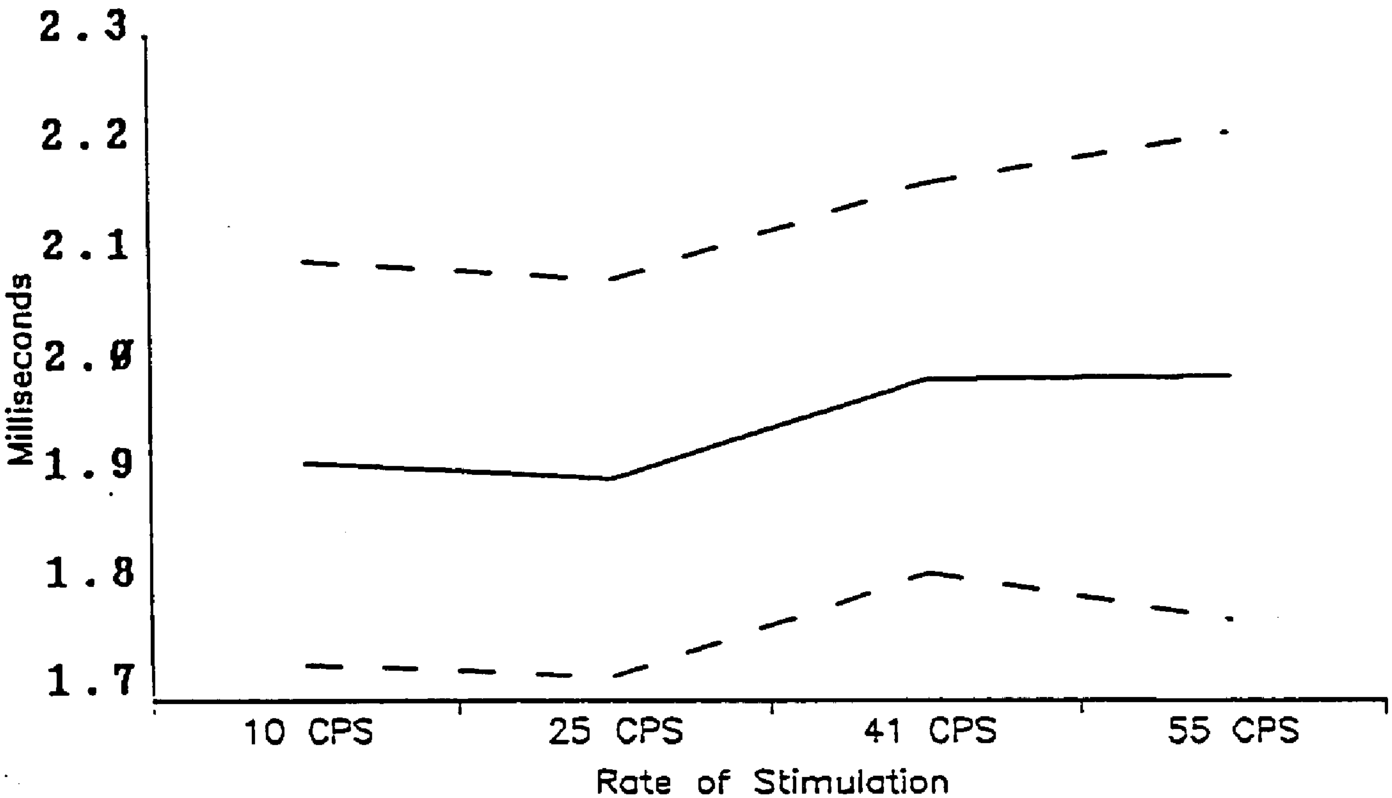


Figure 8
Means and Standard Deviations for
I–V IPL

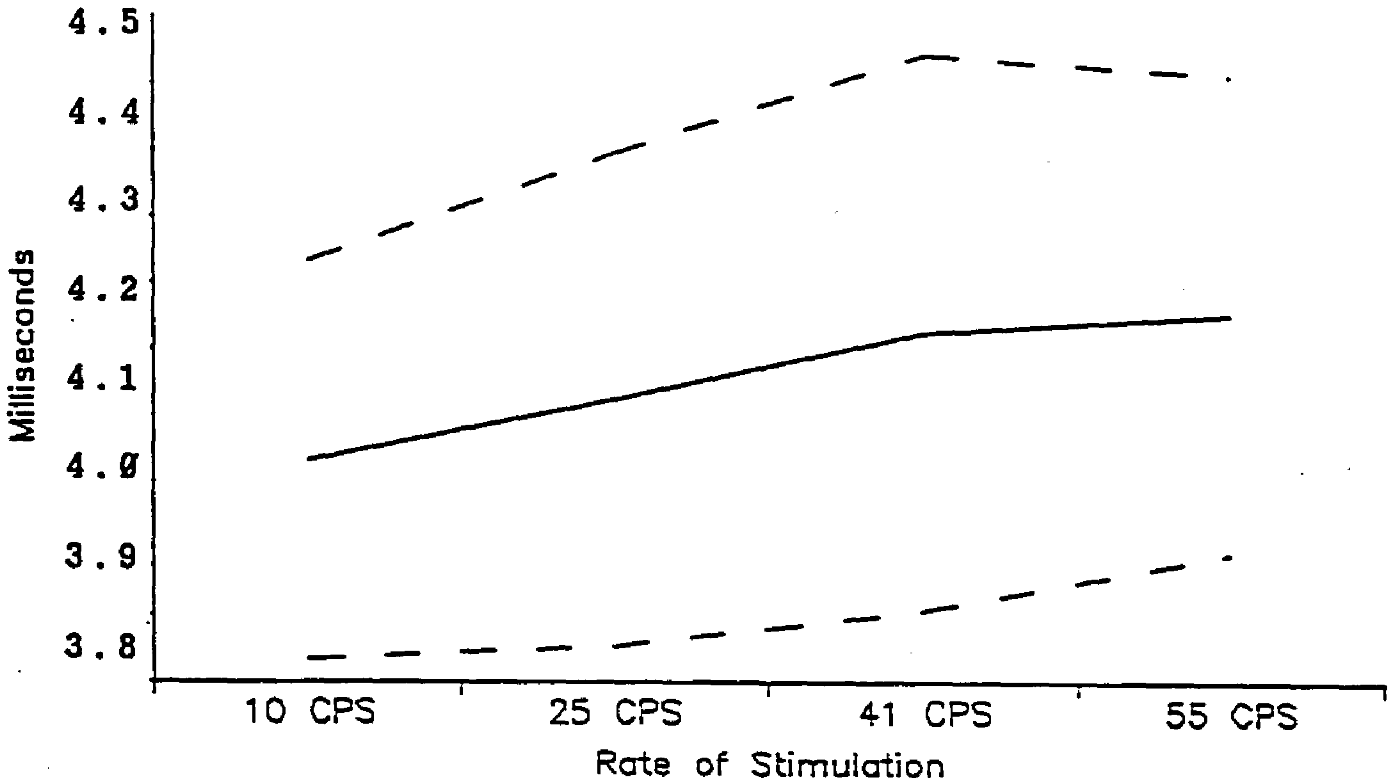


Figure 9
Means and Standard Deviations for
Number of Peaks Measure

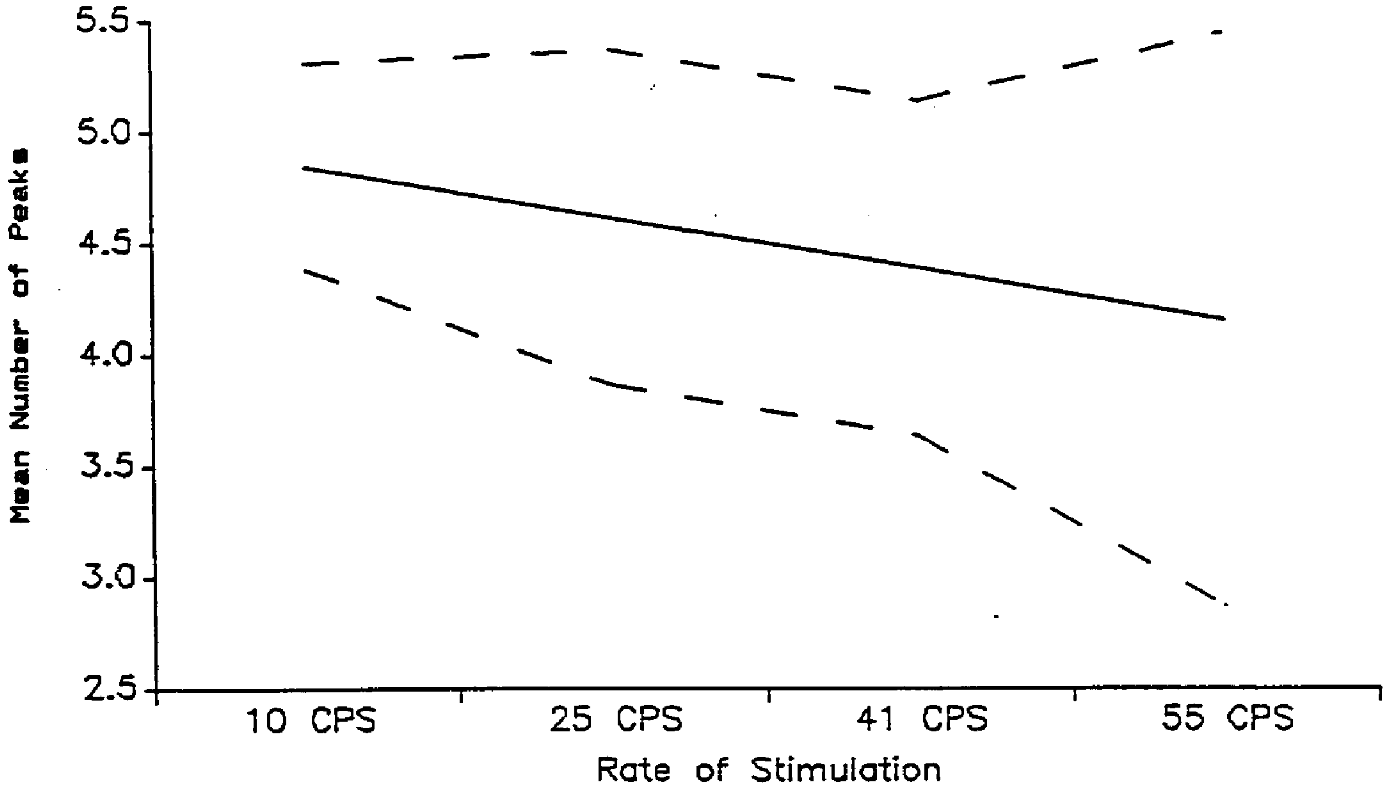


Figure 10
Means and Standard Deviations for
Synchrony Measure 1

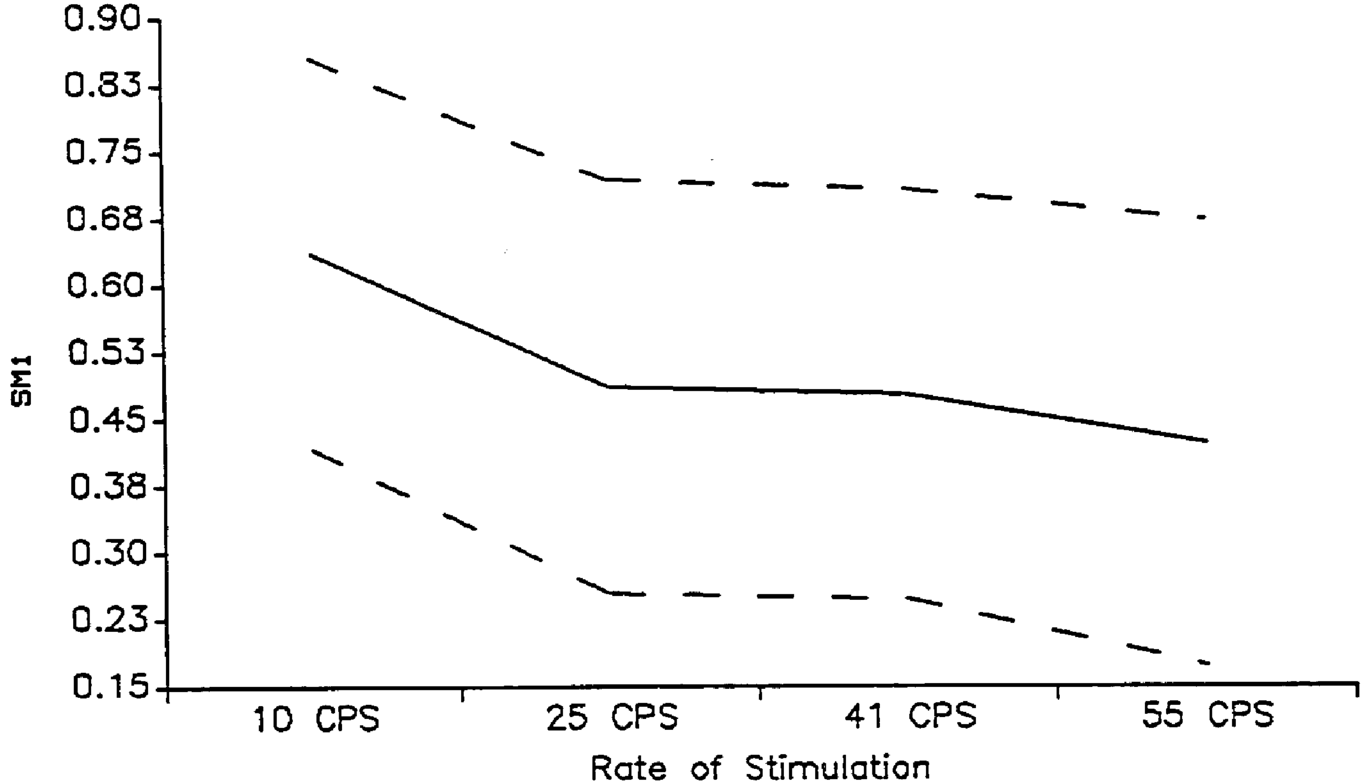


Figure 11
Means and Standard Deviations for
Synchrony Measure 2

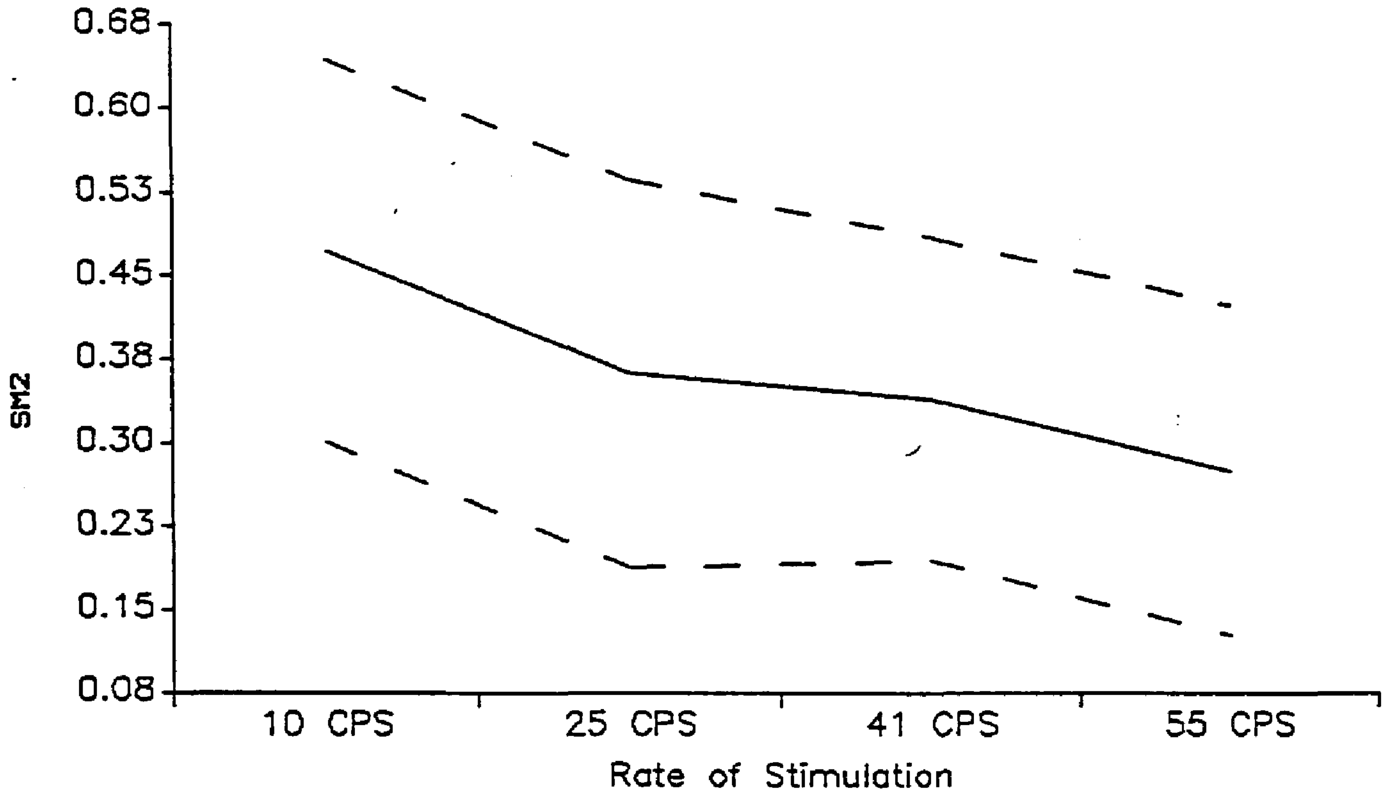


Figure 12
Means and Standard Deviations for
Magnitude Measure 1

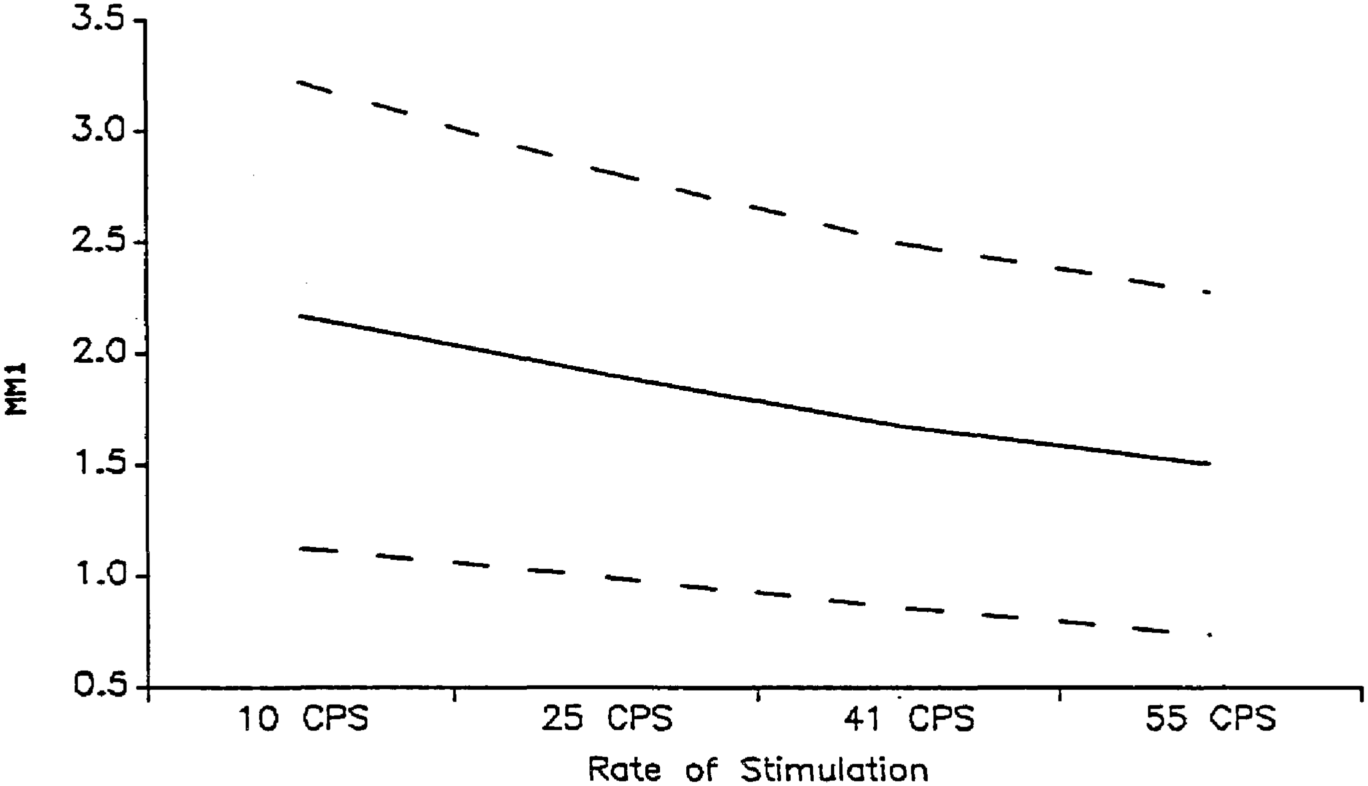


Figure 13
Means and Standard Deviations for
Magnitude Measure 2

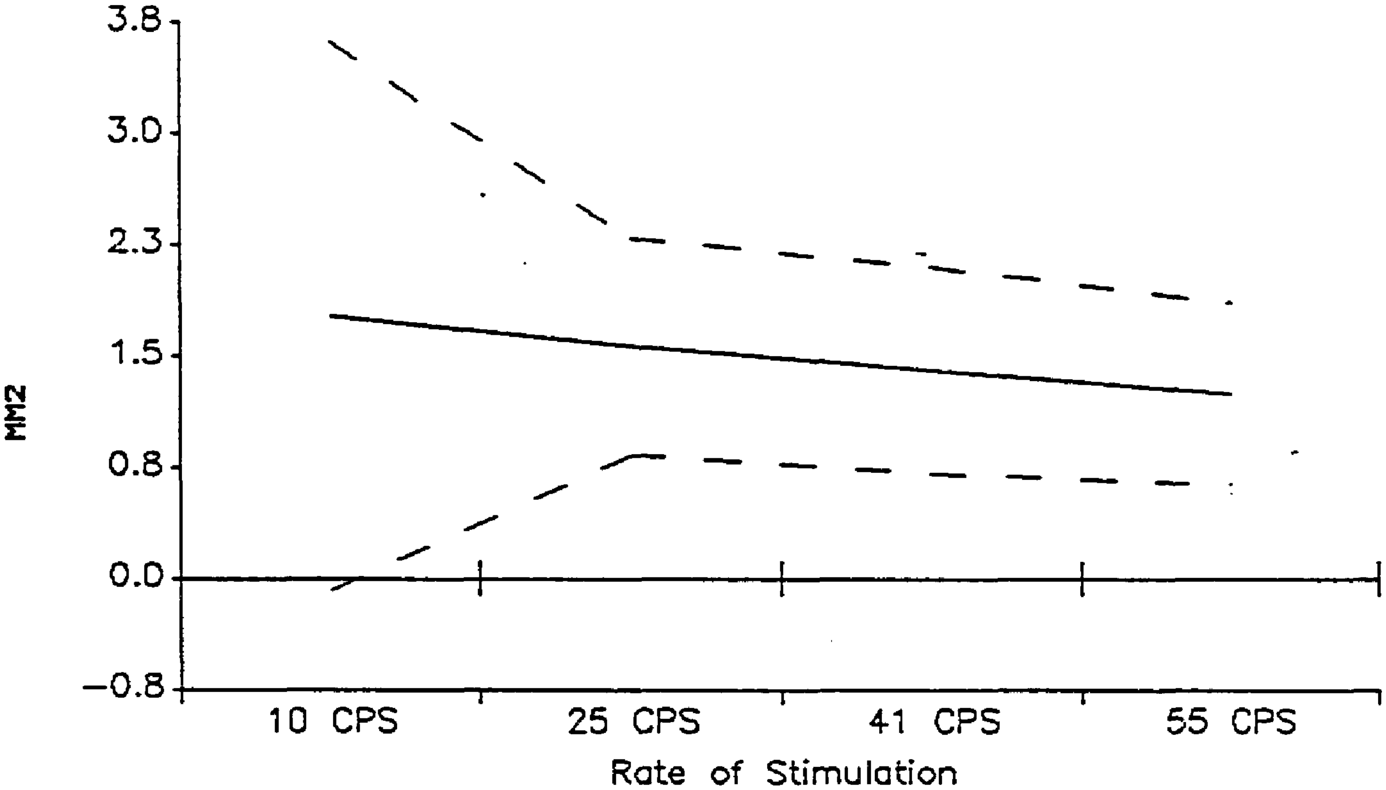


Figure 14

BAER (A) and No-Stimulus Waveform (B) with their Component Synchrony Measure Spectra

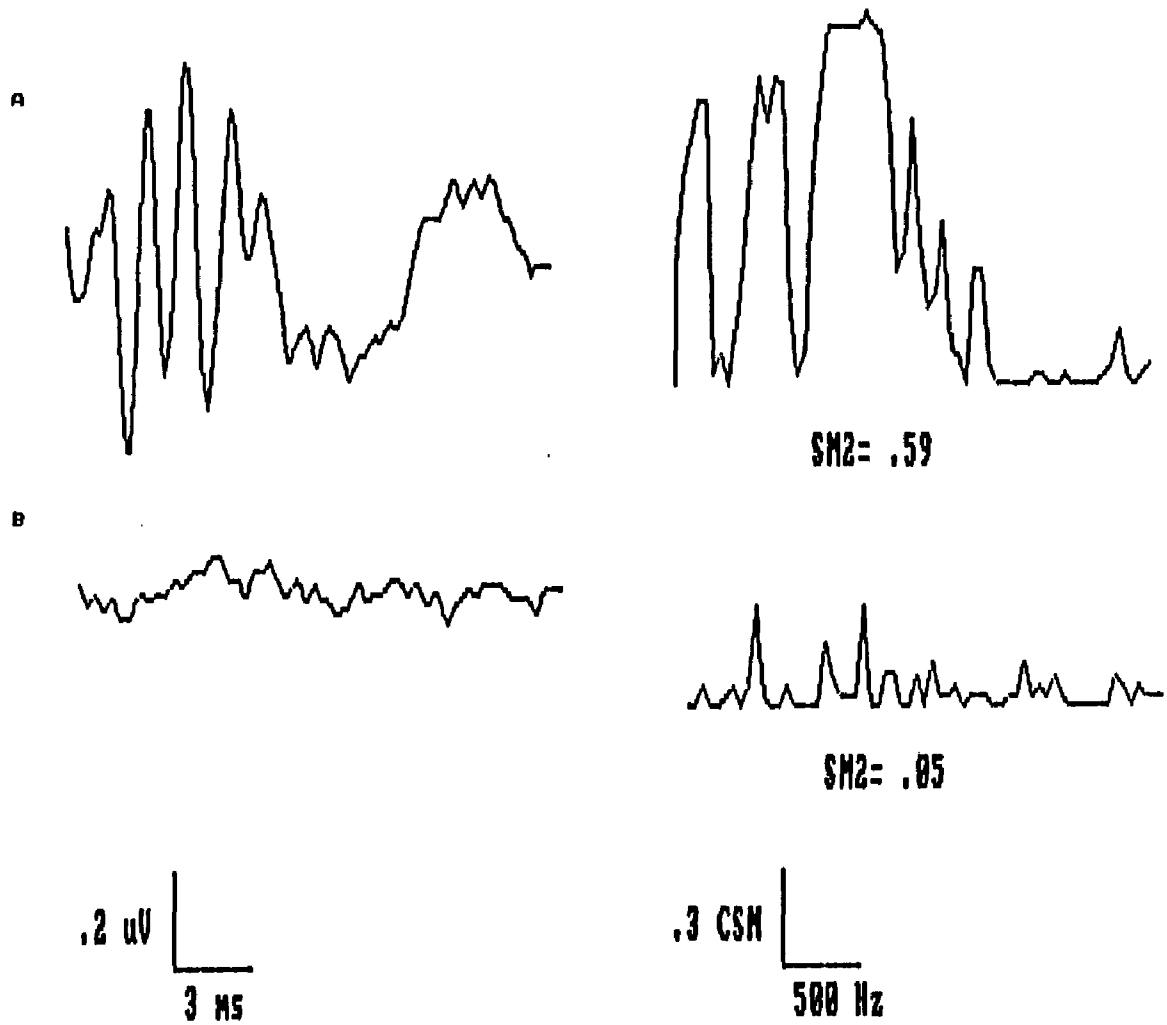


Figure 15

BAERs with Component Synchrony Measure Spectra Across Four Rates of Stimulation

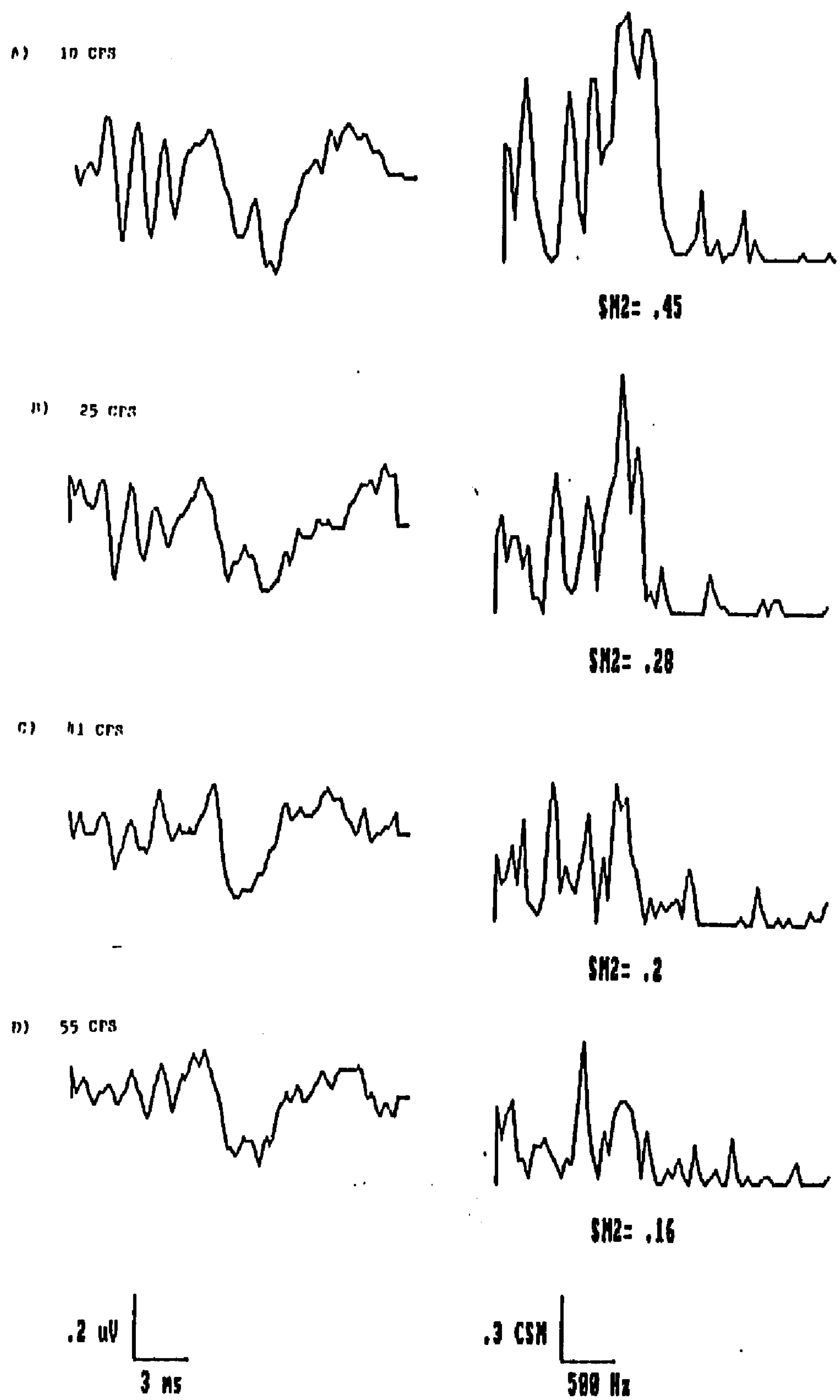


Figure 16

BAERs with Component Synchrony Measure Spectra for Both Ears for Stimulus (A and B) and No-Stimulus (C and D) Conditions

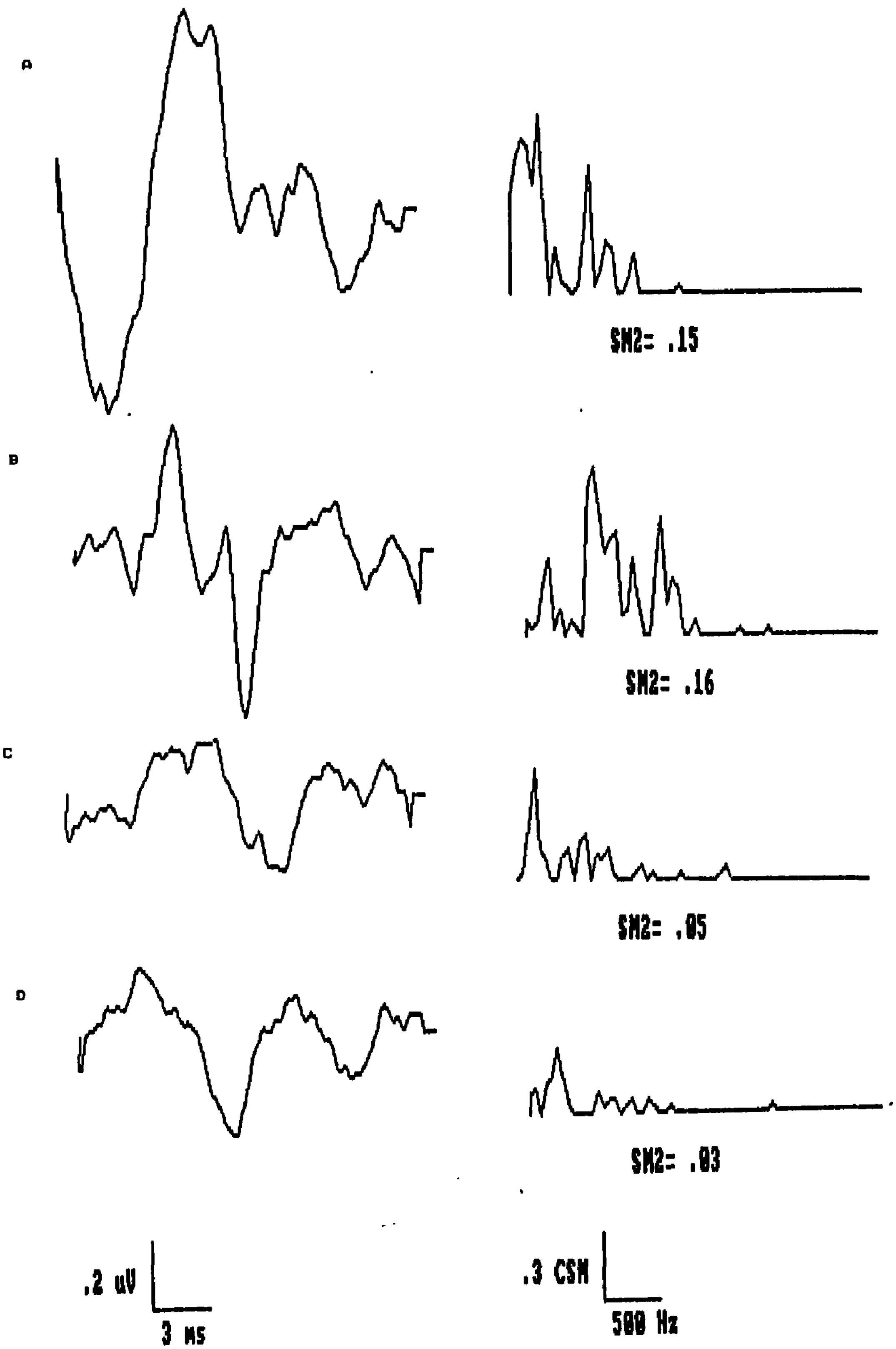


Table 1

Means and Standard Deviations for I-III Inter-Peak Latency for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	2.136	2.170	2.186	2.210
SD	0.182	0.192	0.201	0.220
N	25	23	22	20

Table 2

Means and Standard Deviations for III-V Inter-Peak Latency for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	1.864	1.850	1.940	1.943
SD	0.182	0.179	0.176	0.220
N	25	24	25	21

Table 3

Means and Standard Deviations for I-V Inter-Peak Latency for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	4.000	4.068	4.143	4.164
SD	0.255	0.278	0.313	0.270
N	25	25	23	22

Table 4

Means and Standard Deviations for # of Peaks Present for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	4.846	4.615	4.385	4.154
SD	0.464	0.752	0.752	1.287
N	26	26	26	26

Table 5

Means and Standard Deviations for Synchrony Measure 1 (SM1) for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	.636	.486	.477	.423
SD	.219	.232	.230	.250
N	26	26	26	26

Table 6

Means and Standard Deviations for Synchrony Measure 2 (SM2) for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	.472	.362	.339	.275
SD	.171	.174	.145	.148
N	26	26	26	26

Table 7

Means and Standard Deviations for Magnitude Measure 1 (MM1) for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	2.172	1.906	1.671	1.504
SD	1.048	0.913	0.817	0.769
N	26	26	26	26

Table 8

Means and Standard Deviations for Magnitude Measure 2 (MM2) for Four Rates of Stimulation

	10 CPS	25 CPS	41 CPS	55 CPS
Mean	1.771	1.566	1.406	1.249
SD	1.851	0.729	0.693	0.612
N	26	26	26	26

Table 9

Results of One Way Repeated Measures ANOVA for Each of Eight Measures

	SM2	SM1	I-V IPL	III-V IPL
F=	20.06**	11.83**	10.51**	7.37**
Df.=	(3,75)	(3,75)	(3,57)	(3,60)

	MM1	MM2	#Peaks	I-III IPL
F=	6.70**	6.69**	5.75*	2.06
Df.=	(3,75)	(3,75)	(3,75)	(3,54)

* p (.01
** p (.001

Table 10

Zero Order, Pairwise, Pearson Correlation Coeficients for Rate of Stimulation and Eight Dependent Measures

	Rate	I-III IPL	III-V IPL	I-V IPL
Rate				
I-III IPL	.137 (90)			
III-V IPL	.193 (95)	-.078 (90)		
I-V IPL	.227 (95)	.689 (90)	.669 (90)	
#Peaks	-.290 (104)	-.014 (90)	-.092 (95)	-.291 (95)
SM1	-.300 (104)	.001 (90)	-.124 (95)	-.171 (95)
SM2	-.398 (104)	-.052 (90)	-.225 (95)	-.268 (95)
MM1	-.275 (104)	-.071 (90)	-.316 (95)	-.320 (95)
MM2	-.261 (104)	-.147 (90)	-.374 (95)	-.418 (95)

	#Peaks	SM1	SM2	MM1
#Peaks				
SM1	.547 (104)			
SM2	.524 (104)	.982 (104)		
MM1	.382 (104)	.735 (104)	.738 (104)	
MM2	.365 (104)	.714 (104)	.762 (104)	.950 (104)

Note: Number of pairs used for each correlation appear in parenthesis.

Table 11

Hotelling's ts Between Time and Frequency Domain Variables as Correlated with Rate of Stimulation

		Time Domain Variables			
		I-III IPL (.14)	III-V IPL (.19)	I-V IPL (.23)	#Peaks (-.29)
Freq. Domain Vars.	SM1 (-.30)	3.29 *	3.51 *	3.69 **	0.11
	SM2 (-.40)	4.07 **	4.16 ***	6.11 ***	1.22
	MM1 (-.28)	2.96	3.04 *	3.27 *	0.14
	MM2 (-.26)	2.75	2.87	3.04 *	0.27

* p (.05 (All alpha levels were adjusted for 16
** p (.01 repeated t-tests by multiplying each
*** p (.001 probability value by 16)

Note: Pearson correlation coeficients between rate of stimulation and each measure appear in parentheses.

Table 12

Results of Stepwise Multiple Regression for Seven Measures Predicting Rate of Stimulation

Step Number	Variable Entered	Adjusted R Squared
1	SM2	.1499
2	SM1	.1770
3	# of Peaks	.1875
4	I-III IPL	.1873
5	MM2	.1837
6	MM1	.2023
7	III-V IPL	.1997

Table 13

Comparison of Multiple Regressions for Time Domain versus Frequency Domain Measures

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Time Domain Model:

Rate of Stimulation= I-III IPL + III-V IPL + # of Peaks + Constant

Multiple R = .337

Adjusted Multiple R Squared= .087

$F(3,100) = 4.269$, $p < .01$

Frequency Domain Model:

Rate of Stimulation= SM1 + SM2 + MM1 + MM2 + Constant

Multiple R= .466

Adjusted Multiple R Squared= .186

$F(4,99) = 6.878$, $p < .001$

Table 14

Summary Statistics for Synchrony Measure 2
in Stimulus and No-Stimulus Conditions

	No-Stimulus	Stimulus
N	104	104
Mean	.067	.362
Std. Dev.	.021	.172
Min.	.027	.056
Max.	.141	.786

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