EXPLORING CHILDHOOD AUTISM:

AN ELECTROPHYSIOLOGIC APPROACH

by

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ABSTRACT

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Event-related potentials were recorded from autistic children and normal children of the same age in association with auditory and visual stimulation. In the present investigation, both transmission through the brain of auditory and visual information and short-term storage of this information were examined in a range of experimental conditions. The investigation tested the hypothesis that behavioral impairments of autistic children are associated with aberrant brain processes.

Scalp-recorded potentials in the autistic children were different from those of normal children in the following ways: 1. Cortical auditory evoked potentials were affected by interstimulus interval and by task requirements; 2. Late positive parietal potentials associated with signal stimuli in an auditory discrimination task were markedly variable; 3. Late positivity was seen in parietal waveforms associated with nonsignal stimuli, as well as with the signal stimuli, in the auditory discrimination task; 4. Potentials associated with deletion of expected auditory stimuli and potentials associated with

deletion of expected visual stimuli were infrequent or absent.

Electrophysiologically defined defects in the autistic children were related to impairments in particular stages of sensory information processing that were defined behaviorally. It was proposed that in individual autistic children, defective physiologic processes affect processing of sensory information at one or several levels within the nervous system hierarchy. Further, it was proposed that impaired processes are reflected in a range of aberrant behaviors that depend upon perceptual skills.

It was concluded that the experimental format developed would be useful for obtaining objective physiologic measures of abnormal brain processes and in turn, for providing insight into aberrant forms of human behavior in mental illness.

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CHAPTER I

INTRODUCTION

Clinical features of Childhood Autism were first described by Kanner in 1943. Experimental investigations of the disorder have mainly utilized one of two distinct approaches, employing either psychological or physiological methods. Psychologists have depended soley upon behavioral data, making it difficult to infer the nature of aberrant intracerebral processes associated with the deviant behavior. The physiological approach, on the other hand, relies upon application of specific biologic techniques such as the electroencephalogram (EEG) to the study of certain neurophysiologic processes within the organism. This experimental approach usually obtains no behavioral data, thus limiting the inferences that can be made on the nature of the relations between the observed processes within the organism and the characteristic behavioral disturbances of Childhood Autism. Apparently what is needed is a way of combining the psychological and physiological approaches.

During the past fifteen years an area of research has developed that provides the format for this combination, namely the study of human scalp-recorded, event-related potentials (ERP). The current investigation is intended to assess the psychologic relevance of human brain potential studies to focal areas of research on Childhood Autism. Specifically, an experimental approach to the study of a relation between concomitant variation of brain activity and specific psychologic parameters in autistic children is suggested, employing recording of

ERP concurrent with the performance of tasks requiring the processing of sensory information.

A. Childhood Autism: Problems of Definition, Classification, and Etiology

Atypical behaviors that are considered to be characteristic of children given the diagnostic label Childhood Autism include: poor eye contact; obsessive behaviors; inattention; failure to develop speech or development of only limited speech; bizarre behaviors such as rocking, spinning or handflapping; functional retardation with islets of normal functioning; and unusual responses to stimulation. A variety of behavioral definitions of Childhood Autism exist and each considers the presence of a particular subgroup of the behaviors sufficient to establish the presence of the disorder. In this review I have chosen to define Childhood Autism as a disorder of early childhood in which all of the above behaviors are present.

There is widespread disagreement as to whether or not Childhood Autism is a distinct diagnostic category. Three nosologic views of Childhood Autism have been espoused. Some investigators contend that Childhood Autism and Childhood Schizophrenia form a unitary diagnostic category of Childhood Psychosis (O'Gorman, 1967; Ornitz and Ritvo, 1968b); others view Childhood Autism as one of several types of Childhood Schizophrenia (Fish and Shapiro, 1965; Schopler, 1965; Bettleheim, 1967); and yet another group of investigators regards Childhood Autism as a syndrome distinct from Childhood Schizophrenia

(Rimland, 1964; Eisenberg, 1966).

Attempts to define etiologic factors have resulted in three types of theories of Childhood Autism; non-organic, organic-experiential, and organic. Non-organic theories include both psychodynamic (Bettleheim, 1967) and behavioral (Ferster, 1961) explanations. The psychodynamic view suggests that Childhood Autism is the result of denial of self in defense against threats from a world perceived as hostile. Behavioral theorists explain the disorder as the result of parents' failure to pair primary reinforcement with a wide variety of behaviors. Organic-experiential theories postulate that Childhood Autism is the result of a combination of organic defects or predispositions and maternal deficiency (Goldfarb, 1961; O'Gorman, 1967). Organic theories postulate that Childhood Autism is the result of a central nervous system defect, diffuse sites of impairment (Hutt, Hutt, Lee, and Ounsted, 1964; Bender, 1966; Ornitz, Ritvo, Brown, LaFranchi, Parmelee, and Walter, 1969; Rutter, Bartok, and Newman, 1971) as well as specific sites of impairment (Rimland, 1964) have been suggested. None of these etiologic theories has been either validated or definitively invalidated.

A general impediment to the definition of etiologic factors in psychopathology derives from a feature of the experimental design commonly used in this research: a dichotomy between normal and abnormal is assumed, implying qualitatively different underlying physiologic and psychologic mechanisms. Because psychopathologic entities are often poorly defined, the expectation of fundamentally different pathogenic mechanisms is unlikely to be realized. Individual differences

within categories are usually ignored, impeding efforts to improve the definition of abnormal processes. Furthermore, the lack of adequate criteria for defining psychopathologic conditions may result in an emphasis on entities that are in fact extremely varied in their manifestations and underlying pathophysiology. Nevertheless, behavioral characteristics are used to define casual factors in psychopathology. It appears, then, that attempts to define etiologic factors in mental illness on the assumption that different diagnostic groupings will manifest qualitatively different intracerebral defects are premature at best. At present, investigations are likely to be most fruitful if focused on quantitative distinctions between normal and abnormal processes in individual subjects whose behavioral characteristics are well defined.

B. Behavioral Studies of Childhood Autism

1. Impairment of Sensory Processes

a. Intra-modal sensory processing. The study of sensory processes in Childhood Autism constitutes a major and perhaps the most productive area of research to date. Striking similarities exist between autistic children and some children with severe auditory or visual deficits. Autistic children are characteristically inattentive to auditory or visual stimulation and for this reason are often considered to have impaired hearing or vision. However, this impairment has not been traced to dysfunction at the receptor level or to dysfunction of neural elements of either the auditory or visual system. One explanation for inattentiveness

is that autistic children have elevated sensory thresholds, but the small amount of available data does not support this explanation. For example, Goldfarb (1961) was unable to demonstrate any difference in auditory, visual, or tactile thresholds between normal and autistic children.

Ornitz and Ritvo (1968a, 1968b) and Ornitz et al (1969) suggested that some of the symptoms of Childhood Autism reflect faulty modulation of sensory input. They studied auditory evoked potentials in normal and autistic children during sleep and found relative reduction of response amplitude during the Rapid Eye Movement (REM) stage of sleep in normal as compared to autistic children. They concluded that the phasic inhibition during REM sleep, which is mediated by vestibular nuclei, is impaired in Childhood Autism. They suggested that this dysfunction underlies the faulty processing of sensory information and the attentional defects that are characteristic of Childhood Autism.

Visual discrimination has also been investigated in Childhood Autism. Interpretation of the results is difficult, however, since they seem to be largely dependent upon the test procedures. Hermelin and O'Connor (1965) reported that autistic children perform less well than retarded children on two-choice visual discrimination tasks. On the other hand, Bryson (1970a) reported that autistic children perform within normal limits on a visual matching test and suggested that it is the memory factory inherent in standard discrimination training procedures that is responsible for the poor visual discrimination performance of

autistic children. Using a somewhat different approach to the analysis of sensory processing in autistic children, Hermelin and O'Connor (1967a) found a distinct impairment in performance on visual length discrimination tasks but no impairment in ability to learn position discriminations. Following up this observation, they showed that when visual discrimination tasks are arranged such that movement response cues are available, autistic children perform as well as normals of the same mental age. They concluded that perceptual ability of autistic children is enhanced by specific motor-response cues.

It has been noted that autistic children do not relate appropriately to people or objects. Small, De Meyer, and Milstein (1971) evaluated this impression by measuring Contingent Negative Variation (CNV) activity recorded with scalp electrodes from autistic children and normal children. The Contingent Negative Variation was initially described by Walter (1964a) as a slow negative shift in cortical potentials correlated with expectancy or preparatory set. The negative slow potentials develop in the interval between two successive stimuli the second of which requires cognitive processing or a motor response. Small et al (1971) recorded the CNV (in association with photos of familiar faces and strange faces that followed presentation of a click or flash) from autistic children and from normal children. The autistic children, however, unlike the normals, did not show a differential response to photos of familiar and unfamiliar faces. These investigators concluded that the results support the accepted clinical view that autistic children do not show differential responses to familiar and unfamiliar people - or, in other words, that autistic children do not participate appropriately in social interaction.

b. Development of sensory dominance. Several investigators have suggested that the disturbance in Childhood Autism involves an arrest of sensory development. Schopler (1965) suggested that in light of phylogenetic and ontogenetic trends in normal development from near to distant receptor usage, the adaptational problems of autistic children be considered due to a failure in the normal maturation of sensory integrative mechanisms. In support of this ontogentic sensory retardation view, he reported preference of tactual over visual receptors in autistic children and suggested that the developmental dysfunction is at the receptor level. As previously noted, however, there is no evidence to indicate that basic sensory reception is defective in Childhood Autism. In this connection, Goldfarb (1961) suggested that unusual response patterns in autistic children reflect disturbances in the development of sensory dominance rather than defects in the modality-specific sensory mechanisms themselves. Goldfarb (1956) also observed an increased use of auditory and visual systems by autistic children who show improvement. He considered this change to be an essential precondition for the development of the anticipatory behaviors that are characteristically lacking in these children.

A few studies have reported data comparing autistic and normal children with respect to utilization and effectiveness of various sensory modalities. The findings are in general consistent with the view that sensory preferences of autistic children differ from those of normal children. For example, Hermelin and O'Connor (1964) studied

sensory dominance in autistic children and retarded children with the same Performance I.Q. All of the children responded most readily to light given a choice between light and touch or light and sound. The usual preference for auditory over tactile stimuli seen in normal children was observed only in the subnormal controls; the autistic children responded more readily to tactile stimuli. Goldfarb (1956) also reported that autistic children use tactile receptors more than telereceptors. Contrasting with the observation is another report by Pollack and Goldfarb (1957) that autistic children perform poorly in localizing tactile stimuli. Thus, autistic children may manifest impaired function even in a preferred sensory modality.

c. Sensorimotor and intersensory processing. Associative processing has been the primary focus of a few behavioral investigations. Although autistic children perform normally on certain auditory-vocal tasks such as repetition of word lists (O'Connor and Hermelin, 1967b) and repetition of single words (Bryson, 1970b), they seem to do poorly on others such as auditory-fine motor associations (Bryson, 1970b) and auditory-visual associations (Walker and Birch, 1970; Cowan, Hoddinott, and Wright, 1965). Walker and Birch (1970) used a task that required equation of temporal auditory patterns and visual dot patterns. They found significant differences between autistic children and normal children matched for mental age. The autistic children were inferior to the normal children at each mental age in their ability to perform the required task. Furthermore, in the normal children,

intersensory integrative ability improved with age. This developmental trend was manifested much more weakly in the autistic children. The investigators discussed the data in relation to the possibility that a primary disorder of intersensory integration underlies Childhood Autism. Cowan et al (1965) also reported severe difficulties of autistic children in this class of associative processing tasks. In contrast to the foregoing, O'Connor and Hermelin (1964a, 1967a) found no difference in performance among groups of normal, retarded, and autistic children in performance of cross-modal, visual-tactile matching tasks.

d. Arousal. Both tonic arousal level and arousal responses to stimulation have been extensively studied in Childhood Autism. I have chosen to consider only those aspects of arousal that are related to sensory processing; parameters that influence the transmission of sensory information, and thereby affect the relation between sensory input and behavioral output.

Studying arousal in autistic children, Hermelin and O'Connor (1968) used alpha rhythm as an indicator of arousal state in darkness. This is based on the fact that alpha waves are most evident when subjects are relaxed with closed eyelids. Alpha waves are ordinarily diminished or abolished by opening the eyes or by introducing visual stimulation. The investigators reported no difference between autistic and normal children in darkness or as a consequence of visual stimulation. However, auditory stimulation under these conditions resulted in a greater degree of arousal (i.e., alpha reduction) in the autistic children. In support of this finding, Walter, Aldridge, Cooper, O'Gorman,

McCallum, and Winter (1964), using average amount of alpha rhythym as a measure of arousal, reported greater arousal in response to auditory than to visual stimulation in autistic children compared with institutionalized controls.

Hutt et al (1964) and Hutt, Hutt, Lee, and Ounsted (1965) hypothesized that autistic children are in a chronically high state of arousal. This is manifested by the desynchronized or higher frequency EEG of autistic children compared to normal children of the same chronological age. According to this view, the aberrant responsiveness to sensory stimulation in Childhood Autism is due to blocking of the normal sensory pathways and catastrophic reaction to novel stimulation is due to overactivation of the tonically excited reticular system. Rimland (1964) discussed the fact that these children sometimes appear underaroused and other times overaroused. However, these views are not based on experimental data. Although investigators seem to agree that autistic children appear different than normal children in arousal state and in their responses to specific types of stimulation, the available data are insufficient to establish either as a basic defect in this disorder.

e. Selective attention. Another commonly held view is that the disturbance in Childhood Autism involves impaired ability to selectively attend. Once again, as the following examples will show, investigations do not conclusively support this view. Lovaas, Schreibman, Koegel, and Rehm (1970) used the multicued stimulus complex as a discriminative

stimulus. They reported that when autistic children are presented with a multicued cross-modal stimulus, the children selectively attend to a single cue whereas retarded and normal children attend to two or three. These investigators concluded that in autistic children, control of attention transfer from one aspect of a situation to another is inadequate. A study that does not support this view was reported by Hermelin and O'Connor (1963). They compared selective attention in autistic children and subnormal children in the presence of various simple visual stimuli and in an empty room. These investigators reported that there was no difference between the groups in amount of attention paid to environmental stimuli, and concluded that the autistic children can selectively attend to stimuli and can control and direct responses at least as well as subnormal controls. Thus, as in all of the areas of sensory processing previously reviewed, the demonstration of attentional deficits in autistic children is dependent upon specific experimental conditions. For this reason, hypothetical constructs such as selective attention, arousal, and associational processing are of questionable value in identifying fundamental deficits in Childhood Autism. At present, operational rather than abstract definitions of these processes would seem to be essential.

2. Impairment of Language

Language disturbances are the most striking and ubiquitous impairment in Childhood Autism. The origin of the language deficit remains a subject of controversy. Among the various currently held views are;

abnormal language development (Wing, 1969); absence of maternal speech model (Goldfarb, 1961); central nervous system dysfunction (De Meyer, 1975; Pronovost, Wakstein, and Wakstein, 1966; Rutter, 1966); poor discrimination of social reinforcers (Cunningham, 1968); psychopathology (De Hirsch, 1967); organic brain defects (Churchill, 1972). None of these views, however, are supported by experimental data.

Some of the previously reviewed investigations of specific perceptual functions have yielded evidence suggesting discriminative and associative impairments that might interfere with language development including impaired auditory and visual discrimination; impaired visual-motor, auditory-motor, and auditory-visual associations. Cowan et al (1965) reported poor performance of autistic children on a task requiring association of verbal shape or color labels with a visual stimulus. Bryson (1970b) reported greater difficulty of autistic children in an auditory-visual task than a visual-visual matching task with the same visual stimuli and concluded that the primary disability is in short-term memory rather than intra-sensory processing. The reasoning behind this conclusion is that in the visual-visual task, both stimuli are presented spatially and simultaneously. On the other hand, in the auditory-visual task, the two stimuli are presented sequentially, thereby introducing memory as a factor in correct response choice. Hermelin and O'Connor (1967b) compared auditory-vocal memory of autistic and retarded children and reported a contradictory result, namely no difference in the number of words recalled, suggesting that

simple short-term memory per se was not impaired. It is evident, however, that short-term memory is not the only process involved in intersensory association tasks. Walker and Birch's (1970) study of intersensory pattern matching has already been mentioned. Their results support the view that autistic children have severe auditory-visual associative processing impairments.

Several investigators have described various aspects of communicative impairments in autistic children. Pronovost et al (1966) analyzed speech patterns of autistic children and compared them to those of aphasic children; Ricks and Wing (1975) compared characteristics of verbal language and other forms of communication in normal and autistic children and suggested that the central problem in Childhood Autism is impairment of complex symbolic functioning. Once again, none of the foregoing reports provide experimental data.

Despite some apparently contradictory hypotheses about the basic nature of the language impairment in Childhood Autism and a paucity of experimental data in support of any view or definition of the impairment, it seems clear that autistic children have severe deficits affecting all aspects of communication, not merely speech or verbal language.

C. Critique of Behavioral Approaches to the Study of Childhood Autism

Behavioral studies of Childhood Autism have often been flawed by unsatisfactory controls, poorly defined response measures, and by the general presumption that these children both understand task require-

ments and have normal perception. Even the most elegant studies of sensory information processing in Childhood Autism have often ignored the role of the childrens' characteristically low level of attentiveness in modulation of sensory input. Indeed, given the current poor definition of a relation between attention and performance of tasks requiring sensory information processing, behaviorally defined dysfunction at different stages of information processing can easily be explained as attentional effects rather than defects in the processing of stimulus information per se. Failure to discuss the role of attentional effects on the extent to which stimulus information reaches a specific level in the nervous system is to be distinguished carefully from failure to control attentional effects. The latter constitutes an extremely serious and as yet unresolved experimental shortcoming of physiologic as well as behavioral studies of sensory processing. I will comment further on this problem in the discussion section.

A crucial factor that has contributed to the general failure to consistently define processing of sensory information in autistic children derives from a limitation of the behavioral method itself. The behavioral method alone can not provide specific information on brain processes that are related to dysfunctional behavior. There is a need in research on sensory processes in autistic children for quantitative identification of physiologic abnormalities specific to stages of information processing including sensorimotor sequences.

In conclusion, Childhood Autism is a condition characterized clinically by a number of specific impairments occurring in a variety

of combinations and giving rise to a pattern of aberrant behavior. Although behavioral investigators have failed to establish either the existence of a single definable pathophysiologic process or to identify pathologic mechanisms underlying this disorder, they have obtained evidence of abnormal sensory processes and language. Given the aim of identifying specific information processing defects in autistic children and examining the relation between behaviorally defined defects and physiologically defined defects, the usefulness of a behavioral method used in combination with a particular electrophysiologic method is suggested.

D. Event-Related Potentials: Studies of Sensory Processes and Language

1. Background

Ideas about the functional relation of brain processes and behavior were first formulated over 100 years ago. In 1868 Donders proposed an experimental method for delineating the timing of brain processes associated with simple sensory discrimination and with organization of a motor response. He utilized a behavioral method that compared reaction time (RT) to a known stimulus with time required to respond to a discriminative stimulus. Distinct brain processes were inferred from the behavioral data. A direct test of Donder's ideas about the relation of distinct central processes and specific stages of sensory information processing depended upon the development of appropriate physiologic techniques. These were forthcoming but a short time later and in 1875

Caton reported the first recordings of electrical fluctuations following peripheral stimulation and associated with motor activity from the exposed surface of a rabbit's brain. Availability of electronic amplification made possible the subsequent findings of Berger (1929) who described brain rhythyms (EEG) recorded from the human scalp. Some thirty years later, commercial availability of computers and application of electronic averaging techniques to analysis of the EEG provided the capacity for detecting even smaller brain potentials. The electronic techniques were employed to enhance brain signals that are related consistently in time to observable reference events and to cancel spontaneous brain activity or EEG. This was accomplished by averaging repeated samples of neuroelectric activity with respect to a specified time reference. At first, most applications of the averaging technique to brain activity involved analysis of responses elicited by a stimulus or "evoked potentials" (EP). The method of repeated measurements, however, can also be used to enhance brain signals that are time-locked to another type of objective referrent, namely a motor response. For this reason the term event-related potential (ERP) was soon introduced (Vaughan, 1969) to apply to all brain potentials that can be subject to the averaging technique, not merely to stimulus evoked potentials.

Introduction of the more inclusive appelation, ERP, widens the scope of electrophysiologic studies of brain processes to include study of sensorimotor processes. In effect, it permits the physiologic analysis of brain processes and the behavioral analysis of sensory

information transmission to be carried out within the same experimental framework through use of the information processing model. In general terms, this model describes passage of information from one location to another in space and time within the nervous system. Given availability of the necessary physiologic technique, the RT method provides the experimental paradigm that is essential for study of relations between brain and behavior processes. Finally, coupling of the ERP and RT methods within a unitary conceptual framework and in a range of experimental conditions permits examination of the relation between physiologic events specific to stages of information processing and behavioral events that define different stages of information processing.

2. Event-related potential characteristics

There are four prinicipal types of event-related potentials; sensory evoked potentials, task-related (or association) potentials, motor potentials, and steady potential shifts. Sensory evoked potentials are obligatory brain respones, the recording of which requires a series of brief stimuli. Properties of the responses depend upon stimulus parameters and the state of the organism when it is stimulated. Task-related potentials are brain responses that are associated with an individual's judgment that a given stimulus event, within a set of events, is significant or different. Properties of this response are primarily defined by task variables rather than stimulus variables. Motor potentials are averaged responses that directly precede and

accompany muscle contractions. Steady potential shifts are slow shifts in cortical potentials that are associated with anticipatory processes and with sensory stimulation.

I will discuss only studies of certain sensory evoked potentials (namely, auditory and visual evoked potentials) and task-related potentials because this is the type of neuroelectric data that will be obtained in the present investigation.

3. Sensory Evoked Potentials

a. Introduction. Properties of sensory evoked potentials have been examined in some detail. Reports indicate that waveforms are more reproducible within subjects than between subjects and that a variety of factors influence characteristic properties of the responses. The following examples will illustrate the effect of some experimental variables on amplitude, latency, and habituation of the auditory evoked response and the visual evoked response.

b. Auditory evoked potentials. Although responses evoked by auditory stimulation were first described by Davis (1939), they have not been systematically studied until quite recently. During the past several years, systematic investigations have established the basic pattern of a large number of components in the average potential evoked by auditory stimuli.

i. Subcortical: A very early series of waves (the auditory brainstem response) is recorded in the initial 8msec after auditory stimulation. A consistently observed longer latency potential (the auditory cortical

response) is recorded approximately 50-250msec after auditory stimulation.

Jewett, Romano, and Williston (1970), Hecox and Galambos (1974), and Salamy and McKean (1976) have established the general and age-related properties of the auditory brainstem response. In particular, Jewett et al (1970) observed a series of five to seven positive waves that are reliably recorded within the first 8msec after auditory stimulation and suggested that these waves reflect sequential activation of auditory brainstem nuclei and pathways. Hecox and Galambox (1974) reported a progressive decline in the latency of wave number five from three weeks to two years of age and suggested that this latency measure be used as an index of cerebral maturation. Salamy and McKean (1976) showed that the brainstem evoked potential waveform in infants shows adult patterns by three to six months and that the brainstem evoked response is quite resistant to habituation as a consequence of continued stimulation. Because recording of the auditory brainstem response does not require cooperation on the part of a subject, the response is a useful physiologic measure of hearing in infants, multiply handicapped children,,and/or inattentive subjects. Although the electrophysiologic response gives no information about ability to process auditory information and use it in the production of a specified behavioral response, brainstem (auditory evoked) responses are proving to be a useful diagnostic tool for audiologic and neurologic disorders and a useful measure in the study of physiologic correlates of sensory information processing.

ii. Cortical components: The later components of the auditory evoked responses were first observed by Davis (1939). She described a triphasic waveform characterized by a small positive peak (P1) with a latency of 12-60msec, followed by a large negative peak (N1) with a latency of about 100msec, and a second positive peak (P2) with a latency of approximately 200msec. This cortical response is most prominent in a vertex electrode site.

The effect of repeated stimulation on auditory evoked response amplitude has been studied extensively. Studies of habituation (short-term) of the response have generated contradictory results. There have been reports, on the one hand, that when auditory stimuli are presented repeatedly there is a gradual decrement in response amplitude (Davis, Mast, Yoshie, and Zerlin, 1966). Since behavioral studies have shown that attention decreases rapidly during presentation of the first few in a series of stimuli, loss of attention is not a good explanation of the gradual response decrement. On the other hand, Ritter, Vaughan, and Costa (1968), summing responses to single sequential stimuli across runs, reported rapid short-term decrement of the response recorded in association with repeated stimulation in a two second interstimulus interval (ISI) condition and no response decrement in a ten second ISI condition. This result suggested that the rapid decrease in response amplitude in the shorter ISI condition was not a reflection of attention loss but rather a reflection of refractoriness within the auditory system. These results certainly underline the need in studies of

auditory evoked potentials for careful manipulation of experimental variables and careful selection of averaging procedures in the determination of a definitive answer about habituation. Because habituation is often suggested as an explanation of faulty sensory information processing, the electrophysiologic study of subjects presumed to have such impairments requires great care.

Rate of auditory stimulus presentation is a variable that has been used to study normal children and children with developmental language disabilities. Lowe and Campbell (1965) and Tallal and Piercy (1973b) reported decreased performance only in the latter group on auditory sequencing and auditory memory tasks as ISI decreased. Unfortunately, these studies used nonlanguage deficited children as controls. Thus, it is not possible to tell whether or not deficits in rapid auditory processing were specifically associated with language disability or a reflection of underlying brain damage. In any case, the effect of changes in ISI should certainly be examined in electrophysiologic studies of sensory processing in children with behaviorally defined temporal processing deficits.

Several investigators have studied auditory evoked potentials recorded from schizophrenic patients and/or their children. In this regard, many contradictory results have been reported and, in addition, there exists a small body of consistent data that can be summarized as follows: amplitude of the early peak is no different than in normals and amplitude of component peaks that occur 50msec or more after

stimulus presentation is smaller than in normals (Jones, and Callaway, 1970; Saletu, Itil, and Saletu, 1971); the latency of component peaks is faster (Saletu et al, 1971), the variability of late auditory evoked potential components is greater than in normals and the variability of early components is smaller than in normals (Callaway, Jones, and Donchin, 1970).

c. Visual evoked potentials. Although the brain response that is recorded in association with visual stimulation is not present in the adult form during the first year after birth, a recognizable visual evoked potential can be recorded in newborns. This response is localized in the occipital region of the cortex. Ciganek (1961) described the visual evoked potential recorded in association with unpatterned flash stimulation. The waveform is characterized by three prominent peaks; a positive peak at about 60msec, followed by a negative peak at about 75msec, and a second positive peak at about 100msec. A series of negative and positive peaks with latencies that range from about 110-400msec usually completes the visual evoked response. Short latency visual evoked potential components reflecting activity in subcortical visual structures have not been described.

The waveform of the visual evoked potential is significantly influenced by many variables such as patterning, stimulus intensity and frequency, and hue. MacKay and Jeffrey (1973) have provided an excellent summary of these effects.

Data obtained in studies of visual evoked potentials recorded from schizophrenic patients and/or their children are difficult to interpret

and to summarize because no consistent body of information exists. Several examples follow. Speck, Dim, and Mercer (1966) reported no differences in latency of the response recorded from schizophrenics and normals. Rappaport, Hopkins, Hall, and Belleza (1973) reported longer latencies of the responses recorded from schizophrenics. To complete the confusing picture, Shagass and Schwartz (1965) reported shorter latencies in the schizophrenics. Similarly, reports about amplitude of the visual evoked response have ranged from smaller amplitudes in the schizophrenics (Rappaport, Hopkins, Hall, Belleza, and Hall, 1975; Shagass, Straumanis, Roemer, and Amadeo, 1977) to larger amplitudes (Herman, Mirsky, and Ricks, 1977). There seems, however, to be a modicum of agreement about the increased variability of the visual evoked response in schizophrenics compared to normals (Lifshitz, 1969; Shagass, 1976) - perhaps related to poor diagnostic criteria.

4. Task-Related Potentials

a. Introduction. Event-related potentials recorded from the human scalp in association with sensory stimulation have provided quantitative information about inflexible cerebral information processes consequent to incoming sensory data. Event-related potentials recorded in association with sensory stimulation have also provided information about neural activity related to nonobligatory cerebral analysis of sensory information. These brain responses, task-related potentials, are present only in conditions where a perceptual judgment about stimulus events is required. The waveform of the task-related potential is characterized by two peaks, a negative followed by a positive. The

negative component has a distribution compatible with sources near the primary cortical projection area of the stimulus input, that is to say, this distribution is different in each sensory modality. The positive component can be attributed to sources within modality-unspecific association areas of the parietal cortex (Vaughan, 1969; Simson, Vaughan, and Ritter, 1967a, 1977). The waveform of the task-related response varies considerably more than that of the sensory evoked response and its timing as well as its topography are related to specific experimental conditions.

The positive component (LPC) of task-related potentials has received the most experimental treatment. One reason for this is that the negative component that precedes the LPC is either partially or fully obscured by the concurrent sensory evoked potentials.

The fact that task-related potentials can be generated endogenously and that their properties are related to the meaning or significance of a stimulus rather than to its physical characteristics gives us the possibility of insight into previously unobserved perceptual processes. In attempting to exploit this possibility, it is important that investigators studying the relation of task-related potentials and psychologic constructs give careful consideration to the operational definition of these constructs. To the extent that this concern is exercised, and to the extent that the time course of higher level sensory processes can be experimentally defined, certain aspects of underlying neural activity can be delineated and the relation between complex information

processing activity and cerebral processes can be elucidated. Because of this exciting potentiality and the fact that disorders of perception in autistic children have been studied behaviorally in some detail, study of task-related potentials in these children should receive special attention. The following discussion of task-related potential studies is meant to provide an overview of some experimental models that have been used in this area of research and will be employed in the present study.

b. Experimental variables that affect association cortex activity. Variables that influence the properties of task-related potentials include: changes in the probability of occurrence of an infrequent stimulus, changes in the degree of subjective uncertainty about the type of stimulus, and feedback concerning performance on a discrimination task. The effects of these variables have been studied using simple discrimination procedures and using a paradigm derived from signal theory. In the latter, a subject must detect the presence or absence of a target stimulus presented infrequently within a series of nontarget stimuli. Sutton, Braren, and Zubin (1965) were the first to record task-related potentials in association with a task that required subjects to guess the type (auditory or visual) of test stimulus that might follow a cue. In this experiment several variables were manipulated; the degree of subjects' uncertainty regarding the sensory modality of the signal (stimuli that followed the cue were always light flashes, always clicks, or either a flash or a click), feedback

concerning correctness of a stimulus choice (here, one half of the test stimuli were flashes and one half were clicks), and probability of occurrence of a signal (test stimuli within a run were either one third flashes and two thirds clicks, or two thirds flashes and one third clicks). The investigators reported increases in amplitude of the task-related potentials in association with increases in subjects' uncertainty about the sensory modality of a signal. They also reported increases in response amplitude in association with decreased probability of occurrence of the signal and with the presence of feedback concerning correctness of perceptual judgment. The influence of subjects' uncertainty about stimulus alternatives on amplitude of the task-related potentials has also been studied by Friedman, Simson, Ritter, and Rapin (1975) using visual stimuli and the feedback paradigm, and by Squires, Squires, and Hillyard (1975) in a signal detection task using auditory stimuli without feedback concerning correctness of stimulus choice. Available data indicate that whenever normal subjects are required to evaluate stimuli and to select a target stimulus from among nontargets, a larger LPC follows the selected target (regardless of the type of cue or the stimulus parameters) than the nontargets.

c. Nonlanguage tasks that are related to association cortex activity. Task-related potentials have been recorded in association with detection of shifts in stimulus intensity (Ritter and Vaughan, 1969; Picton and Hillyard, 1974), shifts in stimulus frequency (Hillyard, Squires, Bauer, and Lindsay, 1971; Ritter, Simson, and Vaughan, 1972; Squires et al, 1975),

changes in other stimulus parameters (Smith, Donchin, Cohen, and Starr, 1970; Courchesne, Hillyard, and Galambos, 1975; Kurtzberg, Vaughan, and Kreuzer, 1978), and changes in sensory modality of nontargets (Ford, Roth, Dirks, and Kopell, 1973). Results are consistent with the view that task-related potentials reflect some specific cognitive process and are relatively independent of physical characteristicsof the sensory input. Further support for this view is provided by Sutton, Tueting, Zubin, and John (1967) who reported that task-related potentials can be recorded in association with detection of omitted or missing stimuli within a series of nonsignal stimulus presentations.

5. Language Tasks and Event-Related Potentials

There have been many evoked potential studies of language in normals. Unfortunately, the results of these studies are, by and large, contradictory and seem to raise more questions than they answer concerning electrophysiologic correlates of language information processing. Nevertheless, because the studies do represent a variety of experimental approaches to the study of language (some of which may be useful in future examination of sensory information processing in Childhood Autism) and because they provide data concerning auditory and visual processes (which have been studied behaviorally and identified as aberrant in autistic children), a summary of these reports is germane to this presentation.

Investigators have used visual stimuli to examine evoked potential correlates of language information processing. The hypothesis that

cerebral hemispheres in man are asymmetric with respect to language-related processes is supported by Buchsbaum and Fedio (1969) and Donchin, Johnson, Hernong, and Kutas (1973) who reported differences in ERP recorded from the left and right hemispheres in association with language and nonlanguage stimuli. Shelburne (1972) reported contradictory results. Friedman et al (1975) used visual stimuli to study processing of different types of language information rather than the processing of language in different sides of the brain. Their results are consistent with the view that processing of semantic information is related to latency of the task-related response and processing of syntactic information is related to task-related response amplitude.

Auditory stimuli have also been used to study language information processing. Once again the results are inconsistent. For example: Smith, Donchin, Cohen, and Starr (1970) used the dichotic paradigm developed by Kimura (1961b) and reported no left-greater-than-right differences in ERP recorded in association with verbal and nonverbal stimuli; Haaland (1974) used the same paradigm and reported asymmetric brain responses to verbal and nonverbal stimuli; Friedman et al (1975) and Galambos, Benson, Smith, Schulman-Galambos, and Osier (1975) used diotic stimulation and reported no left-greater-than-right ERP differences associated with language stimuli; Morrell and Salamy (1971), on the other hand, used diotic stimulation and reported hemispheric asymmetry of ERP recorded in association with speech stimuli.

Contradictory results concerning language processing can be explained

in several ways. To begin with, the overwhelming clinical evidence for hemispheric asymmetry in language processing comes from studies of subjects with cerebral lesions and investigations of bilateral asymmetry in evoked responses recorded in association with language stimuli have used normal subjects. In addition, there may be crucial neuroelectric events that we are unable to record or, alternatively, particular experimental designs may have inadvertently eliminated or failed to elicit such crucial events. It is also possible that neurophysiologic differences in hemispheric function are, in actual fact, marginal. In any case, study of what may be the most complex cerebral mechanisms seems premature at a time when the successive stages of sensory information processing that must be components of language processing remain poorly understood.

E. Objectives and Rationale (of Present Study)

1. Objectives

The aim of the present study is to use event-related potentials to examine in individual autistic children both transmission through the brain of auditory and visual information, and short-term storage of this information. The investigation tests the hypothesis that in autistic children aberrant brain processes are associated with behavioral abnormalities.

The auditory and visual (among other) modalities were selected for study because behavioral skills that depend upon auditory and visual processes are characteristically abnormal in autistic children and because audition and vision are the sensory systems that have been

most thoroughly studied in normals.

In order to examine the neural transmission of auditory and visual information, subjects will be tested in a range of experimental conditions that are designed to explore the electrophysiologic concomitants (at different places in the brain) of behaviorally defined dysfunction (at different stages of information processing). In the auditory system, intracerebral neural events will be examined that are related to the processing of information in the auditory brainstem, the auditory cortex, and the parietal cortex; in the visual system neural processes will be examined in the visual cortex and in the parietal cortex.

2. Rationale

Behavioral methods alone do not provide specific information about the nature of intracerebral processes that are related to behavior; they provide only a basis for inferences about brain mechanisms. Thus, given the aim of elucidating the relation between behavior processes and brain processes, an alternative method is needed. The recording of ERP concurrent with performance of tasks requiring sensory information processing is well suited to the study of correlative variation of abnormalities in brain activity and behavior. Furthermore, use of this methodologic format in combination with a range of experimental conditions permits examination of cerebral neuroelectric concomitants of stages of information processing including sensorimotor sequences. Thus, it might be possible to define electrophysiologically defects at particular stages of information transmission and/or to identify defects affecting several stages of the stimulus-response process.

CHAPTER II

METHOD

A. Subjects

Three autistic and three normal children were subjects for these experiments. All subjects were between the age of 14 years and 15 years. The autistic children (patient subjects) were selected from a population of autistic children at Bronx Childrens Psychiatric Center. The normal children (normal subjects) were selected on the basis of normal developmental history and appropriate school placement.

Patient subjects had been diagnosed as autistic on the basis of (i) observation of stereotypic behavior, (ii) observation of poor eye contact, (iii) history of aberrant language development, (iv) impression of functional retardation with islets of age-appropriate function.

Autistic children were selected for the study on the basis of (i) a normal EEG, (ii) a demonstrated preference for the right hand, (iii) ability to obtain scorable results on a battery of neuropsychologic tests.

A battery of neuropsychologic tests was used in the study for the following reasons; to evaluate the clinical impression of severe deficiencies in cognitive functions and in patterns of sensory information processing; and to obtain standardized measures of specific psychologic processes that could be examined in relation to the electrophysiologic data. The patient subjects' ability to take the tests

indicates that they were less impaired than an overall population of autistic children. The reason for not selecting a random sample of (more impaired) autistic children was that a primary goal of the study was to assess the very possibility of using with autistic children the somewhat demanding technological format involved in obtaining accurate encephalographic recordings of evoked potentials. Although the experimental tasks involved are simple, it was assumed that these children would require at least some training to perform them - this requirement was expected to be minimal for the less severely impaired children that were chosen; patient subjects that would have required extensive training were considered inappropriate for the present exploratory electrophysiologic study.

The following neuropsychologic tests were administered: Wechsler Intelligence Scale for Children, WISC-R, (Wechsler, 1974); Peabody Picture Vocabulary Test (Dunn, 1959); Raven Coloured or Standard Progressive Matrices (Raven, 1965); Slossom Drawing Coordination Test (Slossom, 1967); Illinois Test of Psycholinguistic Abilities, ITPA, (Kirk, McCarthy, and Kirk, 1968); Visual Sequential, Auditory Memory, and Sound Blending subtests. Scores obtained on the tests are seen in Table 1.

A clinical summary abstracted from available medical records and a neuropsychologic assessment of each subject follows. R.S. was born in October, 1961. His mother reported that despite a difficult birth her son's early developmental milestones were normal until age two years. At this time R.S. began to speak using single words. However, the use

Table 1: Scores obtained on neuropsychologic tests represent standardized measures of cognitive skills and specific sensory information processing skills.

NEUROPSYCHOLOGIC TEST SCORE DISTRIBUTION

	R.S.	S.N.	H.P.
WECHSLER INTELLIGENCE SCALE FOR CHILDREN - R			
Verbal I.Q.	51	50	59
Performance I.Q.	64	90	77
Full Scale I.Q.	54	67	67
PEABODY PICTURE VOCABULARY TEST			
Mental Age Equivalent	7-0	8-0	9-1
RAVEN COLOURED OR STANDARD PROGRESSIVE MATRICES			
Percentile	85	Below 50 for 11 year old	92
SLOSSOM DRAWING COORDINATION TEST			
Accuracy Score (%)	75	33	92
ILLINOIS TEST OF PSYCHO-LINGUISTIC ABILITIES			
Age Score			
Visual Sequential	8-1	6-10	8-4
Auditory Memory	Unscorable	10-3	8-1
Sound Blending	Unscorable	Unscorable	Unscorable

of phrases and complete sentences failed to develop. Ms. S. described R.S. as a difficult pre-schooler who was disinterested in other people and objects in his surroundings, used limited speech, and had uncontrollable temper tantrums. Feeling unable to manage this child, Ms. S. placed him at age seven years in Rockland Childrens Psychiatric Center (RCPC). At RCPC, R.S. received the diagnosis Childhood Autism. Presenting symptoms included; low frustration tolerance, hyperactivity, unresponsiveness, poor language, negativistic and manneristic behaviors. R.S. remained an in-patient at this facility until at the age of thirteen (because his family had moved to the Bronx) he was transferred to Bronx Childrens Psychiatric Center (BCPC). Upon admission, R.S. was labelled Autistic. He appeared lacking in age appropriate social and cognitive skills. Language development was profoundly retarded and bizarre behaviors such as clapping and rocking were noted.

A speech and language evaluation in 1976 revealed striking receptive and expressive language disabilities. R.S. scored below average for a child his age on tests of receptive syntactic structure and receptive vocabulary. He had difficulty repeating meaningful sentences and incorrectly used pronouns and prepositions. Spontaneous speech was slurred and R.S. spoke in fragments rather than in complete sentences. Results of an audiometric screening were within normal limits.

During the same period, R.S.'s teacher described his excellent drawing skills and particular preference for drawing cartoon-like

figures that were realistically proportioned and delicately detailed. R.S. also demonstrated severe learning disabilities despite the ability to spell some simple words and identify the alphabet letters. On standardized tests he obtained arithmetic, reading, and spelling scores at the pre-school level.

Neuropsychologic evaluation of R.S. in 1977 yielded scores in the mentally deficient range (see Table 1). A noteworthy 13 point difference between Verbal and Performance Scale I.Q. on the WISC-R suggests relatively greater strength in nonverbal than in language-related skills. This was consistent with the low score on the Peabody Picture Vocabulary Test, a test that measures understanding of spoken words, and high scores on the Ravens, a receptive test of visual spatial abilities, and the Slossom Drawing Coordination Test. His inability to blend sounds was reflected in unscorable performance on the Sound Blending subtest of the ITPA. Inability to repeat more than three digits in the forward direction only was reflected in poor performance on the Auditory Memory test and suggests serious deficits in auditory functions. R.S.'s relatively high score on the Visual Sequential Memory test coupled with demonstrated spatial abilities suggest relative strength in visual compared to auditory skills as well as the previously noted strength in nonlanguage-related compared to language-dependent skills.

S.N. was born in July 1962. His parents reported that early development proceeded normally and S.N. walked alone at 12 months but always on his toes and began speaking words at 11 months. However, he

did not seem to understand when he was spoken to. Communicative speech failed to develop and S.N. appeared unresponsive to his surroundings and to other people. When S.N. was three years old, believing he might have some organic hearing impairment, his parents arranged for a hearing evaluation that produced negative results. However, an impression of Childhood Autism was noted. S.N. was then referred to Bellevue Hospital and the diagnosis Childhood Schizophrenia - Autistic Type was confirmed. S.N. was admitted to and remained at Bellevue for one year. He was described as a toe-walking, hyperactive child with strange speech patterns who actively avoided eye contact and physical contact with people. During his stay at the hospital, S.N. developed minimal communicative speech and relations with others improved. S.N. was discharged to his home and during the next five years he attended a private school for emotionally disturbed children. He was described as a perseveratively destructive boy with profoundly impaired communicative and social skills. Around age eleven, self-abusive and aggressive unpredictable episodes became more frequent and occurred with increasing intensity. These violent outburst made it impossible for S.N. to remain at school and his parents felt unable to manage him at home. Thus, residential placement was sought. At age twelve, following a short-term placement at a private facility, S.N. was admitted to BCPC as an in-patient. Upon admission, S.N. received the diagnostic label Childhood Autism. Among the more distinctive characteristics noted were toe-walking, limited and rapid speech, hyperactivity, inattentiveness, and avoidance of physical

contact with people. Head-banging, face-slapping, and other violent tantrum behaviors were also described.

A speech and hearing evaluation in 1975 resulted in test scores that indicated poor understanding of word meaning, inappropriate spontaneous speech patterns, and incorrect use of pronouns and prepositions. Test results also suggested that receptive syntactic language abilities were dysfunctional. Hearing, on the basis of audiometric tests, was normal.

During his stay at BCPC, S.N.'s teacher reported performance at the pre-school level on standardized reading, spelling, and arithmetic tests. S.N.'s graphomotor skills were described as poor. His interest in birth dates and batting averages of baseball players were noted as were his excellent abilities in the rapid and accurate retrieval of this information.

On neuropsychologic tests S.N. achieved a Full Scale I.Q. and a Verbal I.Q. in the mental defective range. The Performance Scale I.Q. was in the average range. A very significant 40 point difference between Verbal and Performance I.Q. suggests relative strength in nonverbal skills. This is consistent with the low score that S.N. obtained on the Peabody. Whereas the low score on the Slossom is consistent with difficulties in the area of graphomotor skills, the low score on the Ravens is indeed difficult to interpret in light of S.N.'s average score on the Performance Scale of the WISC-R. Perhaps the fact that the Ravens does not permit self-correction through

manipulation of parts suggests that perceptual analysis and synthesis as well as visuo-motor coordination were essential factors contributing to relatively high scores on the Performance subtests. The Peabody has the same response requirement as the Ravens and S.N.'s low score on this test might reflect his poor self-control and his serious receptive language impairment. In a similar vein, the Slossom permits no erasures and S.N. probably lost points on this test of graphomotor and visual spatial skills, the former a reported area of weakness, because of his impulsive behaviors. S.N.'s performance on the Auditory Memory test was superior to test limits. He was able to recall seven digits forward and backward suggesting relative strength in auditory as compared to visual skills as well as the previously noted strength in nonlanguage dependent compared to language-related skills.

H.P. was born in September, 1961. Ms. P. reported that her son's early development was normal and that H.P. began saying words at the age of two and using short sentences at the age of three. During the next two years Ms. P. became concerned about the slow development of her son's speech, his failure to appropriately use language, his lack of interest in other people, and his violent temper. H.P. attended kindergarten for one week and because of poor language development, inattentiveness, and uncontrollable temper tantrums, H.P. was referred to a special classroom setting. From 1966 until 1975, H.P. remained in public school classes for disturbed children. During that period he was described as an autistic-like, uncooperative boy with slurred and limited speech. Despite some progress in language skills and social

skills, H.P. became increasingly distractible and unmanageable. A variety of bizarre behaviors such as inappropriate laughing and rocking were also reported. In 1976, H.P. was referred to a day treatment program at BCPC because his behavior had become so impulsive and unpredictable that he was no longer able to be physically contained in a classroom setting. Upon admission to BCPC, H.P. received the diagnosis Childhood Autism. He appeared pre-occupied and unresponsive. Inappropriate behaviors, poor eye contact, and extremely retarded language skills were also noted.

During 1976, a speech and hearing evaluation revealed scores significantly below age-expectancy on tests of receptive and expressive language. Spontaneous speech was slurred and monotone. H.P. had difficulty correctly using prepositions and pronouns and correctly answering questions. Audiometric test results were within normal limits.

Education reports indicated that H.P. achieved arithmetic, spelling, and reading scores at the pre-school level. He had difficulty identifying left and right and did not understand simple concepts such as before and after, more and less. Despite severe cognitive deficits, H.P. appeared very skilled in drawing and his accurate, detailed, and colorful representations of people and animals were described.

In 1977, neuropsychologic evaluation of H.P. resulted in a Full Scale I.Q. of 67. An 18 point difference between the Verbal Scale I.Q. and the Performance Scale I.Q. is noteworthy and suggests

visual spatial reasoning as an area of relative strength contributing to an overall I.Q. that falls in the mentally deficient range. In fact, H.P.'s Performance Scale I.Q. of 77 is within the borderline range of intelligence. This is consistent with the low score achieved on the Peabody and high scores on the Ravens and the Slossom. Extreme difficulty blending sounds is reflected in unscorable results obtained on the Sound Blending test. H.P. obtained a low score on the Auditory Memory test. He was able to recall four digits in the forward direction, and none in the backward direction. This result suggests serious impairment in temporal processing, storage, and/or in retrieval of auditory information. H.P. achieved an age score seven years below the expected level on the Visual Sequential Memory test. This result suggests that H.P. has serious sequencing difficulties and that his main area of strength is in visual abilities that are not dependent upon sequencing, information storage, or language skills.

B. Experimental Conditions

All of the studies were performed in a sound dampened electrostatically shielded recording chamber (Industrial Acoustics Special Series 200) from which all light can be excluded. Ss were seated comfortably on a wooden armchair. Throughout testing, a volunteer remained in the chamber and monitored Ss behavior. Four experimental conditions were employed as follows:

1. Auditory Brainstem Potential

Subjects were instructed to sit still and to listen to sounds. An experimental run consisted of 1000 stimulus presentations. The interstimulus interval was 100msec. In this recording condition, stimuli

were presented binaurally and monaurally. The condition of stimulus delivery in a run was determined randomly prior to the onset of testing. Average potentials associated with the auditory stimuli were obtained in six runs providing a total sample of 6000 auditory brainstem potentials.

2. Auditory Evoked Potentials

Subjects were instructed to sit still and to listen to sounds. An experimental run consisted of 100 stimulus presentations. The inter-stimulus interval was 1sec or 3sec. Stimuli were presented binaurally (1sec ISI) or binaurally and monaurally (3sec ISI). The condition of stimulus delivery in a run was determined randomly prior to the onset of testing. Average potentials associated with the auditory stimuli were obtained in eight runs providing a total sample of 800 auditory evoked potentials.

3. Auditory Discrimination Potentials

Subjects were told that most of the time they would hear a high sound (nonsignal) and once in a while they would hear a low or different sound (signal). Ss were instructed to lift the right index finger each time they heard a low or different sound. During pretest sessions, Ss were taught to perform the discriminative RT task through the use of imitation and continuous verbal reinforcement. Training was considered completed when Ss performed five consecutive correct responses.

An experimental run consisted of 150 stimulus presentations. Stimuli were presented binaurally and at 2sec intervals. Randomly, at an average rate of one per ten stimulus presentations, a high tone (nonsignal) was replaced with a low tone (signal). Approximately 15 signals were presented in a run. Average potentials associated with the nonsignals

and average potentials associated with the signals were obtained in six runs. This provided a total sample of 900 auditory evoked potentials and a total sample of 90 auditory discrimination potentials.

4. Missing Stimulus Potential

In two auditory missing stimulus conditions and two visual missing stimulus conditions Ss were instructed to sit still and to pay attention. In the two auditory conditions, Ss were told that most of the time they would hear a high sound (nonsignal) and occasionally they would note no sound (signal) in the place of a high sound. In the two visual conditions, Ss were told that most of the time they would see a light (nonsignal) and occasionally they would note no light in the place of a light.

Specific task requirements were different in each of the four missing stimulus conditions. In one auditory condition, Ss were told to pay attention to the high sounds and the missing sounds and to make no motor response. In a second auditory condition, Ss were told to lift the right index finger each time the high sound was missing. In one visual condition, Ss were instructed to pay attention to the lights and to the missing lights and to make no motor response. In the second visual condition, Ss were told to lift the right index finger each time the light was missing. The order of the four missing stimulus conditions was randomly determined for each subject.

The subjects were taught to perform the discriminative RT task through the use of imitation and continuous verbal reinforcement. Training sessions preceded test sessions and were considered completed

when subjects performed five consecutive correct RT responses.

An experimental run consisted of 250 stimulus (nonsignals) presentations. The interstimulus interval was 1sec. In the auditory conditions, stimuli were presented binaurally. In the visual conditions, stimuli were presented while Ss fixated on a strobe light. Randomly, at an average rate of one per ten stimulus presentations, a stimulus was omitted (signal). Approximately 25 missing stimulus events occurred in a run. In each condition, average potentials associated with the nonsignals and average potentials associated with the signals were obtained in four runs. This provided a total sample of 1000 sensory evoked potentials and a total sample of 100 missing stimulus potentials.

C. Recording Methods

1. Electrode Application and Placement

The scalp EEG recordings were obtained using gold disc electrodes (Grass). These were fixed in place with bobby pins following vigorous preparation of the skin with acetone and saline electrode jelly. Additional electrode jelly was applied to the electrodes prior to application so as to obtain good electrical contact.

In the auditory brainstem potential condition, an array of three electrodes was used. Electrodes were placed over the two mastoids and over the vertex. An electrode on the tip of the nose was used as reference. In the other experimental conditions, in order to obtain some information about the distribution of the cerebral potentials

under investigation, an array of six electrodes was used. Electrodes (1-6) were placed equidistantly along the midline. An electrode on the tip of the nose was employed as reference in the auditory conditions. Linked ear electrodes were employed as reference in the visual conditions.

2. Recording Apparatus and Procedure

The EEG signals were amplified by low level preamplifiers (Tektronix 3A9 and Tektronix 2A61). In the auditory brainstem condition the preamplifiers (Type 3A9) were set for a bandpass of 1.6-300c/sec. In the other conditions, one set of preamplifiers (Tektronix 3A9) was set for a bandpass of 1.6-100c/sec and the other set of preamplifiers (Tektronix 2A61) was set for an equivalent bandpass of .6-60c/sec. System gain was 8K.

At the beginning of each run, the electrophysiologic data were visually checked to insure freedom from line and muscle artifacts. During the run, the EEG was continuously monitored on a 4-trace oscilloscope (Tektronix 3A74 plug-in).

The stimulus that was presented, the configuration of recording equipment, and the light conditions within the chamber were determined for each condition. In the auditory brainstem condition, the stimulus was a 100usec 90dB SPL click that was generated by an Ortec (4710) Dual Channel Stimulator. A General Radio Company Sound-Level Meter (Type 1551-C) and an Impact Noise Analyzer (General Radio Company Type 1556-B) were used to calibrate the click stimulus. The stimulator was used to drive a laboratory made audioamplifier. In the auditory evoked potential condition, the stimulus was a .5msec 90dB SPL click that was calibrated and generated in the same manner. In all of the auditory conditions, stimuli were delivered through commercial headphones (Koss Pro 4A) and the chamber light was turned on.

The configuration of recording and data processing equipment that was used in the auditory discrimination condition is seen in Figure 1. Two stimuli were presented, a 2000c/sec tone burst and a 1000c/sec tone burst. Each had a rise and decay time of 5msec. The method of limits was used to determine stimulus threshold and the stimuli were delivered at 50dB above subjective threshold. When it was not possible to obtain subjective thresholds, stimuli calibrated with a General Radio Company Sound-Level Meter (Type 1551-C) and a General Radio Company Impact Noise Analyzer (Type 1556-B) and were delivered at 90dB SPL. The tone bursts were generated by a Heathkit Audiogenerator (Model 1G072) that drive a laboratory-made audioamplifier.

The configuration of recording and data processing equipment that was used in the auditory missing stimulus conditions is seen in Figure 2. The configuration of the recording and data processing equipment that was used in the visual missing stimulus conditions is seen in Figure 3. In the auditory missing stimulus conditions, the stimulus (nonsignal) was a 2000c/sec tone burst with a rise and decay time of 5msec. Intensity of the stimulus was determined as in the previous condition. The tone burst was generated by a Heathkit Audiogenerator (Model 1G072) that drove a laboratory-made audioamplifier. In the visual missing stimulus conditions, the light was generated by a Grass (PS2) photic stimulator with the lamp mounted on a floor stand positioned at eye level 4ft from the subject. Dimensions of the flash lamp were: height 7in, width 11½in, depth 8in. The intensity of the light was 375,000 candle power. Duration of the stimulus was 10usec. The chamber light was turned off and ambient light alone was present in the visual condition.

The reaction time response was recorded by means of a lift off key that was made in the laboratory. In the auditory conditions, the RT

Figure 1: Block diagram of recording and data processing equipment used in the auditory discrimination potential studies.

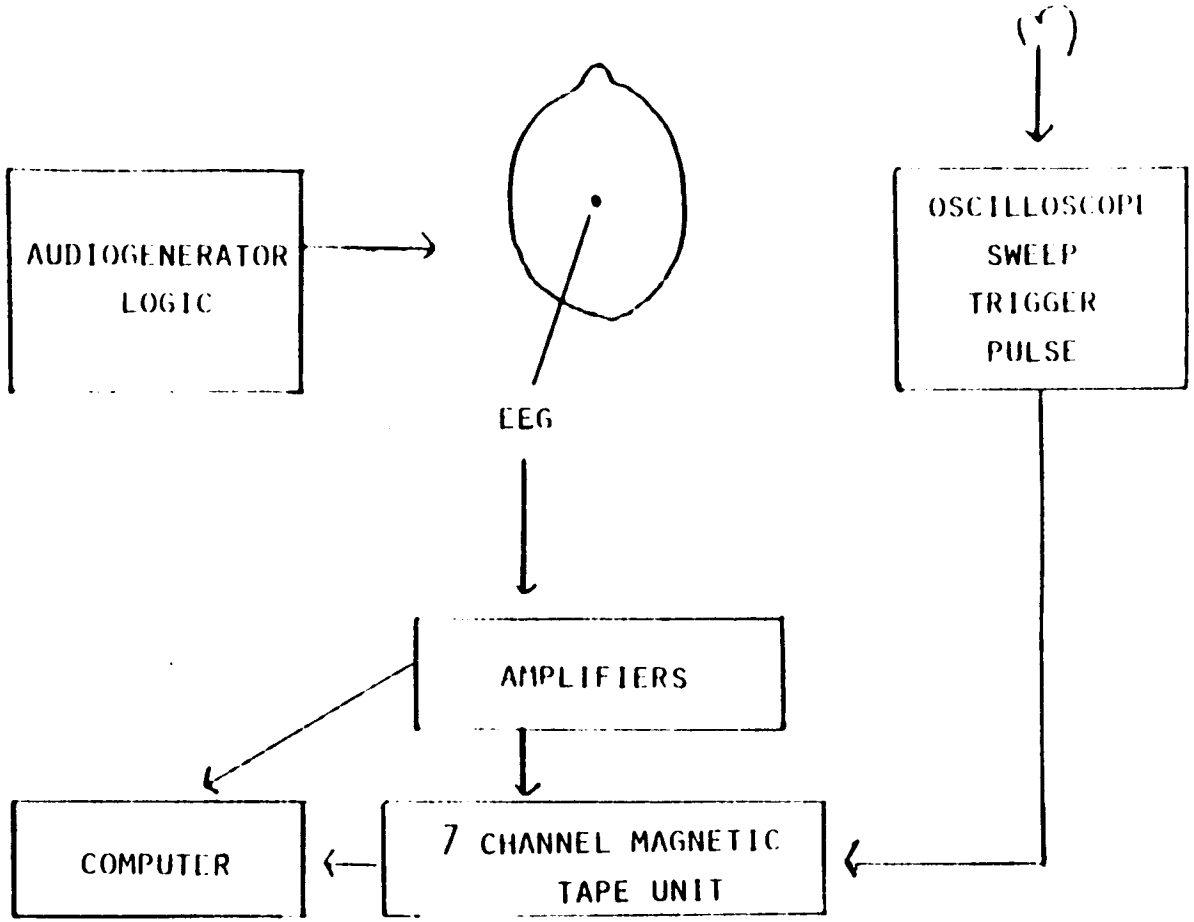
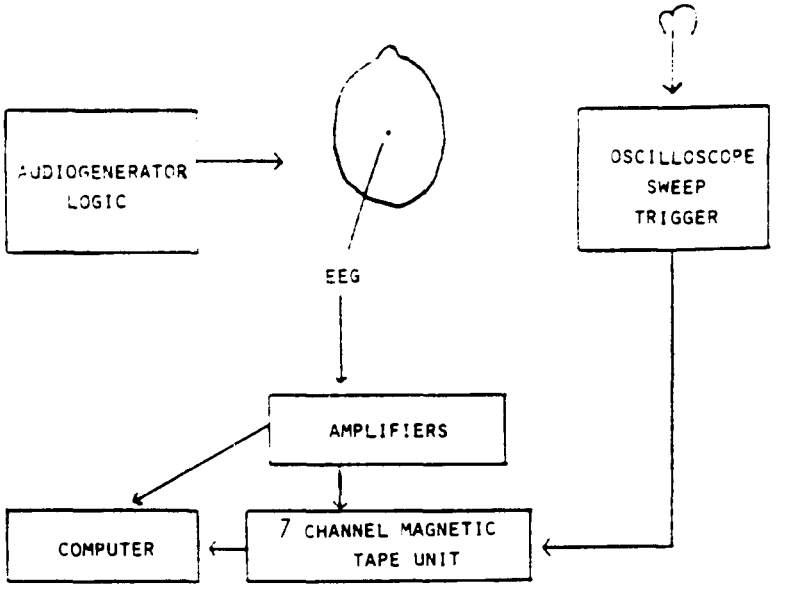

AUDIOGENERATOR
LOGIC
EEG
OSCILLOSCOPE
SWEEP
TRIGGER
PULSE
AMPLIFIERS
COMPUTER
7 CHANNEL MAGNETIC
TAPE UNIT

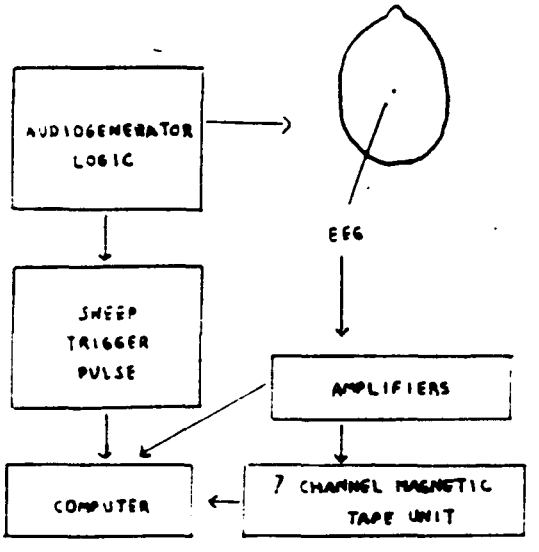
Figure 2: Block diagram of recording and data processing equipment used in the auditory missing stimuli studies.

Upper: Reaction time experiments.

Lower: No reaction time experiments.



MOTOR-RESPONSE CONDITION

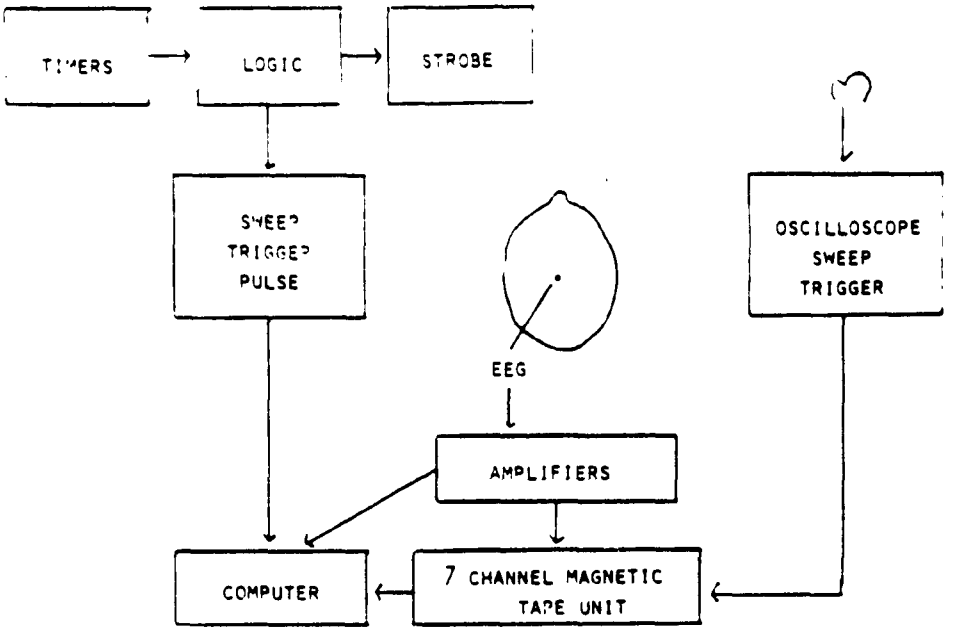


NO-MOTOR-RESPONSE CONDITION

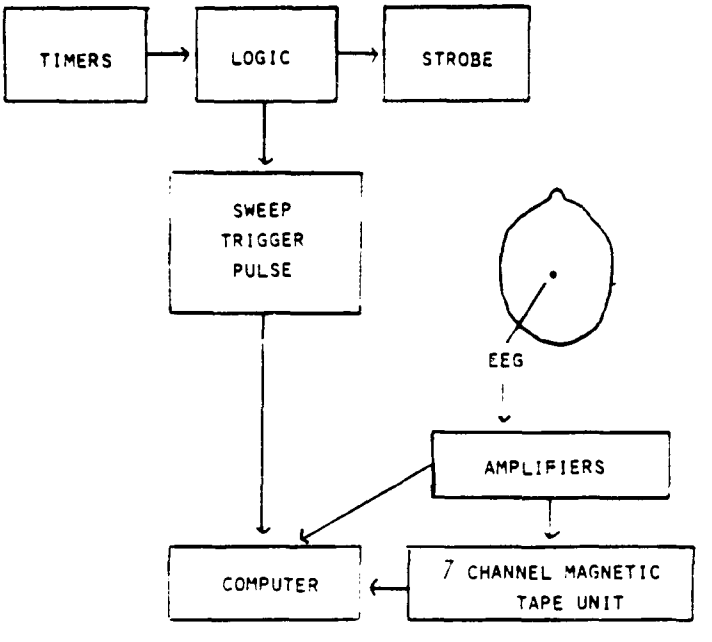
Figure 3: Block diagram of recording and data processing equipment used in the visual missing stimuli studies.

Upper: Reaction time experiments.

Lower: No reaction time experiments.



MOTOR-RESPONSE CONDITION



NO-MOTOR-RESPONSE CONDITION

response was employed to trigger the time base of a second oscilloscope (Tektronix 2B67) used to provide a trigger pulse at the initiation of each lift off. A pulse marking left off was also put on tape. The trigger sensitivity was reset at the onset of a run and was monitored during the run. In the visual conditions, RT responses were recorded in the same manner. The responses were, however, employed to trigger a third oscilloscope (Tektronix 532) providing a pulse at the initiation of each lift off that was put on tape. In the visual conditions, the second oscilloscope (Tektronix 2B67) was triggered by stimulus onset to provide a trigger pulse to the pulse generator (Tektronix PG505) that was used to drive the photic stimulator (Grass PS2), and in turn, generated the visual stimulus. The onset of the stimulus, used to trigger the time base of the second oscilloscope (Tektronix 2B67) was also used to provide a trigger pulse that was recorded on tape. (In the auditory task-related conditions, the RT response provided the trigger pulse and the onset of a stimulus was merely recorded on tape).

The amplified neuroelectric data were recorded at 3 3/4 ips or 7 1/2 ips on magnetic tape employing a 7-track FM tape unit (Honeywell Model 7600) with a frequency response of DC-2.5 KHz. Negative pulses marking signal tones and missing stimuli, and positive pulses marking nonsignal and non-task-related stimuli were recorded on tape.

3. Averaging Procedures

During each experimental run, EEG data were averaged on-line from analog tape using a Nicolet Med-80 computer. After the run, data were averaged off-line. The computer was programmed to sample continuously the electrophysiologic data at a predetermined sampling rate and to store a selected number of samples in memory. When a trigger pulse indicating the occurrence of a stimulus event was sensed by the computer, data that had been previously stored in memory were held and the computer continued to sample for a predetermined time and to add to memory the electrophysiologic data that

followed the trigger pulse. Thus, a pre-trigger and a post-trigger period were included in every data epoch. Finally, in order to provide an average event-related potential for one run, each epoch was added to the sum of data from previous trials and divided by the total number of trials in the run.

In order to minimize the contribution to averaged responses of muscle artifact, the computer was programmed to reject electrophysiologic activity with peak amplitudes larger than two volts.

In order to minimize contamination of data that was related to fluctuations in baseline DC voltage, the computer was programmed to continuously correct baselines by subtracting the calculated DC level of each waveform from every point in that waveform.

Computed averages were written out on a Houston X-Y plotter.

4. Data Analysis

In all of the experimental conditions, data obtained were analyzed in several ways. Averaged cortical potentials were computed for each run. In the task-related conditions, averaged potentials were obtained by separately averaging the nonsignal and the signal trials for each run. The grand mean event-related potentials were also computed, for each child within conditions, in association with the signals. Peak amplitude and peak latency measurements were made on averaged potentials that were comprised of 15 epochs (nonsignal auditory discrimination potentials), 25 epochs (signal missing stimuli potentials), 100 epochs (auditory evoked potentials), 150 epochs (nonsignal auditory discrimination

potentials), 250 epochs (nonsignal missing stimuli potentials), and 1000 epochs (auditory brainstem potentials). Amplitude was measured baseline to peak. The relative contribution of two sources of variance, the variability of the background EEG activity and of the event-related potentials, was assessed by examination of the standard deviation and the standard error of the mean. In the task-related conditions, variability of the background EEG in each child was assessed by computing in association with the signals the point by point standard deviations for each time sample. The standard error of the mean, derived as a measure of variability of the time-locked cortical potentials themselves, is estimated as the standard deviation divided by the square root of the number of samples entering into the mean. It was actually derived by computing point by point standard deviations of four averages obtained in association with the signals in each of the four missing stimulus conditions and six averages obtained in association with the signals in the auditory discrimination condition. Median reaction times were also computed in the task-related conditions. Based upon a conception of the study as an exploratory electrophysiologic examination of Childhood Autism, a comparison of data obtained in the subjects and in the controls was deemed appropriate. Averaged cortical potentials, grand mean event-related potentials, standard deviations, standard error of the means, and median reaction times were therefore inspected and differences were noted across children, within conditions, and across conditions.

CHAPTER III

RESULTS

A. Subcortical Evoked Potentials to Clicks

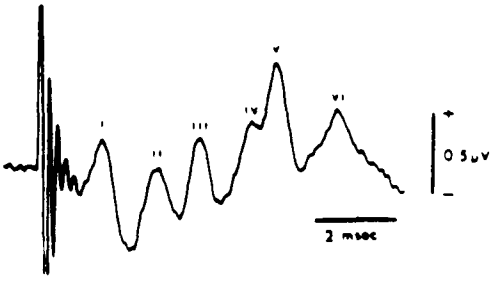
Auditory brainstem potentials were recorded from patient subjects in association with rapid binaural stimulation. The waveforms, recorded for averages of 1000 trials, consisted of a series of positive peaks. The auditory brainstem potentials that were recorded from the patient subjects were within normal limits (Figure 4); specifically, the potentials recorded from R.S. had five positive peaks with latencies that ranged from 1.8 to 7.5 msec; the potentials recorded from H.P. had five positive peaks with latencies that ranged from 1.4 to 7.1msec; in S.N. the earliest of five peaks had a latency of 1.9msec and the latest peak had a latency of 7.1msec.

B. Cortical Evoked Potentials to Clicks

The longer latency auditory evoked potentials elicited by clicks were always largest at the vertex. The average waveforms in response to 100 clicks are shown in Figure 5. In the normal subjects, a characteristic positive-negative-postive (P1-N1-P2) waveform was present in both the 1sec ISI condition and the 3sec ISI condition. A small late negativity and a later positivity were also seen. In the 1sec ISI condition peak latencies were P1 (65-75msec), N1 (90-115msec), P2 (130-190msec); peak amplitudes were P1 (1-2uv), N1 (1-2uv), P2 (3-5uv). In the 3sec ISI condition peak latencies were P1 (45-85msec), N1 (85-130msec), P2 (190-200msec); peak amplitudes were P1 (1-2uv),

Figure 4: Averaged brainstem potentials recorded in response to 1000 clicks from the vertex referred to the nose. Bar beneath the trace indicates onset of click.

NORMAL



PATIENT SUBJECTS

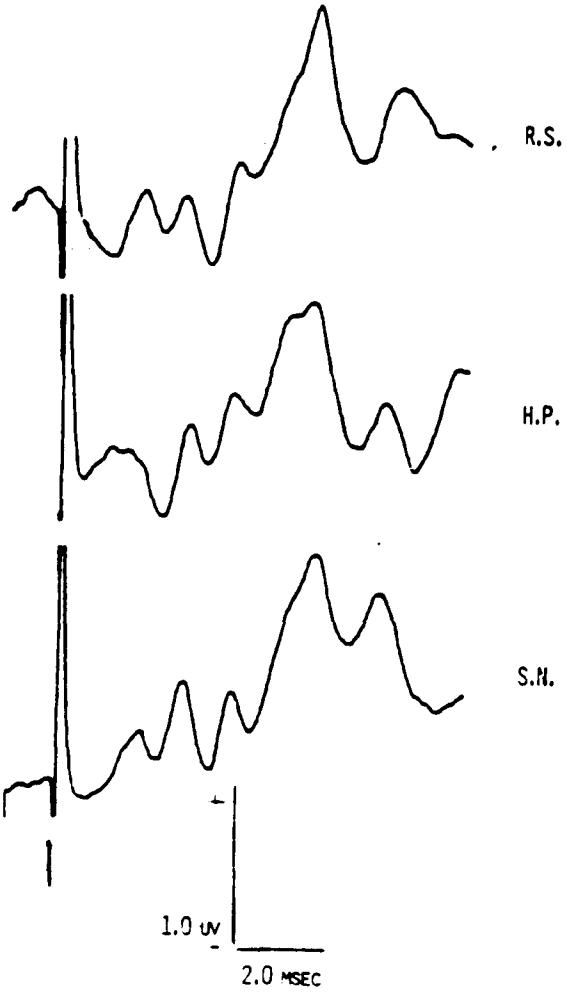
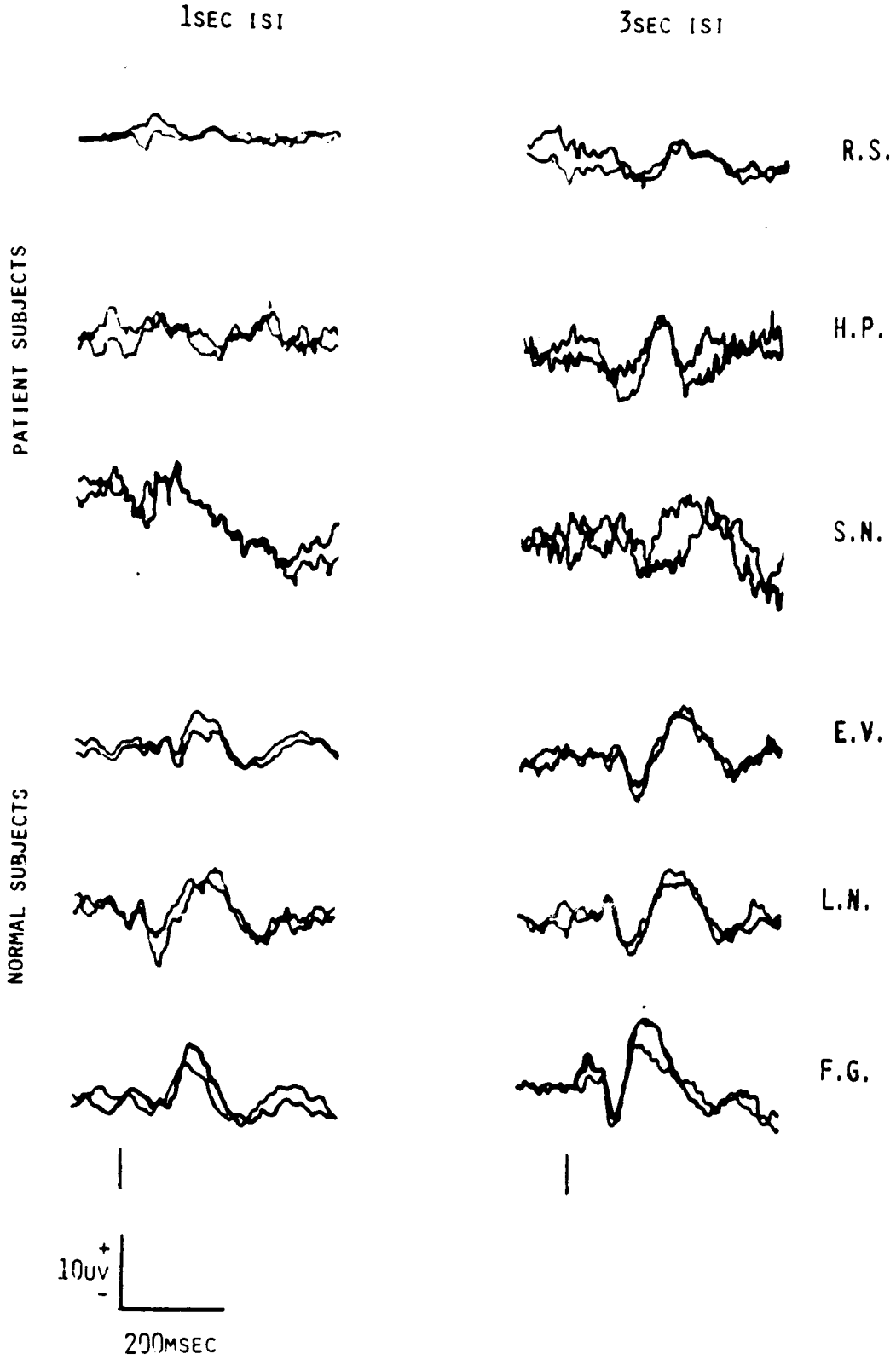


Figure 5: Averaged cortical evoked potentials recorded in response to 100 binaural clicks at the vertex electrode. Two averages recorded in a 1sec ISI and a 3sec ISI condition are superimposed. Bar beneath the trace indicates onset of click.


1SEC ISI
3SEC ISI
PATIENT SUBJECTS
NORMAL SUBJECTS
R.S.
H.P.
S.N.
E.V.
L.N.
F.G.
10UV
+
-
200MSEC

N1 (4-5uv), P2 (5-7uv). Responses were remarkably invariant across runs. In the patient subjects, the w-shaped complex was not seen in the 1sec ISI condition - in R.S., no evoked potential was seen; in H.P. only the first positive peak was present; whereas in S.N. a late aberrant negativity was seen. In order to examine the possibility that the evoked potential decreased rapidly in amplitude (habituation) accounting for the reduced amplitude of the average waveform, potentials were averaged in response to the first two blocks of ten clicks. Activity later than P1 was absent. In the 3sec ISI condition, however, the positive-negative-positive waveform was seen in the patients. Late negativity and later positivity were also seen in S.N. Peak latencies were P1 (50-75msec), N1 (90-120msec), P2 (165-235msec); peak amplitudes were P1 (1-2uv), N1 (1-3uv), P2 (1-4uv) - no different than the normal subjects. In contrast to the normal subjects, considerable variability across runs was seen in the patient subjects. Measurements of the cortical evoked responses to clicks are summarized in Table 2.

No differences were noted in the cortical potentials recorded in association with right ear versus left ear stimulation.

C. Potentials Associated with Auditory Discrimination

1. Responses to Nonsignals

Cortical evoked potentials were averaged in response to 150 non-signal tones (Figure 6). Potentials were seen in all subjects and were always largest at the vertex. In both normal and patient subjects the initial positive peak had a latency of (approximately) 35-55msec followed

Table 2: Latency and amplitude measurements of component peaks of grand mean cortical evoked potentials to clicks. Grand mean waveforms are comprised of averages recorded at the vertex electrode.

MEASUREMENTS OF CORTICAL EVOKED POTENTIALS TO CLICKS

	NORMAL SUBJECTS			PATIENT SUBJECTS		
1 SEC ISI	E.V.	L.N.	F.G.	R.S.	H.P.	S.N.
P1						
Latency	65	75	70	-	50	-
Amplitude	11	2	1	0	3	0
N1						
Latency	100	115	90	-	-	-
Amplitude	2	2	1	0	0	0
P2						
Latency	150	190	130	-	-	-
Amplitude	3	4	5	0	0	0
3 SEC ISI						
P1						
Latency	85	80	45	75	75	50
Amplitude	1	2	1	1	1	2
N1						
Latency	130	115	85	110	90	120
Amplitude	5	4	4	1	3	2
P2						
Latency	200	200	190	190	165	235
Amplitude	5	5	7	1	4	3

Latency in msec
Amplitude in uv

Figure 6: Averaged cortical evoked potentials recorded in response to 150 nonsignal tones at the vertex electrode in the auditory discrimination condition. Bar beneath the trace indicates onset of nonsignal tone.

NORMAL SUBJECTS

E.V.

L.N.

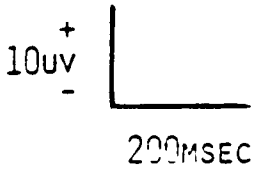
F.G.

PATIENT SUBJECTS

R.S.

H.P.

S.N.



by a large negativity that occurred at about 80-100msec and a second positivity with a latency of about 150-200msec. In L.N., late negativity was seen at 300msec and in F.G. late negativity was seen at 225msec and late positivity at 275msec. In two patient subjects (H.P. and S.N.) late positivity was seen at about 250msec. In all subjects amplitude of P1 was about 2uv and amplitude of N1 was about 5uv. Although amplitude of P1 and N1 were similar in normal and patient subjects, amplitude of P2 in normal subjects was 5-10uv and amplitude of P2 was 0.5-uv in patient subjects - or smaller than in the normals. In contrast to the auditory evoked potentials seen in the 1sec and 3sec ISI condition that required no response, responses seen in the patient subjects in this condition were extremely well developed.

2. Responses to Signals

In both patient and normal subjects inspection of waveforms recorded in response to signal tones from each electrode site revealed a characteristic distribution of the brain responses. Waveforms recorded from one patient subject (S.N.) are shown in Figure 7 to illustrate the scalp topography of potentials in the auditory discrimination condition.

Cortical potentials averaged in response to signal tones were always largest at the parietal site. Grand mean waveforms and their standard errors were computed for six averages of 15 trials recorded from the parietal electrode. Late positivity was seen in all subjects. The potentials are depicted in Figure 8. At the parietal site

Figure 7: Topographic distribution of grand mean waveforms computed in association with signals in the auditory discrimination condition. Waveforms are comprised of six averages of 15 trials recorded at each electrode site from one patient subject.

Bar beneath the trace indicates onset of signal tone.

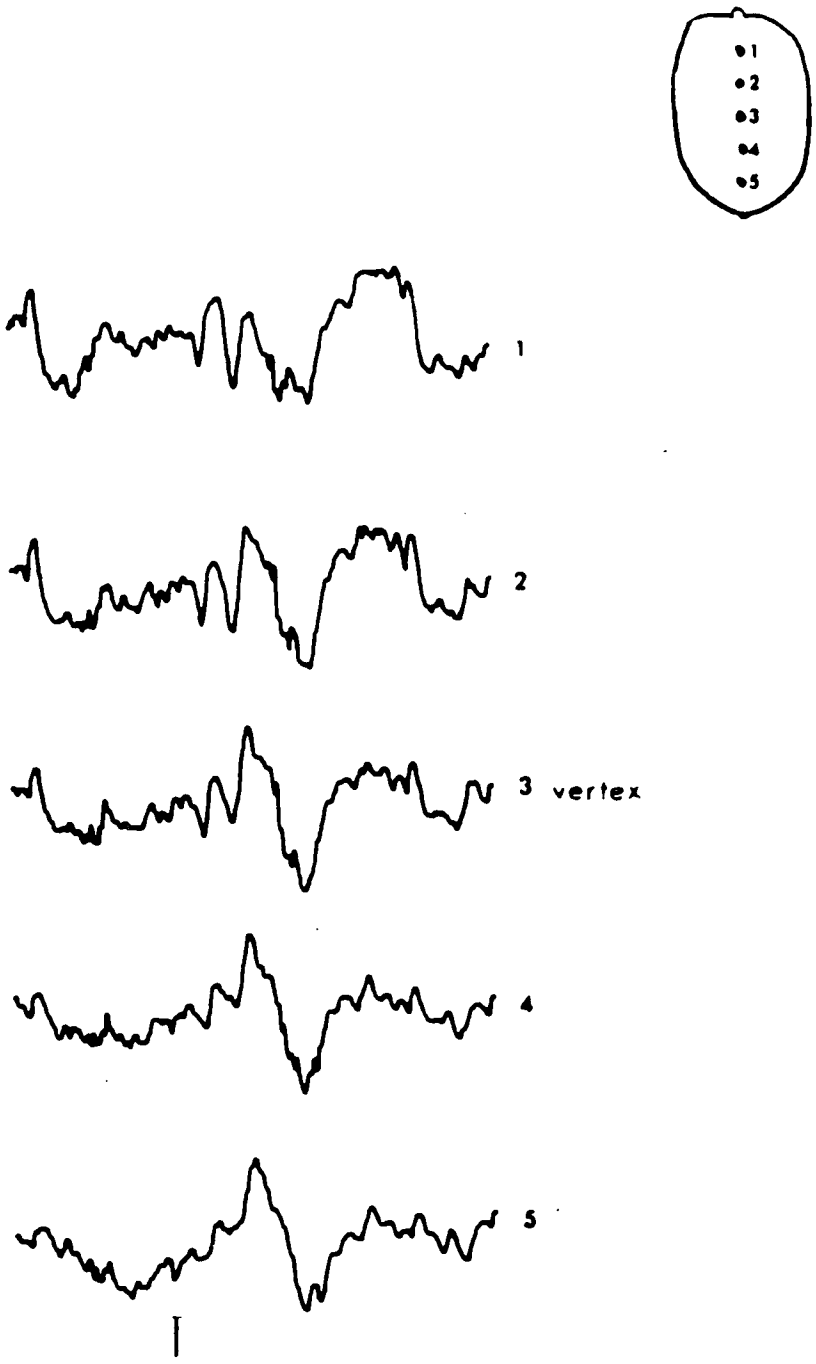

1
2
3
4
5
1
2
3
4
5
vertex
+
20uv
-
200msec

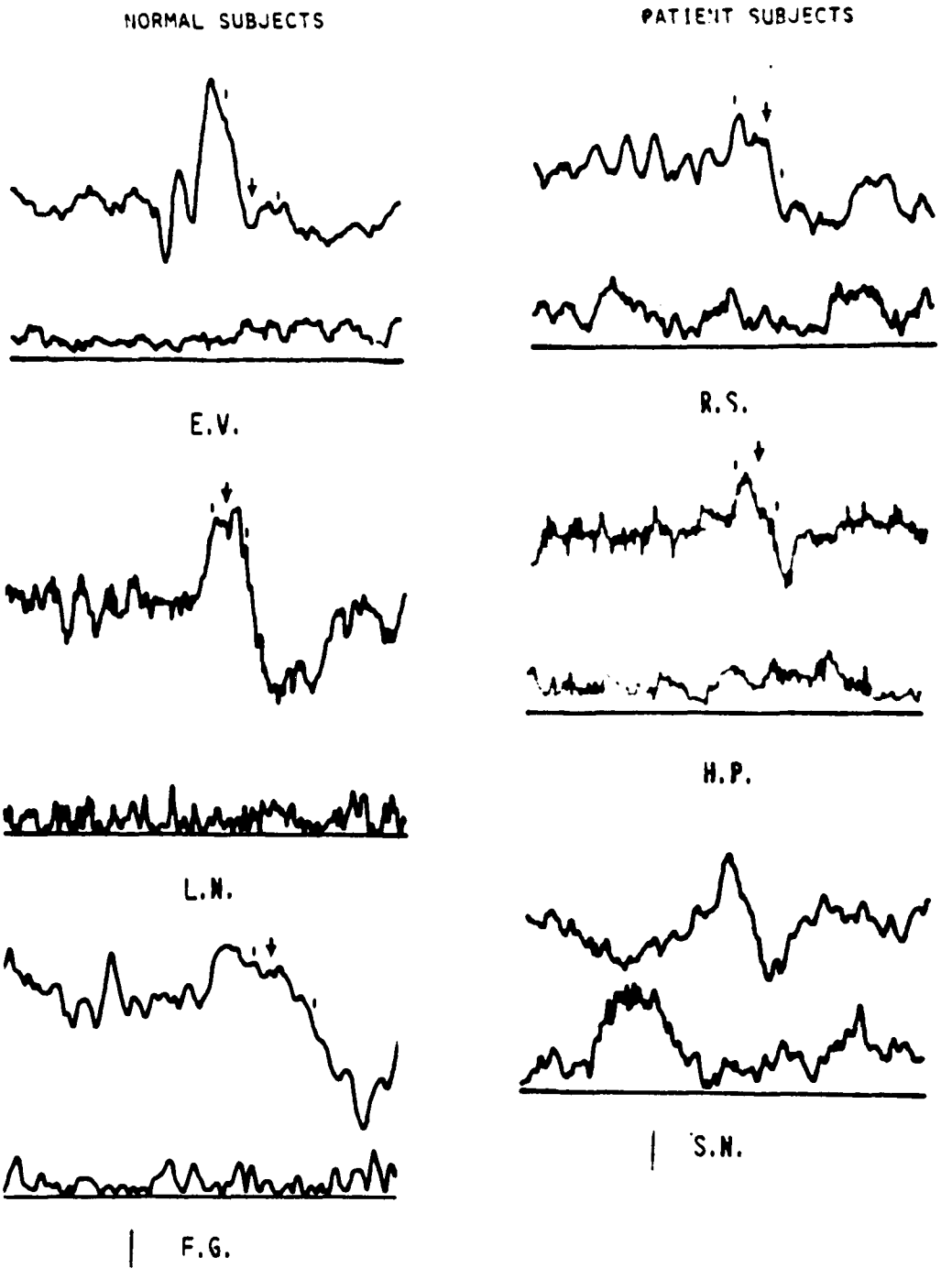
Figure 8: Grand mean waveforms and their standard errors computed in association with signal tones in the auditory discrimination condition. Waveforms are comprised of six averages of 15 trials recorded at the parietal electrode.

Arrow denotes median reaction time. Vertical lines above trace denotes interquartile range of reaction times.

Bar beneath the trace indicates onset of signal tone.

Upper trace represents grand mean waveform.

Lower trace represents standard error.


NORMAL SUBJECTS
PATIENT SUBJECTS
E.V.
R.S.
L.N.
H.P.
F.G.
S.N.
10uv
200MSEC

auditory evoked potentials were seen only in E.V. The late positive activity seen was characteristic of event-related potentials in experimental situations where a perceptual judgment about stimulus events is required (see Introduction section D, 4a). Latency of the LPC was similar in all subjects. In the normal subjects latency was 270msec (E.V.), 320msec (L.N.), and 350msec (F.G.). In the patient subjects latency was 280msec (R.S.), 320msec (H.P.), and 260msec (S.N.). Amplitude of the LPC in the normal subjects was 15uv (E.V.), 8uv (L.N.), and 4uv (F.G.). In the patient subjects amplitude was 2uv (R.S.), 3uv (H.P.), and 10uv (S.N.) - or, smaller than the normals. In the normal subjects variability across the epoch was small and no increase in variability was associated with the LPC. In one normal subject (E.V.), however, increased variability was associated with late negativity at 420msec that followed the LPC. In the patients variability across the epoch was greater than in the normals and - as was the case in the normals, no increased variability was associated with the LPC. In addition, no increase in variability was associated with late negativity seen in H.P. at 500msec and in S.N. at 400msec. Measurements of the last positive components in the waveforms associated with auditory discrimination are summarized in Table 3.

Median reaction times to the signals are noted in Figure 8. In the normal subjects values obtained were 420msec (E.V.), 340msec (L.N.), and 510msec (F.G.). Accuracy of the response was 100%. In the patient subjects median reaction times were 390msec (R.S.) and 370msec (H.P.) -

Table 3: Latency, amplitude, and standard error measurements of late positive components of the grand mean potentials associated with auditory discrimination.
Grand mean waveforms are comprised of averages recorded at the parietal electrode.

MEASUREMENTS OF LATE POSITIVE COMPONENTS IN WAVEFORMS

ASSOCIATED WITH AUDITORY DISCRIMINATION

	NORMAL SUBJECTS			PATIENT SUBJECTS		
	E.V.	L.N.	F.G.	R.S.	H.P.	S.N.
Latency	270	320	350	280	320	260
Amplitude	15	8	4	2	3	10
Standard Error at Point of Measurement	1.0	1.0	1.0	2.0	3.0	3.0

Latency in msec
Amplitude in uv
Standard Error in uv

similar to the values obtained for the normal subjects. One patient subject (S.N.) was unable to learn the RT task. During the training period he was taught to label verbally each stimulus event "high tone" or "low tone". In all patient subjects motor response accuracy was poorer than in the normal subjects; ranging from 80-90%.

D. Missing Stimulus Potentials

1. Auditory Condition

a. Responses to auditory stimuli. Cortical evoked potentials were averaged in response to 250 tones (Figure 9). Potentials were seen in all subjects and were always largest at the vertex site. In both normal and patient subjects a small initial positivity peaked at about 50msec followed by a negative peak at about 100msec and a second positivity that peaked at about 150-200msec. In all subjects peak amplitudes were about P1 (0.5-1uv), N1 (0.5-2uv), and P2 (2-5uv). In contrast to the auditory evoked potentials seen in the 1sec ISI condition that required no response, responses seen in the patient subjects in this condition were well developed and not noticeably different than responses in the normal subjects.

b. Missing stimulus potentials in motor response condition. Averaged cortical potentials associated with the missing stimuli were always largest at the parietal site. Grand mean waveforms and their standard errors were computed for four averages of 25 trials recorded from the parietal electrode. Late positive activity was seen in all normal subjects. The potentials are depicted in Figure 10 which also

Figure 9: Averaged cortical evoked potentials recorded in response to 250 nonsignal tones at the vertex electrode in the auditory missing stimulus conditions.

Bar beneath the trace indicates onset of nonsignal tone.

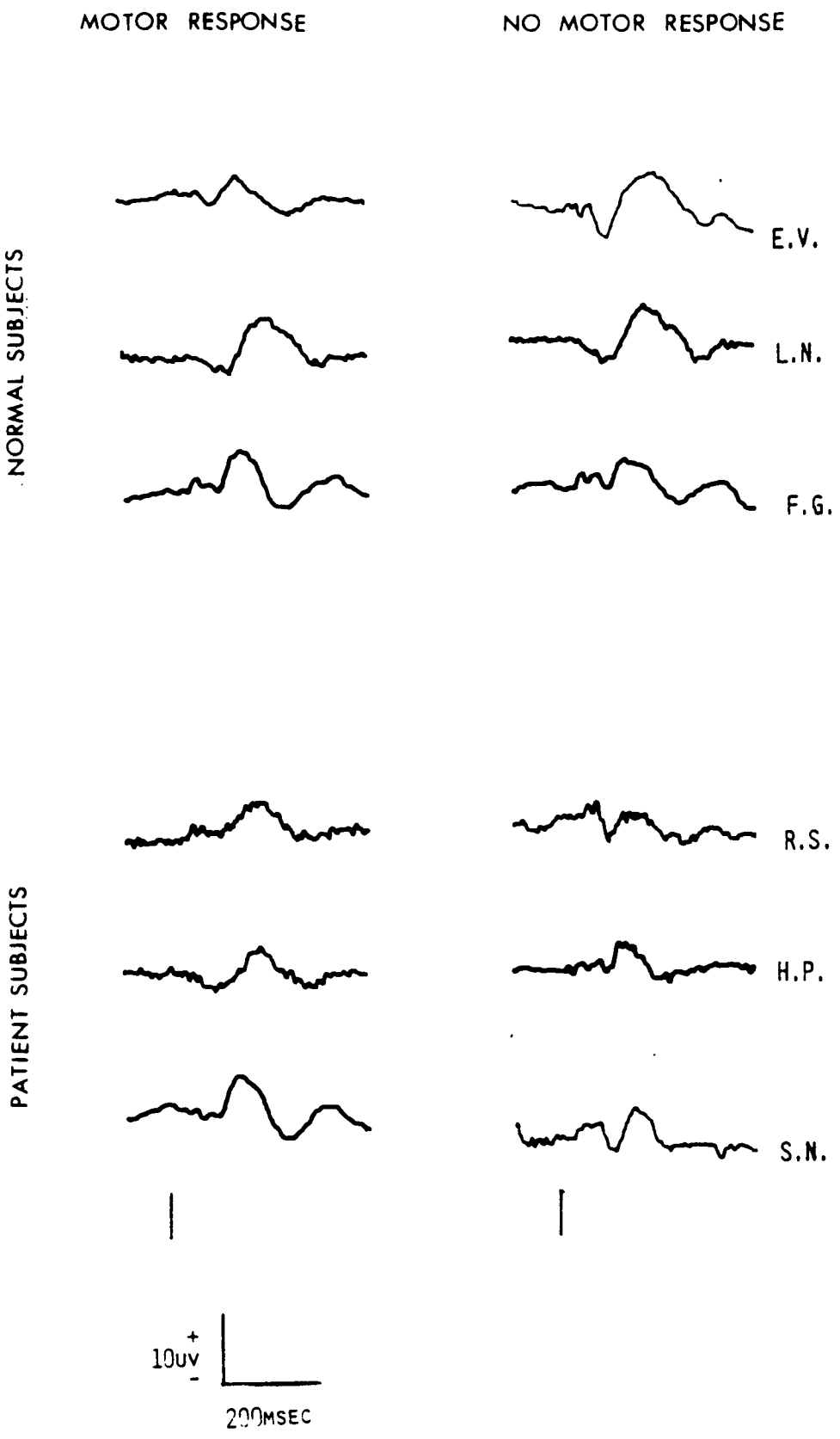
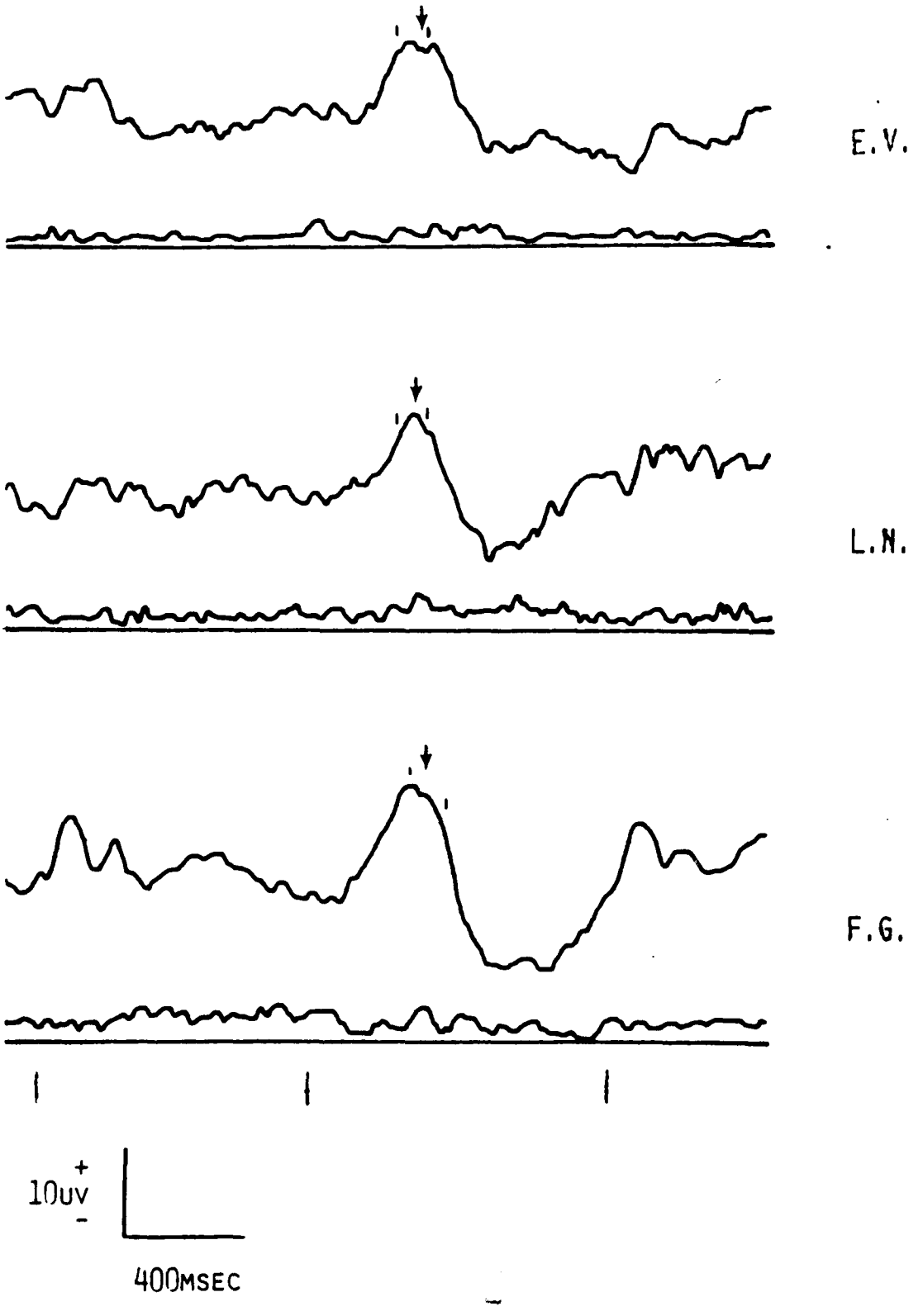

MOTOR RESPONSE
NO MOTOR RESPONSE
NORMAL SUBJECTS
E.V.
L.N.
F.G.
PATIENT SUBJECTS
R.S.
H.P.
S.N.
10uv
200MSEC

Figure 10: Grand mean waveforms and their standard errors computed in association with signals in the motor response (auditory missing stimulus) condition.
Waveforms are comprised of four averages of 25 trials recorded at the parietal electrode from normal subjects.
Arrow denotes median reaction time. Vertical lines above trace denote interquantile range of reaction times.
First and third bars beneath the trace indicate onset of nonsignal tone. Middle bar indicates point in time of stimulus deletion.
Upper trace represents grand mean waveform.
Lower trace represents standard error.


E.V.
L.N.
F.G.
10uv
+
-
400MSEC

shows the standard errors of the means. The brain responses comprised the late positive activity that is characteristic of event-related potentials in experimental situations where expected stimuli are occasionally and randomly deleted (see Introduction section D, 4c). Latency of the LPC was 360msec (E.V. and L.N.) and 370msec (F.G.); amplitude of the LPC was 9uv (E.V.), 8uv (L.N.), and 10uv (F.G.). Variability across the epoch was small and there was no increase in variability associated with the LPC or the later negativity seen in L.N. and F.G. at about 600msec.

Median reaction times to the signals are noted in Figure 10. The values obtained were 360msec (E.V.), 320msec (L.N.), and 380msec (F.G.). Accuracy of the response was 100%.

Late positivity was not seen in grand mean waveforms computed for patient subjects. Absence of the LPC led to an inspection of averaged potentials associated with the missing stimuli and their standard deviations (computed for 25 missing stimuli) recorded from the parietal electrode in four runs. The potentials and their standard deviations are depicted in Figure 11. Waveforms that were recorded from S.N. in the second run and from other patient subjects illustrate the poorly developed LPC that characterized most long latency brain responses recorded from the patient subjects in this condition. Late positivity was seen only in the first run. Latency of the LPC was 400msec and amplitude was 10uv - no different than in the normal subjects. Unlike the normal subjects, however, in all patient subjects variability across the epoch was considerable and probably reflects variability of the

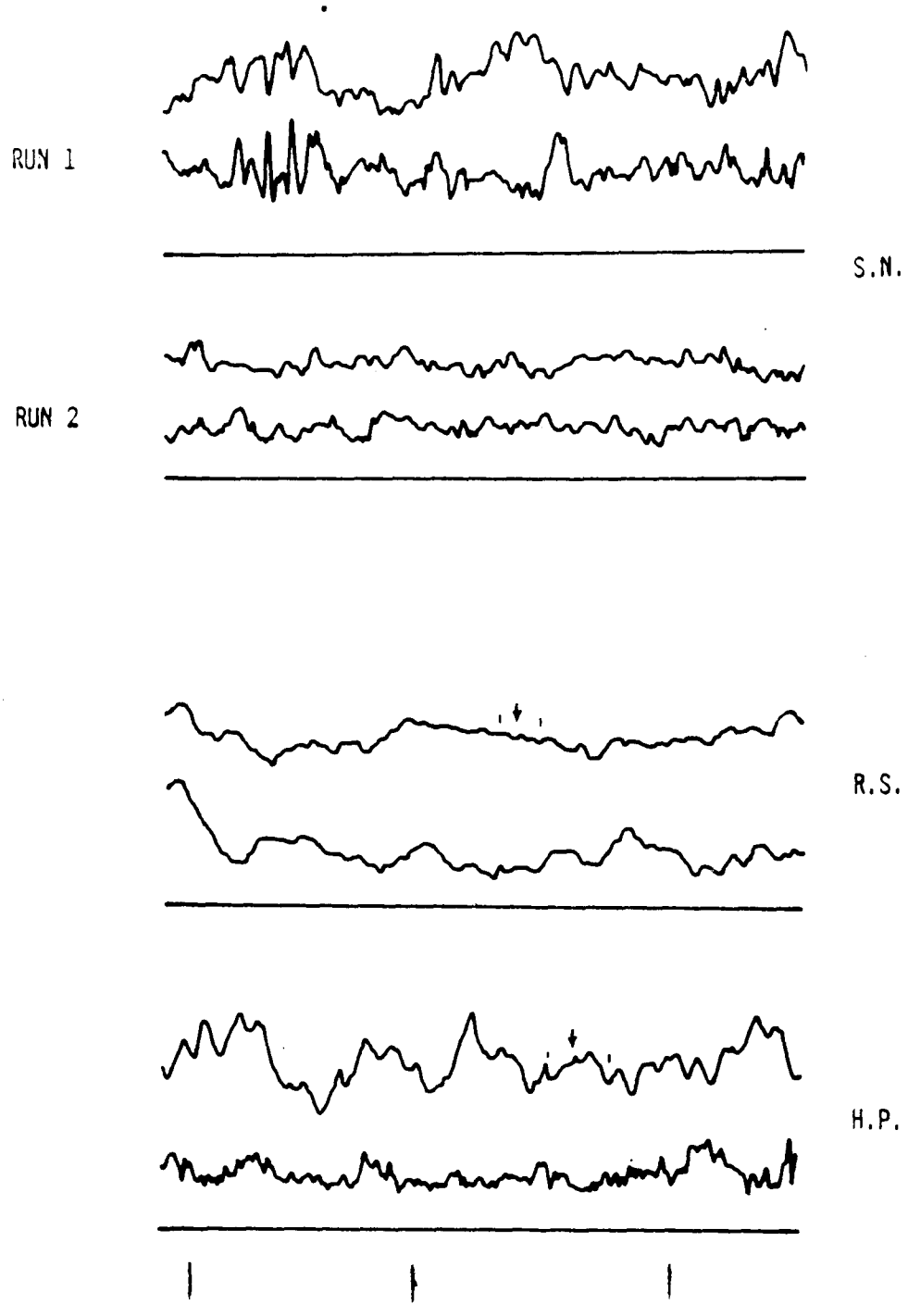
Figure 11: Averaged parietal potentials and their standard deviations computed in association with 25 signals in the motor response (auditory missing stimulus) condition. Averaged potentials were recorded from patient subjects.

Arrow denotes median reaction time. Vertical lines above trace denote interquantile range of reaction times.

First and third bars beneath the trace indicate onset of nonsignal tone. Middle bar indicates point in time of stimulus deletion.

Upper trace represents averaged potential.

Lower trace represents standard deviation.


RUN 1
S.N.
RUN 2
R.S.
H.P.
20uv
+
-
400MSEC

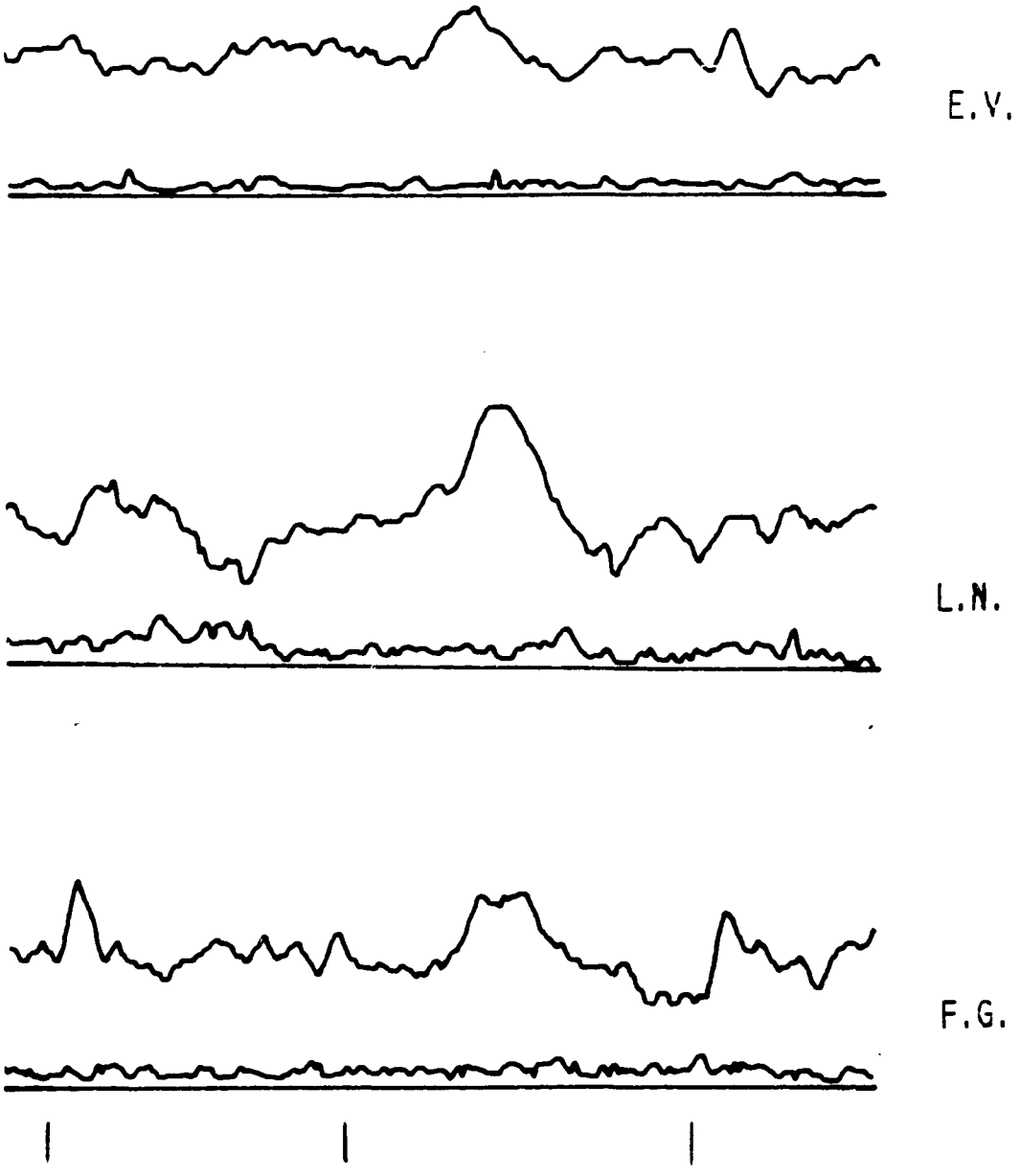
background EEG. No increase was seen in EEG variability in association with late positivity seen in S.N.

Median reaction times to the signals are noted in Figure 11. The values obtained for patient subjects were 390msec (R.S.) and 620msec (H.P.) - only the latter was noticeably larger than values obtained for the normal subjects. Once again one patient subject (S.N.) was unable to learn the required RT task. During the training period he was taught to label verbally each stimulus event "high tone" or "no tone". Motor response accuracy was poorer than in the normal subjects, ranging from 75-90%.

c. Missing stimulus potentials in no motor response condition. Averaged cortical potentials associated with the missing stimuli were always largest at the parietal site. Grand mean waveforms and their standard errors were computed for four averages of 25 trials recorded from the parietal electrode. Late positivity was seen in all normal subjects. The potentials are depicted in Figure 12 which also shows the standard errors of the means. Latency of the LPC was 360msec (E.V.), 400msec (L.N.), and 420msec (F.G.). Amplitude of the LPC was 3uv (E.V.), 10uv (L.N.), and 5uv (F.G.) - smaller than in the motor response condition. Once again, small variability existed across the epoch and variability in association with the LPC and the later negativity (seen in E.V. at 625msec and in L.N. at 650msec) was negligible.

Late positivity was seen in grand mean waveforms computed for patient subjects. Absence of the LPC led to inspection of averaged

Figure 12: Grand mean waveforms and their standard errors computed in association with signals in the no motor response (auditory missing stimulus) condition. Waveforms are comprised of four averages of 25 trials recorded at the parietal electrode from normal subjects.
First and third bars beneath the trace indicate onset of nonsignal tone. Middle bar indicates point in time of stimulus deletion.
Upper trace represents grand mean waveform.
Lower trace represents standard error.


E.V.
L.N.
F.G.
+
10uv
-
400MSEC

potentials associated with the missing stimuli and their standard deviations (computed for 25 missing stimuli) recorded from the parietal electrode in four runs. The potentials and their standard deviations are depicted in Figure 13. Waveforms that were recorded from R.S. in the third run and from the other patients illustrate absence of the LPC that characterized most recordings from patient subjects in this condition. Late positivity seen only in R.S. and only in the fourth run had a latency of 360msec and an amplitude of 2uv - not very different in latency but smaller than the normal subjects. Unlike the normal subjects, however, all patient subjects had responses that varied across the epoch. No increased variability was seen in association with the LPC recorded from R.S.

Measurements of late positive components in the waveforms associated with auditory missing stimuli are summarized in Table 4.

2. Visual Condition

a. Responses to visual stimuli. Visual evoked potentials were averaged in response to 250 flashes (Figure 14). Potentials were seen in all subjects and were always largest at the occipital site. In both normal and patient subjects an early negativity peaked at about 50-80msec and a prominent positivity peaked at about 100-150msec followed by a series of positive peaks (that terminated at about 300msec). Response amplitude in the normal subjects was N1 (1-7uv) and P1 (5-15uv). In the patient subjects amplitude was N1 (1-4uv) and P1 (4-15uv) - or similar to the normal subjects.

Figure 13: Averaged parietal potentials and their standard deviations conputed in association with 25 signals in the no motor response (auditory missing stimulus) condition. Averaged potentials were recorded from patient subjects.
First and third bars beneath the trace indicate onset of nonsignal tone. Middle bar indicates point in time of stimulus deletion.
Upper trace represents averaged potential.
Lower trace represents standard deviation.

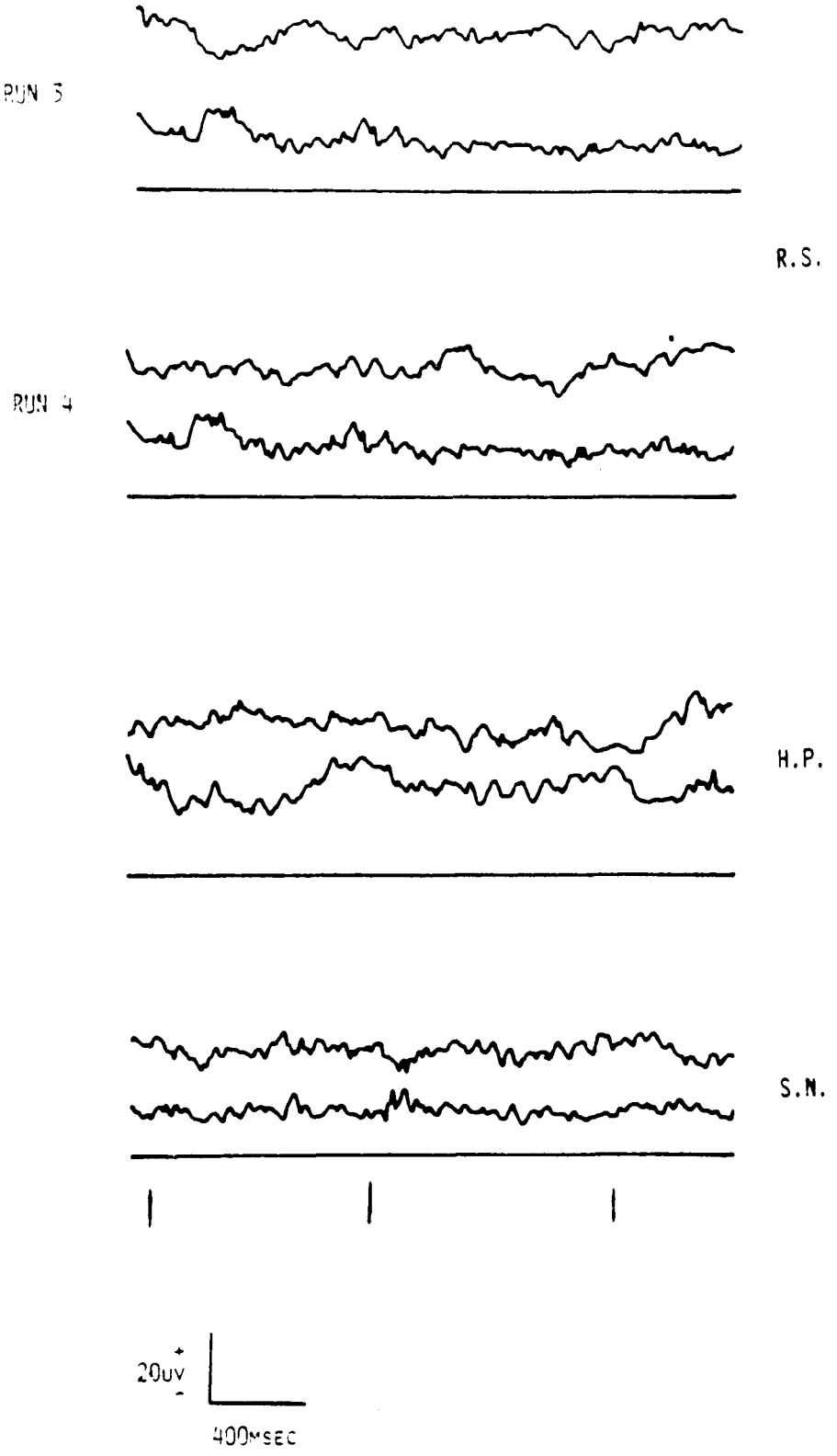

RUN 5
R.S.
RUN 4
H.P.
S.N.
20uv
400MSEC

Table 4: Latency, amplitude, and variability measurements of late positive components of the grand mean potentials and the averaged potentials associated with auditory missing stimuli.
Waveforms were recorded at the parietal electrode.

MEASUREMENTS OF LATE POSITIVE COMPONENTS IN WAVEFORMS ASSOCIATED WITH AUDITORY MISSING STIMULI

NORMAL SUBJECTS

	Motor Response Condition			No Motor Response Condition		
Grand Mean Potentials	E.V.	L.N.	F.G.	E.V.	L.N.	F.G.
Latency	360	360	370	360	400	420
Amplitude	9	8	10	3	10	5
Standard Error at Point of Measurement	1.0	2.0	1.0	1.0	1.0	1.0

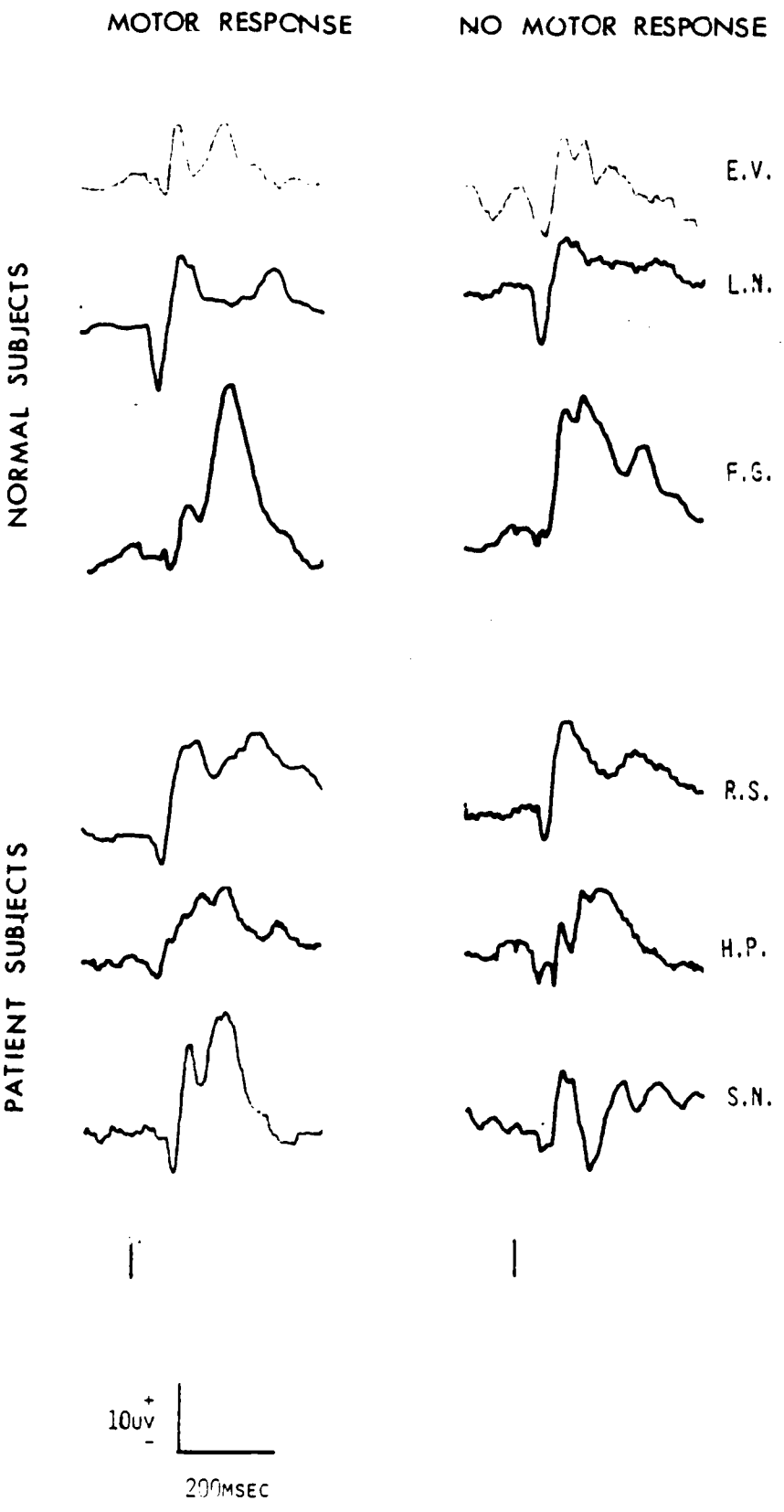
PATIENT SUBJECTS

	Motor Response Condition			No Motor Response Condition		
Averaged Potentials	R.S.	H.P.	S.N.*	R.S.*	H.P.	S.N.
Latency	-	-	400	360	-	-
Amplitude	0	0	10	2	0	0
Standard Error at Point of Measurement	2	2.8	3.4	2.2	3.4	2

*In the motor response condition, measurements for S.N. are for one averaged potential recorded in the first of four runs. In the no motor response condition, measurements for R.S. are for one averaged potential recorded in the last of four runs.

Latency in msec
Amplitude in uv
Standard Error in uv
Standard Deviation in uv

Figure 14: Averaged visual evoked potentials recorded in response to 250 nonsignal flashes at the occipital electrode in the visual missing stimulus conditions. Bar beneath the trace indicates onset of nonsignal flash.


MOTOR RESPONSE
NO MOTOR RESPONSE
NORMAL SUBJECTS
PATIENT SUBJECTS
E.V.
L.N.
F.G.
R.S.
H.P.
S.N.
10uv
200MSEC

b. Missing stimulus potentials in motor response condition. Averaged cortical potentials associated with the missing stimuli were always largest at the occipital site. Grand mean waveforms and their standard errors were computed for four averages of 25 trials recorded from the parietal electrode. Lat positive activity was seen in all normal subjects. The potentials are depicted in Figure 15 which also shows the standard errors of the means. Latency of the LPC was 400msec (E.V.), 400msec (L.N.), and 390msec (F.G.). Amplitude of the LPC was 4uv (E.V.), 4uv (L.N.), and 8uv (F.G.). In all normal subjects variability across the epoch was small and increased variability in association with the LPC was absent.

Median reaction times to the signals are noted in Figure 15. The values obtained were 340msec (E.V.), 460msec (L.N.), and 400msec (F.G.). Accuracy of the response was 100%.

Late positivity was not seen in grand mean waveforms computed for patient subjects. Absence of the LPC led to an inspection of averaged potentials associated with the missing stimuli and their standard deviations (computed for 25 missing stimuli) recorded from the parietal electrode in four runs. The potentials and their standard deviations are depicted in Figure 16. Waveforms that were recorded from H.P. and S.N. illustrate the poorly developed LPC that characterized most brain responses recorded from patient subjects in this condition. Late positivity was seen only in R.S. in runs one and two. Latency of the LPC was 400msec and amplitude was 6uv and 2uv - no different than the LPC seen in normal subjects. However, once again and in contrast to the normal subjects, variability across the epoch was considerable

Figure 15: Grand mean waveforms and their standard errors computed in association with signals in the motor response (visual missing stimulus) condition.
Waveforms are comprised of four averages of 25 trials recorded at the parietal electrode from normal subjects.
Arrow denotes median reaction time. Vertical lines above trace denote interquantile range of reaction times.
First and second bars beneath the trace indicate onset of nonsignal flash. Middle bar indicates point in time of stimulus deletion.
Upper trace represents grand mean waveforms.
Lower trace represents standard error.

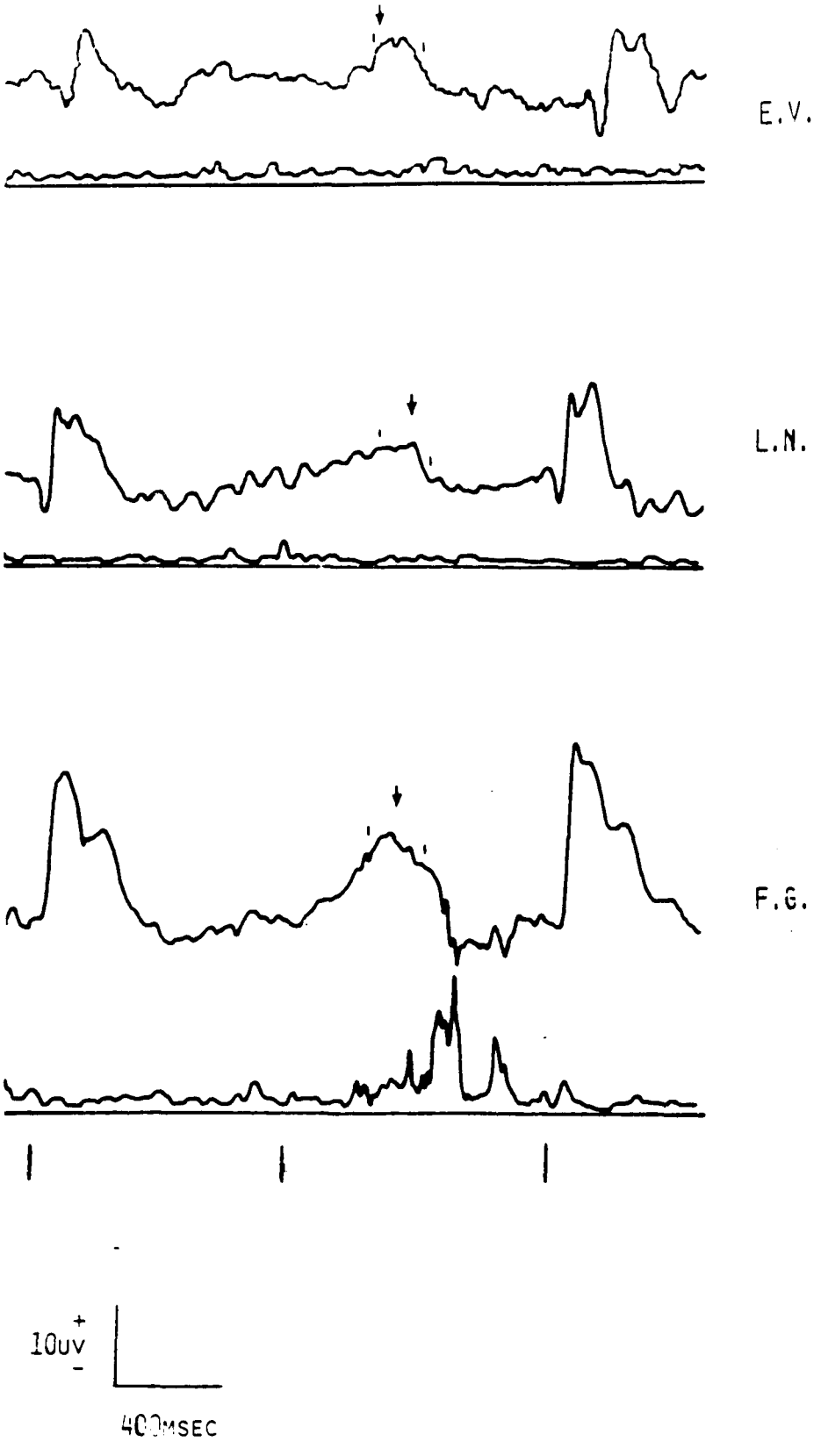

E.V.
L.N.
F.G.
10uv
+
-
400MSEC

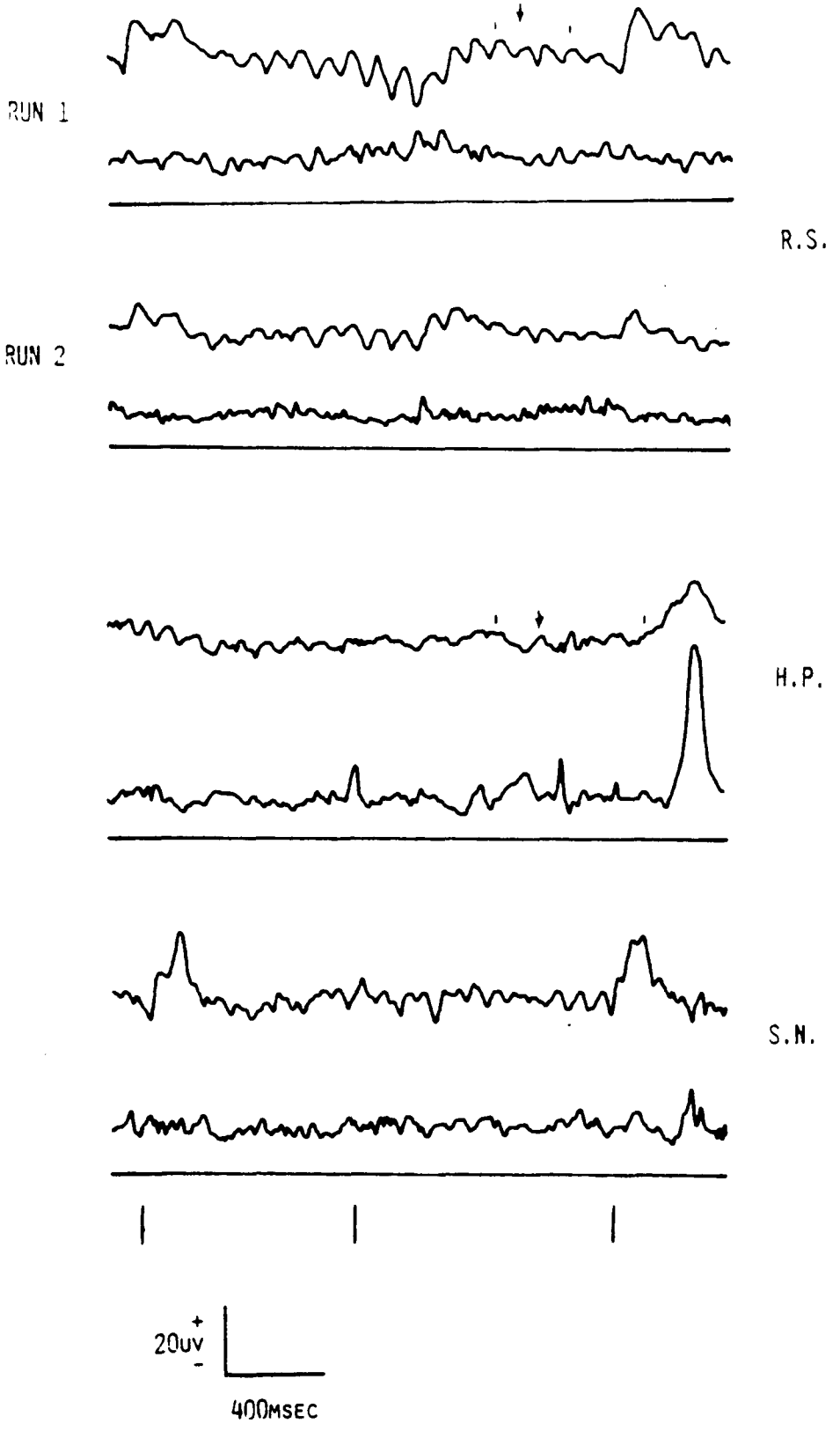
Figure 16: Averaged parietal potentials and their standard deviations computed in association with 25 signals in the motor response (visual missing stimulus) condition. Averaged potentials were recorded from patient subjects.

Arrow denotes median reaction time. Vertical lines above trace denote interquartile range of reaction times.

First and third bars beneath the trace indicate onset of nonsignal flash. Middle bar indicates point in time of stimulus deletion.

Upper trace represents averaged potential.

Lower trace represents standard deviation.


RUN 1
R.S.
RUN 2
H.P.
S.N.
20uv
+
-
400MSEC

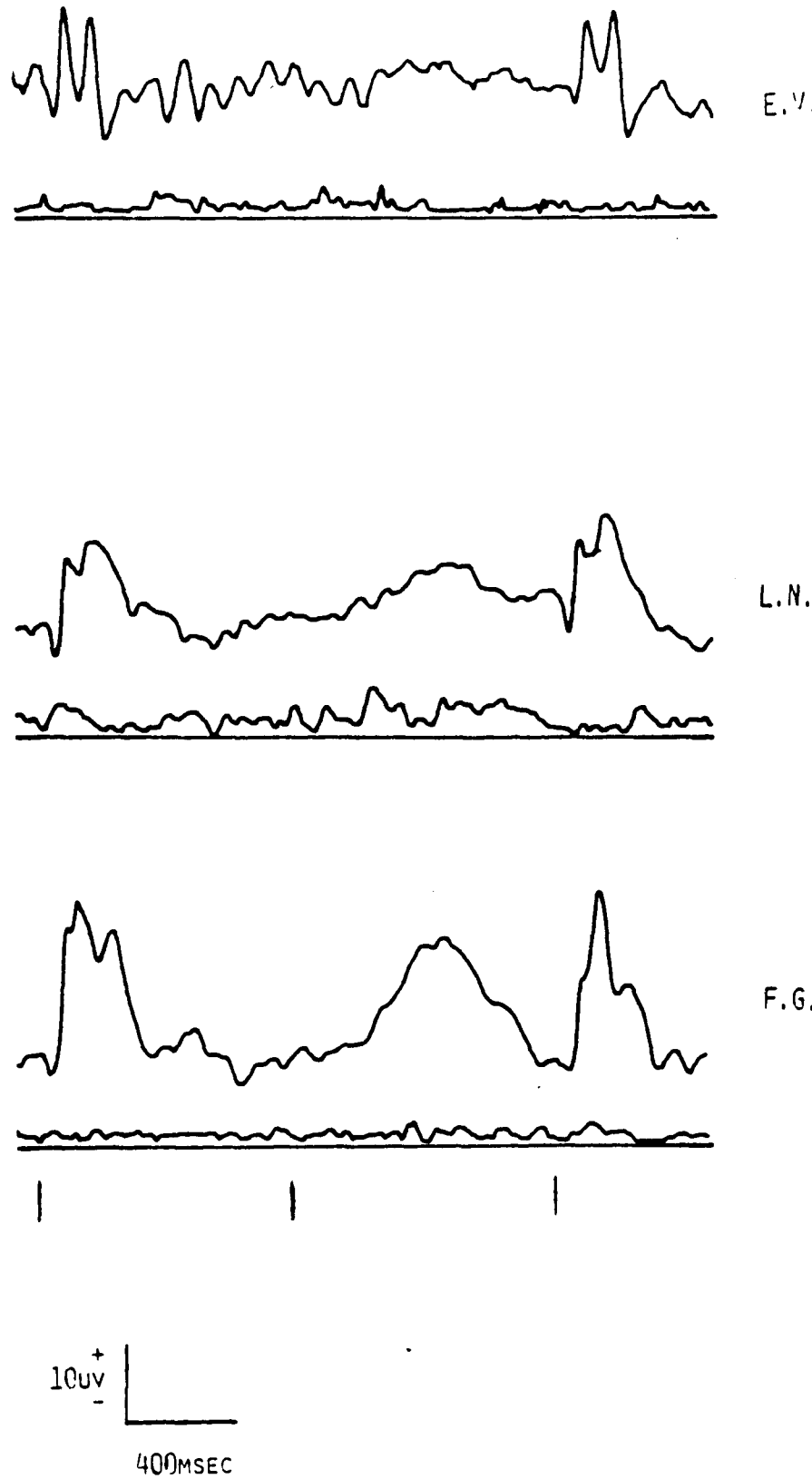
reflecting variability of the background EEG. No increase was seen in variability associated with the LPC recorded from R.S.

Median reaction times to the signals are noted in Figure 16. The values obtained were 660msec and 750msec (H.P.) - larger than the values obtained for normal subjects. S.N. was unable to learn the R.T. task. During the training period he was taught to label verbally each stimulus event "light" or "no light". Motor response accuracy ranging from 70-80% was poorer than in the normal subjects and, in addition, poorer than in the other conditions that required subjects to evaluate stimulus events.

c. Missing stimulus potentials in no motor response condition. Averaged cortical potentials associated with the missing stimuli were always largest at the parietal site. Grand mean waveforms and their standard errors were computed for four averages of 25 trials recorded from the parietal electrode. Late positive activity was seen in all normal subjects. The potentials are depicted in Figure 17 which also shows the standard errors of the means. Latency of the LPC was 400msec (E.V.), 500msec (L.N.), and 500msec (F.G.). Amplitude of the LPC was 3uv (E.V.), 5uv (L.N.), and 11uv (F.G.) - no different than in the motor response condition. No variability across the epoch was noted and variability in association with the LPC was insignificant.

Late positivity was not seen in grand mean waveforms computed for patient subjects. Absence of the LPC led to an inspection of average potentials associated with the missing stimuli, and their standard

Figure 17: Grand mean waveforms and their standard errors computed in association with signals in the no motor response (visual missing stimulus) condition. Waveforms are comprised of 25 trials recorded at the parietal electrode from normal subjects. First and third bars beneath the trace indicate onset of nonsignal flash. Middle bar indicates point in time of stimulus deletion. Upper trace represents grand mean waveform. Lower trace represents standard error.


E.V.
L.N.
F.G.
10uv
+
-
400MSEC

deviations (computed for 25 missing stimuli) recorded from the parietal electrode in four runs. The potentials and their standard deviations are depicted in Figure 18. The waveforms that were recorded from R.S. and H.P. in the second run and the waveform recorded from S.N. illustrate the absence of late positivity that characterized most recordings from patient subjects in this condition. Late positivity seen in the first run in R.S. and H.P. had a latency of 560msec (R.S.) and 460msec (H.P.); amplitude of the LPC was 4uv (R.S.) and 2uv (H.P.) - no different than the LPC seen in normal subjects. Variability across the epoch was very noticeable and, in addition, increased variability in association with late positivity was seen in H.P.

Measurements of late positive components in the waveforms associated with visual missing stimuli are summarized in Table 5.

3. Response-Triggered Parietal Potentials

In order to investigate the absence of averaged potentials associated with missing stimuli in patient subjects, response-locked (as well as stimulus-locked) averaged electrophysiologic activity was computed in association with the RT. Response-triggered late positivity was seen in all normal subjects in six or seven of eight runs. The waves began in synchrony with motor response onset. No response-triggered late positivity was seen in the patient subjects.

Figure 18: Averaged parietal potentials and their standard deviations computed in association with 25 signals in the no motor response (visual missing stimulus) condition. Averaged potentials were recorded from patient subjects.

First and third bars beneath the trace indicate onset of nonsignal flash. Middle bar indicates point in time of stimulus deletion.

Upper trace represents averaged potential.

Lower trace represents standard deviation.

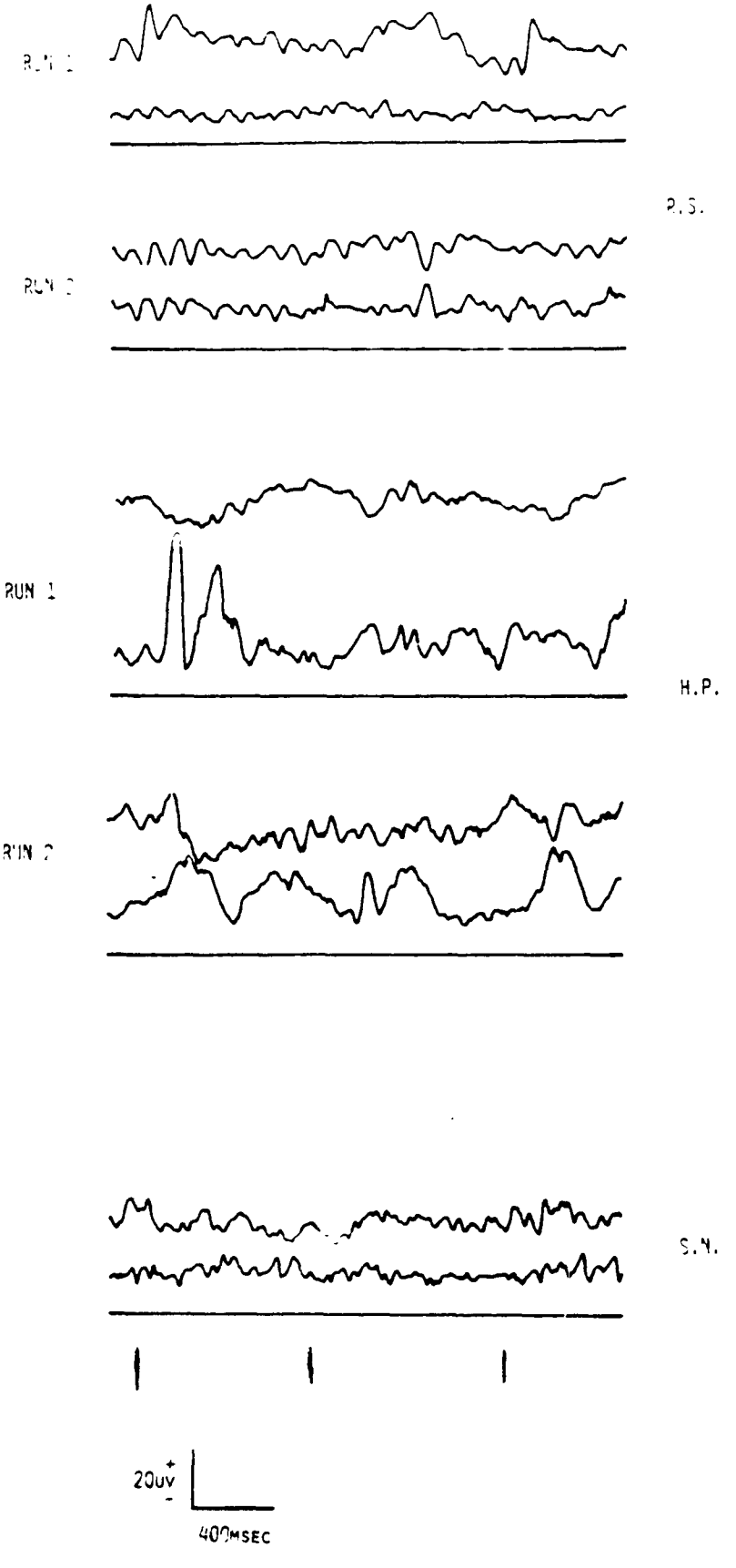

R.S.
RUN 2
RUN 1
H.P.
RUN 2
S.N.
20uv
400MSEC

Table 5: Latency, amplitude, and variability measurements of late positive components of the grand mean potentials and the averaged potentials associated with visual missing stimuli.
Waveforms were recorded at the parietal electrode.

MEASUREMENTS OF LATE POSITIVE COMPONENTS IN WAVEFORMS

ASSOCIATED WITH VISUAL MISSING STIMULUS

NORMAL SUBJECTS

	Motor Response Conditions			No Motor Response Condition		
Grand Mean Potentials	E.V.	L.N.	F.G.	E.V.	L.N.	F.G.
Latency	400	400	390	400	500	500
Amplitude	4	4	8	3	5	11
Standard Error at Point of Measurement	1.0	1.0	1.0	1.0	1.0	1.0

PATIENT SUBJECTS

	Motor Response Condition			No Motor Response Condition		
Averaged Potentials	R.S.*	H.P.	S.N.	R.S.*	H.P.*	S.N.
Latency	400,400	-	-	560	460	-
Amplitude	6, 2	0	0	4	2	0
Standard Error at Point of Measurement	2.8,2	1.8	2.8	2.2	4.8	2

*In the motor response condition, measurements for R.S. are for averaged potentials recorded in the first and second of four runs. In the no motor response condition, measurements for R.S. and H.P. are for averaged potentials recorded in the first of four runs.

Latency in msec
Amplitude in uv
Standard Error in uv
Standard Deviation in uv

CHAPTER IV

DISCUSSION

Event-related potentials were recorded from three autistic children and compared with data obtained from three normal children of the same age. The results suggest that in individual autistic children aberrant brain processes can be defined electrophysiologically. Findings are consistent with the proposal that neurophysiologic deviations at particular stages of information processing can be related to behaviorally defined abnormalities. Thus, results of the present study not only suggest that electrophysiologic methods can be used to study psychopathologic disorders but, in addition, the results add to an increasing body of evidence that the identification of ERP-psychologic process relations may be a fertile area for the study of quantitative indicators of mental illness.

It must be stated at the outset, however, that it would be surprising if an exploratory study of a complex problem such as Childhood Autism were to resolve all aspects of that problem. In the context of the present study, then, the information transmission sequence in individual subjects has been outlined, but detailed analysis of ERP characteristics implicated in processing of sensory information has not been accomplished. Indeed, the many unanswered questions raised by the findings, in turn, encourage future study. For this reason, in the following comments, I have selected for

presentation some important unresolved issues. Answers to these are major objectives of further research and essential to an improved understanding of the nature of psychologic impairments and the functional significance of ERP deviations in Childhood Autism.

A. Subcortical Auditory Evoked Potentials

The waveforms recorded from patient subjects in association with rapid binaural stimulation were within normal limits. The observation suggests that in the autistic children who were studied subcortical processing mechanisms within the auditory pathways were intact. This result is consonant with the findings of Ornitz et al (1968). Using auditory evoked potentials (AEP) recorded in autistic children during sleep, they reported only marginal differences between these children and normal controls. Thus, it appears that although autistic children often resemble children with profound hearing disturbance, their auditory input is not necessarily impaired.

B. Cortical Auditory Evoked Potentials

Longer latency cortical evoked potentials elicited by clicks were recorded from all subjects. In the normal subjects a characteristic triphasic complex was seen both in the 1sec ISI condition and the 3sec ISI condition and responses were remarkably invariant across runs and across conditions. In the patient subjects, however, the positive-negative-positive waveform was not seen in the shorter ISI condition. Because an averaged evoked potential was not seen in either of the first two blocks of ten trials, habituation does not seem to explain this finding. Still, rapid habituation, a central process, in the

initial trials can not be entirely ruled out. Variable latency of the response to single clicks on the other hand, would flatten and reduce the amplitude of the AEP but not abolish it.

In contrast to the 1sec ISI condition, the positive-negative-positive waveform was seen in all patient subjects in the 3sec ISI condition. Although the AEP was more variable than the response recorded in normal subjects, it was not different in latency or amplitude. Absence of the characteristic AEP in the patient subjects in the shorter ISI condition and its presence in the longer ISI condition suggests defective processing of auditory information that is presented rapidly.

Clarification of unanswered questions concerning the nature of the auditory processing impairment that is reflected in these EP data depends upon future study. Important questions here include:

i. What is the role of habituation in impaired processing of rapid auditory information?

ii. Is the impairment modality-specific?

iii. What are the parameters of the impairment in processing of auditory information that is presented rapidly?

C. Potentials Associated with Auditory Discrimination

In contrast to the variable or absent auditory evoked potentials in the no response conditions, responsesto nonsignal tones in the auditory discrimination condition were consistently recorded. Although response latency, and amplitude of P1 and N1 were similar in normal subjects and patient subjects, P2 amplitude was greater in the normals. These results suggest sensitivity of the auditory evoked response in

the patient subjects and not in the normal subjects to task requirements as well as to ISI. They also underlie the need to consider the important role of attentional effects in magnitude of the stimulus information that reaches a specified level in the nervous system.

In this regard, late positivity was seen in the nonsignal ERP of two patients. This finding suggests that some autistic children may be processing all stimuli as signal events - or failing to differentiate signals and nonsignals. Alternatively, the patient subjects may be failing to attend selectively to the signals and, instead, orienting or shifting attention to each event.

The signal ERP contained late positive parietal potentials in patient subjects and normal subjects. Although peak latency was similar in all subjects, peak amplitude was, most often, smaller in the patients. In addition, there was considerable variability in late positive activity recorded in the patient subjects and negligible variability in the normal children. In the patients, the large EEG would have an unfavorable affect on the signal to noise ratio, making it more difficult to see the LPC. Variability of the LPC can be related to variability of the EEG.

The findings here support the notion that autistic children may have impaired ability to register pertinent auditory information in memory and/or impaired ability to determine the match or mismatch of a stimulus to a stored template. Instability of the LPC can also be associated with poor ability to change sensory-motor sets in anticipation of succeeding events - a characteristic of autistic children that is often described behaviorally.

Finally, it should be mentioned that the parietal association

cortex, long regarded as a component of cerebral mechanisms that subserve complex information processing, is among the last to achieve structural maturation. Thus, arrested development of cerebral mechanisms rather than a defective cerebral mechanism can also explain deficiencies in short-term storage of sensory information that are suggested by results of the auditory discrimination experiment.

Further study of discrimination in autistic children is needed to help identify the nature of the LPC deviations in this condition. Questions for future study include:

i. Are the LPC deviations modality-specific?

ii. What are the effects on LPC stability of changes in stimulus and experimental variables?

D. Missing Stimulus Potentials

Auditory and visual potentials were similar in normal and patient subjects in all of the missing stimulus conditions. Responses to the nonsignals in the motor reponse conditions were no different than those in the no motor response conditions. This suggests that in the missing stimulus experiments attention was focused on the stimuli, independent of a motor response requirement. In turn, the task here - in contrast to the no response AEP conditions - enhanced the ERP seen in the autistic children. It is also worth noting that no late positivity was seen in association with nonsignals. This finding suggests that the patient subjects were able to

differentiate signals and nonsignals in this task - unlike the auditory discrimination condition.

Perhaps the most striking finding of this study and certainly one of great interest in the attempt to define a relation between brain processes and behavioral abnormalities, is the fact that brain potentials associated with missing stimuli were rarely seen in patient subjects and observed consistently in normal subjects. Moreover, the motor response requirement did not affect magnitude of the late positive activity in the patient subjects.

Positive missing stimulus potentials (MSP) were, however, usually seen in the first or first two runs. This suggests the possible role of habituation in defective associative or short-term storage processes seen in autistic children. Again - further studies are needed to clarify the role of short-term habituation in the extremely rapid reduction or absence of the MSP in autistic children. Finally, a question raised previously is once again relevant here - namely, is failure in the development of perceptual and cognitive skills related to a slowly emerging and potentially normal functional competence of the parietal association area of the cortex or to a defective critical cortical region?

Two patients were able to learn and perform the RT task fairly accurately. Therefore, absence of the MSP in the two motor response conditions is of particular interest. This result supports the hypothesis that the LPC does not reflect brain events that precede discriminative behavioral responses. An earlier negativity (N2) of the task-related

activity may be related to the decision process in sensory discrimination. Thus, the MSP data should be analyzed to determine the N2 - RT relation.

In this connection, it seems necessary to comment briefly on certain difficulties encountered in the missing stimulus conditions that required the RT task. The two patient subjects who were able to learn the motor response task had enormous difficulty learning it and needed many more training trials here than in the auditory discrimination condition. One explanation is that in the missing stimulus conditions the task was less concrete (responding to the nonappearance of a stimulus event as opposed to a different stimulus event); another is that in these children responses learned in association with one stimulus event are not readily transferred to a second event. In either case, task performance suffered and, in fact, the children had many fasle positives and tended to both anticipate the signals and to move their bodies with each finger lift (RT). The result was that substantial artifact was included in most of the averaged potentials associated with the missing stimuli. Thus,

difficulty in performing the RT task might be related in several ways to the absence of measurable task-related potentials in the missing stimulus motor response conditions. Further, the absence of a reliable motor response measure impedes both the examination of information transmission through the nervous system and the interpretation of neuroelectric data specific to a particular stage of information processing. Thus, in future studies it would certainly be advantageous to invest a good deal of time in training to achieve accurate motor responses.

Clarification of many issues concerning the nature of the short-term storage deficit reflected in the missing stimulus potential data can be major objectives of future research. Some of the important issues here are:

i. The effect on the LPC of probability of occurrence of omitted stimuli.

ii. The effect on the LPC of changes in stimulus as well as experimental variables.

iii. The role of habituation in rapid decrement or absence of the LPC.

E. Relation of Electrophysiologic Data and Neuropsychologic Test Results

The search for a relation between the electrophysiologic data recorded from subjects in a range of experimental conditions (Table 6) and neuropsychologic data reveals several interesting, albeit inconclusive findings. On the one hand, R.S. was the patient subject

Table 6: Measurements of brain potentials recorded from each subject across experimental conditions. Evoked potentials to clicks were recorded at the vertex electrode. Potentials associated with auditory discrimination and with missing stimuli were recorded at the parietal electrode.

MEASUREMENTS OF BRAIN POTENTIALS RECORDED ACROSS EXPERIMENTAL CONDITIONS

	NORMAL SUBJECTS			PATIENT SUBJECTS		
	E.V.	L.N.	F.G.	R.S.	H.P.	S.N.
Evoked Potentials to Clicks						
1sec ISI						
P2						
Latency	150	190	130	-	-	-
Amplitude	3	4	5	0	0	0
3Sec ISI						
P2						
Latency	200	200	190	190	165	235
Amplitude	5	5	7	1	4	3
Potentials Associated with Auditory Discrimination						
Latency	270	320	350	280	320	260
Amplitude	15	8	4	2	3	10
Missing Stimulus Potentials Auditory						
Motor Response Condition						
Latency	360	360	370	-	-	400
Amplitude	9	8	10	0	0	10
No Motor Response Condition						
Latency	360	400	420	360	-	-
Amplitude	3	10	5	2	0	0
Visual						
Motor Response Condition						
Latency	400	400	390	400,400	-	-
Amplitude	4	4	8	6, 2 0		0
No Motor Response Condition						
Latency	400	500	500	560	460	-
Amplitude	3	5	11	4	2	0

Latency in msec
Amplitude in uv

who obtained the lowest age equivalent scores on the Peabody Picture Vocabulary Test and the Auditory Memory Test. Also, in R.S. the smallest auditory evoked potentials were recorded both in association with clicks and in association with nonsignal tones. All of these results suggest the existence of seriously impaired mechanisms mediating processing of auditory information. The defective mechanisms, in turn, most probably contributed to the very low Verbal I.Q. and Full Scale I.Q. that were obtained by this patient subject. On the other hand, H.P. and S.N. were the patient subjects who obtained higher scores on the neuropsychologic tests under consideration and had larger cortical auditory evoked potentials. These findings suggest relatively less defective mechanisms subserving auditory processing. Finally, of all the patient subjects, S.N. obtained the highest score on the Auditory Memory Test. He also had the largest auditory discrimination potentials and the largest auditory missing stimulus potentials. These data support the notion that in S.N. ability to register auditory information in memory was less impaired than in the other patient subjects.

A relation between defective processing of auditory information and specific neurophysiologic dysfunction is supported by the results of DeLong's studies (In Press). DeLong discussed a neuropsychologic interpretation of autism on the basis of consistent changes on pneumoencephalography reflecting specific anatomical pathology in the left medial temporal lobe and seen as dilation of the temporal

horn of the left ventricle. The relation between a lesion of the left medial temporal lobe, poor auditory processing, and profound language deficiency is clear. DeLong suggested a specific left hemisphere lesion and the absence of transfer of specific left hemisphere functions to the nondominant side, it is no surprise that autistic children can often demonstrate fine right hemisphere-related functions associated with preserved islets of age-expected skills. Here - two of the patient subjects, R.S. and H.P., had relatively intact visual spatial and mechanical skills as reflected in high scores on the Ravens and the Slossom Tests. In turn, visual evoked potentials in these children did not differ from the normals. S.N., on the other hand, also had visual evoked potentials that were no different from the normals. He, however, obtained poor scores on the tests of visual spatial abilities suggesting a more diffuse left cortical lesion, a bilateral lesion associated with extremely poor understanding of test requirements, and/or a great need for feedback and self-correction. The latter interpretation, in part, explains this child's high Performance I.Q. in light of poor scores on the tests of visual spatial abilities. Finally, in all patient subjects, the poorly developed late positivity in visual missing stimulus experiments and poor scores on the Visual Sequential Test both support the notion of seriously impaired ability to store in memory sequential information that is presented visually.

In summary, the three patient subjects had cortical responses that differed most from those seen in the normal subjects at the level of associative function and a relation between these data and results of the neuropsychologic test can be inferred easily. This, however,

should not be taken as evidence that the underlying defect in Childhood Autism is at the highest cortical level. Rather, given a larger sample of autistic children, it is hypothesized that a range of defective mechanisms can be demonstrated at all levels within the nervous system hierarchy and can be related, in turn, to a range of aberrant development of specific psychologic processes. Confirmation of this hypothesis awaits the results of future investigations.

F. State of Attention: Relation to Physiologic and Neuropsychologic Data

Serious shortcomings of physiologic as well as behavioral studies of sensory processing and a problem that is central to the issue of interpreting the neuroelectric data obtained in the present study of autistic children, is the problem of controlling attentional state. In studying subjects who are characteristically unresponsive and inattentive, one is always faced with the dilemma of interpreting the role of attention *per se* in the absence of a behavioral and/or a physiologic response. In this study it was intended that the motor response requirement would provide a control of attentional effects. Nevertheless, failure to perform the task with 100% accuracy can not be taken as proof of intermittent inattention and can not be related definitively to the absence of parietal activity characteristically associated with discriminative responding. Behavioral

correlates of attention depend upon careful operational definition of this complex psychological construct. In turn, neuropsychologic correlates of attention require further definition of neural mechanisms subserving the many processing mechanisms that are involved. (In fact, task-related potentials are most often used in the electrophysiologic study of attention and these brain responses must certainly be poor indicators of attentional mechanisms distinct from some as yet unknown number of other associative processing mechanisms.) At present, then, because attentional state is poorly defined and difficult to control, the possibility that attentional effects have determined behavioral and neurophysiologic findings must be considered.

G. Limitations of Event-Related Potentials

Although event-related potentials may provide an exciting possibility for identifying specific aberrant processes that in some way reflect psychopathologic states and have proven of considerable value in the study of neural activities related to the processing of sensory information in animals and in normal humans; still, the potential of the method has serious limitations. These limitations, as the following remarks will show, suggest that ERP studies must always be considered with considerable caution.

i. The investigator must be able to distinguish cerebral activity from extraneous electrical activity. In the context of event-related potentials, electrical activity that is generated by a source that is external to the subject or is independent of the experimental task

must be recognized as spurious. The first type of artifact includes activity that arises from any number of external sources of electrical interference and from recording apparatus defects. The second type of artifact is generated by physiologic variables such as skin resistance and muscle activity. Because of the susceptibility of the method to electrical artifacts, a great deal of attention must be devoted to minimizing the influence of extraneous electrical activity. Studies that fail to accomplish this are prone to serious misinterpretation.

ii. Another problem with the ERP method is related to the fact that human brain potentials can ordinarily be recorded only from the surface of the intact scalp. For this reason, the information that is provided about timing, location, and magnitude of neural events is degraded information. Thus, an ambiguous relation exists between event-related potentials and specific intracranial neural processes. Even detailed and carefully conceptualized studies of human brain potentials with statistically significant results can not be simply interpreted in terms of underlying neural activities in the absence of information concerning the sources that generate the potentials. In turn, in order to locate intracranial sources, animal and human topographic studies are necessary. The fact that this information is still largely unavailable is a serious hindrance to definitive neurophysiologic interpretation of scalp-recorded ERP.

iii. Another limitation of the event-related potential method involves attempts to interpret amplitude as a response measure. Response latency, on the other hand, which is a measure of the timing of neural events, is less equivocal since it is relatively unaffected by the distance of the source from the electrode. Although response amplitude reflects with considerable sensitivity changes in certain stimulus parameters, it is nevertheless an ambiguous measure of the magnitude of underlying neural activities. This is because the magnitude and spatial distribution of the sources that generate the recorded evoked potentials must necessarily influence profoundly the amplitude of event-related potentials. Therefore, interpretation of the amplitude response measure is never simple.

iv. It should be emphasized that the necessity of computer averaging of sequential responses in order to obtain meaningful data is in itself a significant limitation. In averaging, one must sacrifice the specificity and uniqueness of individual responses for the advantage of obtaining an adequate signal to noise ratio. In order for data of this type to be a fully meaningful reflection of underlying neuroelectric processes, it is necessary that the successive responses evoked by a series of identical stimuli be themselves identical. Since such factors as habituation and fatigue are more or less inevitable accompaniments of prolonged stimulus sequences, one must attempt to strike a balance between the loss of response stability and the enhancement of the signal to noise ratio. In any case, conditions of

stimulus delivery must be carefully considered and the subjects' state must be closely monitored.

v. Another limitation of the ERP method is that the averaging technique provides a single datum for each run. Thus, variations among responses to single stimuli are obscured. Information about such variations in neuroelectric activity might provide useful insights into cerebral information processing.

In conclusion, awareness of the many limitations of the event-related potential method suggests that in order to maximize the potential utility of the approach while minimizing its limitations, it is necessary to pay close attention to the adequacy of experimental and subject controls and to utilize critically information about sources that generate the potentials. Despite the many problems confronting investigators that use the method, only the more pressing having been discussed, the availability of this powerful experimental strategy provides an exciting possibility for developing correlations between behavior and brain mechanisms. In turn, the availability of quantitative information about normal neural activities underlying sensory processing and the growing evidence of sensory processing impairments in Childhood Autism suggest that use of the ERP method can improve the quantitative definition of this disorder.

H. Conclusions and Prospects

To summarize, recording and interpretation of the electrophysiologic data obtained in the present study of autistic children are fraught with difficulty. Nevertheless, the ERP recorded in the present

investigation probably reflect neuroelectric activity that occurs during the processing of sensory information and is altered in some as yet ill defined manner. More specifically, the ERP recorded from the autistic children were different than the recordings from the normal children in the following ways: 1. Cortical auditory evoked potentials were affected by ISI and task requirements. 2. Potentials associated with auditory discrimination were noticeably variable. 3. Late positivity was seen in the waveforms associated with nonsignals as well as signals in an auditory discrimination condition. 4. Potentials associated with missing stimuli were infrequent or absent. These findings provide some insight into impaired sensory and central processes. Further, the study demonstrated that defective cerebral functions subserving processing of certain sensory information can be related to specific impairments that can be defined behaviorally.

Since perceptual deficits cut across sensory modalities, perhaps the most parsimonious way of explaining the physiologic and behavioral impairments in Childhood Autism is that there exists in any one child defective physiologic processes that affect processing of sensory information at one or several levels within the nervous system hierarchy. In turn, the impaired processes are reflected in a range of aberrant behaviors that depend upon perceptual skills. This is not meant to imply a unitary etiology or a single disability but merely to define a simple experimentally approachable parameter that lends itself to

a systematic electrophysiologic examination of autistic children.

In my view, the encouraging findings reviewed here suggest that the present experimental format can be useful in defining objective physiologic measures of abnormal brain processes in Childhood Autism. There are many exciting possibilities inherent in the establishment of electrophysiologic correlates of the aberrant behavior of autistic children. For example: the measures may define more reliably the disorder; they may be used to examine the nature of underlying mechanisms; they may provide the basis of objective diagnostic tests and of appropriate rehabilitative procedures.

It should be emphasized, however, that although the analysis of ERP gives considerable promise of insight into sensory and central processes, understanding of the mechanisms of abnormal behavior remains a long-term and difficult goal. On the one hand, the search for a unitary description of brain-behavior correlates in autistic children and answers to questions concerning underlying physiologic determinants of their behavior clearly depends upon the continued study of large numbers of normal children, developmentally disabled children, and children with definable brain defects. On the other, as stated at the outset of this presentation (Introduction, section A) - there are major impediments to the goal of detecting differences among diagnostic groups. Thus, to reiterate, useful clinical indices are most likely to be forthcoming if investigators concentrate their efforts on the exploration of correlative variations of physiologic

and behavioral measures (of specified processes) in individual subjects. Finally, although the suggested investigations are certainly a formidable task, the prospect of an improved understanding of aberrant forms of human behavior in mental illness most assuredly makes the task very worthwhile.

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