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JOHN CLIFFORD BESS

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RECOVERY CYCLE OF THE ACOUSTICALLY-EVOKED POTENTIAL

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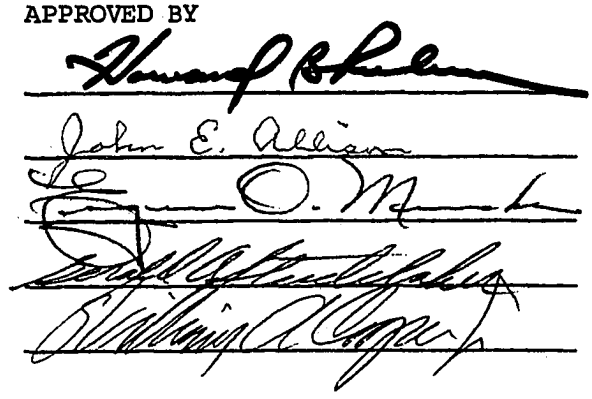

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CHAPTER I

INTRODUCTION

Various aspects of the nervous system's response to environmental stimuli can be observed in the electroencephalogram (EEG). Although responses evoked by sensory stimuli are sometimes visible in the conventional EEG tracing, their amplitudes relative to on-going EEG activity are so small that detection is most often impossible. It has been demonstrated, however, that the visibility of responses evoked by tactile, visual, and auditory stimuli can be enhanced through the summation of a number of responses (22, 24).

The advent and use of the summating or averaging computer has made it possible to obtain a single "averaged" response to acoustic, as well as other types, of sensory stimuli. The averaging technique permits a parcellation of responses to specific stimuli from on-going EEG activity (9, 11, 15, 16, 23, 26, 27, 36, 43, 49, 51, 54). Briefly stated, this technique is based on the concept that the cerebral response to time-locked signals sums in direct proportion to the number of samples, while on-going, non-time-locked "noise" sums approximately as the square root of the number of samples. Thus, repeated sampling produces a favorable increase in the signal-to-noise ratio and a representative "averaged"

picture of the evoked response is obtained.

In audition, responses evoked by administering pairs of acoustic signals have been utilized to determine various parameters of cerebral responsivity. One such parameter is the determination of the recovery cycle of the acoustically-evoked potential. One method of measuring the recovery cycle involves administering pairs of signals, each member of the pair separated from the other by a range of inter-signal intervals. The relative size of the response evoked by the second member of the pair when compared to the response evoked by a single signal has been interpreted as the extent to which the system has recovered its capacity to respond after a given interval. This procedure derives importance from the possibility that the magnitude of response and the rate of recovery may be related to the size of the neural pool available for firing. If the two ears are stimulated at various intervening time intervals, the response to the second signal may differ depending upon which ear is stimulated and which hemisphere is being observed. For instance, if one ear had greater neural representation than the other at some cerebral site, the imbalance might be reflected in a differential rate of recovery of the evoked response in favor of the ear possessing the larger neural representation.

It may be that responses which are evoked by paired and unpaired stimuli and measured at both cerebral hemispheres will yield not only a measure of recovery function but may contribute some indication of the relative roles played by each ear and cerebral hemisphere in processing non-meaningful, non-verbal information.

This experiment will be concerned with the effects of interaural

interaction on some components of electroencephalic responses evoked by auditory stimulation. Specifically, an attempt will be made to determine the recovery cycle of the acoustically-evoked potential as a function of inter-signal interval when each member of a pair of clicks is presented to different ears.

A discussion of the experimental work relating to the investigation of the acoustically-evoked response as well as some of the procedural variables which may affect such a study is presented in the following review of literature.

CHAPTER II

REVIEW OF THE LITERATURE

The purpose of this study was to investigate the effects of interaural interaction on various components of the evoked response. Specifically, it was designed to determine the recovery cycle of the electroencephalic response evoked by monaural stimulation which was preceded by stimulation of the opposite ear. The amplitude characteristics of the evoked response were viewed as a function of inter-signal interval by varying the silent time between signals presented to the two ears.

The following review of the literature will be concerned with quantitative information regarding the recovery cycle of sensory evoked potentials and will not attempt to describe the underlying physiological or neural mechanisms involved in the processing of information. Some general physiological concepts are reviewed in an attempt to assist the reader in understanding the present investigation.

Recovery Function

Cortical recovery cycles have been studied in man and animals for a variety of purposes (3, 13, 33, 40, 46, 48, 64, 68, 71). However, differences in emphasis, procedure, recording techniques, and other technicalities have made it difficult to compare components of the evoked response across studies. These same problems have limited comparisons

between infra-humans and humans. Allison (3) suggested that one of the major problems involved in obtaining comparative data was two-fold in nature. The majority of human studies have relied on only scalp recordings, while animal preparations have utilized a wide variety of pharmacological, surgical, and recording techniques in which it was possible to separate and isolate the individual response components. Unfortunately, the procedures and techniques utilized with human subjects can not be as definitive.

Recently, Goff and his associates (35) attempted to classify and correlate homologous components of evoked potentials among sensory modalities and to differentiate the specific from the non-specific components. They examined the form and distribution of auditory, visual, and somatosensory evoked potentials recorded in the same subjects under similar experimental conditions from an array of electrodes large enough to give a reasonable representation of cranial topography. These authors concluded that the neural substrates involved in the processing of sensory information probably operate in similar ways and thus should produce homologous evoked potentials. However, their similarities become apparent only when the technical sources of variability are minimized.

The determination of the recovery cycle of sensory evoked potentials has provided information relative to the processing of sensory stimuli within the central nervous system. A cycle of recovery can be determined by presenting pairs of signals with varying inter-signal intervals and plotting the amplitude of the evoked response against the inter-signal interval. Some authors (14, 31, 71) have suggested that the relative size of the second response as compared to the first response

of a pair indicates the extent to which the system has recovered its capacity to respond after a given interval. Several investigations (3, 25, 45, 47, 56) have demonstrated that it is possible to differentiate various components of visual and somatosensory evoked responses when utilizing this technique. These studies have shown that different peaks of a complex response will often display different recovery cycles. This differential rate of recovery across response components suggests the possibility that the various peaks may represent origins of discharge at different neural levels.

Excitability Cycles

Like peripheral nerves or other excitable tissue, the aggregate of neurones within the central nervous system, after being activated, undergoes a cycle of excitability changes consisting of a refractory phase and a recovery phase. The interval immediately following stimulation during which a second impulse cannot be initiated has been defined as the refractory phase. The phase following refractoriness is the recovery period (75).

Generally, the refractory period can be considered to be a composite of two phases; the absolute refractory period and the relative refractory period (7). The former implies a brief interval of time following the passage of an impulse in which a second signal, however strong, is unable to evoke a neural response. The latter refers to the interval following the absolute refractory period and during which the excitability cycle gradually returns to normal. For purposes of this discussion the refractory period will be considered synonymous with recovery cycle. The time necessary for the system to regain its original

responsivity may indicate the size of the neural population that comprises the system. Furthermore, it may be that the greater the segment of the total neuronal pool that is available for firing, the faster will be the recovery of response amplitude.

The recovery times of responses elicited from the visual cortex of man and animal as determined by Gastaut and associates (33) were 20 and 40 milliseconds (msec) respectively. According to Tunturi (76), the absolute refractory period at the auditory cortex of the dog to click stimuli lasted from 20 to 100 msec and the duration of the relative refractory period was 100 to 250 msec. It was further shown that prior stimulation of the ipsilateral ear (re the auditory cortex from which measurement was made) in some animals resulted in longer periods of unresponsiveness than when the preceding signal was delivered to the contralateral ear. However, successive stimulation at identical locations in either the ipsilateral or contralateral ear resulted in an absolute unresponsive period of only one millisecond with complete recovery at two milliseconds. Because of the electrode size, it was considered that the results were a reflection of the activity of a composite of relatively numerous neural elements rather than of responses elicited by a single neurone and that the intervals of absolute and relative unresponsiveness tended to increase in duration with the depth of anesthesia.

A phase of facilitation exists as another portion of the excitability cycle, which arises either through the summation of the effects of two or more successive impulses or because of the spatial overlap by which two or more afferents activate the same neurone. This concept has been derived from observations in which the number of neural units

responding to a volley of impulses was increased in number over some previous established level. This phase appeared to be based on a combination of temporal and spatial excitatory processes as well as the neural recovery periods (75).

The degree and duration of the "refractory period" have been found to vary more or less proportionately with the stimulus strength and the number of neurones rendered unresponsive by prior stimulation. No apparent reduction of response amplitude is observed if the initial signal is weak; however, increasing the strength of the initial signal can result in recovery cycles lasting several hundred milliseconds (32). By using paired electrical shocks applied to the optic nerve both Marshall (46) and Clare and Bishop (14) demonstrated the existence of a typical excitability cycle in the visual cortex, composed of a supernormal phase (facilitation) and followed by a lengthy recovery period (from 200 to 3000 msec). A similar phenomenon has been suggested in the auditory system. Rosenzweig and Rosenblith (64) observed that the neural responses to a monaurally presented click recorded from the round window and the auditory cortex of the cat were reduced in size immediately after exposure and the course of their recovery was dependent upon the intensity, frequency, and duration of the signal.

In addition to the normal excitability cycle, there is a period of variation, unique to the sensory area, in which the cortex does not appear to return to normal following the completion of the usual excitability cycle, but tends to undergo a further cyclic waxing and waning (3, 13, 32, 40, 44, 64, 77). Jarcho's (40) observations of responses from somesthetic and auditory cortexes in animals failed to show recovery

curves that were characteristic of facilitation or of lengthy recovery periods; however, when relatively light anesthesia was induced, the recovery functions demonstrated "bizarre notching and occasionally rather regular undulations". Chang (13) reported animal recovery curves which illustrated only small variations in amplitude that were "suggestive of periodic changes in the excitability of the cortex following auditory stimulation". When auditory signals were replaced with an electrical shock to the cortex, the recovery curves demonstrated large cyclical variations not unlike the cortical responses induced by sound stimulation. Rosenzweig and Rosenblith (64), in their investigation of recovery functions in the anesthetized cat, suggested that at the auditory cortex there were always cyclical alternations in the response amplitude initiated by the second member of a click-pair, but the prominence of the cycles was dependent upon the intensity of these signals and upon such physiological conditions as temperature and depth of anesthesia. These authors demonstrated this cyclic activity in recovery functions as the intensity of the first member of a click-pair was varied systematically. When the first member of the pair was weak, the recovery function was nearly monotonic although small cyclical variations were seen. When this member was made stronger, the cyclical activity became more prominent. They concluded that intensity variation of auditory signals has differential effects on the cyclical and monotonic components of cortical recovery functions.

Recently, Webster (77) demonstrated a difference in waveform between the auditory recovery cycles obtained from anesthetized and unanesthetized animals. The recovery cycle for the anesthetized animals displayed an initial depression (0-40 msec) in responsivity followed by

facilitation (50-80 msec), then another depression (100-125 msec) followed by facilitation (125-160 msec). He stated that the evoked response initiated by the second member of a click-pair "can be either facilitated or depressed, according to where in the phase of activity induced by the first click the responses to the second click arrives". Webster further suggested that the refractory processes have been confused with habituation and the observed wave-like activity consisted of alternate peaks of excitation and inhibition. It was reported further, that complete recovery at subcortical areas may take as long as several seconds. This slow recovery process has also been demonstrated at the auditory cortex (19, 64).

Allison (3), was unable to demonstrate this wave-like activity in his effort to define the somatosensory recovery function in man. He suggested that the evidence presented by King and his associates (44) may explain the absence of such effects in human recovery functions. King and associates demonstrated that small doses of barbiturates or the observance of EEG synchrony tended to enhance facilitation peaks while arousal abolished them. Similar effects have been reported by Evarts and associates (31) who found that the visual recovery cycle of a normal cat was depressed more and showed less facilitatory peaks during wakefulness than during sleep. The subjects in Allisons' (3) study and those in the present study were unanesthetized, awake, and alert; conditions which tended to minimize EEG synchrony. Thus, the experimental conditions imposed on the subjects did not favor the appearance of marked facilitation or cyclic effects.

These, then, are some of the concepts in which the constituents

of the excitability or recovery cycle may be expressed without a complete understanding of the underlying chemical and physiological mechanisms. Inherent within these constructs, however, is the implication that the excitability cycles of neurones are essential determinates of the magnitude of cortical responsiveness, whether spontaneous or evoked (14).

All references to measurements in recovery function presented in subsequent sections of this chapter are defined as the ratio of R2 to R1, i.e., the amplitude of the response initiated by the second member of a pair of stimuli expressed as a percentage of the first member of the pair.

Psychophysical State

Since the observations of Berger (6) and Adrain and Matthews (2) regarding the effects of arousal on cerebral responsivity, several investigations have been concerned with the extent to which the state of alertness may influence evoked potentials and their recovery cycles. The following studies indicate that the evoked response and recovery cycles are altered by the subject's state of awareness.

The early work of P. A. Davis (21) indicates that specific electroencephalic activity evoked by a sudden change in the environment, e.g., onset or offset of an acoustic signal (on-effect), becomes more prominent as subjects progress from alertness to sleep. H. Davis and associates (18) presented evidence to support this finding and showed that the amplitude changes associated with the "on-effect" increased progressively as the subjects' psychophysical state changed.

Derbyshire and McDermott (29) and Roth and associates (61), reported that latency modifications in the "K" complex were associated

with stages of alertness. When stimuli were presented at minimal intensities, the conditions of sleep and drowsiness produced an increase in latency as compared to conditions of maximum alertness.

Other investigators (34, 53, 78) observed various components of the evoked response during different stages of sleep and submitted that its waveform was altered across the different stages of sleep and was not unlike that observed in the on-going EEG activity during conditions of drowsiness and sleep.

The previously mentioned studies and others (17, 38, 42, 73) present evidence regarding the role of attention in evoked responsivity and indicate that the psychophysiologic state of the organism, when viewed on a continuum from vigilance to sleep, has a marked effect on the average acoustically-evoked potential.

Schwartz and Shagass (67) determined the effect of different states of alertness on cortical somatosensory and auditory recovery cycles in anesthetized cats. Evoked responses to 100 pairs of acoustic and 100 pairs of somatosensory stimuli were recorded at the cerebral cortex. Intervals between pairs of stimuli were varied from 10 to 190 msec. In turn, each pair of stimuli was separated by an interval of 1.6 seconds. The results of this study demonstrated a significant reduction in the amplitude of the somatosensory evoked potential as a function of decreased attention; however, consistent findings were reported only for this modality. The authors stated that the averaging of 100 responses failed to produce reliable records of acoustically-evoked potentials "...probably because the auditory cortex is remote from the surface". All animals displayed consistent EEG changes within a sensory modality, but the

changes were not completely consistent among animals nor between modalities, i.e., amplitudes increased in some instances and decreased in others. In the non-alert state, the percentage of recovery was consistently higher than in the alert state. Following the administration of drugs (antidepressants), a longer separation between pairs was necessary in order to reach comparable levels of recovery. Greater fluctuations in the percentage of recovery were reported for the auditory modality. Schwartz and Shagass concluded that, although measured at the cortex, recovery changes were probably not cortical in origin and that a change in the recovery of one sensory modality may prove to be a valid indication of generalized changes in central nervous system excitability.

Allison (4) indicated that the recovery cycle affords another test of cortical functioning during wakefulness and sleep and suggested that recovery and the observed changes in recovery between the states of waking, slow sleep, and rapid sleep (as defined by the frequency of the on-going EEG) were entirely a consequence of intra-cortical events. His investigation of cortical and subcortical evoked responses to electrical stimuli illustrated that following stimulation, during periods of wakefulness, a rapid phase of recovery occurred and reached its maximum at inter-signal intervals (ISI's) of 6 to 13 msec. This initial peak recovery was then followed by a period of depression (non-recovery) which lasted from 150 to 200 msec. The depression phase was shown to be considerably longer during wakefulness than during slow sleep. However, the amount of recovery observed was greater during the condition of rapid sleep than during periods of wakefulness. The condition of slow sleep produced a greater percentage of recovery than did the other two

conditions. Allison proposed that during the condition of rapid sleep the cortex was in a state of heightened responsiveness as compared with the waking state. The resultant increase in amplitude of the evoked response appeared to be a result of "active" processes within the cortex. He also suggested that the increased recovery observed during the condition of slow sleep may be associated with some type of cortical inhibitory mechanism.

Evarts and his associates (31) reported similar findings during their investigation of visually-evoked potentials at the cortex of anesthetized cats. Their data indicated that waking and sleeping animals displayed a supra-normal recovery cycle (facilitation) at ISI's of 3.2 to 10 msec. This period of facilitation was immediately followed by a recovery period which lasted from 16 to 200 msec. The condition of sleep produced a higher percentage of recovery at the short ISI's and a shorter recovery period at the longer ISI's. They suggested that the recovery cycle was influenced not only by the time interval between pairs of stimuli but varied as a function of stimulus intensity, position of the recording electrodes, and other procedural variables.

Shagass and Schwartz (68, 70, 71) have engaged in extensive investigations of human evoked potentials as indexes of psychiatric problems. These authors concerned themselves with somatosensory recovery functions on groups of normal and psychiatric patients before and after drug therapy. Their results were based on 207 subjects of whom 40 were non-patients. The recovery curves exhibited by the patient population were significantly different from the non-patient in two respects. First, the normals or controls initially (before 20 msec ISI) reached a greater

percentage of recovery than did the patients. Second, the normals demonstrated more facilitation during the ISI's of 100 to 300 msec than did the patients. Findings regarding the treatment effects on the patient population indicated a progressive increase in the observed percentage of recovery as a function of continued treatment. The authors concluded that improvement in recovery was apparently a correlate of the clinical disorder and not a fixed characteristic of the individual. Additional information suggested that as a remission of symptoms occurred and the individual approached normalcy, a reduction in response amplitude of the evoked potential was observed. Shagass and Schwartz further stated that apparently this reduction was a product of the action of the treatments (drugs). Other investigators (57, 58, 60, 72) have observed a similar diminution of response amplitude and a reduction in the recovery cycle resulting from the administration of drugs.

Recording Site

In 1939, P. A. Davis (21) observed that the acoustically-evoked response was greatest when recording at the vertex. Later, Bancaud and his associates (5) named the large response, which appeared to center at the vertex, the "V potential" to emphasize its anatomical distribution. Since that time, numerous investigators have substantiated the fact that the maximal amplitude of the evoked response may be recorded at the vertex or near vertex position.

Derbyshire and his associates (28) indicated that the recording site which produced the greatest responsivity for auditory stimuli was three centimeters lateral to the midline in the plane between the subject's ear and was referenced to the contralateral earlobe or mastoid.

Similar results reported by McCandless and Best (50) indicated that maximum amplitude of responses were obtained when recording from the central area of the interaural plane.

Abe (1) observed that the amplitude of the acoustically-evoked response decreased progressively as the distance from the vertex was increased. Davis and Zerlin (20) also reported that the distribution of the vertex potential extended laterally in the interaural plane and anterior-posterior in the coronal plane and likened its distribution to the position of a cap placed on the front of the head.

The International Ten-Twenty Electrode System (41) has been successful in standardizing scalp electrode positions. Traditional anatomical terms were employed to designate the positions overlying the various lobes of the brain and subsequent anatomical studies were carried out to determine the cortical areas located beneath each of the standard electrode positions in the average brain.

Inter-signal Interval

As early as 1953, Pearl, Galambos, and Glorig (55) reported that the number of discernible responses were decreased when auditory stimuli were presented too rapidly, i.e., faster than 10 per second. Abe (1) was unable to obtain evoked responses to click stimuli separated by intervals of 500 msec or less. However, he was able to observe an evoked response when the interval was lengthened to 750 msec. McCandless and Best (49) examined the response evoked by clicks presented at rates of 0.5 per second to 3.0 per second and observed a reduction in response amplitude concomitant with a latency shift at repetition rates faster than 2.0 per second.

Clinically, Rapin (59) and Derbyshire and his associates (29) advocated that the greatest response amplitude was obtained when irregular inter-signal intervals of 10 to 30 seconds were utilized.

H. Davis and his associates (19) stated that the major positive and negative components of the acoustically-evoked response demonstrated no latency shifts until the ISI's were shorter than 500 msec. At shorter ISI's, the waveform was altered with a concomitant reduction in amplitude which might be explained on the basis of superimposition of relatively late components of the preceding response on the early components of the succeeding response. Davis and Zerlin (20) reported in their investigation of human acoustically-evoked potentials that probably 10 seconds were necessary for the evoked response to regain its original amplitude and that at ISI's of one second the individual response amplitude was only 25 percent of maximum.

H. Davis and his associates (19) reported recovery functions of the human acoustically-evoked potential from interpolated data and indicated that ISI's greater than six seconds, and probably as much as 10 seconds, were required for complete recovery of the vertex potential. Data presented by these authors demonstrated that the response evoked by the second member of a click-pair presented to one ear when separated by a 500 msec ISI was only 1/3 to 1/2 the amplitude of the response evoked by the first member of the pair. Additional information indicated that if the signals were presented in pairs with short intervals between each member, but considerably longer intervals between the pairs, the recovery following the first response was greater than if the intervals were all brief and regular.

Shagass and Schwartz (68, 70, 71), in a previously discussed investigation involving psychophysiologic state and recovery functions, stated that little change, if any, was observed when single signals or pairs of signals were separated by intervals greater than 2.0 to 2.5 seconds. These authors separated pairs of signals in steps of five milliseconds from ISI's of 10 to 40 msec and in steps of 10 msec from ISI's of 50 to 190 msec. They emphasized that "these intervals by no means represent a complete description of the recovery curve but were selected so as not to lengthen an already long procedure". These investigators indicated that the human somatosensory recovery curve was generally biphasic; the initial phase of full recovery or facilitation occurred at an ISI of 20 msec and again at approximately 100 msec, with an intervening phase of response depression. However, they suggested that the intervals associated with recovery and non-recovery appeared to be dependent upon the length of the nerve which must be traversed during stimulation.

Allison (3) described the recovery cycle of several components of somatosensory evoked potentials in humans and reported that the recovery cycle of the long-latency component (apparently the vertex potential) was virtually complete in two seconds, depending upon recording location and other variables. However, two of his normal subjects demonstrated considerable recovery as early as 300 msec, although responsiveness was not normal until an interval of two to three seconds. Two other subjects showed a much slower rate of recovery which was not complete at an interval of four seconds. ISI's of 0.1, 500, and 1000 msec demonstrated the greatest reduction in recovery for the component in question. In addition, the negative and positive phases of the component were

shifted earlier by as much as 20 and 40 msec respectively.

Laterality

Previous discussion has been concerned with some of the factors that influence the determination of recovery cycles among sensory evoked potentials. Most of the data presented thus far, unless stated otherwise, has been obtained under conditions of monaural signal presentations with responses recorded at either the vertex position or a position overlying the cerebral hemisphere contralateral to the ear receiving the signal.

Extensive literature now exists regarding ipsilateral and contralateral auditory asymmetry for the preception of dichotically-presented verbal materials. There is abundant evidence indicating that the asymmetrical functioning of the two halves of the brain for speech are reflected in the unequal perception of words and other specialized materials presented dichotically to the left and right ears. To date, however, little information has been advanced regarding cerebral functioning and the processing of non-verbal, non-meaningful materials. The remainder of this review will be limited to the literature pertaining to hemisphere and ear differences in the processing of non-verbal information.

Previous reports, describing the relative amplitudes of ipsilateral and contralateral responses during alternate stimulation of both ears, are in disagreement regarding the size and the significance of the observed differences. Rosenzweig (62) obtained evidence from a study of cats which indicated that the contralateral auditory pathways were stronger than the ipsilateral in terms of amplitude of the response. Bremer (12) found that the contralateral response was three times the

size of the ipsilateral response in the cat. Woolsy and Walzl (79) noticed some differences between contralateral and ipsilateral responses in the cat but believed that these differences were not significant.

In 1946, Tunturi (76) reported that the contralateral responses to electrical stimuli in the dog were slightly greater than those observed at the ipsilateral auditory cortex. His conclusions were based on the observation that stimulation of either ear would completely block the response to subsequent stimulation of the other ear. He submitted that the two ears were represented at the auditory cortex by two overlapping neural populations and not two different populations as proposed by Boring (8).

In order to demonstrate the overlap, Tunturi (76) stimulated a group of neural fibers located in symmetrical parts of the cochleas of opposite ears and recorded responses from a single point located at each cerebral hemisphere in anesthetized dogs. Responses evoked at subcortical areas were also recorded. Two electrical signals of equal strength, delivered in succession to opposite ears, resulted in an absolutely unresponsive period to the second stimulus. This unresponsive period, lasting 20 to 100 msec, was recorded at the cortex ipsilateral to the ear receiving the first signal. This period was followed by a second phase during which the response to the second stimulus gradually increased in size until it reached its former magnitude. The second phase was reported to last from 100 to 250 msec or longer. In most of the experiments, preceding stimulation of the ipsilateral ear resulted in longer periods of unresponsiveness than for preceding stimulation of the contralateral ear. In addition, the amplitude of responses

contralateral to stimulation were greater than those of the ipsilateral side. It was suggested, however, that alterations in response amplitude and changes in recovery periods were influenced by the depth of anesthesia and the physiological condition of the animal. Large cyclical variations in cerebral responsivity were also reported. These findings are in agreement with those of Marshall (46) who reported an absolute period of unresponsiveness, 25 to 30 msec in duration, to successive stimulation at the same spot on the skin of anesthetized cats.

Rosenzweig and Rosenblith (64) presented evidence in agreement with that of Tunturi (76) regarding the role played by each ear and hemisphere in the processing of information. These authors proposed that at the auditory cortex the response evoked by a signal was altered when another signal preceded it and the extent of the alteration was dependent upon the time interval between the two signals. The observed differences were reflected in a reduction of response amplitude and a change of waveform. Pairs of acoustic clicks (0.1 msec in duration) of equal intensity were presented at various inter-signal intervals to alternate ears of anesthetized cats. The initial member of each click-pair was always presented to the right ear while responses were recorded at the left auditory cortex. When the interval between members of the click-pair was seven msec or less, only a single response was observed. However, when the ISI was increased, the waveform of the response became biphasic. Apparently, the small response initiated by the second member of the pair was superimposed on the response created by the first member. When the interval between pairs was extended to approximately 90 msec, the response evoked by the second member reached maximum recovery and subsequent

increases in ISI's resulted in cyclic alternations of responsivity. Rosenzweig and Rosenblith further reported that the long duration of cortical recovery cycles were characteristic of their animals and that cortical functions were "profoundly affected by the depth of anesthesia, temperature of the animal, and the general physiologic state of the animal". The data presented by these authors indicated that in all aspects of the recovery cycle the response evoked by the second member of a click-pair was more strongly depressed by a prior signal to the same ear than by a prior signal to the opposite ear. This evidence suggested that the cortical projections from the two ears were not entirely in common, although their overlap may be considerable.

Additional data presented by Rosenzweig (62) indicated that differences in response amplitude and in the percentage of recovery were observed depending on whether or not a prior signal was delivered first to the ear ipsilateral to the cortical electrode or the ear contralateral to the electrode. When the first member of a click-pair was presented to the ipsilateral ear, the response amplitude and the percentage of recovery decreased as a function of reduction of the ISI. There was less decrease in the response amplitude and a greater increase in the percentage of recovery when the first member was presented to the contralateral ear. The amplitude of the response evoked by a single contralateral click was found to be almost as large as the response to simultaneous or nearly simultaneous clicks at the two ears. The amplitude of the response at either hemisphere was larger when the contralateral ear received initial stimulation. This author also noted that when the ears were stimulated in the order of left-right a larger response was

evoked at the right auditory cortex than at the left. The converse was found to be true for right-left stimulation. Order differences were reported to be consistent at intervals of less than one millisecond.

In a later investigation, Rosenzweig (63) demonstrated that the amplitude of cerebral responses evoked by click-pairs presented alternately to the left and right ears of anesthetized cats were not absolutely symmetrical. When recorded from an electrode located at the left cerebral hemisphere, the order of left-right stimulation produced a smaller response than did the order of right-left stimulation at an ISI of approximately one msec. The pattern of signal presentations did not appear to influence the response amplitude when the ISI was decreased to 0.2 and 0.1 msec. The order of left-right stimulation consistently resulted in larger responses regardless of the interval between pairs when responses were recorded from the right cerebral hemisphere. This information indicated that, at least for click stimuli, responsivity was largest at the cerebral hemisphere contralateral to the ear receiving initial stimulation, whether it was the right or left ear.

Although not specifically mentioned by Rosenzweig (63), his data also suggest a "hemispheredness" in favor of the right cerebral hemisphere. The fact that the left ear-right hemisphere maintained its relationship of larger amplitude rather than the right ear-left hemisphere, even at the lowest ISI's measured, indicates the possibility of a hemispheric predominance in favor of the right cerebral cortex. Whether this is indicative of left "e[illegible]" remains open to question.

As previously mentioned, the laterality effects in audition for the perception of verbal materials are not within the scope of this

discussion. Suffice it to say that the processing of verbal information and speech functions for the majority of individuals are represented in the left cerebral hemisphere (10).

Milner (52) demonstrated that the performance on some subtests of the Seashore Measures of Musical Talents was affected by a right temporal lobectomy but not by a left temporal lobectomy. Her findings indicated that the perception of tonal patterns and tonal quality depended more on right temporal activity than on left temporal activity. She concluded that if a relative ear superiority for melodic patterns could be elicited, it would be in the direction opposite to that for spoken digits. To demonstrate this relationship, Milner presented different melodic patterns to a group of normal subjects, all of whom had been previously tested on the digits task. She found that a significantly greater number of accurate identifications were made when the melody patterns task was presented to the left ear than when it was presented to the right ear. This was the converse of the results obtained on the digits task.

In a later portion of the same investigation, Milner (52) reported data for recorded clicks. Utilizing a variation of the Broadbent task, two different groups of clicks, varying in number from one to six, were presented to the two ears over a two-second time interval. The subject was to report the number of clicks arriving at each ear. Thus, if the subject heard three clicks in the left ear and five clicks in the right ear, he reported "three and five". Responses were obtained from 14 normal subjects whom she previously tested on the digits task. The results for the two tests were found to be different. A higher score

for the digits task was found for the right ear, while a slight, though statistically insignificant, difference for the clicks, was observed in favor of the left ear.

Justification for the Present Study

The determination of the recovery cycles of the acoustically-evoked potential provides a reasonable approach toward elucidating functioning of the central auditory mechanism. Thus far, the primary focus of attention has not been directed toward the relative roles played by each ear and cerebral hemisphere in the processing of information. Some authors (8, 12, 63, 76, 79) have suggested that if the two ears are stimulated by paired signals presented at various intervening time intervals the response evoked by the second signal may differ depending on which ear received the initial signal and which hemisphere was being observed.

The present study was designed to investigate the recovery cycle of the acoustically-evoked potential as a function of inter-signal interval when each member of a pair of clicks was presented to different ears and responses were recorded from positions overlying each of the cerebral hemispheres. A description of the experimental apparatus, subject sample, and procedures utilized are outlined in detail in the following chapter.

CHAPTER III

PROCEDURE AND INSTRUMENTATION

This experiment was designed to investigate the amplitude characteristics of electroencephalic responses evoked by pairs of clicks, each member of which was presented to opposite ears.

The instrumentation utilized in this study consisted of several pulse generators and waveform generators, a central programming unit, FM tape system, recording electrodes, amplifiers, attenuators, earphones, computer and monitor oscilloscope. The pulse and waveform generators were used in conjunction with a pre-set central programming unit to produce and control the temporal order of auditory signals. Trigger pulses and on-going EEG activity were simultaneously recorded and stored on separate channels of magnetic tape. The trigger pulses initiated by the tape system allowed responses for the right and left ears to be retrieved separately during the analysis phase of the study. The signals produced by pulse generators were fed through matching-pads into attenuators and into the appropriate earphones.

Encephalic potentials between two pairs of electrodes attached to the scalp of each subject were amplified, fed through 60 Hz filters, and paralleled into a summing computer, FM tape system, and monitor oscilloscope. The computer provided on-line monitoring of one experimental condition concurrent with the tape recording of all conditions.

Evoked responses were obtained at a single sensation level for each subject under four experimental conditions and twelve treatment conditions. A total of 60 samples were used to obtain an averaged, or summed, response.

A detailed description of subjects, instrumentation, and procedure is presented in the subsequent sections.

Subjects

Data were collected from four adult males who demonstrated normal hearing, a negative history of chronic ear pathology, and a negative neurological history. Each subject was required to undergo a brief screening procedure. This procedure included a pure tone air-conduction screening examination at 15-dB HL (re ISO, 1964) at octave frequencies of 250 through 4000 Hz and a sampling of EEG activity. All subjects whose EEG exhibited myogenic activity in excess of 160 μv were excluded from the experimental group. Subject fatigue was minimized by limiting the length of each experimental session and providing sufficient periods of rest. It was suggested to all subjects that they be well-rested prior to participation in this study in order to reduce the possibility of sleep contamination during the recording sessions. Once a subject was selected for inclusion in the experimental group, the responses obtained during each recording session were used for data if they were relatively free from the influence of myogenic activity. During the entire investigation ten recording sessions were repeated because of myogenic contamination.

Apparatus

All testing was completed in an acoustically-treated, electrically shielded, two-room suite at the Speech and Hearing Center, University of Oklahoma Medical Center.

Screening Apparatus

A pure tone audiometer (Beltone, Model 15C) feeding either of two air-conduction receivers (Telephonics, TDH-39, 10Z) was used in the hearing screening examination. The acoustic output of each receiver was measured with an audiometric calibration unit (Western Electric 640AA Condensor Microphone: Western Electrical-Acoustical Laboratory, Inc., Condensor Microphone Complement, Type D/E or Allison Laboratory, Model 300) at regular intervals by the clinical staff at the University of Oklahoma Medical Center Speech and Hearing Clinic.

Experimental Test Apparatus

The experimental apparatus is represented by the flow diagrams shown in Figures 1 and 2. Many components were utilized in both the recording and analysis phases of this experiment.

Recording Apparatus. A pre-set central programming system (Grason-Stadler Modular Programming Series 1200) controlled the temporal sequencing of all signals. This unit supplied triggers to a pair of waveform generators (Tektronix, Type 162) which in turn triggered two pulse generators (Tektronix, Type 161). The pulse generators delivered a 0.1-msec, 50-volt square pulse to either of two attenuators (Hewlett-Packard, Model 350-AR) loaded with minimum-loss pads (not shown in Figure 1). The output of each attenuator was then fed to either of two

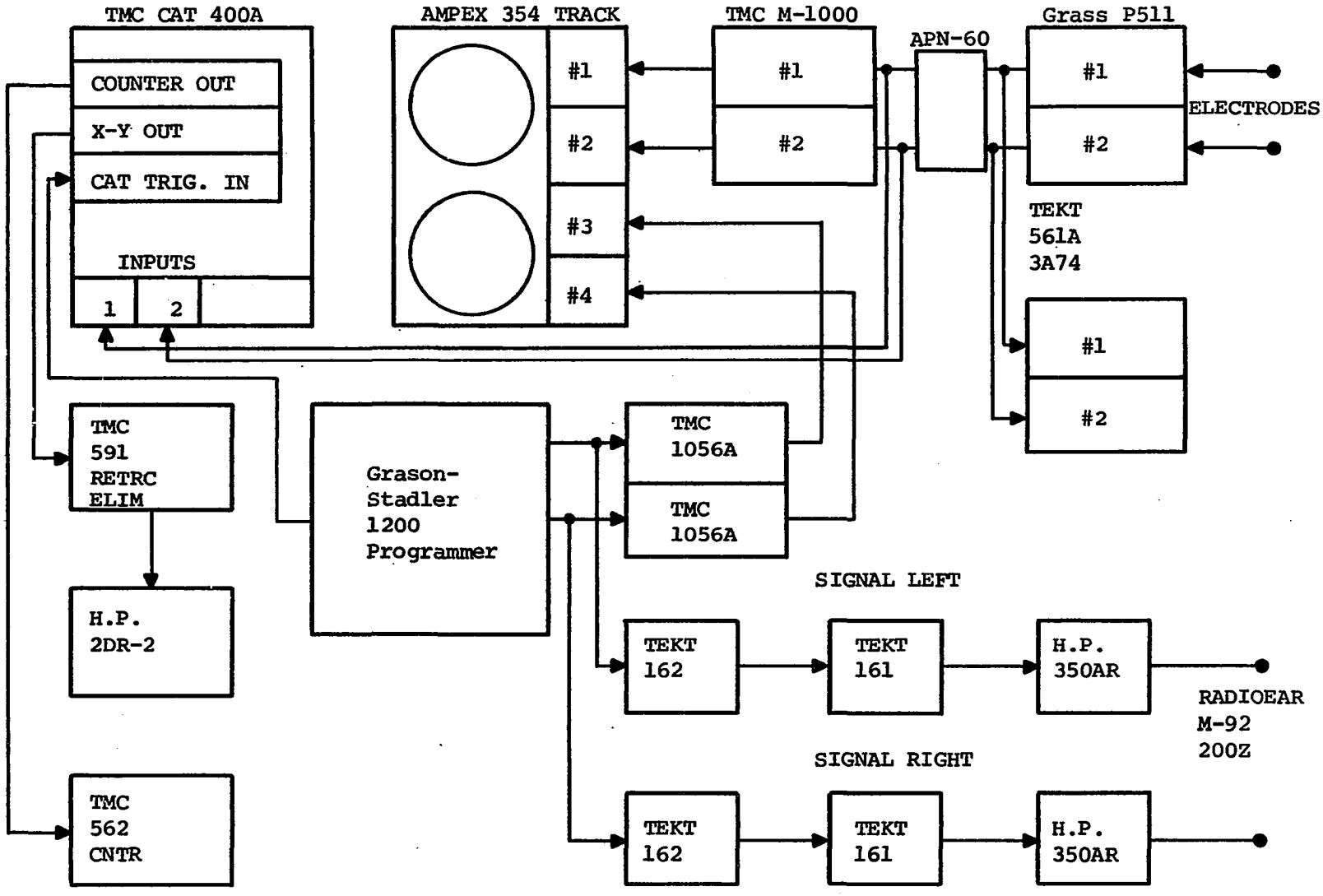


Figure 1--Flow diagram of apparatus used for recording and signal presentation.

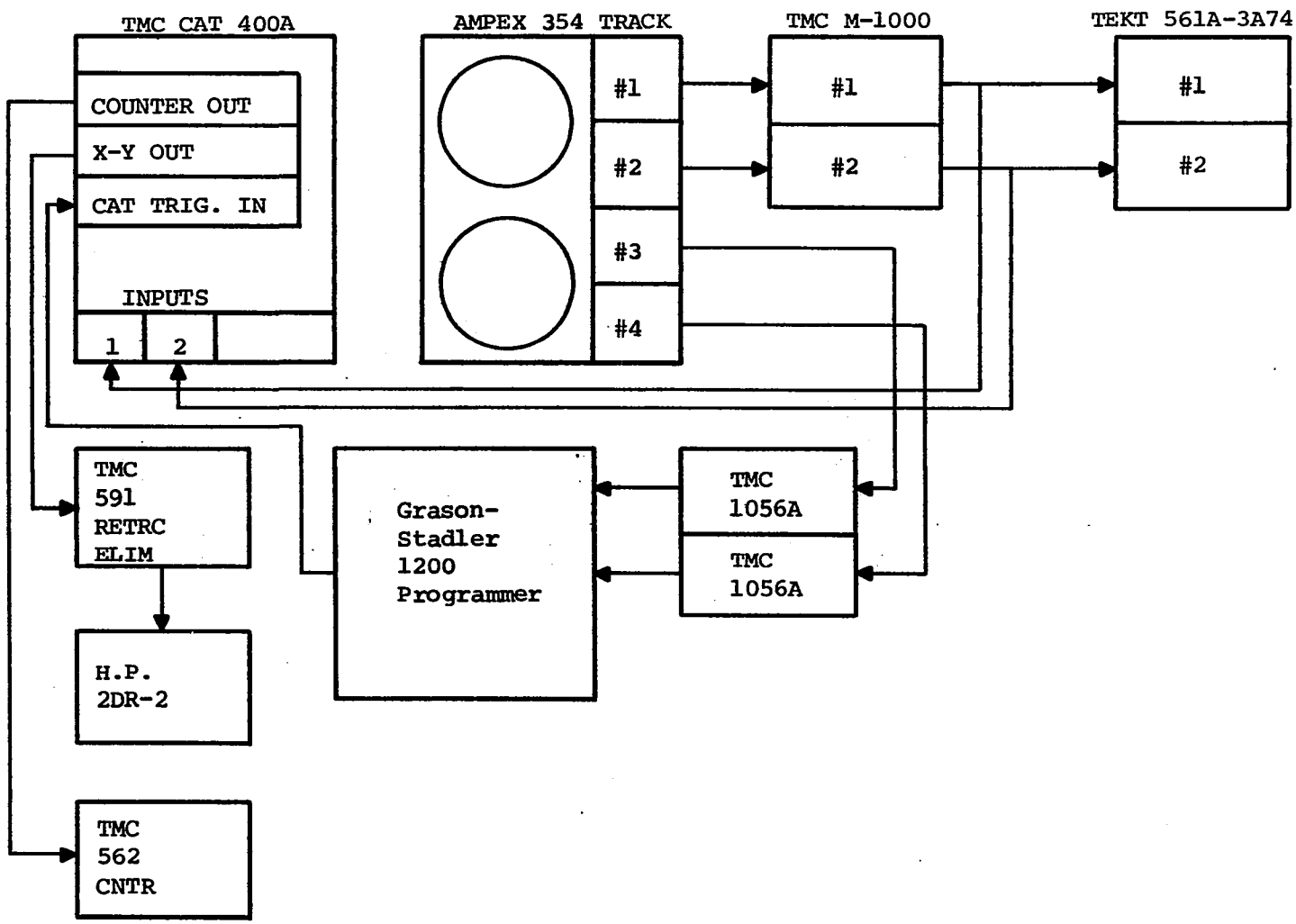


Figure 2--Flow diagram of apparatus used for analysis.

insert receivers (Radioear, Model M-92, 200Z) producing an acoustic click. The acoustic output of each receiver was viewed on an oscilloscope prior to a recording session to insure equivalent polarities and voltage outputs across channels with equivalent inputs.

Recording electrodes conducted on-going EEG activity from the scalp through a patch board to amplifiers (Grass, P5 Series, Type P511) set at a gain of 25,000 (approximately 88-dB). This amplified signal was fed in parallel to: an FM tape system (TMC, Model 700/1400) where it was stored on a single track of a seven track magnetic tape; a four-trace monitor oscilloscope (Tektronix, Model 561-A with Type 3A74 four-trace amplifier and Type 67 time-base); a 60-Hz notch filter (A. P. Circuit Corporation, APN-60); and to a summing computer [Technical Measurement Corporation, Model 400A (CAT)]. The computer was pre-set to accumulate incoming data for a 500-msec period following the stimulus. During the recording phase of the experiment, the computer was used only as a monitor and provided on-line information. The oscilloscope permitted continuous monitoring of the on-going EEG activity in each of the four channels, providing information about the psychophysiological state of the subject and electrode placement. The pre-set programming unit delivered a trigger to start the computer sweep concurrent with each signal series. Triggers were recorded on separate channels of magnetic tape by two synchronous trigger units (TMC, Model 1056-A) which also were utilized in separately retrieving left and right ear responses in the analysis phase of this study. An interval-timer (TSI Model 361) served as a counter to aid in the presentation of the same number of stimuli in each experimental condition.

Analysis Apparatus. A flow diagram of the apparatus used for the analysis of the tape-recorded electroencephalic data is shown in Figure 2. These data were fed from the FM tape system into the computer. Trigger pulses on each of two tracks of the magnetic tape were utilized to trigger the computer for the separate accumulation of responses to right and left ear stimulation. These pulses also went to the programming system which interpreted them in order to activate and deactivate computer channels and to place the computer in the "add" or "subtract" mode at appropriate times. Graphic recordings of off-line data analyzed by the computer were obtained with the use of an X-Y plotter (Moseley, Hewlett-Packard, Model 2DR-2) under computer control.

Calibration Procedure

The procedures used to calibrate the system are recorded in Appendix A. Calibration procedures for the CAT and the X-Y plotter were supplied by their respective manufacturers. The stability of the computer's analog-to-digital converters was checked periodically in accordance with procedures developed in this laboratory (65).

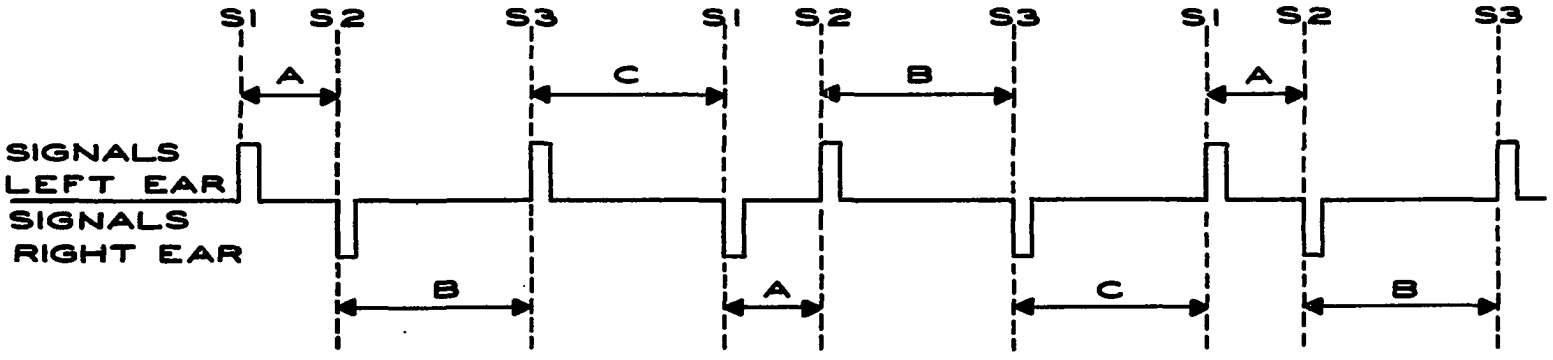
Experimental Procedures

This study was designed to investigate the manner in which the recovery cycle of the acoustically-evoked potential was affected when predisposing signals were presented to the ear opposite the test ear and evoked responses were recorded from scalp positions located over each cerebral hemisphere. Signals consisted of click-pairs and single clicks presented alternately to each ear (it will be convenient to refer to the first member of the click-pair as S1, the second member of the pair as S2,

and to the single click as S3). The corresponding responses are designated R1, R2, and R3. A schematic diagram indicating the pattern and order of signal presentation is shown in Figure 3. Programming permitted each member of a click-pair to be delivered to opposite ears and to be separated in time by a variable interval (ISI). Interspersed between the click-pairs were single clicks alternately presented to each ear. The single click (S3) served the purpose of providing a reference against which to judge the recovery of R2 delivered to the same ear. Responses to single clicks (R3) were also used to remove the direct contamination of R1 on R2 which may occur when the ISI is short enough to encroach on the latency domain of the evoked response. It is important to note that R3, evoked by stimulation of the right ear was subtracted from R1, the response to the first member of the click-pair evoked by stimulation of the same ear which might otherwise have contaminated R2 evoked by stimulating the left ear. R3, evoked by stimulation of the right ear, also served as a reference for R2, evoked by right-ear stimulation. The same relationships were true for left-ear stimulation.

Responses to clicks were obtained during four different combinations of signal presentations and recording locations. The nomenclature utilized in designating the order of signal presentations was S-R,L (signal presented first to the right ear, separated in time by the ISI, and followed by a signal presented to the left ear). S-L,R designates the converse manner of presentation.

Recording locations were determined in accordance with the International Ten-Twenty Electrode System (41) and are designated as C3 for the left cerebral hemisphere and C4 for the right cerebral hemisphere.



LEGEND

S1, S2, S3--Signals presented in consecutive order to appropriate ears.

A----------Inter-Signal Interval (ISI), Independent Parameter.

B----------Standard Recovery Interval of 6000 msec after the presentation of a click-pair.

C----------Standard Recovery Interval of 6000 msec after the presentation of a single click.

Figure 3--Paradigm of signal presentation.

The C3 and C4 scalp positions are located 30 percent above each pre-auricular notch on either side of the head. Identical positions may also be determined by locating two points, each 20 percent lateral to the vertex position on either side of the head.

The rational for recording potentials evoked from these two electrode positions was that the often observed myogenic contamination is minimal at these loci due to the absence of large underlying muscle groups and the evoked cerebral responsivity is relatively large because of the proximity of the vertex position. Simultaneous recordings from electrode positions overlying each cerebral hemisphere also provided the opportunity to observe the existence or non-existence of hemispheric differences as a function of ear stimulation or ISI.

Evoked responses for each combination of signal presentation (S-R,L and S-L,R) and recording location (C3 and C4) were obtained during each of the treatment conditions (ISI's). The intervals between members of the click-pair were as follows: 1, 3, 5, 10, 30, 50, 100, 300, 500, 1000, 3000, and 5000 msec. The treatment conditions were presented to all subjects in descending order beginning with the longest interval. While this manner of presentation may have introduced an order effect, the reduction of subject fatigue and the decline in psychological unpleasantness associated with lengthy recording sessions were sufficient to justify this order of presentation. Initial stimulation of the right and left ears was counter-balanced across subjects.

It should be reiterated that the complex pattern of signal presentations and recording locations allowed each subject to serve as his own control for all ISI's and for any combination of signal presentation

and recording location. Assumedly, any fluctuation or alteration in attention or psychophysiological state would affect the responses evoked by each member of the click-pair and the response evoked by the single click in the same manner since each member of the click-pair, as well as the single click, were alternately presented to the right and left ears and simultaneous recordings were obtained from both cerebral hemispheres. Thus, any changes that influence subject variability would presumably affect each ear and hemisphere approximately equally under any given condition. A pilot study conducted at the University of Oklahoma Medical Center revealed that an interval of 6000 msec is a sufficiently long silent time between stimuli to permit complete recovery of the response componentry in the range of 75 to 300 msec. Programming allowed this silent interval to be introduced between responses evoked by single clicks and click-pairs. Presumably, the response initiated by a predisposing signal delivered to either ear will not influence or contaminate the succeeding response evoked by a signal presented to the opposite ear when separated by this time interval.

Each experimental session consumed approximately three hours which included electrode placement, threshold determination, and rest periods. Seven to nine recording sessions were necessary to collect data for all experimental conditions.

The equipment was calibrated and checked before and after each experimental session. It was decided prior to engaging in the experiment that, if, for any reason, the equipment was found to be out of calibration or otherwise malfunctioning following or during an experimental session, the data would be discarded and the session repeated at a later

time. At no time was it necessary to exercise this precaution.

After a subject was seated in a comfortable reclining chair in the test room, the electrodes were positioned and insert receivers were placed in both ears. Instructions were given for the determination of sensitivity threshold for clicks. Threshold was determined using an ascending technique in 2-dB steps and was defined as the lowest intensity to which a subject responded two out of three times. The signal intensity level utilized under all experimental conditions was 50-dB sensation level.

Responses were recorded from the scalp utilizing two bipolar montages located at electrode positions C3 and C4 referred to the respective left and right ear lobes. A ground electrode was placed at the forehead. The electrode positions were determined by actual measurements in accordance with the International Ten-Twenty Electrode System (41). Presumedly, these scalp locations permit the recording of the underlying electrical activity of each cerebral hemisphere at or near the Fissure of Rolando. Prior to electrode placement the respective scalp areas were cleaned with alcohol. The electrodes, filled with an electrolytic suspension (Sanborn EKG Sol), were then held in place by collodion placed over a gauze patch and dried with pressurized air.

Subjects were allowed to read materials of their own selection during each experimental session, however, they were instructed to try to remain as quiet as possible and to keep bodily movements at a minimum. Recently, Keating (42) has demonstrated that reading produced less intra-run variability than other types of activity or no activity at all.

In summary, sampling and experimental errors were mitigated by

controlling the following sources of variation: (1) appropriate calibration checks before and after each experimental session, (2) the use of young normal-hearing adults, (3) prior sampling of individual EEG activity to insure observable evoked responsivity, (4) recording sessions which were not unduly long, (5) recording evoked responses from each subject under all experimental conditions in as brief a time as is possible, and (6) the use of properly shielded, grounded, and sound-treated test suites.

Measurement of Data

After the data had been recorded, analyzed, and graphically displayed by the X-Y plotter, the evoked responses were visually examined in order to determine which components of the response were common to all subjects and present in all experimental conditions. After careful inspection of the data it appeared that there were three components whose recurrence warranted consideration. These three components were as follows:

Component 1--first prominent negativity after 80 msec.

Component 2--first prominent positivity after component 1: approximately 125-175 msec.

Component 3--the major negativity after component 2: approximately 225-275 msec.

The polarity of each of the components described above represents the positivity or negativity with respect to the slope of the component which immediately precedes it and has no reference to a zero base line.

These three components were selected since they were common to each subject in all experimental conditions and no estimation of missing data was necessary. Where some question existed regarding the location

of data points, final decisions were made by judgmental agreement among experienced workers. It was recognized that, in setting the latency limits mentioned for each component, it was likely that sub-components (e.g., "shoulders") may be interchanged across subjects and conditions. However, the compelling nature of the general configuration remained the criterion, since it has not yet been possible to parcel out and systematically classify the sub-components.

After the response components were selected for analysis, they were measured to determine the amplitude difference between a response initiated by a single click and that elicited by the second member of a click-pair for each combination of electrode location and experimental condition. Additional measurements were undertaken to determine whether or not a latency shift existed among the experimental conditions. (See Appendix A for calculation of system amplification and readout). The tabulated data for each subject under each experimental condition can be found in Appendix B.

Classification of Components

The data points utilized by this investigation are coincidental with the traditional method of classification (19, 37, 38, 39) of N1-P2-N2 of components (Figure 4). A more recent and expandable method of evoked response classification (35) indicates that the data measurements utilized by this investigation correspond to N4b, P5a, and N6a components (Figure 4).

The data resulting from the previously described procedures are presented and discussed in the following chapter.

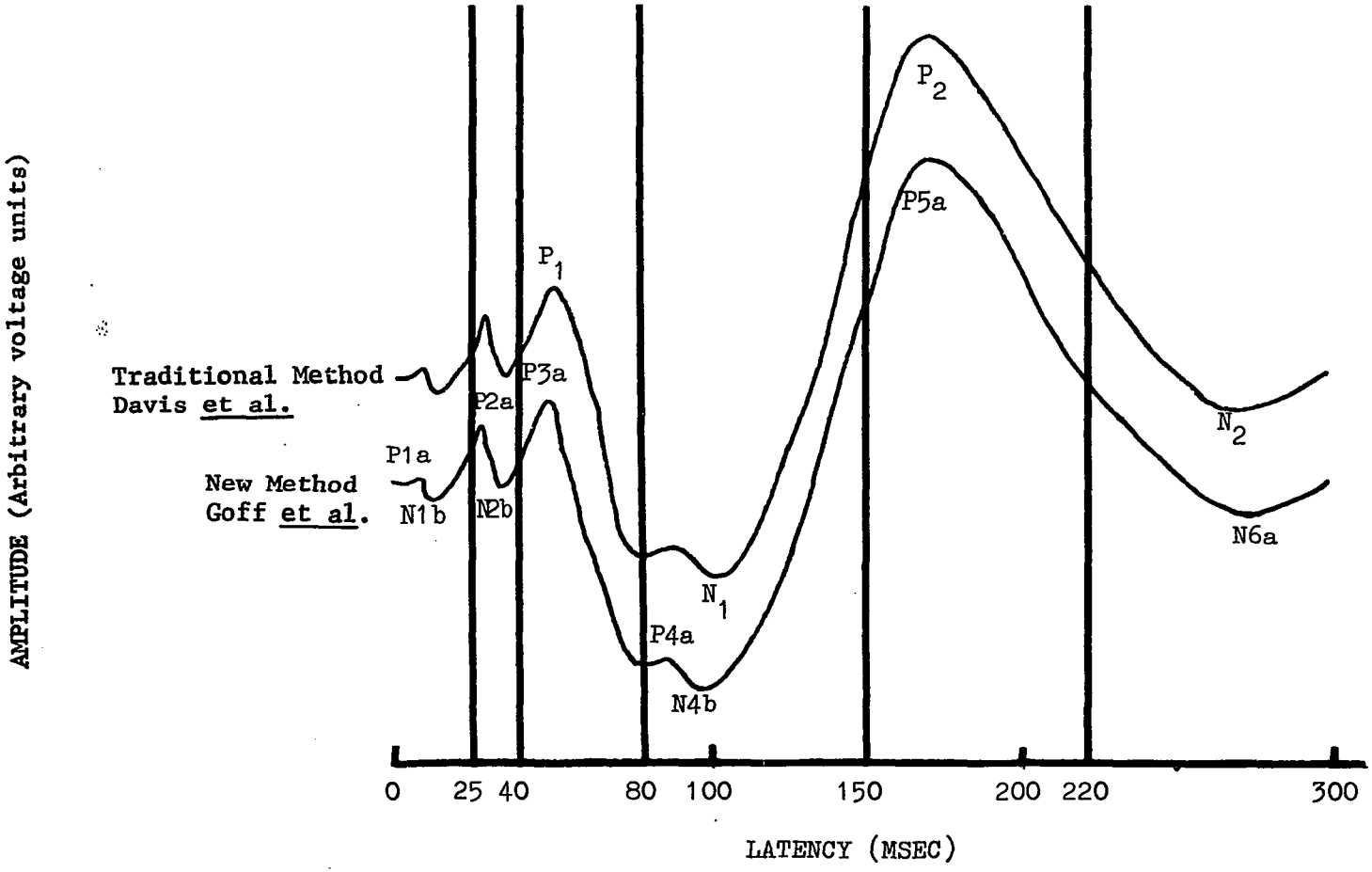


Figure 4--Representation of latencies for component classification contrasting the Traditional System and the Constant Latency System.

CHAPTER IV

RESULTS AND DISCUSSION

The purpose of the present investigation was to determine the recovery cycle of the acoustically-evoked potential as a function of inter-signal interval when each member of a click-pair was presented to opposite ears. Brief clicks, presented at 50-dB sensation level to four subjects, elicited electroencephalic potentials under four experimental conditions. Responses to single clicks and click-pairs presented alternately to the right and left ears were recorded from a bipolar montage located over each cerebral hemisphere. These were stored on magnetic tape and subsequently summed by computer program and printed out in graphic form. Measurements of amplitudes and latencies of these data were accomplished manually.

The recovery cycle of the acoustically-evoked potential, utilizing right and left ear stimulation, was determined for each subject by obtaining responses under twelve treatment conditions at a single sensation level. These data were collected during a three week period.

The derivation of the recovery cycle involved the measurement of the amplitude of responses evoked by members of a click-pair that had been presented to opposite ears, R1 and R2, and the measurement of the amplitude of responses initiated by single clicks, R3, presented to either ear. R3 provided a reference against which to judge the response evoked

by either member of the click-pair and was also used to remove the direct contamination of R1 on R2 at ISI's which were short enough to cause direct overlap of responses. The resulting information permitted the use of each subject as his own control under each of the twelve treatment conditions. The combined response of R1 and R2 represented the contaminated R2 response. This response, evoked by the second member of the click-pair was often overlapped temporally by R1, the response to the first member of the pair. To remove this contamination, R3, the response to a single click was subtracted from the complex (R1, R2). Previously in this paper the computation was designated as [R1, R2 - R3], however, for clarity and convenience to the reader the results of this computation will be represented in subsequent discussions as R2 (the uncontaminated response).

The latency of a single peak of the evoked potential, as well as the peak-to-peak amplitudes of three points, were measured. Averages, medians and ranges of these data were calculated for each experimental condition across subjects. The mean amplitudes provided group data from which percentages of recovery were computed. The computation utilized in determining the percentage of recovery is presented in a later section of this chapter. The data obtained from individual subjects can be found in Appendix B. When applicable, comparisons will be made with data reported by other investigators.

Subject Variability

The mean peak-to-peak amplitudes of the single component utilized in amplitude measurements (Figure 5), regardless of the ear stimulated or recording location, graphically illustrate the well-known fact of high intersubject variability for R3, the response evoked by a single click

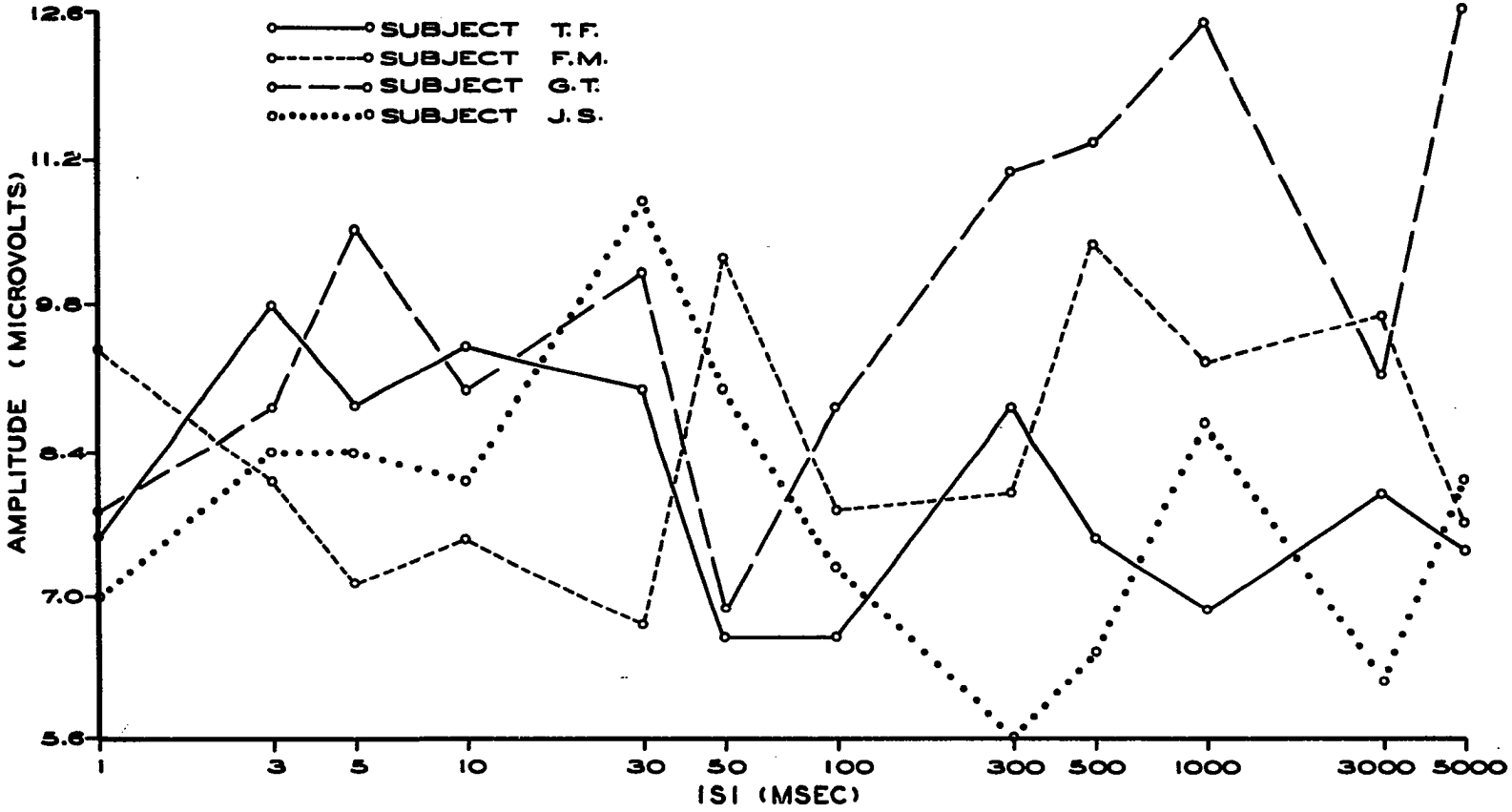


Figure 5--Mean peak-to-peak amplitudes of the N1-P2-N2 component of responses (R3) evoked by a single click without regard to ear stimulated or electrode position.

(19, 20, 30, 80). Intersubject differences across all treatment conditions ranged from a low of 5.6 microvolts to a high of 12.4 microvolts, while the mean intrasubject differences ranged from 6.9 to 12.4 microvolts. The mean amplitude values shown in Figure 5 suggested that there may be a tendency towards less intersubject variability at the shorter ISI's and that a non-linear increase in variability seemed to occur with an increase in ISI. This increase may be due to the fact that at the longer ISI's approximately twice as much time was needed to complete each recording session and the factors of subject fatigue, attention, and psychological unpleasantness associated with the task tended to increase the variability as a function of recording time. There did not appear to be any particular subject who consistently contributed to the variability across treatment conditions.

The intersubject and intrasubject variability were also reflected in the individual data when recording location and signal presentation were taken into consideration (Figures 6, 7, 8, 9).

The use of averaging techniques in the investigation of sensory evoked potentials is based on the assumption that the polarity and voltage of on-going EEG activity that are not initiated by sensory stimuli are random over time with respect to the stimulus and that positive and negative voltages added algebraically will sum toward zero as the number of samples approaches infinity. However, this assumption is somewhat mitigated by a number of the variables which may alter or influence the waveform in one way or another during an averaging procedure.

Recently, Keating (42) demonstrated that the variability of several components of the acoustically-evoked potential were affected by

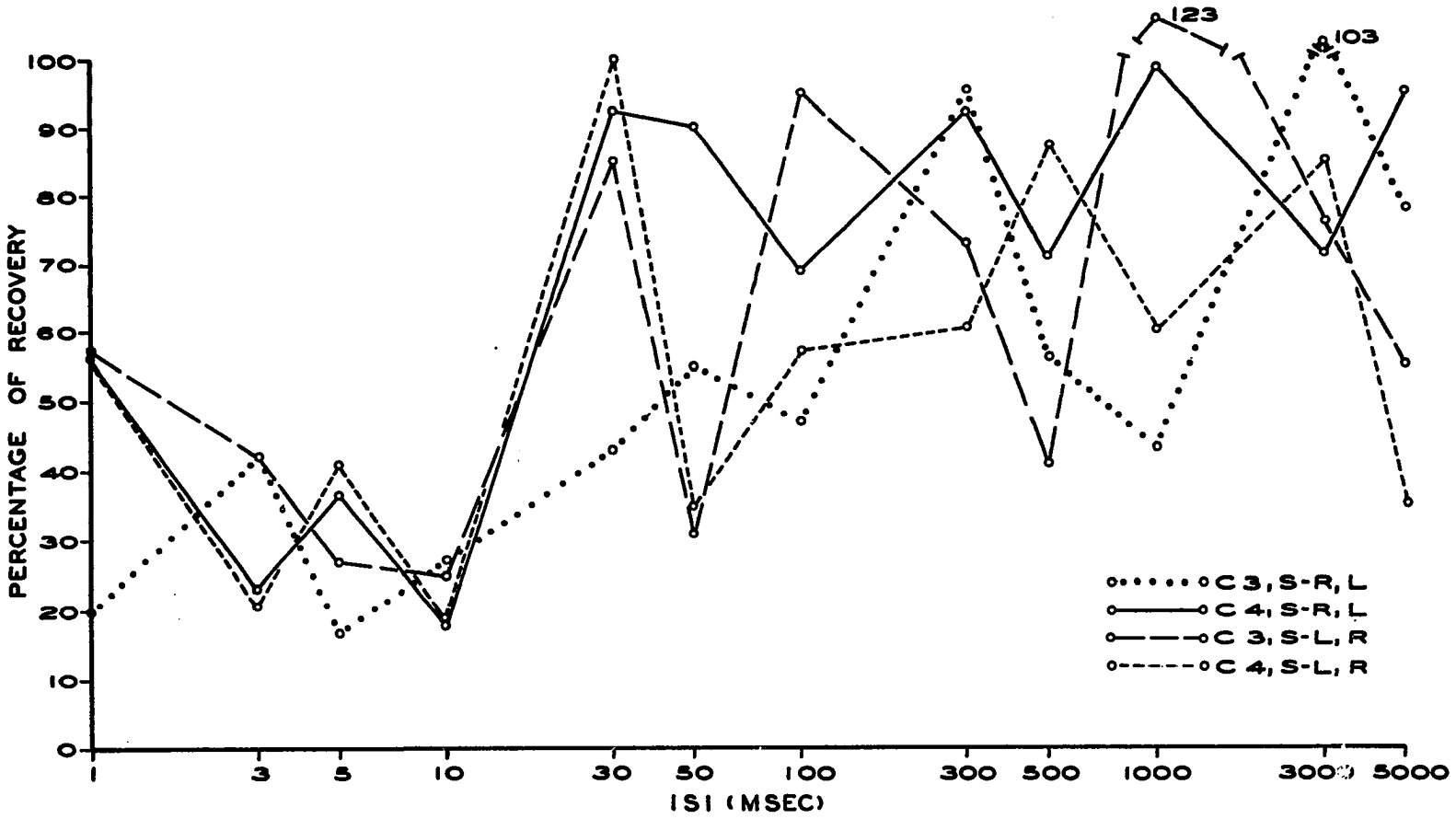


Figure 6--Subject T. F., percentage of recovery (R2/R3) of N1-P2-N2 component.

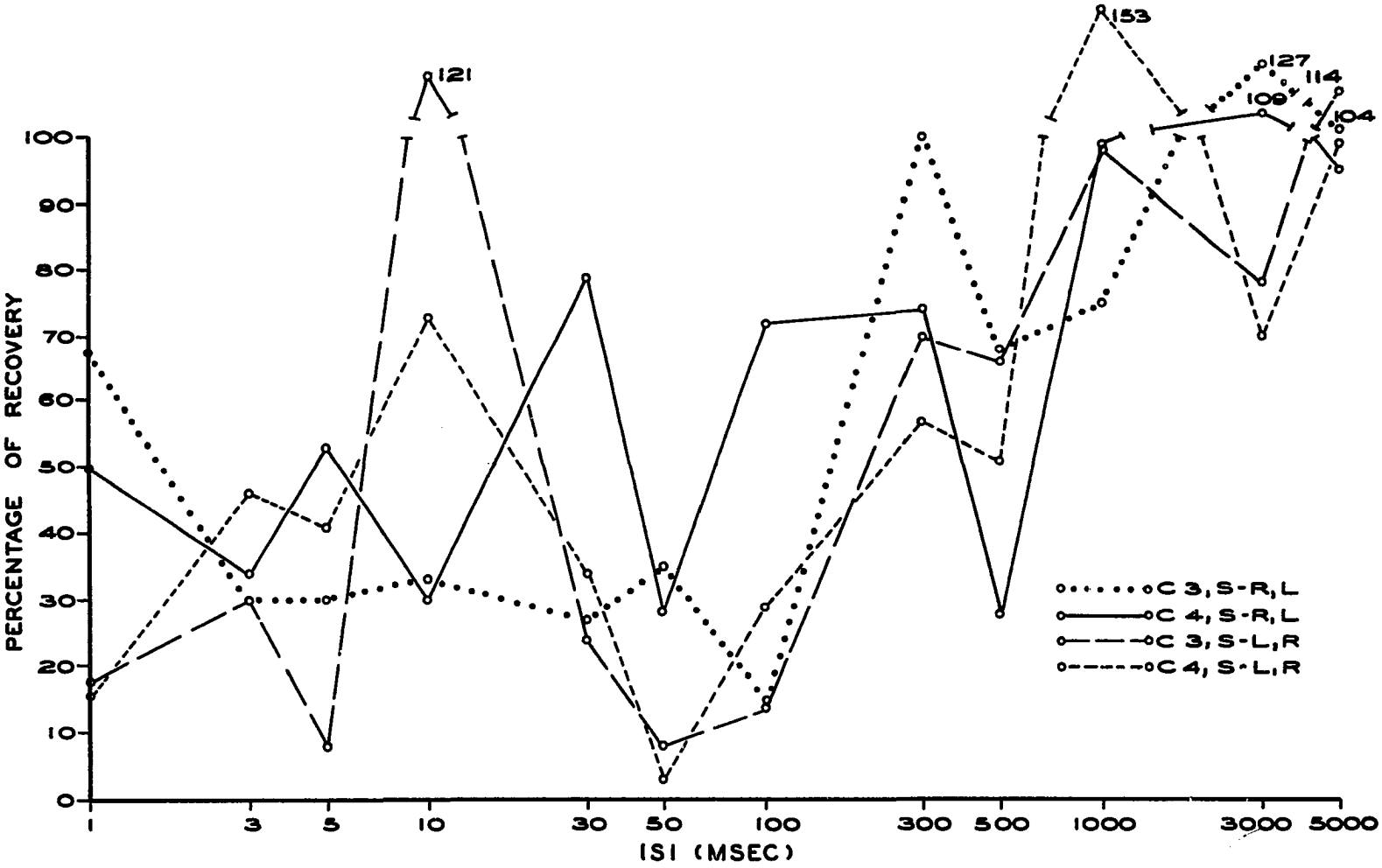


Figure 7--Subject F. M., percentage of recovery (R2/R3) of N1-P2-N2 component.

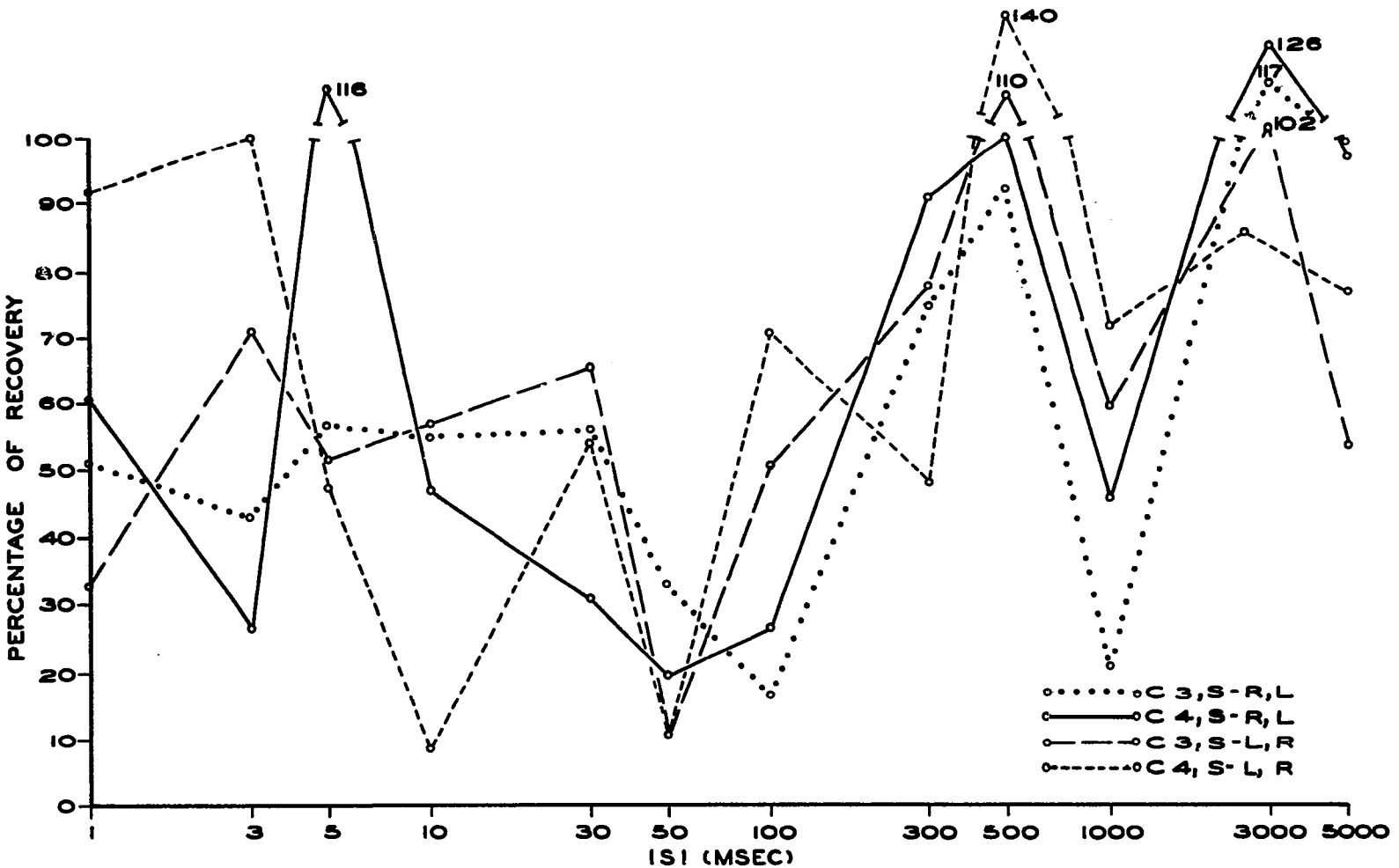


Figure 8--Subject G. T., percentage of recovery (R2/R3) of N1-P2-N2 component.

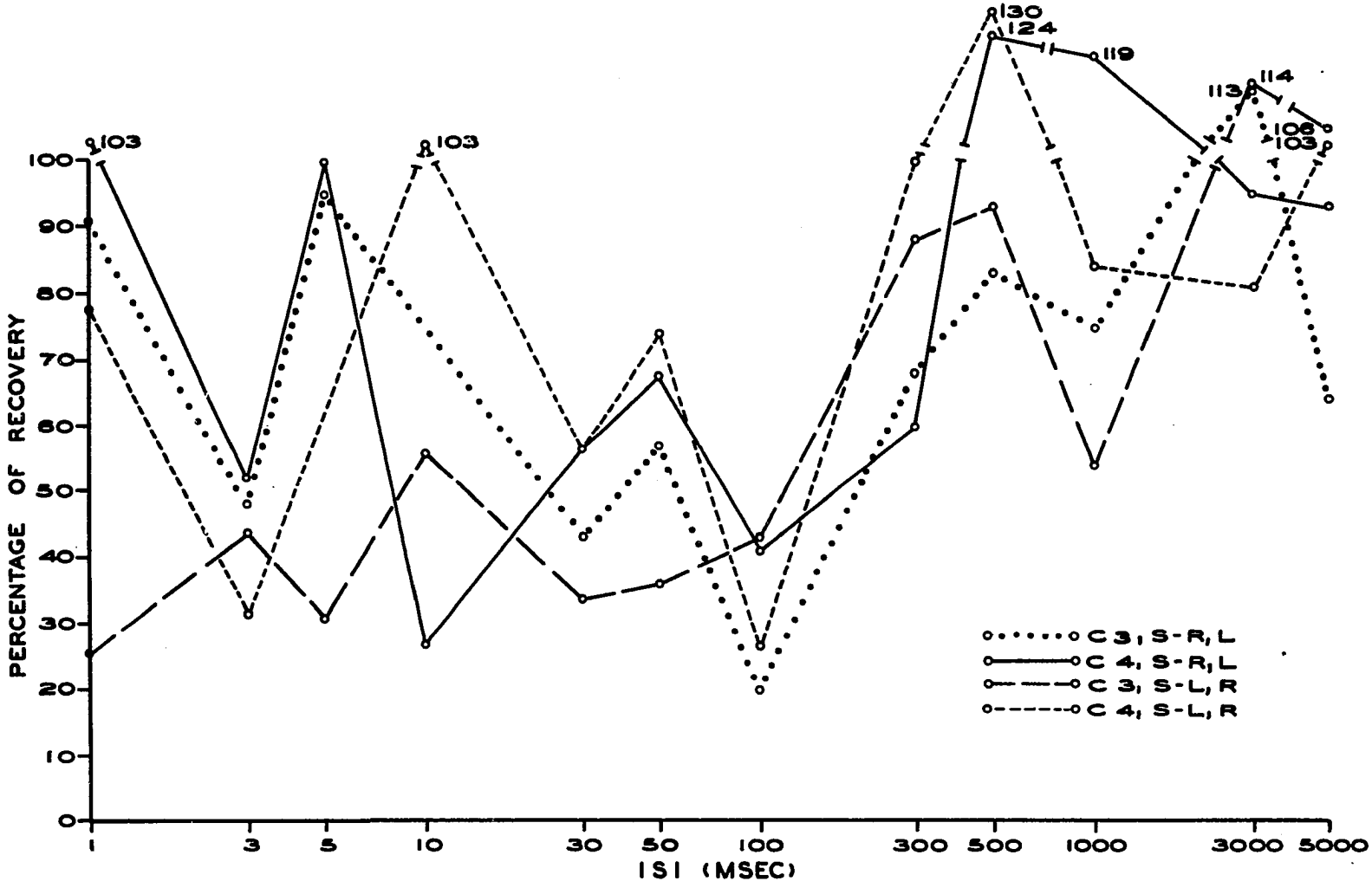


Figure 9--Subject J. S., percentage or recovery (R2/R3) of N1-P2-N2 component.

the task which the subject was required to perform during the accumulation of an average. Conditions of quiet produced a greater amount of variability than did conditions of discrimination or reading. Other factors such as subject fatigue, attention, restlessness, and the psychological unpleasantness of the task itself also lead to an increased amount of variability which cannot be adequately controlled.

The apparent solution to the problem of controlling subject variability is to increase the total number of accumulations obtained during an averaging procedure. However, this increase does not always produce a small variance. The larger the number of accumulations required to obtain a "low-noise" tracing, the longer the subject must remain in the recording session maintaining his state of alertness and a relatively motionless position. Obviously, the interactions produced by these two factors need not provide an evoked potential associated with a small amount of subject variability and might well increase the problem.

Latency

Prior to computing amplitude measurements, it was necessary to determine the presence or absence of a shift in latency associated with one or more treatment conditions. The latency point utilized for this measurement was the first major negativity that occurred after 80 msec. This point was selected for two reasons. It was common to tracings of both R3 and R2 and it was the only configurational landmark that was unambiguously identifiable in the data of all subjects under all treatment conditions. The mean latency differences between the response to a single click and that of a click-pair are shown as a function of ISI in Table 1. Only a minimal latency shift occurred under any experimental

TABLE 1

MEAN LATENCY DIFFERENCES (MSEC) BETWEEN R2 AND R3
OF FIRST MAJOR NEGATIVE COMPONENT

ISI	1	3	5	10	30	50	100	300	500	1000	3000	5000
S-R,L C3	-1.25	0.0	-3.0	-1.50	-1.75	.50	-11.0	0.0	4.0	6.75	-4.75	2.0
S-R,L C4	12.25	2.75	-1.75	-5.25	0.0	.75	-13.5	-3.75	10.50	0.0	-8.0	5.0
S-L,R C3	1.75	.25	3.50	0.0	-1.25	-7.25	- 5.25	3.25	-4.75	-1.50	2.0	2.25
S-L,R C4	.50	-.75	.75	-1.75	2.75	.25	2.0	3.50	0.0	5.50	-3.25	3.25

condition regardless of right or left ear stimulation or recording location. Furthermore, the exceptionally low values observed exhibit no trend across conditions and fluctuate close to zero (Figure 10); that is, no consistent shifts in latency were observed as a function of treatment conditions (ISI's), right or left ear stimulation, or right or left hemisphere recording locations. It should be noted that equipment fluctuations during the analysis and write-out phases of this experiment can account for only ± 1 msec in latency variability.

Amplitude

Peak-to-peak amplitude measurements were computed at three previously described latency points: N1-P2-N2. The configuration bounded by these three points proved to be the most characteristic and stable sequence of components of the evoked potential across all subjects under all treatment conditions. It was treated as a unitary response in that the amplitude of N1-P2 was added to that of P2-N2. This was done with no implication that these components were derived from the same neurological substrate, although such, indeed, might be the case. In this manner the total amplitude values were obtained for R3 at the prescribed latencies for each subject under all treatment conditions and for all possible ear and hemisphere combinations. Amplitude values of R2 were obtained, similarly, at the latencies established by R3. Once these two values had been established, the percentage of recovery was computed as:

$$\frac{R2}{R3} = \text{percent of recovery}$$

The range, mean, and median values for this computation are

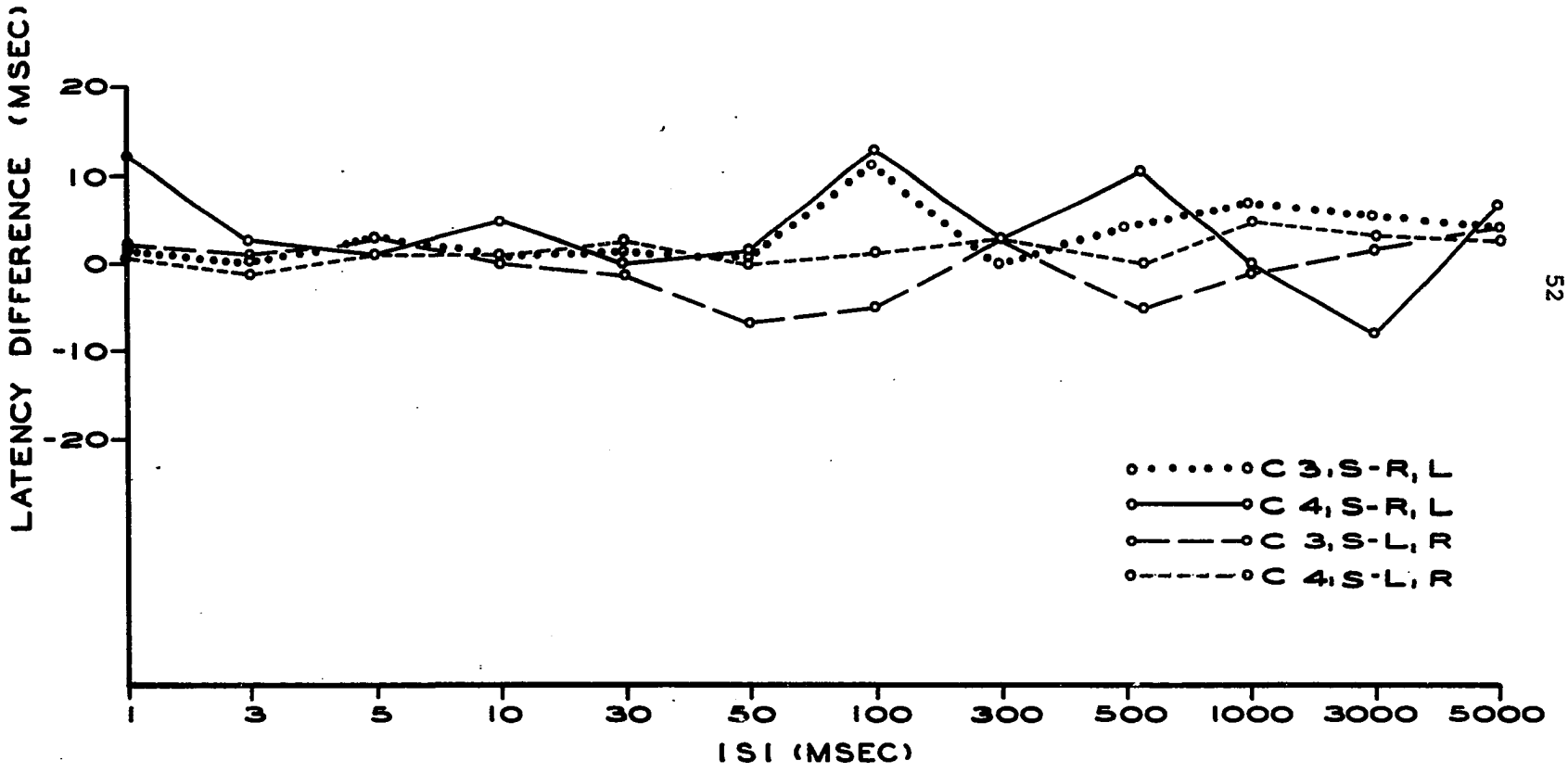


Figure 10--Mean latency differences between R2 and R3 for first major negative component.

presented in Table 2. All measures of central tendency demonstrated the effects of relatively large magnitudes of intersubject and intrasubject variability. Visual representations of the mean and median values are shown in Figures 11 and 12. Despite the extreme amplitude values used in the calculation of means, both measures of central tendency are in close agreement.

Treatment Effects

The effects produced by varying the inter-signal interval between members of a pair of acoustic clicks delivered to opposite ears at a single sensation level are graphically represented in Figures 11 and 12. The values for the mean and median percent of recovery indicated a general tendency for less than full recovery to exist from approximately 1 msec to 100 msec. However, a marked increase in recovery to approximately 75 percent was observed at 300 msec. The response continued to recover until, at 3000 msec, essentially full recovery was achieved. In addition, these data suggested the possibility of hyper-recovery or facilitation at particular ISI's e.g., 500 and 3000 msec. The meaning of these results is obscure at this time despite the fact that this phenomenon has been observed elsewhere. Shagass and Schwartz (7) demonstrated that during the determination of the recovery cycle of the somatosensory evoked potential psychiatric patients exhibited a biphasic recovery function with full recovery or facilitation present at 20 msec and again at approximately 100 msec. Facilitation, however, was not observed in normals until 100 to 300 msec.

The mean values shown in Figure 11 were averaged across all subjects in order to demonstrate the general configuration of the recovery

TABLE 2

RANGE DIFFERENCE, MEAN, AND MEDIAN VALUES COMPUTED IN PERCENTAGE OF RECOVERY AT 12 INTER-SIGNAL INTERVALS, TWO ELECTRODE POSITIONS (LEFT, C3; RIGHT, C4), AND TWO PRESENTATION PATTERNS OF SIGNAL LATERALITY (S-R,L; S-L,R)

ISI (MSEC)	Range Differences				Mean				Median				ISI (MSEC)
	C3		C4		C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	71	39	53	76	58	34	68	61	60	30	59	67	1
3	18	41	29	79	41	47	34	50	43	43	31	39	3
5	78	44	79	19	50	30	77	47	49	29	77	44	5
10	47	96	29	94	47	65	31	51	44	57	29	46	10
30	29	61	61	66	42	52	65	61	43	50	68	56	30
50	24	28	70	69	45	22	52	30	45	21	48	23	50
100	32	81	45	44	25	51	52	46	19	47	55	42	100
300	32	18	32	52	85	77	79	66	85	76	83	59	300
500	36	69	96	89	75	78	81	102	76	80	86	109	500
1000	54	69	73	93	54	84	91	92	59	79	98	78	1000
3000	24	38	55	16	115	93	100	81	115	90	102	83	3000
5000	40	60	4	68	86	82	95	79	88	81	95	88	5000

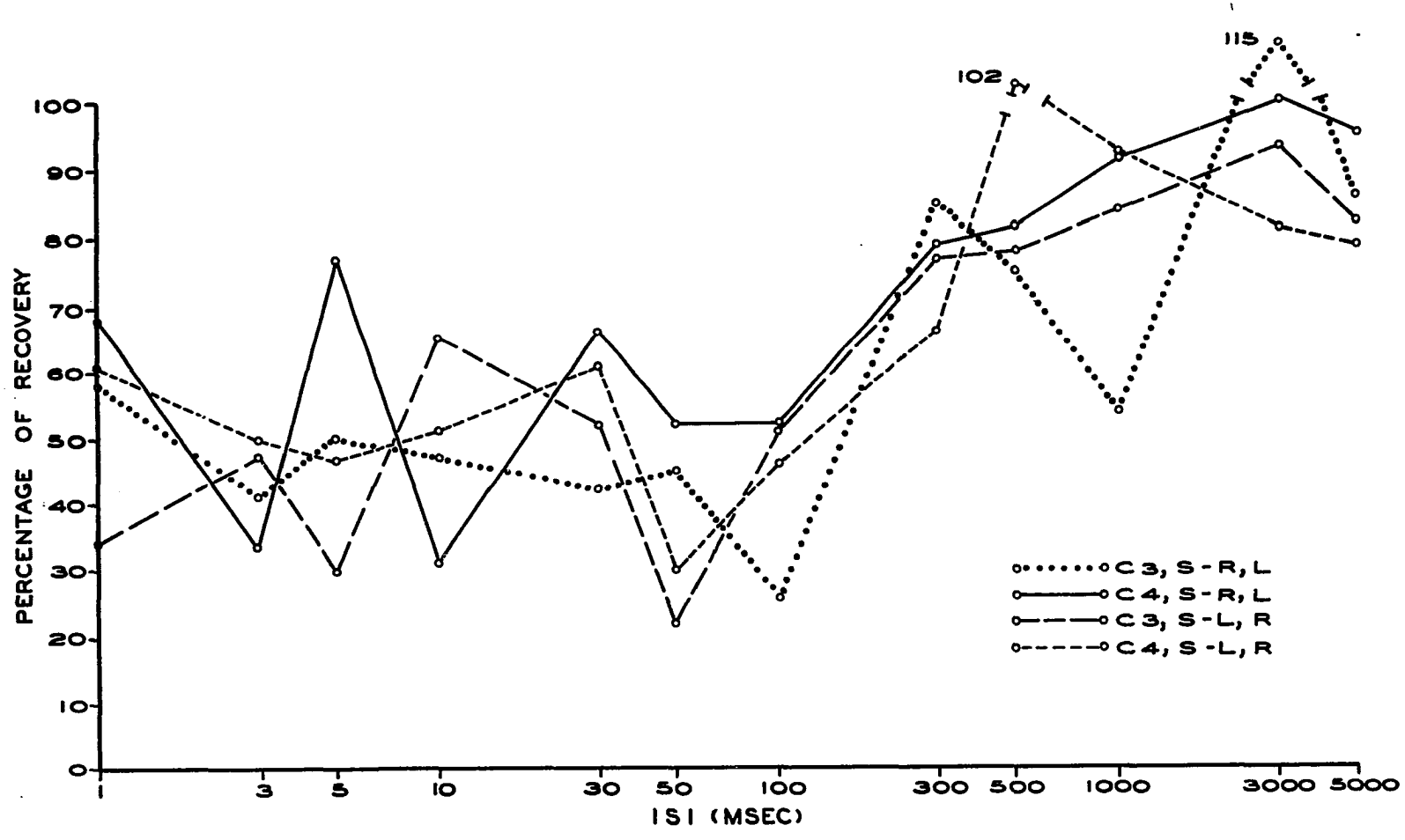


Figure 11--Mean percentage of recovery (R2/R3) of N1-P2-N2 component.

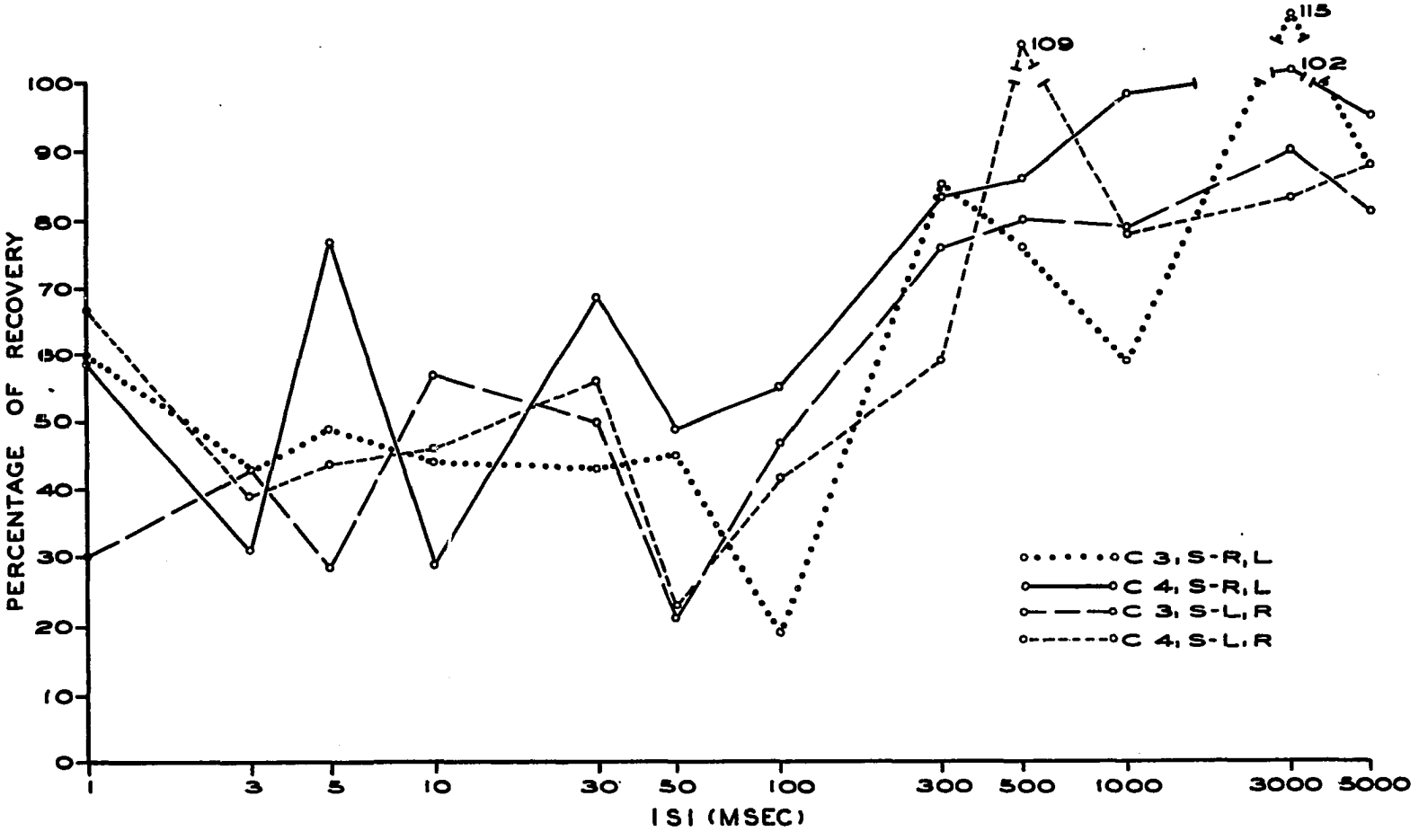


Figure 12--Median percentage of recovery (R2/R3) of N1-P2-N2 component.

cycle as a function of inter-signal interval without regard to ear stimulated or recording location (Figure 13). This configuration indicated that response recovery did not appear to be markedly influenced as the ISI was varied between 1 msec and 30 msec. However, between intervals of 50 and 3000 msec a gradual increase in the percentage of recovery was observed. These data, like those in Figures 11 and 12, suggest a general tendency for less than full recovery to exist from approximately 1 msec to 50 msec, where the general order of magnitude is 40 to 50 percent. An increase in recovery is observed from 50 msec to 300 msec and the recovery curve continue to rise toward essentially full recovery at 3000 msec.

It is interesting that the results of the present investigation do not demonstrate the complete obliteration of cerebral responsivity at any ISI. These findings are in contrast with the results obtained by Ruhm (66) during a monaural recovery study in which a total absence of responsivity was observed at ISI's of 1, 4, 8 and 10 msec. Allison (3) presented evidence that during the recording of somatosensory evoked potentials two subjects demonstrated considerable recovery as early as 300 msec, although complete responsivity was not obtained until an interval of 2000-3000 msec. However, in four other subjects, the recovery cycle was much slower and was not complete at an ISI of 4000 msec. The high amount of intersubject and intrasubject variability obtained during this investigation precluded comparisons such as these, however, the findings suggest complete recovery by approximately 3000 msec.

Although the measures of central tendency show that a signal presented to one ear is not capable of obliterating cerebral responsivity

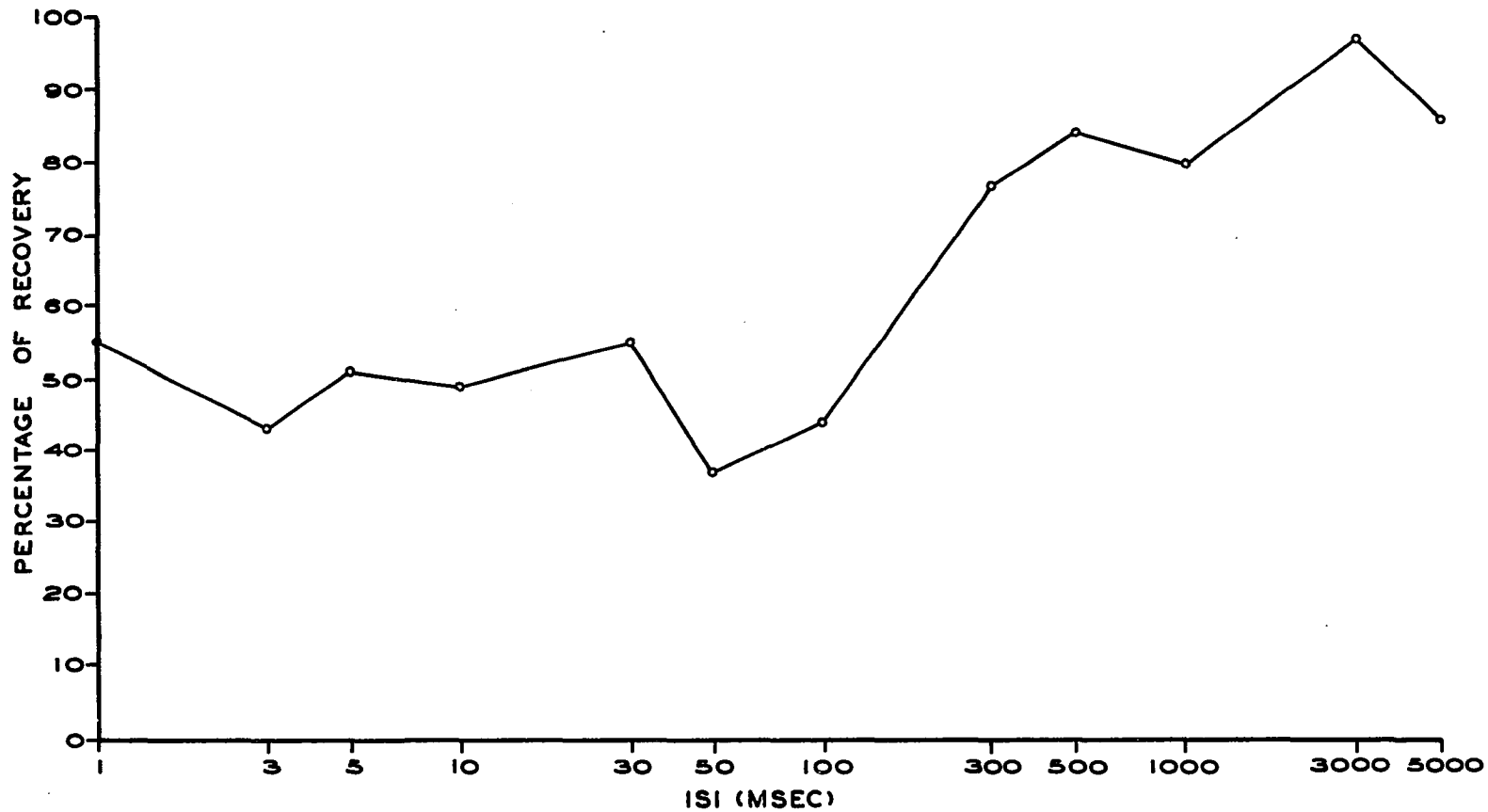


Figure 13--Grand mean percentage of recovery (R2/R3) of N1-P2-N2 component for all subjects without regard to ear stimulated or electrode location.

evoked by the subsequent stimulation of the opposite ear, individual subjects demonstrated a decrease in responsivity at the 50 msec or 100 msec ISI (Figures 6, 7, 8, 9). This effect was shown by all subjects except subject T. F. (Figure 6). The effect is also suggested in the median data, Figure 12, where all but conditions C4, S-R,L illustrate it.

Ear and Hemisphere Effects

The median data for all combinations of ear stimulated and scalp recording sites are presented in Figures 11 and 12. No consistent interactions between ears or hemispheres were observed when signals were presented in right-left or left-right order and recordings were obtained simultaneously from areas over the ipsilateral and contralateral cerebral hemispheres. However, the condition of C4, S-R,L, as shown in the median data (Figure 12), evidenced a considerable amount of recovery at the short ISI's of 5 and 30 msec. Unfortunately, it was not possible to resolve whether or not the increased recovery was artifactual, resulting from the high degree of subject variability or whether this particular combination of signal presentation and recording location enhanced the recovery process at short ISI's. Further investigation of this finding is warranted when the factors contributing to subject variability have been thoroughly investigated.

It was anticipated that a differential effect in favor of one ear or one hemisphere might be observed in the acoustically-evoked potentials. There was no indication of such an effect. Of course, these negative results do not preclude the possibility that this phenomenon might be recorded under different experimental conditions. For example, an observation of increased responsivity or inhibition would be more

likely if the technique employed reduced the intersubject and intrasubject variability and approached the neurological substrates directly rather than from a scalp recording. There is ample evidence (8, 12, 63, 76, 79) that cortical and sub-cortical recordings of sensory evoked potentials clearly demonstrate a preponderance of one ear or one hemisphere when the locations of the recording electrodes, relative intensity of signals, and psychophysiological state of the subject are suitable.

The possibility exists that the two ears are represented at the auditory cortex by two different populations of neural units (8). However, the physiological evidence presented by Rosenzweig (62) indicates that the two ears are not represented by independent populations but by overlapping neural populations and that upon successive stimulation an interaction between the two populations occurs. The extent to which these two populations overlap remains unanswered. It is possible that the overlap is extensive and the ipsilateral population is largely contained within the contralateral population so that many of the units which respond to ipsilateral stimulation also respond to contralateral stimulation. The results of animal investigations (63) suggest the ipsilateral representation to be approximately three-fourths the size of the contralateral representation.

It has been demonstrated by Rosenzweig (62, 63) that the two populations are not entirely independent. Simultaneous stimulation of the two ears in anesthetized cats usually resulted in a partial summation; that is, the combined response was somewhat larger than the response initiated by a single signal presented to the contralateral ear, It was not as large, however, as the combined ipsilateral and contralateral

responses. Independent populations would presumably yield an aggregate response twice that of a single response.

The presentation of paired stimuli provides some estimate of the relative number of neural units which comprise the two auditory populations. Presumably, when one ear is stimulated the neural impulses are distributed to the neuronal population representing that ear. However, when a second signal is presented within a relatively short interval, some of the previously excited units may not be capable of firing due to prior stimulation. Hence, the more overlap between the two populations, the more units the second signal will find inexcitable.

The amount and extent of inexcitability appears to be associated with the temporal relationships of the signal. Ruhm (66) has recently established that monaural presentations of paired auditory stimuli result in a total absence of responsivity at short ISI's. Rosenzweig and Rosenblith (64) have also indicated that, in all aspects of the somatosensory recovery cycle, the second response is more strongly depressed by a prior signal to the same ear than by a prior signal to the opposite ear. These results suggest that the projections from the two ears are not entirely common, although their overlap may be considerable.

The results of the present investigation support the hypothesis that the number of neural units found inexcitable by the second signal appear to be associated with the temporal relationships of signal presentations. This was evidenced by the fact that it was not possible to demonstrate less than approximately 40 to 50 percent recovery at the shortest ISI's when signals were alternately presented to both ears at a constant sensation level. The probability of demonstrating the total

absence of responsivity during binaural stimulation may be a function of, not only ISI and order of signal presentation, but of such variables as the relative intensities of the two signals.

Suggestions for Future Research

In the past decade advances in technology have furthered considerable research in the area of sensory evoked potentials. However, many areas of interest have remained untouched.

The effects of time and intensity on the recovery cycle of the acoustically-evoked potential should be considered. The existence of a time-intensity trading relationship between ears or between hemispheres resulting in enhancement or inhibition of responsivity should be explored when one or both parameters are varied. Perhaps a neural compensation exists for increased intensity at short ISI's and it may be possible to drive the recovery cycle to zero percent recovery with a differential time and intensity trade.

A cross-modality comparison of the recovery cycle of sensory evoked potentials would lend new information regarding the processing of information within the central nervous system. The available evidence (3, 4) suggests that the recovery function of sensory evoked potentials may have a longer time course within the same modality than in interactions across modalities. If explored further, such comparisons might elucidate similar relationships between priorities of attentiveness and the neurological substrates that mediate them.

CHAPTER V

SUMMARY AND CONCLUSIONS

The use of signal averaging for the investigation of electroencephalic potentials has provided some indicants of the complex processing of sensory stimuli within the central nervous system. Recently, investigators have been concerned with the determination of various components of the potentials evoked by specific sensory modalities. Various inferences and conclusions have been drawn relative to the averaged or summed response across sensory modalities, thus providing increased knowledge relative to the role the central nervous system plays in processing sensory information.

In audition, the determination of the recovery cycle of the acoustically-evoked potential has provided some estimate of cerebral responsivity. The recovery cycle may be determined by administering pairs of stimuli separated by varying intervals. The relative size of the second response of a pair, compared to the first response, indicates the extent to which the system has recovered its capacity to respond after a given interval. The magnitude of the response and the rate of recovery should serve not only as a measure of recovery function but also might provide some indication of the relative roles played by each ear and cerebral hemisphere in the processing of auditory information.

Experimental Design

The purpose of this study was to determine the recovery cycle of the acoustically-evoked potential as a function of inter-signal interval when each member of paired stimuli were presented to opposite ears and evoked potentials were recorded from areas overlying both cerebral hemispheres.

Evoked responses to clicks presented at 50-dB sensation level were obtained from normal-hearing subjects. The 0.1-msec clicks were presented alternately to the right and left ears during each of four experimental conditions. The temporal sequencing of these signals allowed a total of 60 clicks to be accumulated to obtain an average. Data for right and left ear stimulation, as well as recordings from areas overlying the right and left hemispheres, were stored separately on magnetic tape along with trigger pulses that enabled the data to be retrieved separately during the analysis phase of the study.

The responses evoked by click-pairs presented alternately at 50-dB sensation level to the right and left ears were obtained for each subject at twelve different inter-signal intervals; 1, 3, 5, 10, 30, 50, 100, 300, 500, 1000, 3000, and 5000 msec. The response evoked by a single click was interspersed among the responses to click-pairs. This response served as a criterion against which to judge tne responses evoked by both members of the click-pair. The response evoked by a single click was also subtracted from the combined response of the click-pair, leaving only the effects produced by one predisposing signal upon the other.

Measures of central tendency and variability were obtained for all subjects during each treatment condition and under all combinations of

signal presentations and recording locations.

Results and Conclusions

The results of this investigation indicate that when paired acoustic signals are delivered to opposite ears at a 50-dB sensation level and separated by various intervals, only a partial reduction in evoked cerebral responsivity is observed. This reduction in responsivity is related to the inter-signal interval. However, the intersubject and intrasubject variability of the N1-P2-N2 component was of such magnitude that a definitive estimate of recovery cycle was not possible. There was a general tendency for less than full recovery to exist from approximately 1 msec to 100 msec. At 300 msec a noticeable increase in recovery occurred. This increase continued until approximately 3000 msec where full recovery was observed.

The latency of the first major negativity occurring after 80 msec was not affected by the treatment conditions applied. No consistent shifts in latency were observed at any combination of signal presentation and recording location. It would appear that the undefined neurological substrates utilized in processing auditory information with respect to latency are not necessarily the same as those which comprise the magnitude gradients of cerebral responsivity. The fact that interaural recovery functions, unlike monaural functions, do not go through a complete refractory phase supports the concept of bilateral neurological representation of each ear. The failure to demonstrate a differential rate of recovery between hemispheres or between ears does not mitigate the possibility that this phenomenon might be observed under different experimental conditions.

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APPENDIXES

APPENDIX A

CALIBRATION PROCEDURES

RECORDING INSTRUMENTATION

Step 1. Turn on equipment and allow a warm-up period of at least one hour prior to calibration.

Step 2. Adjust the output of the audio oscillator (Hewlett-Packard 201C).

(a) Connect output of oscillator to input of Darcy DMM (VAC) in parallel with EXT. CAL. Input of P511.

(b) Adjust oscillator attenuator to read 1.73v RMS.

Step 3. Gain calibration of P511 amplifiers.

(a) Set Input switch to CAL.

(b) Set Fall Time Constant switch to 1.

(c) Set Amplification switch to 50 x 1000.

(d) Set Rise Time Constant switch to .3.

(e) Connect output of oscillator (100 Hz at 1.730v RMS) to EXT. CAL. Input.

(f) Connect output of P511 to DMM (VAC) and read 1.76v by adjusting ADJ. CAL. knob.

Step 4. Place P511 amplifiers in operating position.

(a) Set Input switch to USE.

(b) Set Calibrator switch to 200 μv.

(c) Set CAL. switch to A.C.

(d) Set Fall Time Constant switch to 1.

(e) Set amplification switch to 50 x 1000.

(f) Set Rise Time Constant switch to .1.

Step 5. Balance DC level of the 60-Hz filter (A.P. Circuit Corporation, APN-60).

(a) Short the input to ground.

(b) Connect the filter output to the DMM (Darcy 440).

(c) Set the DMM on VDC.

(d) Adjust the DC pot on filter to read 0v on DMM.

Step 6. The calibration procedures for the CAT, FM Tape System, and X-Y plotter were supplied by their respective manufacturers. The calibration procedure for the analog-to-digital converters was done in accordance with procedures developed in this laboratory.

Record Calibration Signal

Step 1. Calibrate frequency output of audio oscillator (Hewlett-Packard 201C) for 30 Hz.

(a) Connect output of audio oscillator to input of interval timer and universal counter (TSI Model 361).

(b) Adjust frequency control on audio oscillator to read 30 Hz on TSI.

Step 2. Calibrate P511 amplifiers for 25,000 gain (See Step 3, Recording Instrumentation).

Step 3. Connect output of audio oscillator to microvolter (General Radio Type 548C) set for μv output.

Step 4. Adjust output of audio oscillator for 2.2μv input to microvolter. Set output of microvolter for 10μv.

Step 5. Connect output of microvolter in parallel with 600 ohm load resistor to grids 1 and 2 of P511 amplifier.

Step 6. Connect output of P511 amplifier to input of data converter (Mnemotron M1000).

Step 7. Parallel the output of data converter and monitor scope and CAT monitor.

Step 8. Record the calibration signal on magnetic tape at 3 and 3/4 IPS.

Step 9. Play back the recorded 10μv signal at 7 and 1/2 IPS through the data converter to the CAT. Accumulate 60 samples. Use input converter Grason-Stadler 1211) set for sine wave operation and CAT trigger units (Grason-Stadler 1056A) for triggers and synchronization.

Calculation of System Amplification and Readout

Step 1. Using the X-Y plotter, write out the average of 60 accumulations of the 10μv amplified sine wave on calibrated graph paper.

Step 2. Determine the amplitude of the sine wave in inches (7.3).

Step 3. Calculate the value of 1μv (.73 inches).

Step 4. Calculate the value of 1 inch (1.3698μv).

Step 5. Determine the value of 1/10 inch (.13698μv).

APPENDIX B

INDIVIDUAL SUBJECT DATA

TABLE 3

INDIVIDUAL AMPLITUDE DATA (MICROVOLTS) OF MAJOR
N1-P2-N2 COMPONENT FOR SUBJECT T.F.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	8.5	7.1	8.0	6.3	1.7	4.1	4.5	3.5	1
3	6.3	5.6	8.4	19.0	2.7	2.4	2.0	3.9	3
5	4.9	6.3	10.6	13.4	0.8	1.7	3.9	5.5	5
10	9.2	11.6	7.8	9.0	2.5	2.9	1.4	1.7	10
30	7.8	4.6	10.8	12.5	3.4	3.9	9.9	12.5	30
50	6.9	6.9	5.5	7.3	3.8	2.1	4.9	2.5	50
100	5.0	5.6	8.3	7.1	2.4	5.3	5.7	4.1	100
300	7.7	7.1	11.8	8.4	7.3	5.2	10.8	5.0	300
500	6.7	8.5	5.9	8.8	3.8	3.5	4.2	7.7	500
1000	6.4	6.2	7.6	7.3	2.8	7.6	7.4	4.3	1000
3000	9.0	5.7	9.7	7.7	9.2	4.3	6.9	6.6	3000
5000	8.3	5.9	8.8	6.4	6.4	3.2	8.4	2.2	5000

TABLE 4

INDIVIDUAL AMPLITUDE DATA (MICROVOLTS) OF MAJOR
N1-P2-N2 COMPONENT FOR SUBJECT F.M.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	7.4	9.4	7.0	13.6	5.0	1.7	3.5	2.1	1
3	7.4	6.0	9.5	9.7	2.2	1.8	3.2	4.5	3
5	6.6	5.5	6.6	9.7	2.0	0.4	3.5	3.9	5
10	8.4	5.3	6.6	9.9	2.8	6.4	2.0	7.3	10
30	4.6	8.3	6.0	7.8	1.3	2.0	4.8	2.7	30
50	10.4	8.3	12.2	10.1	3.6	0.7	3.4	0.3	50
100	7.3	9.9	6.0	8.3	1.1	1.4	4.3	2.4	100
300	5.6	9.0	8.1	9.4	5.6	6.3	6.0	5.3	300
500	3.9	11.2	11.1	15.4	2.7	7.4	3.1	7.8	500
1000	7.3	7.4	13.3	9.0	5.5	7.3	13.0	13.7	1000
3000	3.6	7.7	10.9	16.1	4.6	6.0	11.9	11.3	3000
5000	7.8	7.8	5.3	9.9	8.1	9.0	5.0	9.8	5000

TABLE 5

INDIVIDUAL AMPLITUDE DATA (MICROVOLTS) OF MAJOR
N1-P2-N2 COMPONENT FOR SUBJECT G.T.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	7.4	5.9	9.4	8.7	3.8	2.0	5.7	8.0	1
3	6.2	10.9	6.3	11.8	2.7	7.7	1.2	11.8	3
5	10.5	9.0	9.7	13.0	6.0	4.6	11.2	6.0	5
10	8.1	7.6	10.8	9.4	4.5	4.3	5.0	0.8	10
30	10.2	9.0	11.8	9.5	5.7	5.9	3.6	5.2	30
50	5.6	7.4	5.7	8.7	1.8	0.8	1.1	1.0	50
100	7.4	9.9	11.8	6.3	1.3	5.0	3.2	4.5	100
300	8.0	9.7	13.3	13.3	6.0	12.5	12.0	6.4	300
500	12.2	8.3	14.0	11.1	11.2	9.1	14.0	15.5	500
1000	8.1	11.5	15.0	15.3	1.7	6.9	6.9	10.9	1000
3000	6.6	6.0	13.9	9.9	7.7	6.2	17.5	8.5	3000
5000	11.3	11.8	12.3	15.0	11.2	6.3	11.9	11.5	5000

TABLE 6

INDIVIDUAL AMPLITUDE DATA (MICROVOLTS) OF MAJOR
N1-P2-N2 COMPONENT FOR SUBJECT J.S.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	4.6	7.4	4.5	11.6	4.2	2.0	4.6	9.1	1
3	9.1	8.8	6.2	9.5	4.3	3.9	3.2	3.1	3
5	7.8	8.5	5.3	11.6	7.4	2.7	5.3	7.0	5
10	7.0	9.0	5.2	11.1	5.2	5.0	1.4	11.3	10
30	8.4	12.5	8.8	13.4	3.6	4.2	5.0	7.7	30
50	5.9	12.2	5.2	12.7	3.4	4.3	3.5	9.2	50
100	6.9	6.4	10.6	5.2	1.4	2.8	4.3	1.4	100
300	3.5	7.1	4.2	7.7	2.4	6.3	2.5	7.7	300
500	6.4	3.8	10.1	5.2	5.3	3.5	12.5	6.7	500
1000	7.8	5.2	15.5	6.3	5.9	2.8	18.5	5.3	1000
3000	4.2	4.9	9.0	6.7	4.8	5.6	8.5	5.5	3000
5000	7.7	4.5	12.3	8.0	4.9	4.8	11.5	8.3	5000

TABLE 7

INDIVIDUAL LATENCY DATA (MILLISECONDS) OF COMPONENT #1;
FIRST MAJOR NEGATIVITY OCCURRING AFTER 80 MSEC,
FOR SUBJECT T.F.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	85	78	80	75	80	72	70	95	1
3	110	80	103	85	110	83	90	84	3
5	85	80	83	77	90	85	89	86	5
10	85	80	88	85	87	80	110	80	10
30	80	103	85	110	90	110	90	120	30
50	80	80	80	85	92	90	80	85	50
100	85	85	75	75	91	75	80	72	100
300	93	85	85	80	87	83	83	85	300
500	95	75	90	80	93	87	95	80	500
1000	80	100	80	100	91	80	82	80	1000
3000	85	97	90	85	80	105	80	95	3000
5000	77	85	84	100	80	85	85	85	5000

TABLE 8

INDIVIDUAL LATENCY DATA (MILLISECONDS) OF COMPONENT #1;
FIRST MAJOR NEGATIVITY OCCURRING AFTER 80 MSEC,
FOR SUBJECT F.M.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	100	103	100	105	106	108	105	110	1
3	95	90	97	85	99	105	95	78	3
5	85	103	80	95	70	90	80	85	5
10	85	93	83	90	95	95	83	100	10
30	75	87	90	85	77	65	80	75	30
50	110	100	112	95	112	95	110	90	50
100	107	85	105	87	128	80	105	87	100
300	92	95	93	90	98	90	86	93	300
500	100	87	98	82	98	62	95	45	500
1000	90	95	93	90	90	80	92	90	1000
3000	100	65	97	100	92	67	96	92	3000
5000	95	100	96	95	96	104	93	103	5000

TABLE 9

INDIVIDUAL LATENCY DATA (MILLISECONDS) OF COMPONENT #1;
FIRST MAJOR NEGATIVITY OCCURRING AFTER 80 MSEC,
FOR SUBJECT G.T.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	105	95	100	93	105	97	103	105	1
3	95	110	77	120	90	120	90	120	3
5	126	100	126	98	122	100	127	106	5
10	103	95	102	100	98	97	102	110	10
30	97	85	97	85	80	88	85	100	30
50	95	92	95	95	100	85	97	90	50
100	112	103	120	103	97	105	105	115	100
300	80	95	75	110	87	102	90	112	300
500	97	110	97	101	120	102	105	95	500
1000	95	87	90	85	90	85	107	95	1000
3000	110	98	110	87	115	105	120	108	3000
5000	103	110	105	115	100	90	94	95	5000

TABLE 10

INDIVIDUAL LATENCY DATA (MILLISECONDS) OF COMPONENT #1;
FIRST MAJOR NEGATIVITY OCCURRING AFTER 80 MSEC,
FOR SUBJECT J.S.

ISI (MSEC)	(R3)				(R1, R2 - R3)				ISI (MSEC)
	C3		C4		C3		C4		
	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	S-R,L	S-L,R	
1	108	108	103	100	100	112	103	112	1
3	110	115	110	108	110	90	115	105	3
5	100	95	112	95	100	115	99	95	5
10	100	108	120	90	93	110	105	96	10
30	90	110	90	105	100	115	96	90	30
50	110	95	115	89	120	95	112	92	50
100	103	88	101	95	112	145	103	140	100
300	120	90	120	85	100	90	100	90	300
500	100	105	110	110	100	110	100	111	500
1000	100	105	111	105	100	115	115	115	1000
3000	120	108	106	112	120	110	117	121	3000
5000	100	95	100	100	90	103	100	107	5000