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AT HIGH RISK TO MANIFEST SCHIZOPHRENIA.

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Neuroelectric Correlates of Children
at High Risk to Manifest Schizophrenia

by

Allan Frosch

A dissertation submitted to the Graduate
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1977

This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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Abstract

NEUROELECTRIC CORRELATES OF CHILDREN
AT HIGH RISK TO MANIFEST SCHIZOPHRENIA

by

Allan Frosch

Adviser: Professor Steven J. Ellman

The electroencephalogram (EEG) and the auditory evoked response (AER) were studied in a group of children at (genetic) high risk to manifest schizophrenia and in a group of control subjects. Differences between the groups were interpreted along the lines of disordered arousal for the high risk subjects. The configuration of EEG and AER findings in the high risk subjects could be interpreted as indicating either increased or decreased arousal and, therefore, the findings were dubbed "paradoxical".

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I am dedicating my thesis to my wife, Helen, whose support, encouragement and love are greatly appreciated.

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Chapter I

Introduction

The introduction section will be broken up into the following parts:

- A. Introductory comments on the concept of schizophrenia
 - 1. Importance of the problem
 - 2. Preliminary comments on the aetiology of schizophrenia
 - 3. Some considerations concerning the "construction of reality"
 - 4. Neurophysiological speculations
 - 5. Further consideration of psychological dysfunction and experimental support.
- B. Difficulties inherent in research strategy for the study of schizophrenia and an alternative approach
 - 1. Subject selection (general)
- C. High risk research – a review of the literature
 - 1. The EEG and the AER
- D. Some concluding comments concerning research strategy
- E. Aim of the present study.

A. Introductory Comments on the Concept of Schizophrenia

The first classification of "schizophrenia" as a "disease entity" was made by Kraepelin (1896). Kraepelin used Morel's term "dementia praecox" to refer to a clinical picture whose common characteristic

was termination in a "peculiar weakened state of mind" (Kraepelin, 1896, cited by McGhie, 1969, p. 39). Bleuler (1911) was the first to use the term "schizophrenia", replacing Kraepelin's "dementia praecox". Bleuler's use of the term schizophrenia emphasized a "splitting" process which Bleuler regarded as the basic characteristic of the disorder. Bleuler's observations led him to state three primary symptoms as most characteristic of schizophrenia: 1) a thought disorder; 2) a flattening or inappropriateness of affect; and 3) a loss of volition. For Bleuler, these symptoms were a consequence of a "splitting off of the different psychic functions so that the cognitive, affective and volitional functions ceased to operate in a unitary, congruous way" (Bleuler, 1911, cited by McGhie, 1969, pp. 39-43).

Although retaining Kraepelin's sub-divisions of hebephrenia, catatonia and paranoid schizophrenia (Bleuler also included "simple" schizophrenia), Bleuler, like so many investigators who followed him, was struck by the heterogeneous nature of the diagnostic group. His term, the "group of schizophrenias", has been replaced by the current term "spectrum of schizophrenic disorders" (Rosenthal, 1974). Although the subcategories of hebephrenia, catatonia, paranoid and simple schizophrenia are still currently used, there is widespread agreement that the term schizophrenia does not represent a unitary disease entity. In particular, the paranoid schizophrenic has been

shown to differ along a number of psychological and biological dimensions in comparison to the three other subcategories of schizophrenia (CF. Silverman, 1967). And some investigators (e.g. McGhie, 1969) have suggested that many patients classified as paranoid schizophrenics should be grouped under the category of paranoid psychosis.

1. Importance of the Problem

While recognition of some of the difficulties involved in schizophrenia research (e.g. diagnoses, effects of hospitalization, etc.) would seem to discourage major research efforts into the etiology of schizophrenia, quite the opposite has been the case. Research efforts in the area of schizophrenia have been widespread and diverse (e.g. psychological, neurological, biochemical, etc.). And recognition of the heterogeneous nature of the schizophrenic population has not curtailed the hope of discovering common "mechanisms" of dysfunction among the various schizophrenic groups.

Quite clearly, the intense research interest in schizophrenia, in spite of some of the difficulties posed, is a consequence of the disorder itself, i.e., some of the more dramatic aspects of the disorder such as neologisms and "bizarre" behavior, as well as the widespread occurrence of schizophrenia. In the U.S., for example, in 1966 there were nearly 250,000 resident schizophrenic patients in state and county mental hospitals. As Gunderson et al. (1974) point

out, however, this figure is not at all indicative of the number of schizophrenic patients in the U.S. These authors note that since the mid-1940's, there has been a shift in the locus of treatment for mental patients — out of hospitals and into community facilities such as day care centers, half-way houses and the like. In 1955, for example, 125,000 patients were discharged from mental hospitals, whereas 419,000 patients were discharged in 1971 (1974, pp. 18-20). As Gundersou et al. point out, the increased number of discharges does not indicate that more patients are being "cured", but, instead, is more directly related to the growing number of alternative treatment facilities which have become available. Since approximately fifty percent of all inpatients are diagnosed as suffering from some form of schizophrenia, or falling along the schizophrenic spectrum, the figure of 250,000 schizophrenics is, at best, a conservative estimate.

It is also clear that the occurrence of schizophrenia cuts across cultural boundaries. Each of the fifteen republics which constitute the U.S.S.R., for example, have major institutes which are actively involved in research into the aetiology of schizophrenia (Brown et al., 1973). In addition, the Institute of Psychiatry in Moscow — under the direct auspices of the Society Academy of Medical Sciences — has undertaken major research efforts into the causes of schizophrenia (1973). (See also Bleuler, 1972, for a discussion of schizophrenia in Germany and Switzerland, and Mednick &

Schulsinger (1973) for the occurrence of schizophrenia in the Scandanavian countries.)

2. Preliminary Comments on the Aetiology of Schizophrenia

Beginning with the work of Kraepelin and Bleuler, a commonly noted characteristic of schizophrenic patients has been their difficulty in processing both external and internal information. Bleuler, for example, noted that his schizophrenic patients seemed easily distractible by external stimuli. He further noted that even those patients who appeared to pay little or no attention to the external world, upon closer examination, appeared to be bombarded by a number of external events of little or no concern to them. In a similar vein, Schilder (1951) described schizophrenic patients as being unable to pursue what he referred to as the "determinative idea". For Schilder, schizophrenic patients were constantly being bombarded by thoughts and ideas that had little or no relevance to the mainstream of their thinking. The underlying ideas of both Bleuler and Schilder were, of course, quite similar: the schizophrenic patient seems unable to discard or inhibit extraneous information (exogenous or endogenous) and seems flooded with a mass of sense impressions. Freeman et al. (1958) described a state of "undifferentiated attention" which led to a confusion of the "internal" and "external" worlds of the schizophrenic patient. The central notion in the work of Freeman et al. (1958, 1966; McGhie & Chapman, 1961; McGhie,

1969) has been a disturbance in attentional behavior which leads to extreme difficulty in the selection of relevant information. This inability or deficit in the process of selection of relevant information has been considered one of the most distinctive features of schizophrenia (Freeman et al., 1966; McGhie, 1969). McGhie and Chapman (1961) have observed that this difficulty seems most pronounced with young patients during the onset of the disorder.

3. Some Considerations Concerning the "Construction of Reality"

Modern-day psychology has taken the position that the world we perceive is a personal construction, as opposed to a direct registration of events. On the basis of present needs, past experiences and future expectations, man is able to select and categorize sense data (both endogenous and exogenous) and thereby construct his "time-bound" reality, i.e., his reality at that moment in time. In order to comprehend his present reality, man compares current information with models constructed from past experiences. Thus, man is constantly constructing and reconstructing an external and internal reality. Through the process of selection of input, classification along a number of dimensions and eventual comparison to internal standards or models, we create reality. These (re)constructions of reality are further appraised as to their "goodness" or "badness", "pleasure" or "displeasure", and so on. Furthermore, the

products of these constructions, i.e., the consequences in terms of overt motoric behavior, are appraised, as well as the various steps of the process (CF. Bowlby, 1969, pp. 104-124).

Inherent in this overall process of appraisal, or information processing, is some "mechanism" which can inhibit or block redundant (and presumably) maladaptive information. Freud (1920), for example, referred to a cortical mechanism (Reizschutz) which, in conjunction with the sense organs, acted as a special integument or membrane to ward off stimuli. In recent years, Broadbent (1958; Broadbent & Heron, 1962) has been an eloquent proponent of the notion that to function effectively, man must select from a variety of stimuli. Broadbent has elaborated on the concept of a "filter mechanism" which helps the organism select relevant and discard (or screen out) irrelevant information from the array of sensory input. The selected information is eventually fed into a limited capacity decision channel with connections to a long-term memory system. Thus, new information may be integrated with previously stored information. Broadbent conceives of the filtering mechanism as having a permanent "bias" toward the processing of novel stimuli. This insures that both the selection and subsequent processing of information will be focused on the most important aspects of the stimulus array. In this fashion, our perceptions are synthesized and an inner and outer reality is created.

Broadbent's ideas are of particular importance with reference to schizophrenia. Calloway (1970), for example, noting the impressive body of literature which indicates that many schizophrenics can be characterized as having disordered levels of arousal (e.g. Claridge, 1967; Venables, 1967; Kornetsky & Mirsky, 1966; Itil et al., 1972), high distractibility (Shakow, 1962; Freeman et al., 1969) and poor habituation to stimuli (Zahn et al., 1968), uses a computer analogy to help account for some of these findings. Based on this analogy, human beings are conceptualized as having a central decision-making mechanism with a limited information capacity. According to Calloway, the schizophrenic begins with a heightened level of cortical arousal which leads to heightened distractibility or "hypersensitivity" to stimuli. When this occurs, the central decision-making mechanism (or channel) becomes overloaded. This leads to a further increase in arousal which, in turn, leads to more overload; eventually, a "vicious cycle" is established and perpetuated. In a similar vein, McGhie (1969) describes such a situation as leading to a "passive mode of perception". The schizophrenic person is "obliged" to process (or attempt to process) all stimuli, regardless of its informational or adaptive value. (Although beyond the scope of the present paper, it is of interest to explore the relationship between involuntary behavior -- or loss of volition -- and passivity. For an intriguing discussion of this relationship, see

Haley, 1965, and Gil & Brenman, 1959.)

It is reasonably clear that, even in this preliminary discussion of schizophrenia, the concepts of arousal and attention are of paramount importance. Both concepts have been of great interest in the field of psychology. Both concepts, however, have been conceptualized in a number of different ways and have often been used interchangeably. (For an elucidating discussion of attention and arousal, see Berlyne, 1960, 1969; see Also Vaughan & Ritter, 1974; and Woorden, 1966). In the present context, the term "attention" will be used to refer to its selective function, i.e., the selection or allocation of cognitive mechanisms (Neisser, 1967) of stimuli with high information and/or adaptive value to the organism, and "non-attention" (i.e., no allocation of certain cognitive mechanisms) to those stimuli with little or no informational or adaptive value (Berlyne, 1969; McGhie, 1969). The term "arousal" will be used to refer to an organism's readiness to react, or to how "wide awake" or alert the organism is. "The lower pole of the continuum is represented by sleep or coma, while the upper pole would be reached in states of frantic excitement" (Berlyne, 1960, p. 48). In the context of the present discussion on the construction of "reality", arousal and attention are viewed as separate but interrelated aspects of a relatively ongoing process or behavioral system. It seems apparent that a person would have great difficulty in exercising the selective processes of this behavioral system (i.e., attention) while in coma or heightened states of activation or excitability. It is assumed that for a person to

exercise some selectivity in relation to both external and internal stimuli, there must be a context of "acceptable" arousal, or organismic readiness, which facilitates these selective processes.

4. Neurophysiological Speculations

There has been a great deal of interest in specifying the neurophysiological locus of the postulated psychological dysfunctions in schizophrenia. The reticular system with "its strategic location at the crossroads for incoming and outgoing messages and its apparent ability to sample all such activity and to develop from it a more lasting influence in a form of alerting and attention" (Lindsley, 1961) has been a prime candidate for CNS malfunction in schizophrenia. This brainstem component which appears instrumental in both alerting the organism as well as the inhibition of stimulation along sensory pathways, has received the attention of a great many investigators. Fish (1963), for example, has postulated that overactivity of the reticular system may be the neurophysiological basis of schizophrenia. He notes that such activity could be the end product of several pathways: a) a biochemical disturbance or lesion within the reticular system itself; b) focal activity of structures which influence reticular activity; and d) failure of cortical inhibitory influences. As Erlenmeyer-Kimling (1968) has pointed out, all of these possibilities can be under genetic control as well as non-hereditary in nature.

It is known that special pathways to the reticular system allow

the cortex to exert centrifugal control over the reticular system (Luria, 1966; Sokolov, 1960). It has been suggested (Sokolov, 1960; McGhie, 1969) that some information may reach the cortex prior to its arrival in the reticular system so that the cortex may analyze input and then inhibit its passage through the reticular system. Along these lines, Sokolov (1960) has proposed a model in which information travels by separate pathways to the cerebral cortex and reticular system. If the stimulus is familiar, i.e., it matches a cortical model, the cortex can inhibit further processing at the reticular level. If, however, the information is novel, i.e., there is no match between the incoming information and an existing model, further reticular processing takes place and eventuates in an "orienting" response.

While any research into the aetiology of schizophrenia must ultimately concern itself with neurophysiological aspects of the disorder, current neurophysiological hypotheses are highly speculative and have been mentioned to provide some background for some of the psychological propositions. While these latter propositions can also be thought of as speculative, the support received from numerous experiments make their consideration more tenable. For the remainder of this section of the paper, some of the proposed psychological dysfunctions will be amplified in the light of experi-

mental data.

5. Further Considerations of Psychological Dysfunction and
Experimental Support

Of the many characteristics that have been proposed to distinguish schizophrenics from non-schizophrenics (see Grinker & Holzman, 1973), the existence of a thought disorder has received the most attention and widespread agreement among investigators.

Weckowicz and Blewett (1959) have suggested that the inability of the schizophrenic to selectively attend to relevant information may play a major role in the eventual manifestation of a thought disorder.

In a similar vein, Shakow (1962) has proposed that the disordered thinking so characteristic of schizophrenics may be attributable to a dysfunction in the scanning process which takes place before a response to a stimulus is made. Shakow, like the investigators previously mentioned, takes the position that the schizophrenic person is unable to select out the material relevant for an optimal response (1962, p. 9). Shakow's concept of "segmental set" will be discussed in connection with Calloway's work in a later section of this paper.

Silverman (1964, 1967) has proposed a "sensory input-processing-ideational gating" mechanism which, in schizophrenia, functions to distort environmental data. Silverman conceptualizes the operations of this mechanism as a more or less automatic adjustment to the en-

vironment which emerges in the course of development and which is shaped by both constitutional and environmental factors. Although the terminology is different, Silverman's concept of a gating mechanism is quite similar to Broadbent's notion of a filtering mechanism (see Silverman, 1964, footnote p. 375). Lehmann (1966) has suggested a dysfunction, possibly constitutional, in some central (i.e., cortical) processing apparatus which leads to the oft-reported experience in schizophrenia of sensory bombardment or overload. Escalona and Heider (1959) have suggested that predispositions toward disordered approaches toward environmental stimuli may be present in the earliest days of life, thus echoing the notions of the previously mentioned investigators regarding the influence of constitutional factors on an organism's information processing capabilities.

McGhie (1969) has discussed some of the profound consequences of a breakdown or dysfunction of some filtering or gating mechanism which functions to select and inhibit endogenous and exogenous information:

"Consciousness would be flooded with an undifferentiated mass of incoming sensory data, transmitted from the environment via the sense organs. To this involuntary tide of impressions there would be added the diverse internal images, and their associations, which would no longer be coordinated with incoming information. Perception would revert to the passive and involuntary assimilative process of early childhood and, if the incoming flood were to carry on unchecked, it would gradually sweep away the stable constructs of a former reality." (P. 49)

McGhie provides a host of phenomenological reports of young schizophrenic patients during the early stages of their disorder which lends support to the description provided above:

"I can't concentrate. It's a diversion that troubles me ... the sounds are coming through to me but I feel my mind cannot cope with everything."

"It's as if I'm too wide awake - very, very alert. I can't relax at all. Everything seems to go through me. I just can't shut things out."

"I notice so much more about things ... all sorts of little things ... pick up my attention"

"My thoughts get all jumbled up ... my trouble is I've got too many thoughts ... when I'm trying to think of something, I'm like a runaway engine, running along a line where someone keeps changing the points." (1969, p. 45-49)

Cameron (1951) has also been struck by the schizophrenic's experience of being overwhelmed by a constant stream of internal and external stimuli. Cameron has proposed two stages in the formation of a delusion. The first stage is one of hypervigilance, where perceptions are diffuse and unstructured. It is during this stage, according to Cameron, that the schizophrenic begins to experience confusion between reality and unreality, or a confusion between what is "out there" and what emanates from within. Cameron, however, postulates a subsequent restrictive-distortive stage. During this stage, a delusion (or delusional system) is constructed. Although the delusion leads to a distortion of reality, it may also

serve the purpose of reducing the confusion, uncertainty and subsequent anxiety of the initial stage. Cameron's proposals touch on an important issue in any discussion of schizophrenia. It concerns the notion that the particular symptom formation of the patient is an attempt to resolve some of the unacceptable feelings and impulses which are inherent in the schizophrenic process. Silverman (1964), for example, has postulated that the idiosyncratic operations of the schizophrenic gating mechanism is the ultimate defensive resolution to an otherwise unacceptable situation. These notions apply to neurotic as well as psychotic (e.g. schizophrenia) disorders, and their discussion is well beyond the scope of the present paper. Some cursory comments, however, will be made following the section reporting on experimental evidence which lends support to the general concepts of psychological dysfunction outlined up to this point. (For a detailed and stimulating discussion on the relationship between "symptom choice" and the various subgroups of schizophrenia, see Silverman's paper, 1964.)

Experimental Support for Psychological Hypotheses

There is an impressive body of literature which indicates that the scalp-recorded electroencephalogram (EEG) bears a functional relationship to underlying brain processes (Gibbs & Gibbs, 1941; Lifshitz & Gradijan, 1974). Thus, it seems reasonable to expect the EEG to reflect some of the pathological mental functioning asso-

ciated with schizophrenia. It is not surprising, therefore, that the EEG has received such widespread usage in the study of schizophrenia. One of the first investigators to utilize the EEG in the study of schizophrenia was Lemere (1936). Lemere reported a diminution of alpha activity in the EEGs of schizophrenics in comparison to normal controls. Davis (1940) reported that the EEGs of schizophrenics contained "choppy patterns", i.e., disorganized low voltage (5-10 microvolts) fast activity (26-50 cps). She regarded such activity in the EEGs of schizophrenics as a consequence of "cerebral irritation", i.e., the bombardment of the cortex from subcortical sources, or as a result of unsynchronized activity within the CNS (see Davis, 1940; see also Abenson, 1970). Davis also observed that the more unstable (i.e., disorganized low voltage activity) the EEG, the more unstable the patient's behavior. These observations have been confirmed by Brazier (1962).

Davis' findings of increased fast, low voltage activity have been replicated by an impressive number of subsequent investigators. Lester and Edwards (1966), for example, have demonstrated that the EEGs of chronic schizophrenics had a greater incidence of low voltage fast activity in comparison to normal controls. Similar findings have been reported by Giannitrapani (1971). In his review of the literature on the EEG and schizophrenia, Abenson reports that the most common abnormality in the EEGs of schizophrenics has been

the high incidence of low voltage fast activity and a diminution in the alpha rhythm. In his own study, Abenson (1970) compared the EEGs of 210 chronic schizophrenics (mean age 48.6 years) with 100 normal controls (mean age 44.9 years). Abenson's findings paralleled the host of previously reported results, i.e., increased low voltage fast activity ("choppy records") and a diminution of alpha activity. Abenson viewed such findings as indicative of schizophrenic instability traceable to some generalized brain disorder. Itil et al. (1971, 1972) have also reported an increase in fast beta activity (around 24 cps) and a diminution of alpha activity. Itil and his colleagues have also reported an increase in slow wave activity (both delta and theta) in the EEG records of many of their schizophrenic subjects in comparison to normal and psychotic (not schizophrenic) controls. The Itil group have also reported similar findings in the EEG records of psychotic (not schizophrenic) children. Lifshitz and Gradjan (1972, 1974) have also reported an increase in low voltage fast activity and, in accordance with Itil et al., an increase in slow wave activity in the EEGs of some adult schizophrenic subjects.

At this point in the discussion, the focus has been confined to the frequency characteristics of the EEGs of schizophrenic subjects. Another measure of the EEG which has been extensively utilized in schizophrenic research is the amplitude variability of the EEG as reflected by the coefficient of variability (CV). (The CV is computed

as follows:

$$CV = \frac{\text{standard deviation}}{\text{mean amplitude}} \quad \frac{\text{s.d.})}{\text{amp.})}$$

Walter (1953) and Snezhnevsky (1961) have described a lack of amplitude variability or "crystallization" of the EEG in many schizophrenics. Goldstein et al. (1965) did an amplitude analysis of the EEG recorded at occiput for a group of adult schizophrenics and normal controls. The CV was significantly smaller in the schizophrenic group in comparison to the normal controls. The CV was smallest in those schizophrenics with catatonic symptomatology.

Goldstein et al. (1963) have previously demonstrated a decrease in the CV following the ingestion of amphetamines in normals and an increase in the CV following the ingestion of phenothiazines in normals. Goldstein (1963, 1965) argues that the CV is inversely related to the level of activation (1965, p. 357), and postulates that many schizophrenics suffer from a condition of cortical over-arousal. Majerrison et al. (1968) have also reported a lowered CV in schizophrenic subjects and suggest:

"Those schizophrenics with relatively invariable EEGs may be the ones with more highly aroused states of cortical activation ... and (also) deficient in basic mechanisms ... that are ordinarily operative in sensory input processing." (P. 40)

Lifshitz and Gradijan (1972, 1974) also report that the occipital area CV of the EEG is smaller in schizophrenic patients in compari-

son to normal controls.

Further support for the hypothesis of disordered levels of arousal in many schizophrenics comes from a host of investigators who have used a variety of measures as indicators of arousal. Mirsky (1960), for example, has used the continuous performance test (CPT) as a measure of arousal. Kornetsky and Mirsky (1966) have proposed that performance on the CPT is dependent on brain areas which include the reticular activating system. The Wechsler Digit Symbol Substitution Test (DSST) was selected by Mirsky as a task representing dependence on cortical structures and relatively independent of subcortical, midbrain structures. Mirsky, who is a strong proponent of the hyper-arousal hypothesis in schizophrenia, predicted that schizophrenics would do poorly on the CPT but reasonably well on the DSST. These predictions were confirmed by Orzack and Kornetsky (1966) and lend further support to the hypothesis that many schizophrenics are in a state of heightened cortical activation or hyperarousal. Additional support for this position comes from the study of Venables and Wing (1962), who have shown that many schizophrenic patients have a high level of fusion for paired light flashes. Venables (1967) has also observed a positive association between the two-flash threshold and the degree of social withdrawal of schizophrenic patients. This has led to the suggestion that the social withdrawal of the schizophrenic patient is a defensive reac-

tion aimed at limiting stimulation and thus reducing an unacceptable level of heightened arousal (Venables, 1967; McGhie, 1969; Silverman, 1964). Venables (1967) has suggested that for many schizophrenics, cortical activity is not being controlled by the regulatory action of the reticular system. This leads to an inability to respond selectively to significant stimuli and, thus, to an indiscriminate arousal reaction to all stimuli.

While it is reasonably clear that the vast majority of researchers who have studied cortical arousal in schizophrenia subscribe to the notion that many schizophrenics suffer from heightened states of arousal (see Kornetsky & Mirsky, 1966 for an excellent review), the findings of increased low and high frequency activity in the EEGs of many schizophrenics makes the hypothesis of a constant state of cortical hyperarousal somewhat problematic. Itil and his colleagues (1972, 1974) have postulated a highly variable state of "vigilance" in schizophrenia with continual fluctuation (decrease and increase) over short time periods. Claridge (1967) has formulated a model of arousal based on two functionally related systems; these are the tonic arousal system and the arousal modulating system. For Claridge, the function of the tonic system is to maintain some overall level of arousal. The function of the modulating system is two-fold: 1) the modulating system regulates the activity of the tonic system and thus may be conceptualized as having (or serving)

a homeostatic function; 2) the modulating system is also seen as performing as a filter for incoming information; thus, relevant information is facilitated and irrelevant information is inhibited.

Claridge postulates that in schizophrenia, the two systems become functionally dissociated due to a breakdown in feedback mechanisms. The effect of the proposed dissociation depends on which of the two systems are predominant in their function. Based on his model, Claridge has proposed that all schizophrenics can suffer from both high and low levels of arousal.

Although the EEG has been thought of as reflecting ongoing neural activity, it has not been considered a measure which adequately reflects the organism's (cortical) responsivity to the presentation of a brief external event. Since evoked responses (ERs) are time-locked to an external stimulus (Vaughan & Ritter, 1974), they are believed to reflect some aspect of the organism's information-processing mechanisms, or, stated differently, ERs may represent a neuroelectric correlate of behavioral systems which subserve the organism's capacity to "act on" (i.e., select-inhibit) exogenous information. As has been mentioned throughout this paper, a primary emphasis in schizophrenia research has been the schizophrenic's (postulated) dysfunction (or inability) in information-processing tasks. It seems reasonable, therefore, that ERs, like the EEG, would receive a great deal of attention in investigations

concerned with the aetiology of schizophrenia; in point of fact, this has been the case. Shagass (1969), for example, has produced an impressive amount of literature on the visual and somatosensory ERs and schizophrenia. In recent years, however, the auditory evoked response (AER) has been of growing importance as a neuroelectric measure in the study of postulated attentional dysfunctions in the "group of schizohhrenias".

In a series of studies, Calloway and Jones (1970, 1965, 1969) have used the AER to investigate attentional dysfunctions in schizophrenia. Jones et al. (1965) have compared the waveforms of two subsets of AERs generated to tones of 1000 Hz and 600 Hz. The tones were presented in a haphazard pattern. Jones et al. report lower correlations (more varaibility) in the schizophrenic group in comparison to normal and psychiatric (not schizophrenic) controls. The theoretical orientation of this study was rooted in Shakow's concept of segmental set. Shakow (1962) has found that schizophrenics have a tendency to form multiple disarticulated approaches to tasks. The many reports presented in the present paper of the inability of the schizophrenic to disregard redundant or unimportant aspects of the environment lend some support to Shakow's notion. As Jones et al. additionally point out, Shakow's notion of segmental set is also reflected in the marked variability of response and in the fragmented concepts of many schizophrenics (1965, p. 33). Jones et al. offer-

ed the following explanation for their results: the non-schizophrenic subjects treated the two randomly presented tones as part of the background. Since there was no reason to discriminate between them, the AERs to the tones of 1000 Hz and 600 Hz would, as predicted, be similar. The schizophrenic subjects, on the other hand, with their associated attentional defect (or segmental set) continued to discriminate between the two tones in the absence of any apparent reason to do so. In a subsequent study, Calloway, Jones and Donchin (1969) investigated the possibility that the dissimilar AERs in the schizophrenic group could be produced by more variable AERs to tones unrelated to pitch and/or more variable AERs as a result of a "noisy" background EEG independent of responses to particular stimuli. In this study (1969), two AER wave forms were generated following 320 presentations of a 1000 Hz tone. To control for background variability, i.e., a noisy EEG, the 500-msec. period preceding each tone presentation was digitized and a coefficient of variability (CV) was computed by dividing the maximum standard deviation by the maximum peak-to-peak amplitude of the summed evoked responses. The results of this study were in agreement with the earlier work of these authors: the schizophrenics had significantly lower product-moment correlations between the two sets of AERs than did the normal controls. These findings have been interpreted along the lines of increased variability in the AERs of the schizo-

phrenics. No difference was found between the normals and schizophrenics in the CV of the 500-msec. period preceding tone onset. Therefore, background variability was ruled out as a significant factor in the increased variability of the AERs of the schizophrenics (p. 426). Calloway et al. (1969) have suggested that a general increased response variability seems to be a central factor in schizophrenic thought process disorder (see also Calloway, 1970; and Broen, 1968) and, therefore, the dissimilarity between the two subsets of AERs to the tones of 1000 Hz reflects the generalized response variability which seems to play such a ubiquitous role in the schizophrenic makeup (1969, p. 426). Calloway (1969) and his associates have also reported that a reduction in variability (higher correlations between the two AER wave forms from the same subject) is positively correlated with clinical improvement; there is an inverse relationship between AER variability and cognitive performance and there is a positive relationship between AER variability and a thought disorder (pp. 420-421).

Similar findings have been reported by Saletu et al. (1971), who have studied the AERs of schizophrenics. These authors compared the AERs of schizophrenics with "thought process disorders" (TPD) with the AERs of schizophrenics with no thought process disorders (NTPD) and a group of normal volunteers. Bleuler's definition of a thought process disorder was used: a fragmentation of the thinking

process, a loosening into overtly disconnected but well differentiated percepts and thoughts (Bleuler, 1911, cited by Saletu et al., 1971). Saletu et al. describe the thoughts of their patients with TPD as disorganized, bizzare, diffuse and incoherent, with a loosening of associations and perseverations (p. 118). Saletu and his co-workers used judges to rate the similarity of AER wave forms (four AER wave forms per subject). Variability was judged to be the greatest in the first group (TPD), less so in the second group (NTPD), and the AERs showed the greatest consistency in the group of normal volunteers. Saletu et al. have also reported latency differences to the various components of the AER between the three groups. The schizophrenics had shorter latencies than the normal volunteers, and those schizophrenics with TPD had shorter latencies than the group of schizophrenics with NTPD. The amplitude of the normal subjects was higher than either of the schizophrenic groups.

The difficulties involved in trying to relate various components of the AER to underlying cerebral processes, specifically those that (presumably) subserve attention, has received a great deal of discussion (e.g., see Calloway et al., 1969; Vaughan & Ritter, 1974). Both Naatanen (1967) and Tecce (1972) have commented on the difficulty of separating the effects of arousal and attention when interpreting the AER and contingent negative variation (CNV), respectively. Similar views have also been expressed by Karlin (1970), who

has argued that amplitude differences in the AER may reflect the effects of differential preparatory states rather than different stimulus significance. Vaughan and Ritter (1974) have noted that the P200 component of the AER, which has often been considered a neurophysiological correlate of attention, is plagued by a number of interpretive difficulties; these include the weight one gives to minute changes in the amplitude of P200, as well as changes in the opposite direction within and between subjects (p. 147). In general, however, changes in amplitude and/or latency of the early components of the AER (less than 200 msec.) have usually been associated with changes in arousal or the activation level of the organism (CF. Shagass et al., 1969). Along these lines, it is of interest to note that Vaughan and Ritter (1974) have suggested that the positive component of the AER occurring approximately 300 msec. after tone onset (P300) may be an attractive candidate for a postulated, but unspecified, attentional mechanism (pp. 147-148). These authors note that the AER reflects activity in its primary receiving area of the cortex, i.e., the auditory cortex (Vaughan & Ritter, 1970). These authors also point out that the P300 component of the AER is part of an evoked potential whose origin has been demonstrated to be in the parieto-temporal cortex, and thus appropriately labeled the association cortex potential (ACP) (Vaughan, 1970; Vaughan & Ritter, 1970). While the ACP temporally overlaps the AER, only the latter portion

of the ACP (i.e., P300) is ordinarily visible in the AER (Vaughan & Ritter, 1974).

While it is reasonable to assume that P300 reflects a different aspect or stage of information processing in comparison to the earlier components of the AER (see also Sutton et al., 1965), the factors that elicit P300 have not been clearly understood. Earlier studies (Sutton et al., 1965; Ritter et al., 1968) suggested that the ACP was associated with stimulus uncertainty or the unexpected presentation of a stimulus. Vaughan and Ritter (1974) have noted, however, that when the difficulty of the discrimination between the infrequent and frequent stimulus is increased, the ACP was observed to all stimuli.

"This result led us to conclude that the ACP could not merely reflect stimulus uncertainty or the occurrence of a mismatch in the comparison between a template for predicted stimulus and the (infrequent) signal stimulus, but must be related to a less clearly specifiable operation which we vaguely designated 'cognitive stimulus evaluation'." (Vaughan & Ritter, 1974, p. 148)

Since P300 (for the remainder of this paper, the ACP will be referred to as P300) has been associated with subjective evaluation of a stimulus, and since attention to unimportant or redundant stimuli has played such a significant role in schizophrenic research, P300 takes on special significance. In this context, a study by Roth and Cannon (1972) is of interest. These authors compared the amplitude of P300 for 21 adult schizophrenics and 21 age-matched

controls. All subjects were told to ignore the stimuli (tone bursts). The control group had a larger P300 amplitude to infrequent stimuli than did the schizophrenics.

A good many studies have been reported which indicate that schizophrenics and children at high risk to manifest schizophrenia do not seem to habituate as quickly as normal subjects on a variety of measures (Zahn, 1964; Mednick & Schulsinger, 1973; see also Itil et al., 1974, and p. 35 of this paper). Although the present study has not been specifically designed to study habituation, the AER wave forms between the groups will be compared over the course of time (see data analysis section for details) with special interest in the P300 component.

It is clear that the use of the AER in schizophrenic research has been, to a great extent, to identify some neuroelectric correlate of attention. The results of these studies have been difficult to interpret because of the lack of knowledge concerning the AER, as well as the ambiguity in the use of the concept of attention. If, for example, the P300 component of the AER is to be considered a neuroelectric correlate of the "orienting response" (Roth & Cannon, 1972), does the decreased amplitude of P300 in the Roth and Cannon study indicate that schizophrenics are less easily distractible by infrequent and (apparently) unimportant stimuli than normal controls? To argue that this is so would be to go against a voluminous body of

literature which indicates quite the opposite. As Vaughan and Ritter (1974) have pointed out, changes in amplitude of the AER cannot be equated with shifts in attention, and any interpretation of the AER and its various components must be with great caution.

Quite clearly, the vast majority of the studies investigating attentional behavior in schizophrenics have indicated that many schizophrenics are unable to focus on that part of the environment relevant to the current task (Cameron, 1938, 1939). In support of this notion, Chapman (1956) and Chapman and Taylor (1957) have demonstrated that, in a card-sorting task, schizophrenics were more easily distracted by irrelevant items on response cards in comparison to normal controls. Payne (1964) has also suggested that schizophrenics process more irrelevant information than non-schizophrenics. Payne attributes this to some disturbance in selective attention. For Payne, it is some defect in the mechanism of attention, specifically, a defect in the filtering aspect of attention which accounts for the disordered thoughts and associations so characteristic of schizophrenics. According to Payne, the schizophrenic, when approaching a task, becomes distracted by irrelevant stimuli (both internal and external); selective perception becomes impossible. In dealing with a problem, irrelevant stimuli may lead to the mass confusion and "inappropriate" emotions so often associated with schizophrenia. Along these same lines, Shakow and Juston (1936) have

shown that in a visual signal tracking task, the level of schizophrenic performance fell sharply when either visual or auditory distracting stimuli were introduced. Weckowitz and Blewett (1959) seem to have summed up much of the research on attention and schizophrenia by comparing the (postulated) breakdown in some filtering mechanism to the opening of a set of floodgates, whereby the cortex becomes flooded with irrelevant information and the maintenance of a set becomes impossible.

B. Difficulties Inherent in Research Strategy for the Study of Schizophrenia and an Alternative Approach

In an attempt to understand schizophrenia, most researchers have viewed the adult schizophrenic as the legitimate source of inquiry. Research efforts of this nature have been plagued by an inability to delineate aetiological factors from those that are an effect of the disorder. The use of drugs, for example, provides one of the most complicating factors in all schizophrenic research. Withholding drugs from acutely ill schizophrenic patients is, for various ethical and practical reasons, not possible. Yet, Hughes (1961) has stated, in relation to neuroelectric measures, that at least ten days following discontinuation of phenothiazines is necessary for such measures to return to "normal" or some baseline level. In the previously mentioned study by Roth and Cannon, these authors point

out that medication did have an effect on reducing the amplitude of the AER. Similar comments concerning the confounding effects of medication have been mentioned by Jones et al. (1970). Mucovitch and Katzelenbogen (1948) have stated that the EEG does not return to normal until ten months following electro-convulsive shock therapy (ECT). In addition to these more obvious complications which arise with research which focuses on the "ill", i.e., schizophrenic patient, the length of hospitalization and general malaise produced by the disorder make it difficult to separate causative influences from the effects of the disorder. All of the studies discussed at this point in the present paper have employed a "retrospective" research strategy, i.e., hospitalized schizophrenics have been used as subjects. The subjects have, unless otherwise stated, all been adults. Studies of this nature, while providing necessary insights into the structure of schizophrenia, cannot investigate incipient processes which, over the course of time, may lead to the manifestation of schizophrenia.

In an attempt to circumvent this problem, i.e., the delineation of factors that may exert a causative influence from those that are a product of the disorder, a relatively new research strategy has been employed. Children are selected who, by some criteria, are considered to be at high risk for eventually manifesting schizophrenia in comparison to the population at large. By following these children

from their early childhood, investigators hope to identify pre-existing biochemical, physiological, psychological, or life history characteristics which consistently differentiate those who ultimately develop schizophrenia from those who do not (Erlenmeyer-Kimling, 1971; Mosher, 1974). Mosher (1974) has pointed out that prospective high risk studies represent a predictable stage in the evolution of psychiatric research: a commitment to the study of the development of schizophrenia following an immersion by researchers in the structural aspects of the disorder. Whereas the adult schizophrenic is the legitimate source of inquiry into structure, the child (at high risk) is the legitimate source of inquiry into development (p. 13).

While the strategy for following children at high risk for manifesting schizophrenia offers an opportunity for testing aetiological hypotheses, it is not without formidable problems of its own. A major problem is the identification and selection of the high risk children. Another problem facing the high risk researcher is that of the selection of research measures. A measure chosen as highly promising at the beginning of a research project may appear outmoded and irrelevant at the conclusion of the study 15-20 years later. Does the measure in fact differentiate between those subjects who eventually manifest schizophrenia and those who do not? What inferences can be drawn from the measure regarding the aetiology of schizophrenia?

These problems have led investigators utilizing high risk prospective research strategies to note that in high risk research, the risk is for the investigator as well as the identified child. While espousing many of the advantages of high risk research, Rosenthal (1974) expresses a note of caution to investigators entering the field: "I am grateful enough to have survived most of my high risk period. I hope you survive yours" (p. 40). Before reviewing the high risk research, some preliminary discussion will be given to the problem of subject selection. The selection of research measures will be discussed following the review of the high risk literature.

1. Subject Selection (General)

The investigator employing a prospective research strategy must optimize the chances that a substantial proportion of the children selected for study will actually manifest schizophrenia at some point in their lives. Fortunately, the risk of manifesting schizophrenia in the population at large is only about 1-2% (Yolles, 1969). For the prospective researcher, however, this presents a formidable problem. To select subjects from the population at large without screening procedures increases the risk to researchers to an intollerable level. In order to insure that a substantial proportion of subjects will actually manifest schizophrenia, the initial subject pool would have to be so large that the sheer logistics and economics would make this type of research unfeasible. In order to reduce this risk to the

investigator, a number of approaches have been proposed for the selection of high risk subjects, e.g., selection of disordered children, selection of subjects from the lower socio-economic class, selection of subjects with a history of birth complications (see Garmezy & Stretimen, 1974a, pp. 18-30); the use of genetically-defined populations is preferred by risk researchers over all the current alternatives (Garmezy & Streitman, 1974a).

The strategy of using genetically defined populations was first presented by Pearson and Kely in 1957. Approximately 10-16% of children with one schizophrenic parent can be expected to develop schizophrenia during adolescence or adulthood (Heston et al., 1966), compared to a 1-2% risk in the general population. The risk for children of affected fathers is the same as for children of affected mothers (Erlenmeyer-Kimling, 1970). Children with two affected parents are at higher risk; 35-40% of such children are expected to manifest schizophrenia (Erlenmeyer-Kimling, 1970). As Pearson and Kely (1957) have pointed out, screening of unselected populations of children would require samples at least ten times as large as those drawn on children with a schizophrenic parent in order to obtain a comparable number of pre-schizophrenic subjects. As Garmezy and Stretiman have emphasized, the critical reality for subject selection in high risk research is not adherence to a particular model, but, instead, is one of determining how best to raise the base rate for

predicted schizophrenia. "Thus, genetic susceptibility has become a prime method for selecting samples of vulnerable children, however, the intensity of advocacy of a genetic model of etiology seems to vary widely among those involved in risk research." (1974a, p. 21)

C. High Risk Research

Although high risk prospective research is still in its infancy and the variables that receive primary emphasis vary from study to study, it is possible to discern certain patterns or directions of the research. High risk researchers, like the retrospective researchers who preceded them, them emphasized the schizophrenic's difficulty in information processing tasks. Included under this term are such notions as disordered levels of arousal, hypersensitivity, distractibility, etc.

One of the research programs for the study of high risk children was conducted by Mednick and Schulsinger (1968) who tested adolescents (15.5 mean age) with one schizophrenic parent. (The study was begun in 1962.) Mednick and Schulsinger compared high risk subjects and a group of normal controls under "normal" and "stressful" conditions. (The stressful condition consisted of a loud, unpleasant noise for 4.5 secs. over nine trials.) All results refer to the galvanic skin response (GSR). The results indicated that under the stress condition, the high risk subjects had more rapid latencies,

greater amplitude, were slow in habituating to the stress stimuli and had more generalized responses in comparison to the normal control group. The measure which best differentiated between the two groups was the rate of recovery (number ohms per second) of the GSR following the stress stimuli. Mednick and Schulsinger describe the high risk subjects as being highly susceptible to a broad range of stimuli that are capable of stimulating an already-sensitive autonomic nervous system (see also Silber, 1966). Many of the Mednick and Schulsinger findings are comparable to the results from the studies of adult schizophrenics. Mednick (1955) and Rodnick and Garnezy (1957), for example, have reported that adult schizophrenics have over-generalized GSR responses, and Zahn (1964) reports that chronic schizophrenics are slower to habituate (GSR) to stimuli than normal controls. Mednick (1973) has reported that approximately five years after completion of the initial testing, twelve of the high risk subjects (total N = 97) had been hospitalized for psychiatric disturbances and, in addition, eight had been diagnosed as severely schizoid, delinquent, or alcoholic. Mednick designated these twenty subjects as the "sick" group and compared their original GSR responses to the original GSR responses of twenty high risk subjects with no signs of pathology. The sick group had GSR responses of greater amplitude to the stress stimuli, and also had more rapid conditioning and shorter latencies to the stress stimuli. Once again, the measure

that best differentiated between the groups was the rate of recovery of the GSR following the stress stimuli. While it is unclear what underlying processes this measure may reflect (personal communication, Drs. Mednick and Venables, February 29, 1975), it remains the measure that best differentiates between the high risk and control group as well as between the "sick" and "well" high risk subjects (in their study).

In addition to the GSR data, Mednick and Schulsinger (1973) have found that the high risk subjects were significantly slower than the controls on portions of the WISC that required continuous concentration. As an informal observation, Mednick has noted that the high risk subjects seemed to react to excitement by withdrawal. This is similar to McGhie's observation (1969) that catatonic subjects seemed to have the highest level of arousal of all schizophrenic patients. Mednick and Schulsinger (1973) have tentatively concluded that early evidence of autonomic dysfunction may predict serious adult psychopathology. Schacter (1970) is also interested in studying psychophysiological responsiveness of children at risk. His subjects are neonates with schizophrenic mothers. Preliminary reports from the Schacter study indicate that some of the high risk subjects had a marked increase in heart rate acceleration over the testing session (cited by Garnezy, 1974, pp. 31-33).

Erlenmeyer-Kimling, Rainer and Mednick (1971) have studied the children of one (father or mother) and two schizophrenic parents. A primary emphasis in this study was the investigation of "defective filtering" and "stimulus overload" in the risk group. All results refer

to the GSR and include only the high risk children with one schizophrenic parent. Comparing 29 high risk subjects to 23 normal controls, Erlenmeyer-Kimling et al. report no difference on baseline measures, no consistent differences in the amplitude of responses to an unconditioned stimulus (a loud noise) and no difference between the groups in habituation. Response latency was significantly longer in the high risk group (Erlenmeyer-Kimling et al., 1977a). These authors report, in fact, that recovery time seemed somewhat faster in the controls (no statistics reported). The Erlenmeyer-Kimling group also report that many children did not show conditioning, and that such failures were less frequent among controls (Erlenmeyer-Kimling et al., 1977a; see also Garnezy, 1974, pp. 53-60). At a high risk conference at New York State Psychiatric Institute (February 29, 1975), Mednick and Erlenmeyer-Kimling discussed some of the differences in psychophysiological findings between the original Mednick and Schulsinger study and the Erlenmeyer-Kimling et al. study. Two reasons were suggested to account for these differences: 1) The subjects in the Erlenmeyer-Kimling study were younger than the children in the Mednick and Schulsinger study (mean age 9.5 vs. 15.5); and 2) although the design and procedure were the same in both studies, the children were treated substantially differently. Mednick instructed his experimenters to make the testing sessions as stressful as possible. Erlenmeyer-Kimling, however, instructed her experimenters to conduct the testing sessions in as easy and relaxed way as possible.

Erlenmeyer-Kimling et al. (1977b; see also Rutschman et al., 1977) also compared both groups' performance on the continuous performance task (CPT). Kornetsky and Mirsky (1966) have suggested that the CPT

is dependent upon midbrain and brainstem structures that mediate arousal. Erlenmeyer-Kimling et al. state that preliminary analyses indicate that the high risk subjects have significant performance deficits on the CPT in comparison to normal controls. These findings are consistent with data from chronic schizophrenics (Orzack & Kometsky, 1966) and lend additional support to the notion that disordered levels of arousal plays a significant role in the schizophrenic make-up. Gallant (1972) has also used the CPT as a measure of continuous attention with high risk children. He compared the performance of five-year-olds with a schizophrenic mother to age-matched children with psychotic (not schizophrenic) mother and age-matched controls (non-psychotic, non-schizophrenic) mothers. The children with schizophrenic mothers had significant performance deficits in comparison to both control groups. In the same study, Gallant also used the Hidden Figures Test and the Children's Embedded Figures Test as measures of selective attention. A coding test and an intelligence test were employed as non-attentional measures. Performance deficits were only found on the attentional measures. Gallant repeated the study with the same subjects one year later. At this time, no differences were found between the two groups. Gallant interprets these latter findings as evidence of "catching up" in the risk children's ability to inhibit irrelevant, non-task related stimuli (1972).

Anthony (1972) has studied children with one schizophrenic parent. The emphasis of this study was a "living-in" experience with the family, to provide data for evaluating the degree of susceptibility to the pathogenic influences at work in the environment. In

addition, Anthony and his staff bring each child into the laboratory for tests of information-processing ability and psychophysiological responsivity. Preliminary reports (cited by Garmezy, 1974, pp. 57-59) suggest some similarity between the psychophysiological data from Anthony's study and the Mednick and Schulsinger (1973) study. Anthony reports, for example, that the high risk children do not seem to habituate as well as the normal controls, and do not differentiate between stimuli as well as the normal controls (i.e., the high risk children seem to have overgeneralized responses). More recent reports, however, indicate that these latter findings are not specific to high risk subjects (personal communication, Dr. Erlenmeyer-Kimling, April 25, 1977).

Weintraub and Neal (1974) also studied the children of one schizophrenic parent. They tested each child's ability to ignore distracting information using auditorily-presented material. At this time, no results have been reported. In a similar vein, Wynne (1974) is interested in taking measures of psychophysiological responsivity and measures of sensory integration and information-processing in children with schizophrenic mothers (results not reported).

Garmezy (1974) has studied the children of schizophrenic mothers. In a preliminary report (1974, p. 65), he mentions finding "attentional" dysfunctions with these children (no details given). Garmezy indicates that in the future, more emphasis will be given to the construct of attention: "A broadened attack on the attention construct is

programmed for the future, in which studies will be conducted simultaneously at three levels of functioning — at the neurophysiological level, at the behavioral level in laboratory tasks, and at the behavioral level in a naturalistic setting (1974, pp. 65-66).

The only neuroelectric study of high risk children was done by Itil et al. (1974). These authors investigated children between the ages of 10-12 (mean age = 11 years) in Copenhagen, Denmark, who were considered at high risk for manifesting schizophrenia (schizophrenic mothers). Itil has been critical of retrospective research (Itil, 1972; Saletu et al., 1971), and states that the opportunity to study children before the manifestation of schizophrenia was most welcome (1974). Itil et al. have suggested that neuroelectric research with high risk children could lead to the establishment of "common neurophysiological characteristics" of schizophrenia, if they exist, long before the outbreak of the actual disorder (1974, pp. 896-899). The results of the Itil et al. study were as follows:

EEG

The high risk children had more delta activity (1.3-3.5 cps), more fast beta activity (above 18 cps), higher average frequencies, less alpha activity, less amplitude variability, and lesser average absolute amplitude in comparison to normal controls (1974). (It is worth mentioning that what Itil et al. mean when they say "more", is percentage of time spent in a particular band width. It is more common, however, for the amount of power (or amplitude) to be employed as the referent for "more", e.g., CF. Lifshitz and Gradijan,

1972, 1974.) Itil et al. (1974) have compared the EEG data of adult schizophrenics, psychotic children, and the high risk children. All three groups were different than normal controls and were characterized by more slow wave activity, less fast alpha activity, and less amplitude variability (a lowered CV). Commenting on their findings with high risk children, Itil et al. point out the similarity of neurophysiological patterns of high risk children to those of adult schizophrenics. Noting the appearance of increased slow and fast activity in the EEG records of adult schizophrenics and high risk children, Itil et al. interpret their findings along the lines of a fluctuating state of arousal hypothesis (see p.20 of this paper).

AER

For each subject, five averaged AERs were generated, each containing fifty individual AERs. Each of the five averaged responses were plotted and the latencies of the various peaks was determined. Itil et al. report that the high risk group had shorter latencies than the control group. The latency differences reached the level of statistical significance at peaks occurring approximately 40 msec., and between 100-200 msec. following stimulus onset. There were no significant differences in amplitude between the two groups. Using a discriminant function analysis, it was possible to discriminate between the two groups at the $p = .01$ level of significance. Itil and his coworkers also report that shorter latencies between 100-200 msec. in the high risk group were most pronounced when the AER wave forms were based on the last 50 (of a total of 250) responses. In the control group, however, shorter latencies occurred earlier in

the recording session, i.e., when the AERs were based on 50 responses occurring between 150-200 stimulus presentations. These findings have been interpreted as a lack of habituation in the high risk group (p. 896).

In discussing his results, Itil emphasizes the similarity in the AERs of the high risk group, adult chronic schizophrenics, and psychotic children. He suggests that differences in latency may indicate a potential, or predisposition, for becoming schizophrenic, while the amplitudes are affected only when the disease is clinically manifest in later life (p. 898). Along these same lines, the differences in latency of the early components with high risk children as compared to differences in the later components (see Saletu et al., 1971) with adult schizophrenics, may indicate that different aspects of the "information processing system" are differently affected, depending on the state of the disorder, i.e., incipient or manifest. As mentioned earlier in this paper, the early components of the AER have been generally associated with activation or arousal; the later components, however, have been more often associated with attention. It is interesting to consider the speculation that the various neurophysiological systems that subserve the general term information processing are differentially affected during the course of development and that the system that subserves arousal may become dysfunctional early in the course of development and, at some later point in time, interfere with the organism's capacity to "act on", i.e., select and inhibit, endogenous and exogenous information.

1. The EEG and the AER

An assumption inherent in all high risk research is that indicators of vulnerability to schizophrenia are to be found at relatively early ages and that they show themselves as emerging difficulties in areas continuous with the behavioral deficiencies observed in adult schizophrenics (CF. Erlenmeyer-Kimling, 1971). In the present study, the EEG and the AER are employed as the dependent variables. Both measures have been shown to be deviant in a great many adult schizophrenics in comparison to normal and psychiatric controls. In addition, both measures, when studied in children at high risk to manifest schizophrenia, have been shown to be deviant in comparison to normal controls, and are comparable to the findings from adult schizophrenics and psychotic children. Thus, the choice of the EEG and the AER seems reasonable in view of the experimental evidence. Both measures are also thought to reflect certain aspects of information processing, i.e., the organism's capacity to select and inhibit external and internal stimuli. The EEG and the AER have been implicated in states of disordered arousal, attention, heightened distractibility and the like. Since disordered levels of arousal and/or attention have played such a major role in structural as well as aetiological considerations in the area of schizophrenic research, the choice of the EEG and the AER in the proposed study has theoretical as well as pragmatic value.

Since the time of Darwin, a basic foundation in the behavioral sciences has been the belief that those behaviors which contribute to the survival of the species will continue in the organism's beha-

vioral repertoire, while those that do not will be eliminated — or the species will perish. In short, the behavior must have functional consequences, i.e., it must promote survival. In biological systems, the function of a system are those consequences of the system's activity which led to its having been evolved and which leads to its continuing to remain in the equipment of the species. As Bowlby (1969, pp. 72-76) has emphasized, however, function is used to refer to a collection of individuals (or the species) not to a particular individual or member of the species. In a particular individual, the activity of behavioral systems may have consequences that fail to promote the survival of the species. Examples of this are both Cameron's and Silverman's discussion of the "defensive" aspects of certain information processing maneuvers of schizophrenic patients. Clearly, the establishment of delusional systems would not be expected to contribute to the survival of the species. These maneuvers, however, may serve some "part-function" for particular individuals of the species. The purpose of the present paper, however, is not to discuss or elucidate the defensive (or what has been termed here the part-functional) consequences of information processing maneuvers or strategies. For further discussion of this, see Arieti (1961) and Rapaport (1951).

The purpose of the present paper is to investigate those aspects of information processing which, both pragmatically and theoretically, seem to play such an important role in schizophrenia. It is assumed that information processing behavior(s) are subserved by integrates of neurophysiological systems, plastic in nature, whose

final structure is determined by the interaction of constitutional and environmental factors. The EEG and the AER are considered neuro-electric correlates of these neurophysiological systems. Thus, the study of these measures can provide the investigator with a "peep-hole" into the development of systems whose final structure will determine its functional adaptiveness in the species' environment of evolutionary adaptiveness.

D. Some Concluding Comments Concerning Research Strategy

Research in the area of schizophrenia has always been characterized by an inconsistency of findings. Some of this inconsistency, no doubt, has been a result of the retrospective approach generally employed. Factors such as hospitalization, effects of drugs, etc., may all contribute to this inconsistency. The movement toward high risk prospective research increases the investigators' chances of separating causative influences from products of the disorder. There are difficulties, however, which are not eliminated by a change in research strategy. One of these difficulties is the growing belief that the group of people who constitute the schizophrenic population are a heterogeneous group. If this is correct, and nearly all researchers in the area would readily agree, then inconsistency of findings should not be unexpected and a greater emphasis must be placed on those aspects of schizophrenia that, to some extent, appear to cut across the schizophrenic spectrum. Even a cursory review of the myriad studies of schizophrenia indicates that such areas as "arousal", "attention", and "distractibility" (very often these are subsumed under the more

general rubric "information processing") constitute a major thrust of most research efforts. This confluence of theoretical notions continues in the relatively new area of high risk research — only more so. That the preponderance of investigators in a particular area of research simultaneously find themselves drawn toward certain hypotheses, is, quite clearly, no proof at all that the hypotheses are correct. It does seem to suggest, however, that the hypotheses under consideration are timely, that the data force their consideration at this particular juncture and, finally, that the hypotheses should be worked out in further detail and thoroughly explored before progress toward more definitive theories can be made.

E. Aim of the Present Study

In the present study, an attempt has been made to extend some of the findings predominant in the retrospective research and the very early stages of high risk research. A group of children at (genetic) high risk to manifest schizophrenia has been compared to a group of normal controls, i.e., children not at high risk to manifest schizophrenia. The AER has been used as a measure of responsivity to external stimuli and the EEG has been employed as a measure of cortical arousal.

The use of the EEG and the AER reflects a general scientific trend in any new area of research, i.e., from the general toward the specific. There is a certain amount of "heuristic optimism" involved in such an approach. With specific reference to high risk research, it is hoped that a general research strategy at the beginning stages of

investigation will lead to more specific conceptual and empirical criteria as subsequent studies are generated.

Chapter II

Hypotheses

In order to test the notion that disordered levels of cortical arousal exists before the manifestation of schizophrenia, and is therefore not merely a product of the disorder, a comparison of the frequency characteristics and amplitude variability of the EEGs of the high risk (HR) and normal control (NC) subjects was made.

Hypothesis 1.

It was hypothesized that the frequency characteristics of the EEGs of the HR subjects would differ significantly from the frequency characteristics of the NC subjects. Based on previous research with adult schizophrenics and children at high risk to manifest schizophrenia, the power spectra of the HR subjects was expected to be characterized by more power in the β_1 and β_2 band widths (14.31 Hz-30.00 Hz), an increased amount of power in the delta and theta band widths (1.30 Hz-7.16 Hz), less power in the alpha band width (7.81 Hz-13.65 Hz), and lesser average amplitude in comparison to the NC subjects.

Hypothesis 2.

It was hypothesized that HR subjects would have significantly lower CVs than the NC subjects.

Comparisons of the power spectra and CVs between groups was made within and between conditions (see section on data analysis). These comparisons allow for a partial test of the notion that many schizophrenics can be characterized by a fluctuating state of cor-

tical arousal. More pronounced changes between conditions for the HR subjects, for example, would lend support to this hypothesis.

In order to test the notion that disordered responsivity to external stimuli exists before the manifestation of schizophrenia, a comparison of the AERs of the HR and NC subjects was made.

Hypothesis 3.

It was hypothesized that there would be a significant difference in the variability of the AER wave form of the HR subjects in comparison to the NC subjects.

Hypothesis 4.

Differences were hypothesized to various components of the AER wave form between the two groups. Based on previous research with adult schizophrenics and children at high risk to manifest schizophrenia, differences in latency, as opposed to amplitude differences, were expected between the two groups. With respect to these latency differences, it was expected that the HR subjects would be characterized by shorter latencies than the NC subjects, and that these differences would be most pronounced in reference to the early components of the AER wave form, i.e., those peaks at or before 200 msec. following tone onset.

Chapter III

Methods and Procedures

The methods section will be broken up into the following parts:

- A. Subjects
 - 1. Genetic factors and some general considerations
 - 2. Characteristics of subjects used
 - 3. Subject sampling procedures
- B. Laboratory procedures
- C. Data analysis

A. Subjects

The experimental subjects in the present study are considered to have a potentially high risk of manifesting schizophrenia compared to the risk in the population at large. These HR subjects have been drawn from a genetically defined population.

The present study is part of a larger ongoing study of children at HR to manifest schizophrenia, conducted by Dr. L. Erlenmeyer-Kimling and Dr. J. Rainer at the New York State Psychiatric Institute. The HR and NC subjects in the present study were drawn from a larger pool of subjects connected with this ongoing study. Although subjects in the present study were not individually matched, consideration was given during subject selection to age and sex so that the groups are well matched along these dimensions. The primary criteria for selection, however, has been a subject's availability to participate in the study at the time of selection. In creating the original subject pool matching variables (in addition to the age and

sex of the child) included the socioeconomic level and ethnic background of the family. In addition, an attempt was made to equate the number of paranoid and non-paranoid patients (i.e., father or mother of the child to be studied). This, however, was not accomplished. The number of clearly diagnosed paranoid patients in the present study is, however, quite small. Nevertheless, the children of a paranoid parent can be subjected to a post hoc analysis.

HR Subjects

Subjects in this group were all between the ages of 7-12 at the time of initial contact. All subjects had one schizophrenic parent (at least one hospitalization with a diagnosis of schizophrenia), either father or mother. The subjects, however, were free of any psychopathological or neuropathological symptomatology and were drug-free. The number of subjects in this group was 34.

NC Subjects

Subjects in this group were all between the ages of 7-12 at the time of initial contact. No subjects in this group had a parent with a history of psychiatric hospitalization. The subjects were free of any psychopathological or neuropathological symptomatology and were drug-free. The number of subjects in this group was 32.

Sampling Procedures (HR)

Schizophrenic patients with two or more children in the age range of 7-12 were located by screening all consecutive admissions to several state hospitals, clinics, and one county hospital in New York metropolitan area, between June, 1971 and December, 1972. All patients whose children were selected were white, English-speaking,

married and still living with his or her spouse (i.e., with the other biological parent of the children of interest), and were between the ages of 25-50.

Diagnostic evaluations were made independently from patients' hospital records by two staff psychiatrists at the New York State Psychiatric Institute and one psychiatric resident. All diagnoses were made without knowledge of the hospital diagnosis or of any medications which may have been prescribed by the hospital. Unless all three psychiatrists agreed on a diagnosis of schizophrenia, the patient was excluded from further consideration.

Sampling Procedures (NC)

NC subjects were obtained through the cooperation of the Nassau and Rockland counties school systems. Letters were sent to the families in these school districts with two or more children between the ages of 7-12. These letters requested the voluntary cooperation of "mentally healthy" families. The names of both parents of a control subject were checked against the Department of Mental Hygiene files. Any child with a parent who had a history of psychiatric hospitalization was eliminated from the study. All parents of selected children were white, English-speaking, married and still living with his or her spouse (i.e., with the other biological parent of the children of interest) and were between the ages of 25-50.

Each of the HR subjects and NC subjects selected to participate in the ongoing study by Drs. Erlenmeyer-Kimling and Ranier were brought into the laboratory to be tested on a number of measures. These included a modified Lincoln-Oseretsky Test of motor impair-

ment, attention span measures, and psychophysiological measures. All subjects who participated in the study have had a good deal of contact with various members of the investigative team. In addition to a previous visit to the laboratory, this contact over time also included home visits by staff personnel. Neuroelectric measures were not previously taken, however, and the application of electrodes for the recording of the EEG and the AER has been a new experience for each of the subjects. The families of each of the subjects received \$25.00.

B. Laboratory Procedures

All subjects who participated in the study were picked up at their home by a limousine service and delivered to the laboratory at 9:00 A.M. A typical day at the laboratory lasted approximately 8 hours. The neuroelectric measures lasted approximately 30 minutes. The remaining time was devoted to paper and pencil tests, an interview, psychophysiological measures, and a neurological examination. These latter measures will not be included in the present study.

Two subjects a day were tested. As one subject was tested on neuroelectric and psychophysiological measures in the morning, the second subject went through the other procedures. This procedure was reversed in the afternoon. Lunch was prepared for each subject by staff personnel (not the experimenters). At the end of the day, each subject was driven home by the limousine service.

When a subject entered the laboratory, staff personnel attempted to alleviate any possible anxiety regarding the testing situation. All

subjects were introduced to the experimenters and a brief explanation of recording equipment was offered. The actual running of subjects was done by two experimenters (A.F. and A.B.). All subjects were identified by a code number. Neither experimenter had knowledge of a subject's code number before that subject was actually run. Thus, all subjects were run in a blind fashion. The interviews and paper and pencil tests were not administered by the experimenters. The neurological examination was conducted by a neurologist connected with the Neurological Institute.

EEG

The EEG was recorded in two one-minute sessions, one at the beginning and one at the end of an entire series of psychophysiological measures lasting approximately one and one-half hours. Recordings were made from vertex (C2) and occiput (2 cm. above theinion along the midline) and referenced to the left earlobe. Beckman biopotential (11 mm.) electrodes were employed. Eye movements (EM) were recorded from a supraorbital electrode at the right eye, referenced to the left earlobe. Beckman Dynograph amplifiers (type #482 M8) and preamplifiers (type #481 B) were used. The frequency response of the amplifier system was set to .03-30 Hz, with 6 db per octave roll-off.

Following electrode placements, a check of resistances was made using a portable (Simpson-260) ohm meter. Resistance under 8K ohms was considered acceptable. Immediately after this initial resistance check, a subject was seated in a comfortable leather armchair with a reclining back. The subject was asked to relax as much

as possible. The lights in the subject's room were extinguished. There was sufficient illumination from a window between the subject and instrument rooms, however, to allow subjects to view a target of concentric circles on the opposite wall. Subjects were asked not to move their heads during the recording of the EEG. All subjects were instructed to look at the target (10.5 inches away from the subject's chair, 66 inches off the ground). At this point, a second check of electrode resistance was made using the Beckman resistance meter. A final check of electrode resistance, also using the Beckman resistance meter, was made following the second minute of EEG recording at the conclusion of the testing procedure.

Each subject's EEG was simultaneously recorded on polygraph paper and FM tape. A Beckman type RM Dynograph Recorder and Hewlett-Packard Magnetic Recording System (model #3520 B) was calibrated before testing each subject. Calibration was accomplished by generating a 2 cm. deflection on the Beckman which was equivalent to a one-volt deflection on the FM recorder. This one-volt deflection is equivalent to a .1 mV signal from the subject.

Immediately prior to recording a subject's EEG, the experimenter spoke to the subject over an intercom. Subjects were encouraged to relax, to keep their head and neck relatively immobile, and to look at the target. Subjects were told that the procedure would take about one minute. After recording actually began, the experimenter was able to observe the subject through a window separating the two rooms. Thus, any untoward movement or dozing could be detected by direct observation, as well as by monitoring the polygraph paper.

For the EEG, only the occiput placement was analyzed (see section on data analysis).

AER

Immediately following the recording of the first minute of EEG, AERs were recorded. The recording time lasted 20-25 minutes. The recording conditions and electrode placements were exactly the same as in the EEG procedure. During the AER procedure, a series of 360 click-free, 1000 Hz, 70 db, 500 msec. tones were generated over a set of Sharpe (HA-10A) earphones. The tones were generated by a Heathkit Sine-Square Audio Generator (model 1G-18). The interval between tone presentations (i.e., the interstimulus interval) was manually controlled by the experimenter and haphazardly varied between 1.75 minutes and 3 seconds. All subjects received the following instructions before beginning the AER procedure:

"I want you to look at the target on the wall opposite to you. I want you to do this so that your eyes don't move too much. Everyone blinks and moves their eyes, so I don't expect you not to move your eyes at all. I just want you to move your eyes as little as possible. You will hear some tones over the headphones while you are looking at the target. Try to ignore the tones. Are you ready?"

As in the EEG procedure, subjects were observed through the window to check for dozing and excessive movements. This was also accomplished by monitoring the polygraph paper. For the AER, only the vertex placement was analyzed (see section on data analysis).

C. Data Analysis

EEG

For each of the two conditions, ten 6-second epochs were sub-

mitted to the time series spectral analysis program (BMD 03T). For each of the ten epochs, all frequencies above 30 Hz were filtered out and a spectral analysis was performed. Following this, log transformations were computed for each of the ten-power spectra. The means and standard deviations (SD) were then computed. Thus, for each subject, a mean (amplitude) and SD was computed at each of the frequency band widths. There were 22 separate band widths, from 1.3-28.9 Hz. Each of the band widths was 1.3 Hz wide. The means and SDs of the ten power spectra were used in the analysis of the frequency characteristics of the EEG. A diagram of this is presented for one subject below.

	<u>Condition 1</u>	<u>Condition 2</u>
	F 1.3-28.9	F 1.3-28.9
Subject 1	mean* mean	mean mean
	SD SD	SD SD

* where the means are the means of $\log \mu V^2$

While the spectral analysis permits the investigator to look at the frequency characteristics of the EEG, it does not provide a measure of amplitude variability. Amplitude variability was measured by computing a $CV\left(\frac{SD}{\text{mean amplitude}}\right)$ of the total EEG as well as a

at each of the frequency band widths. The CV were computed without performing any logarithmic transformations of the data (c F. Lifshitz and Gradijan, 1974). Thus, with reference to the diagram presented above, in the computation of the CV, the means are the means of μV^2 .

Three separate stepwise multiple linear regressions (MLR) were performed on conditions 1 and 2 separately. The squared multiple correlation (R^2) of the MLR represents the proportion of the total variance that can be predicted using a linear equation. For the first MLR, the independent variables were the measures of power ($\log uv^2$) at each of the band widths as well as a measure of power for the overall (or total) EEG, and the age and sex of the subjects. For the second MLR, the independent variables were the CV at each of the band widths as well as a CV of the total EEG, and the age and sex of the subjects. The third MLR used the variables employed in the final steps of the first two MLRs and was used to predict group membership. A multiple discriminant function analysis (MDF) was also performed on conditions 1 and 2 separately. Unlike the MLR which used only those variables which appeared in the final step of the regression equation, the MDF employs all the variables, i.e., both power and CV at the separate band widths and for the total EEG, and is used to predict group membership.

Comparisons of power (i.e., frequency characteristics) and amplitude variability (i.e., CV at delta (1.30-3.25 Hz), theta (3.90-7.16 Hz), alpha (7.81-13.65 Hz), beta₁ (14.31-20.16 Hz), and beta₂ (20.18-30.00 Hz), as well as total power and total CV was made between the groups within each condition using a one-way ANOVA with sex and age as the covariates. The same analysis was made between the groups across conditions using a split-plot repeated measures ANOVA with sex and age as the covariates (Winer, 1971, p. 518). Amplitude graphs were generated for each subject

and the mean amplitude and mean frequency of the alpha peaks were scored in a blind fashion. These measures were compared within and across conditions using the same statistical designs mentioned above.

AER

The 500-msec. period following tone onset was digitized for all 360 stimuli on a PDP-12 computer. In order to check for a "noisy" background level of EEG activity, the 500-msec. period preceding tone onset was also digitized.

The digitized data was averaged using a computer program on an IBM 370 that contained the following specifications: Each trial was edited for EMs. Discursions on the EM channel greater than a 2-cm. deflection (.1 mV) led to a rejection of that trial. All trials where the data was out of range of the FM recorder (due to momentary DC shifts or movements of the head and neck area), were similiary discarded.

The first two hundred "good" (see criteria stated above) trials were averaged for each subject for each condition, i.e., following tone onset (AER) and preceding tone onset (background EEG). This averaging procedure produced point-by-point means and SDs across the two hundred trials. Since there was a 2-msec. interval between samples during the digitization procedure, the output consisted of 250 means and SDs per condition per subject. An average SD was then computed for seven time epochs, 128 msec. wide, with centers at 64, 196, 238, 256, 310, 384 and 448 msec. This was done for both the 500-msec. period prior to and following tone onset. In

order to determine if the background activity of the EEG is having a significant effect on the AER, the pre-stimulus condition was compared between groups using a one-way ANOVA for each of the seven SDs. In order to determine if there was a significant difference in the variability of the AER wave forms between groups, a one-way ANOVA was performed for each of the seven SDs of the 500-msec. period following tone onset.

An AER wave form based on 200 responses was graphed for each subject. Each subject's AER wave form was hand-scored in blind fashion so that latency and amplitude measurements could be made on the identifiable peaks. (Both positive and negative deflections will be referred to as peaks.) Although the latency and amplitude of all identifiable peaks have been recorded, only the values at approximately 100 msec., 200 msec., and 300 msec. following tone onset were reported. The scoring of these components was accomplished in the following fashion: the most negative peak occurring between 80-160 msec. following tone onset was designated as N100; the most positive peak occurring between 180-250 msec. following tone onset was designated as P200; and the most positive peak occurring between 280-350 msec. following tone onset was designated at P300. If there was more than one identifiable peak occurring at approximately the same time, the greater of the two values was always used. For N100, the "greater" value was considered the value with the greatest negativity. Thus, -5.30 was considered greater than -5.25. Amplitude was always scored from baseline to peak.

For N100, P200 and P300, separate ANOVAs were performed for

the latency and amplitude values. Cochran's C and the Bartlett Box F tests for homogeneity were also employed, using the SD at the latency and amplitude values at the peaks under consideration. A (stepwise) MLR and MDF were performed using the amplitude and latency values. The rationale for this analysis is exactly the same as the rationale presented for the EEG analysis.

In addition to the analysis of the AERs based on 200 responses, AERs for both groups were calculated based on (approximately) the first ten, second ten, the last ten, and next to last ten responses per subject. The latency values for N100, P200 and P300 were then compared between groups. This procedure allows for a partial test of the "habituation" hypothesis.

An expectation based on previous high risk research is that approximately 10-16% of the HR subjects will manifest schizophrenia at some point in their lives. While no such prediction was made in the present study, it was of interest, nevertheless, to see if two separate subgroups of HR subjects could be determined at this time. A method used for accomplishing this was to transform the scores of all the subjects into standard scores (Z scores). Thus, it was possible to determine how, and with what strength, a particular subject differed from all other subjects. Z score transformations (based on the mean and SD of the groups combined) were made for each subject's total power, as well as for the power at delta, theta, alpha, β_1 and β_2 . The same transformations were made for the CV. All Z scores transformations of the EEG measures were based on the combined scores of conditions 1 and 2. Z scores transformations were also made for

each subject's latency and amplitude scores on N100, P200 and P300 of the AER. A subjects was considered deviant if he had a Z score of at least ± 1 SD away from the mean on at least one of the measures of power and at least one of the measures of the CV. In addition, a subject must also be deviant on at least one of the AER measures. If a subject had a Z score between $\pm .95$ and $\pm .99$, this score was not rounded off to ± 1.00 unless the subject was considered deviant. For example, if subject XYZ had Z scores at or above ± 1.00 at the CV and AER measures, and a Z score of $\pm .98$ on any of the power measures, this latter Z score was not rounded off to ± 1.00 . If, however, he had a Z score of at least ± 1.00 on any of the power measures, in addition to the score of $\pm .98$, then the subject would be considered deviant and the score of $\pm .98$ would be rounded off to ± 1.00 .

A further method for delineating a subgroup of deviant subjects was to assign one point to Z scores ± 1 SD from the mean, two points for Z scores ± 2 SD from the mean, and so on. Using the same hypothetical example of subject XYZ, if he had a Z score of +1 and +2 at power (say at delta and total) and Z scores of -1 at CV (e.g., at total) and a Z score of +1 at latency P300, his total deviance score would be 5. Subjects with deviance scores above the median of all other deviant subjects were considered highly deviant (HD).

All subjects in the present study were, as mentioned earlier, tested on a number of psychophysiological measures. The scoring of these measures was accomplished by a separate team of investigators who were able to delineate a subgroup of subjects. The subgroup was characterized by: 1) high absolute threshold; 2) low uncomfortable

threshold; 3) high heart rate during the presentation of uncomfortable stimuli; 4) large skin conductance response to the uncomfortable stimuli; and 5) more variability of the squeeze response in a magnitude estimation procedure. The stimulus for the above-mentioned measures was white noise (Fein et al., 1974). The subjects in this group who were considered deviant on the neuroelectric measures as well, have also been classified as HD.

The final step in the analysis of the neuroelectric data was to perform a stepwise MDF analysis using the values from the EEG and AER analysis. The EEG values were combined across conditions. The stepwise MDF analysis uses basically the same mathematics as the MLR and has the advantage of predicting group membership. Thus, one step is needed instead of two.

Chapter IV

Results

The results section will be broken up into the following parts:

A. EEG Analysis

1. MLR and MDF Analysis - Condition 1
2. MLR and MDF Analysis - Condition 2
3. Power Analysis
4. CV Analysis
5. Alpha Analysis

B. AER Analysis

1. Measures of Latency, Amplitude and Variability
2. Delineation of a Subgroup: The High Deviant Subjects
3. EEG and AER Measures used to Predict Group Membership

A. EEG Analysis

1. MLR and MDF Analysis - Condition 1

Knowledge of the power at 12.0 Hz, 14.6 Hz, 22.4 Hz, 17.2 Hz, 4.2 Hz, and 8.1 Hz, reduces the error in predicting group membership by 24.6% (p .008).

Knowledge of the CV at 10.7 Hz, 14.6 Hz, 28.9 Hz, and 13.3 Hz, reduces the error in predicting group membership by 30.5% (p .000).

Using both power and the CV in the regression equation, 30.5% of the variability in predicting group membership can be accounted for by knowledge of the CVs at 10.7 Hz, 14.6 Hz, 28.9 Hz, and 13.3 Hz (p .000).

Using a stepwise MLR and knowledge of the CVs at 10.7 Hz, 14.6 Hz, 28.9 Hz, and 13.3 Hz, allows for a predictive accuracy of 70% (p .01). Twenty-nine out of thirty-four HR subjects are correctly placed in their appropriate group, and twenty-one out of thirty-two NC subjects are correctly assigned to their appropriate group.

Employing an MDF analysis, it is possible to assign thirty-two out of thirty-four HR subjects to their correct group, and thirty out of thirty-two NC subjects to their appropriate group. The accuracy in predicting group membership is 96.9% (p .000).

2. MLR and MDF Analysis - Condition 2

Knowledge of the power at 25.0 Hz, 12.0 Hz, 13.3 Hz, and 22.4 Hz accounts for 19.9% of the variability in predicting a subject's group (p .01).

Knowledge of the CV at 1.6 Hz reduces the variability in predicting group membership by 6.4% (p .04).

Using both power and the CV in the regression equation, 20.5% of the variability in predicting group membership can be accounted for by knowledge of the power at 25.0 Hz, and the CVs at 10.7 Hz, 28.9 Hz, and 26.3 Hz (p .008).

Using a stepwise MLR, and knowledge of the power at 25.0 Hz, and the CVs at 10.7 Hz, 28.9 Hz, and 26.3 Hz, allows for a predictive accuracy of 69% (p .05). Twenty-three out of thirty-four HR subjects are correctly assigned to their appropriate group, and twenty-three out of thirty-two NC subjects are correctly assigned to their appropriate group.

Using an MDF analysis, it is possible to assign thirty-two out of thirty-four HR subjects to their correct group, and thirty out of thirty-two NC subjects to their correct group. This is a predictive accuracy of 96.9% ($p < .000$).

3. Power Analysis (across and within conditions) (ANOVAs)

The power values for each group at delta, theta, alpha, β_1 , β_2 and total power are presented in Table 1 and graphically displayed in Figures 1, 2 and 3.

Delta. Across conditions, younger subjects are associated with increased power ($p < .02$). In condition 1 (younger) males are associated with increased power ($p < .01$).

Theta. Across conditions, younger subjects produce more power in the theta band width than older subjects ($p < .005$). In condition 1 (younger), males are associated with increased power ($p < .01$) and in condition 2, younger subjects are associated with increased power ($p < .001$).

Alpha. Across conditions, younger subjects produce more power in the alpha band width in comparison to older subjects ($p < .02$). The association between age and power reaches significance in condition 2 ($p < .01$).

Beta₂. The NC subjects produce significantly more power across conditions in the β_2 band width than do the HR subjects ($p < .04$). This relationship is significant in condition 2 ($p < .04$).

Total. Across conditions, the NC subjects produce significantly greater total power than do the HR subjects ($p < .05$). The group difference approaches significance in condition 2 ($p < .059$). Across

Table 1

Power values for 34 HR and 32 NC subjects in the indicated band widths within and across conditions and significance (sig.) of differences between the two groups.

<u>EEG band widths</u>	<u>Condition 1</u>			<u>Condition 2</u>			<u>Conditions 1 and 2</u>		
	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>
Delta	9.70	9.72	n.s.	9.69	9.53	n.s.	9.68	9.62	n.s.
Theta	7.87	7.98	n.s.	7.87	7.87	n.s.	7.87	7.93	n.s.
Alpha	7.17	7.27	n.s.	7.16	7.29	n.s.	7.17	7.28	n.s.
Beta ₁	5.96	6.05	n.s.	5.98	6.13	n.s.	5.97	6.09	n.s.
Beta ₂	4.82	5.04	n.s.	4.85	5.22	.04	4.83	5.13	.04
Total	6.47	6.62	n.s.	6.48	6.65	.059	6.48	6.63	.05

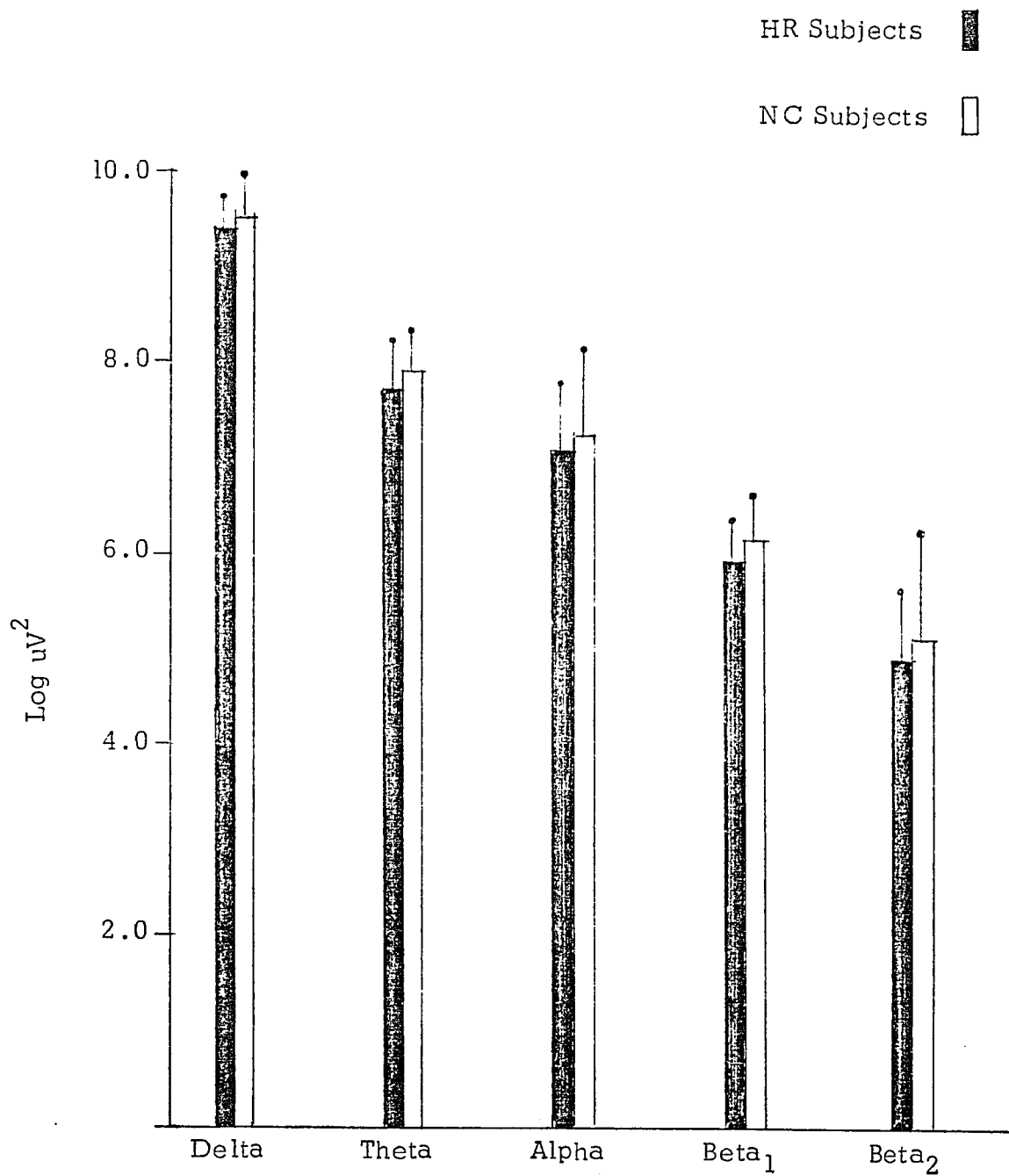


Figure 1. Electroencephalographic power plotted on a linear scale for the indicated band widths. The height of the bar indicates the mean for either 34 HR subjects or 32 NC subjects. The dot above the bar shows one standard deviation. Condition 1.

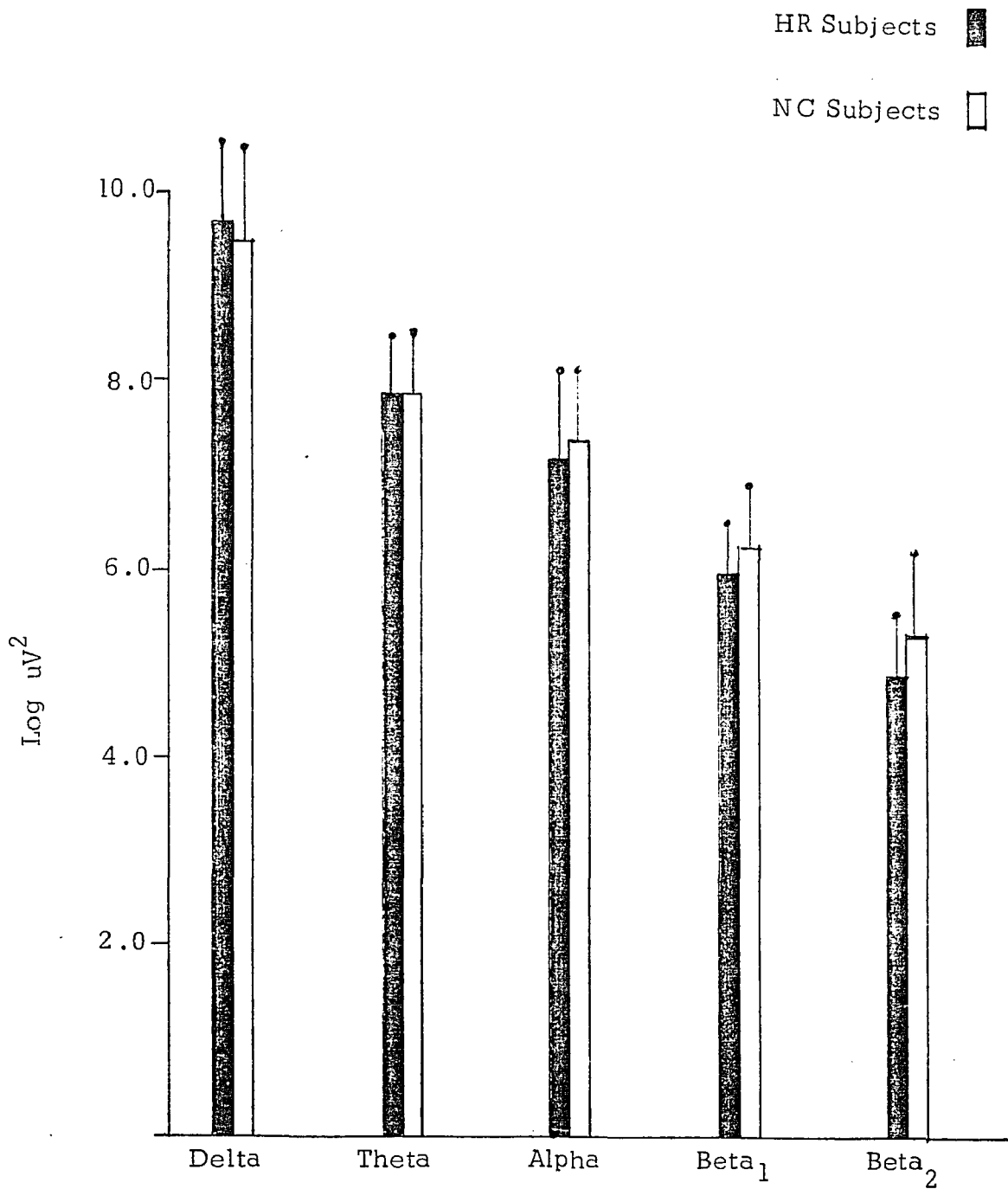


Figure 2. Electroencephalographic power plotted on a linear scale for the indicated band widths. The height of the bar indicates the mean for either 34 HR subjects or 32 NC subjects. The dot above the bar shows one standard deviation. Condition 2.

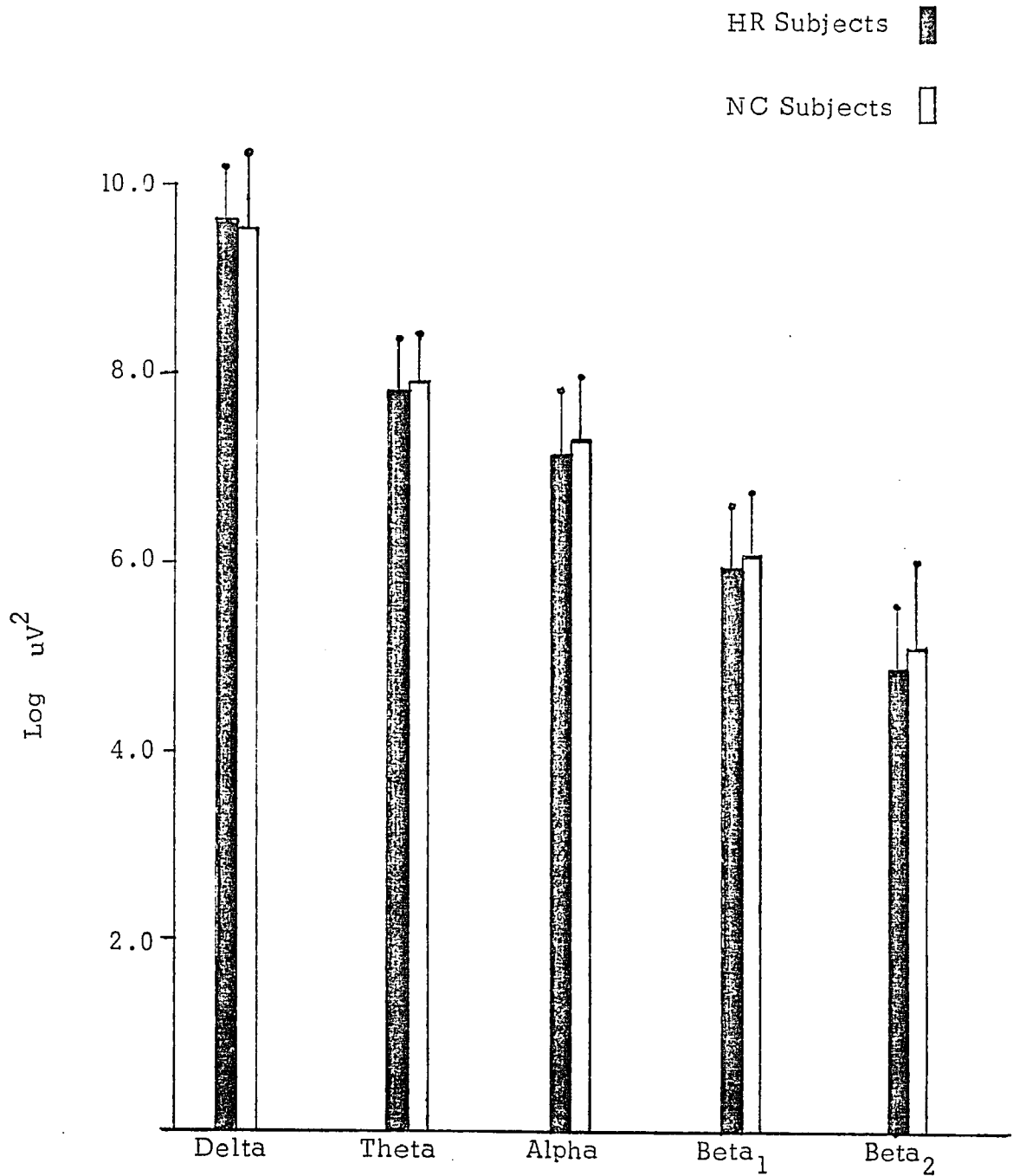


Figure 3. Electroencephalographic power plotted on a linear scale for the indicated band widths. The height of the bar indicates the mean for either 34 HR subjects or 32 NC subjects. The dot above the bar shows one standard deviation. Conditions 1 and 2.

conditions, younger subjects are associated with increased power (p .04).

4. CV Analysis (across and within conditions) (ANOVAs)

The CV values for each group at delta, theta, alpha, beta₁, beta₂ and the total CV are presented in Table 2 and graphically displayed in Figures 4, 5 and 6.

Delta. Across conditions, the HR subjects have a significantly lower CV in relation to the NC subjects (p .04). The difference between the groups is significant in condition 2 (p .04). The CV in condition 2 is significantly greater than the CV in condition 1 (p .01). Across conditions, females have a greater CV than males (p .05).

Theta. The CV in condition 2 is significantly greater than the CV in condition 1 (p .01).

Alpha. Across conditions, the CV for the HR subjects at the alpha band width is significantly less than the CV for the NC subjects (p .01). The difference between the groups is significant in condition 1 (p .01).

Beta₁. Across conditions, the HR subjects have a significantly lower CV in relation to the NC subjects (p .01). This difference between the groups reaches significance in condition 1 (p .02).

Total. Across conditions, the HR subjects have a significantly lower CV in relation to the NC subjects (p .03). This relationship reaches significance in condition 2 (p .05). The CV is greater in condition 2 than in condition 1 (p .01). Across conditions, females are associated with an increased CV (p .02).

Table 2

CVs for 34 HR and 32 NC subjects in the indicated band widths within and across conditions and significance (sig.) of differences between the two groups.

<u>EEG band widths</u>	<u>Condition 1</u>			<u>Condition 2</u>			<u>Conditions 1 and 2</u>		
	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>
Delta	.77	.78	n.s.	.81	.98	.04	.77	.88	.04
Theta	.57	.64	n.s.	.65	.72	n.s.	.61	.68	n.s.
Alpha	.60	.77	.01	.64	.73	n.s.	.62	.75	.01
Beta ₁	.54	.65	.01	.60	.67	n.s.	.57	.66	.01
Beta ₂	.65	.73	n.s.	.73	.80	n.s.	.69	.77	n.s.

Table 3

Comparisons of power and frequency of the alpha peaks within and across conditions and significance (sig.) of differences. (N = HR 34, NC 32)

	<u>Condition 1</u>			<u>Condition 2</u>			<u>Conditions 1 and 2</u>		
	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>	<u>HR</u>	<u>NC</u>	<u>(sig.)</u>
Power	7.81	8.03	n.s.	7.67	7.92	n.s.	7.74	7.98	n.s.
Frequency	9.91	9.69	n.s.	7.27	9.24	n.s.	9.60	9.47	n.s.

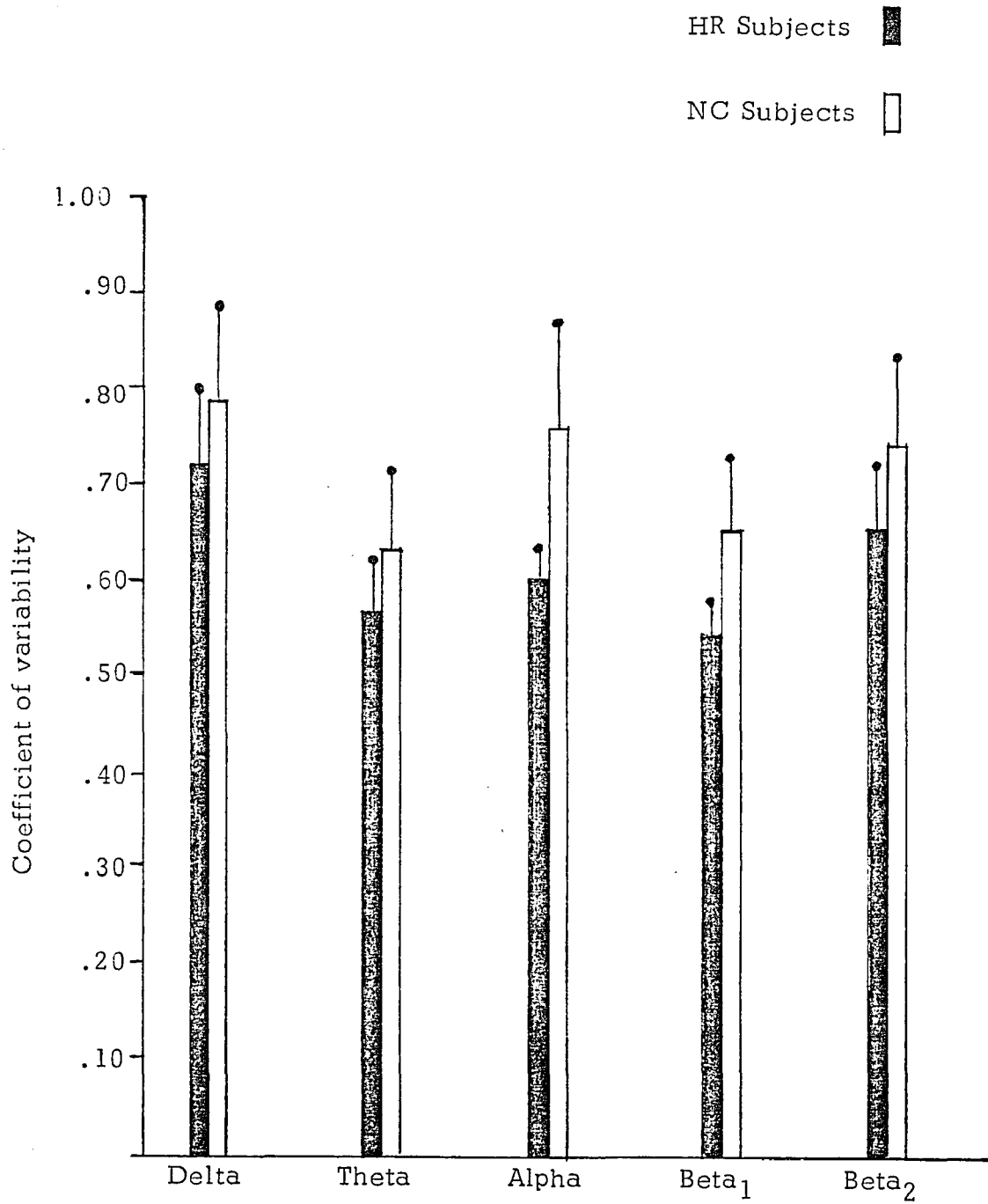


Figure 4. The heights of the bars indicate the mean values for the coefficient of variability of the power in the indicated band widths for the same population of 34 HR and 32 NC subjects as presented in the first three figures. The lines above the bars indicate one standard deviation for these populations; the vertical scale is linear. Condition 1.

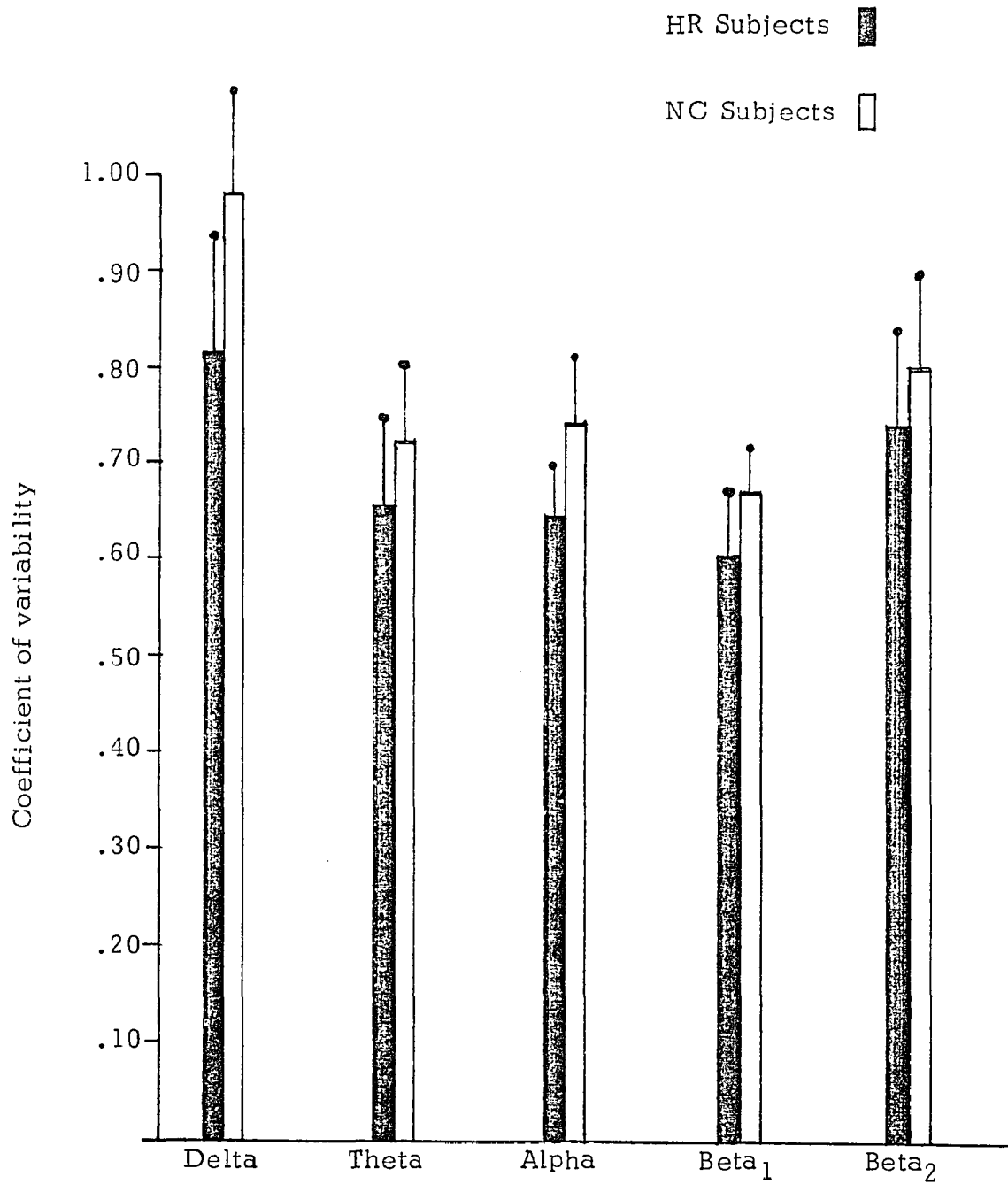


Figure 5. The heights of the bars indicate the mean values for the coefficient of variability of the power in the indicated band widths for the same population of 34 HR and 32 NC subjects as presented in the first three figures. The lines above the bars indicate one standard deviation for these populations; the vertical scale is linear. Condition 2.

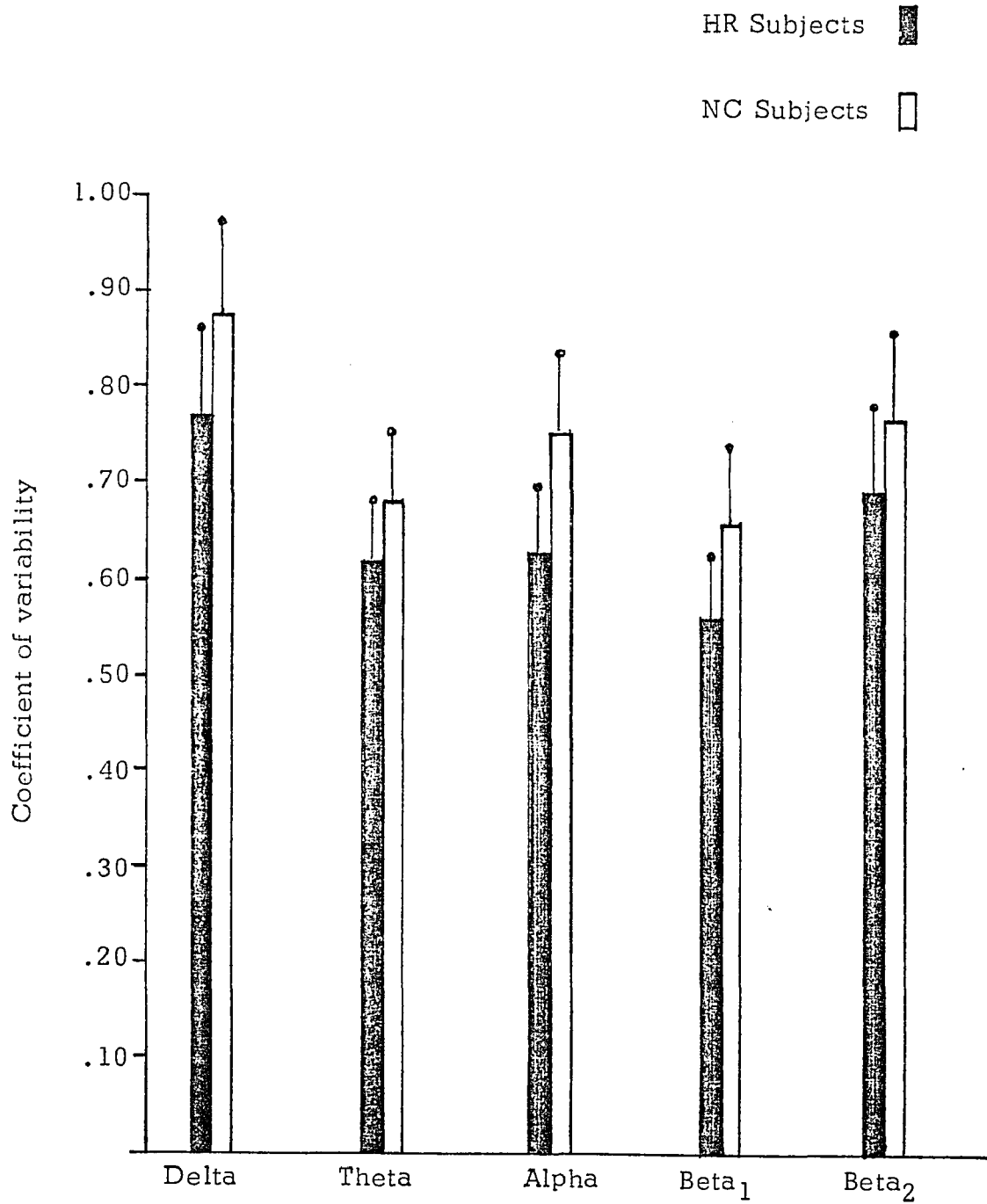


Figure 6. The heights of the bars indicate the mean values for the coefficient of variability of the power in the indicated bandwidths for the same population of 34 HR and 32 NC subjects as presented in the first three figures. The lines above the bars indicate one standard deviation for these populations; the vertical scale is linear. Conditions 1 and 2.

5. Alpha Analysis

The (mean) amplitude and (mean) frequency of the alpha peaks for both groups in each condition are presented in Table 3. No difference between the groups was found on either measure.

B. AER Analysis

1. Measures of Latency, Amplitude and Variability

The seven SDs of the 500-msec. period following tone onset were compared between groups and indicated no difference in the variability of the AER wave form between the HR and NC subjects. The SDs of the 500-msec. period preceding each tone onset were also compared between the groups and no differences were found. The amplitude and latency values for N100, P200, and P300 were compared between groups (see Table 4). The amplitude at N100 was significantly greater for the HR subjects in comparison to the NC subjects ($p = .04$). Using Cochran's C and the Bartlett Box F tests for homogeneity of variances, the HR subjects were found to have greater latency variability for N100 than the NC subjects ($p = .02, .05$) and greater amplitude variability for P200 ($p = .005, .008$). These values are presented in Table 5.

Latency measures for N100, P200 and P300 based on the first twenty and last twenty responses were compared between groups for ten HR and ten NC subjects, and no differences were found (see Table 6).

The results of the stepwise MLR and MDF analysis were not significant.

Table 4

Latency and amplitude values for 31 HR and 25 NC subjects at N100, P200, and P300 and significance (sig.) of differences between the groups.

	HR	NC	Sig.
N100			
Latency	120.45 msec.	125.60 msec.	ns
Amplitude	- 7.01 Uv	- 5.29 Uv	.04
P200			
Latency	197.93 msec.	185.36 msec.	ns
Amplitude	3.58 Uv	3.99 Uv	ns
P300			
Latency	303.19 msec.	292.96 msec.	ns
Amplitude	5.22 Uv	4.91 Uv	ns

Table 5

Standard deviations (SDs) for 31 HR and 25 NC subjects at N100, P200, and P300 and tests for homogeneity of variances.

	<u>HR</u>	<u>NC</u>	<u>Cochran's C</u>	<u>Sig.</u>	<u>Bartlett Box F</u>	<u>Sig.</u>
N100						
Latency	35.25	23.80	.68	.02	3.83	.05
Amplitude	3.11	3.36	.53	ns	.15	ns
P200						
Latency	33.85	44.40	.63	ns	1.81	ns
Amplitude	3.61	1.99	.76	.005	7.01	.008
P300						
Latency	45.44	35.26	.62	ns	1.64	ns
Amplitude	2.67	2.42	.54	ns	.25	ns

Table 6

Latency measures for 10 HR and 10 NC subjects based on the first twenty and last twenty responses and significance (sig.) of differences between the groups.

	<u>LN100</u>		<u>LP 200</u>		<u>LP 300</u>	
	<u>First 20</u>	<u>Last 20</u>	<u>First 20</u>	<u>Last 20</u>	<u>First 20</u>	<u>Last 20</u>
HR	133.1	133.3	190.0	196.9	296.1	295.4
NC	123.1	125.4	184.5	186.5	278.3	276.4

Differences:

HR	+ .2		+6.9		- .7	
		ns		ns		ns
NC	+2.3		+2.0		-1.9	

A graphic representation of an AER wave form for one HR and one NC subject is presented in Figures 7 and 8.

2. Delineation of a Subgroup: The High Deviant Subjects

(The delineation of a HD group was based on 53 subjects who had both EEG and AER measures. There were 23 NC subjects and 30 HR subjects.)

There are twelve subjects who are considered deviant. Of these twelve subjects, nine are HR subjects and three are NC subjects. There are six subjects who are considered highly deviant (HD). These subjects have a Z score average equal to or greater than the median Z score (9) of all of the deviant subjects. Of the six HD subjects, four are HR subjects and two are NC subjects. In addition to these subjects, a subgroup of five subjects have been identified on a psychophysiological task as being significantly deviant from all of the other subjects ($N=70$). These subjects were characterized as having a high absolute threshold and a low uncomfortable threshold. The stimulus was white noise. All five subjects were HR subjects. Of these five subjects, two were considered deviant on the neuroelectric measures, i.e., Z scores ± 1 SD from the mean on power, CV, and the AER. Of the remaining three subjects, one had Z scores of at least ± 1 SD from the mean on the AER and the CV, one had Z scores of at least ± 1 SD from the mean on power and the CV, and the remaining subject had Z scores of at least ± 1 SD from the mean on power, and a Z score of $-.92$ on the CV and $+.97$ on the AER. The two subjects who were identified as deviant on the psychophysiological task as well as on the neuroelectric measures are considered to be HD. Thus, the total

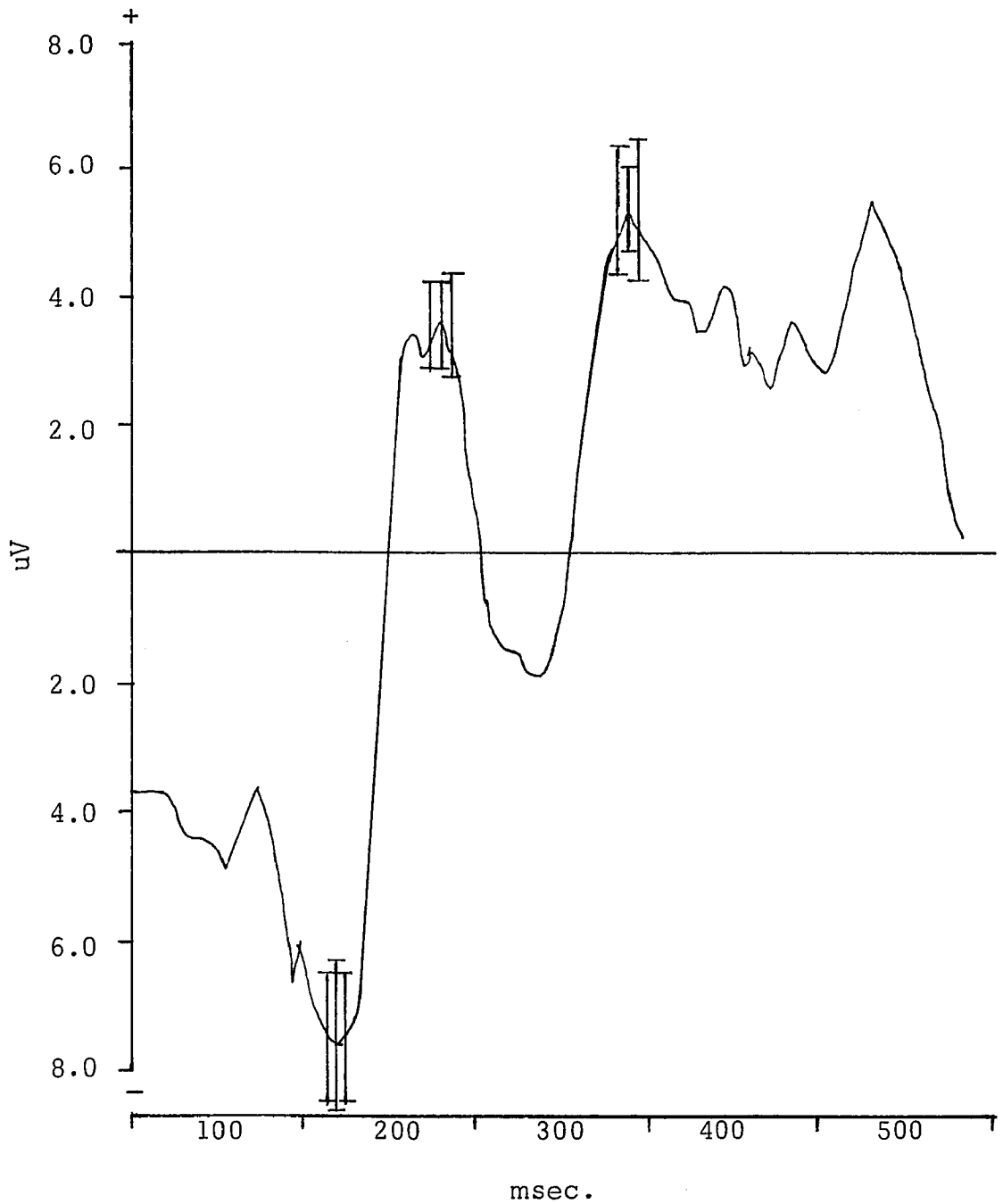


Figure 7. An AER for one HR subject in response to 200 tone presentations. Standard errors of the mean are presented at and around N100, P200 and P300.

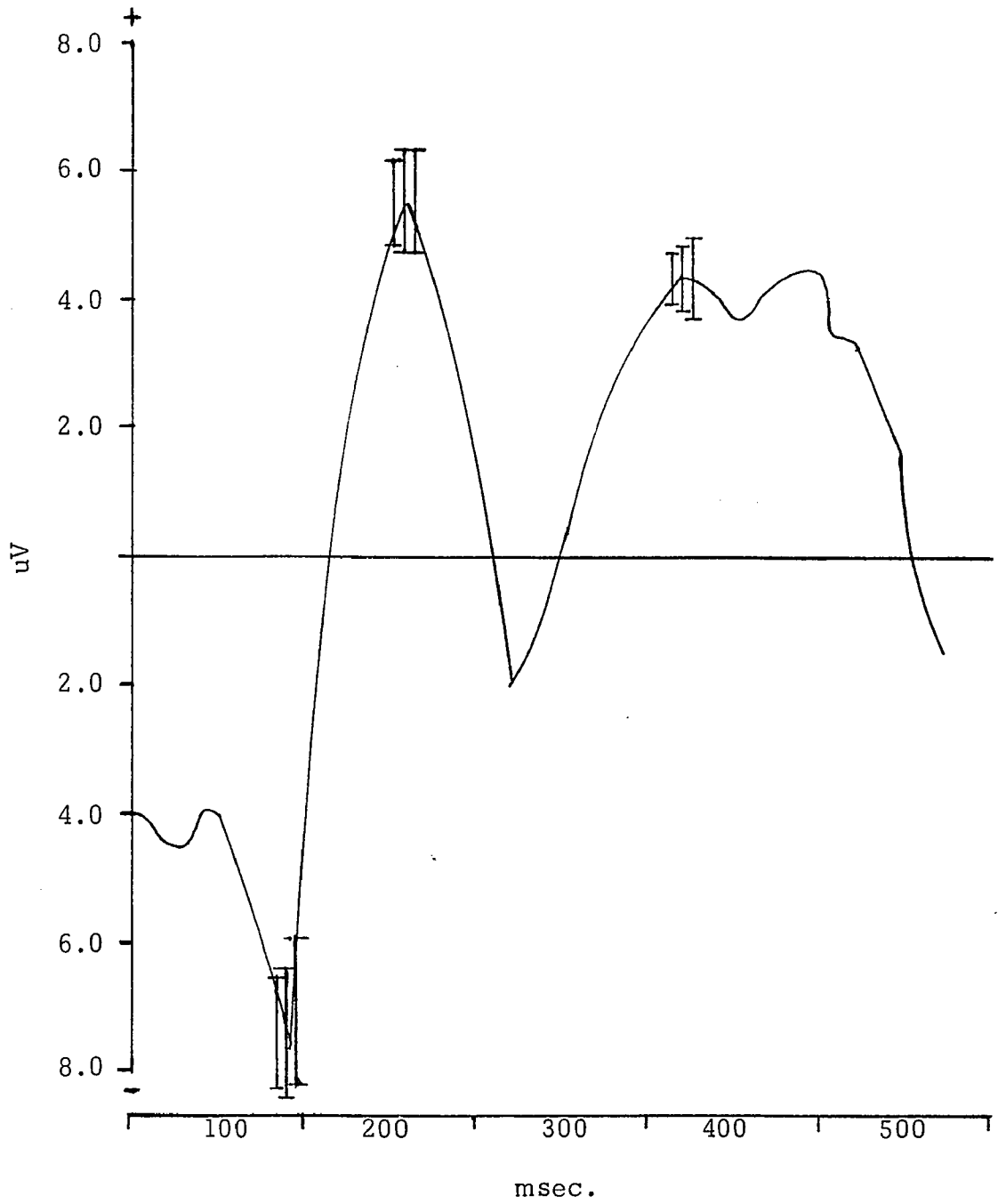


Figure 8. An AER for one NC subject in response to 200 tone presentations. Standard errors of the mean are presented at and around N100, P200 and P300.

number of subjects considered to be HD is eight. Of these eight subjects, six are HR. A profile of these eight subjects is presented in Table 7.

For six of the HD subjects, the measures of power and variability of the EEG have 100% within-subject reliability. Thus, if a subject had a minus Z score on one measure of power (e.g., delta), he had minus Z scores on all other measures of power. The same held true for the CV. This within-subject reliability did not hold true for the two subjects who were considered HD based on psychophysiological and neuroelectric measures. As can be seen in Table 7, there was no consistent relationship between Z scores on power and Z scores on the CV. Looking at the EEG records of the HD subjects (excluding the two who were deviant on the psychophysiological measures), three tentative patterns can be discerned: For two subjects (one HR, one NC), minus Z scores on power were accompanied by plus Z scores on the CV; for two subjects (both HR), minus Z scores on power were accompanied by minus Z scores on the CV; and for the remaining two subjects (one HR, one NC), the EEG profile was characterized by positive Z scores on both power and the CV. On the AER measures, the HD subjects were characterized by shorter latencies and lower amplitudes than the rest of the subjects (see Table 8).

3. EEG and AER Measures used to Predict Group Membership (across conditions)

Using a stepwise multiple discriminant function analysis, knowledge of the CV at 1.6 Hz, 9.4 Hz, 10.7 Hz, 14.6 Hz, 22.4 Hz, and knowledge of the power at 5.5 Hz, 9.4 Hz., and knowledge of the

Table 7

A profile of the 8 High Deviant (HD) subjects with: age, sex, Z scores for the power and CV measures, and Z scores for the AER measures. Subjects labeled 100 have schizophrenic mothers, subjects labeled 200 have schizophrenic fathers, and subjects labeled 700 are NC subjects. The last two subjects (*) are deviant on the psychophysiological measures and have been included in the subgroup of HD subjects.

<u>Subject number</u>	<u>Sex</u>	<u>Age</u>	<u>Power</u>	<u>Band widths</u>	<u>CV</u>	<u>AER</u>
100301	F	12.9	- .40	Delta	+1.11	LN100 -2.57
			-1.30	Theta	+ .80	AN100 - .19
			-1.02	Alpha	+1.21	LP 200 -2.56
			- .01	Beta 1	+1.43	AP 200 + .20
			- .23	Beta 2	+1.06	LP 300 -1.47
			- .50	Total	+1.33	AP 300 - .09
101401	M	11.4	-1.44	Delta	-1.33	LN100 -2.12
			-1.74	Theta	- .14	AN100 + .83
			-1.72	Alpha	-1.05	LP 200 -2.24
			-1.80	Beta 1	- .95	AP 200 - .60
			-1.33	Beta 2	- .94	LP 300 -1.72
			-2.15	Total	-1.26	AP 300 - .05
200102	F	8.5	+1.07	Delta	+1.96	LN100 - .02
			+1.34	Theta	+2.94	AN100 - .52
			+ .82	Alpha	+1.45	LP 200 - .24
			+1.13	Beta 1	+1.60	AP 200 -1.48
			+ .44	Beta 2	+2.77	LP 300 - .64
			+1.29	Total	+2.42	AP 300 - .25
200602	F	12.1	-1.19	Delta	-1.48	LN100 + .04
			-1.74	Theta	-1.37	AN100 -1.20
			-2.23	Alpha	- .88	LP 200 - .38
			-1.43	Beta 1	- .50	AP 200 - .26
			- .25	Beta 2	- .97	LP 300 + .96
			-1.65	Total	-1.55	AP 300 +1.09
700701	M	12.1	-1.08	Delta	+1.40	LN100 - .16
			-1.34	Theta	+1.42	AN100 + .91

<u>Subject number</u>	<u>Sex</u>	<u>Age</u>	<u>Power</u>	<u>Band widths</u>	<u>CV</u>	<u>AER</u>
			-1.14	Alpha	+2.54	LP 200 - .56
			-2.23	Beta 1	+2.04	AP 200 +1.74
			-1.19	Beta 2	+3.69	LP 300 +1.29
			-1.86	Total	+1.66	AP 300 + .004
701502	M	12.1	+ .85	Delta	+1.16	LN100 - .48
			+1.34	Theta	+1.06	AN100 +1.23
			+1.23	Alpha	+ .05	LP 200 - .67
			+ .87	Beta 1	+1.69	AP 200 - .02
			+ .48	Beta 2	+2.00	LP 300 -1.13
			+1.19	Total	+1.04	AP 300 -1.52
100304*	M	8.2	+1.14	Delta	-1.19	LN100 + .37
			+ .80	Theta	- .06	AN100 +1.60
			- .35	Alpha	+ .66	LP 200 + .70
			-1.17	Beta 1	+1.54	AP 200 + .74
			-1.13	Beta 2	- .26	LP 300 + .18
			- .70	Total	- .95	AP 300 - .98
200604*	M	10.1	+ .53	Delta	+ .90	LN100 - .81
			- .24	Theta	+1.12	AN100 +1.23
			-1.23	Alpha	- .71	LP 200 - .45
			- .61	Beta 1	- .08	AP 200 - .53
			- .69	Beta 2	- .07	LP 300 + .78
			- .87	Total	+ .93	AP 300 - .80

Table 8

Mean latency and amplitude values for 8 HD subjects and the associated Z scores at LN100, AN100, LP200, LP300, and AP300.

	<u>Z Score</u>		<u>Z Score</u>
LN100 = 100.75	-.72	AN100 = -4.62	+.55
LP 200 = 166.50	-.70	AP 200 = 3.69	-.03
LP 300 = 289.24	-.22	AP 300 = 4.25	-.14

AER values for latency at 121.4 msec. (L N100), 191.8 msec. (L P200), and the amplitude at N100, 37% of the variance in predicting group membership can be accounted for. Twenty-five out of thirty HR subjects can be correctly assigned to their group, and eighteen out of twenty-three NC subjects can be correctly assigned to their group. The predictive accuracy is 81.13% and is significant at the .02 level.

The three most "powerful" individual variables, i.e., the three variables with the three highest univariate F-ratios with 1 and 51 df are: the CV at 14.6 Hz ($F = 7.59$, $p = .01$), the CV at 10.7 Hz ($F = 6.86$, $p = .025$), and the CV at 12.0 Hz ($F = 5.76$, $p = .025$).

The most "powerful" combination of variables, i.e., the smallest combination of variables with the most predictive accuracy, is the amplitude at N100, the CV at 10.7 Hz, and the power at 5.5 Hz. This combination of variables reduces the variability in predicting group membership by 20%. Twenty-two out of thirty HR subjects can be assigned to their correct group, and seventeen out of twenty-three NC subjects can be assigned to their correct group. The predictive accuracy is 73.80% and is significant at the .01 level.

Chapter V

Discussion

The discussion section will be broken up into the following parts:

- A. The Data in Relation to the Four Hypotheses
- B. The EEG Measures and an Arousal Hypothesis: The Paradoxical Effect
- C. The HD Subjects (AER)
- D. The HD Subjects (EEG)
- E. Summary and Conclusions
- F. Suggestions for Future Research

A. The Data in Relation to the Four Hypotheses

Hypothesis 1

The data lends some support to the first hypothesis. As predicted, the HR subjects do produce significantly less amplitude across the power spectra than the NC subjects, and a difference in frequency characteristics between the two groups was also found. The data does not, however, support the notion that the HR subjects would be characterized by a significantly greater production of power in the delta and theta, and β_1 and β_2 band widths, and significantly less power in the alpha band width. There are no differences between the groups at the slow frequencies (delta and theta), nor are there any differences between the groups at the alpha band width. The finding that the NC subjects produce significantly more power in the β_2 band width in comparison to the HR subjects is contrary to the expectation of hypothesis one. These findings do not

support an increased level of arousal hypothesis in the HR subjects. The decreased levels of power across the frequency spectra may indicate a certain amount of unsynchronized activity and/or lower levels of cortical arousal. This latter suggestion also receives support from the decreased power in the β_2 band width. The differences between conditions one and two are not of interpretive significance.

Hypothesis 2

The data supports the second hypothesis. The HR subjects have a significantly lowered CV in relation to the NC subjects. These findings lend support to an increased level of arousal hypothesis. The differences between conditions one and two are not of interpretive significance.

Hypothesis 3

In comparing the SDs at seven centers across the AER period, no differences were found between the groups. The findings that the SDs of the HR subjects were greater than the SDs of the NC subjects at L N100 and A P200 does, however, lend some support to the third hypothesis, which predicts differences in the variability of the AER wave form between the groups.

Hypothesis 4

With respect to the fourth hypothesis, a significant difference was found between the two groups at A N100. An expectation of the fourth hypothesis was that latency differences were more likely than amplitude differences, and, therefore, the difference in amplitude was somewhat unexpected and lends only partial support to this hypo-

thesis.

B. The EEG Measures and an Arousal Hypothesis: The Paradoxical Effect

If the CV is considered inversely related to level of arousal, then the HR subjects in the present study seem to have a "paradoxical" arousal pattern. The frequency characteristics of the EEGs of the HR subjects does not suggest increased arousal. The lower beta power can, in fact, lend some presumptive support to the notion of a decreased level of arousal. These findings, along with a lowered CV, is what is meant by a paradoxical effect. One EEG measure indicates the HR subjects are in a state of heightened arousal, while a second EEG measure suggests quite the opposite. Another way of viewing the CV is, for the moment at least, to disregard (or strenuously doubt) previous notions concerning its relationship to cortical arousal. This, in effect, places the CV in the same category as Mednick's measure of recovery of the GSR, which he found to be the best predictor variable between the high risk and control groups although he was not able to postulate the underlying process(es) reflected by this measure. For the remainder of this discussion, however, the CV will be considered to have an inverse relationship to cortical arousal. The ramifications of this notion will be explored in the context of the findings from the AER as well as the EEG.

The paradoxical nature of the EEG findings is continued to some extent when the results of the AER analysis are considered. The increased variability to LN100 in the HR group, along with the fact that

the HR subjects have shorter latency times (not significant) at N100 can, to some extent at least, be taken as providing tentative support for an increased level of arousal hypothesis. The argument might be presented in the following way: The early components of the AER have typically been associated with processes reflecting organismic arousal and there does seem to be some activity around the latency for L N100. It is of interest, states the proponent of an increased arousal hypothesis, that the latency at N100 is the only place where the latency is shorter for the HR subjects in comparison to the NCs (although not significantly shorter). The argument is not very convincing. If the AER findings were taken as supporting an increased arousal hypothesis, it would be expected that they would fall along the lines reported by Itil et al. (1974), and Saletu et al. (1971), i.e., shorter latencies (especially to the earlier components) and lowered amplitudes. (In point of fact, the HR subjects in the present study had significantly greater amplitude values at N100 than did the NC subjects.) The analysis of the HD subjects produces a pattern of AERs characterized by shorter latencies and lower amplitudes in relation to the rest of the subjects.

C. The HD Subjects (AER)

It was possible in the present study to tease out a group of eight subjects who were classified as HD. Based on previous studies, an expectation was that approximately 10-16% of all children with one schizophrenic parent to become schizophrenic. In the group of HD subjects, six are HR subjects. The number of HR subjects in the

original group from which the HD subjects were drawn was thirty. Thus, the HR subjects who are also HD account for approximately 20% of the high risk group. As mentioned throughout this paper, a subgroup of 20% of the population is in general agreement with expectations based on previous investigations of children at high risk to manifest schizophrenia.

The AER wave forms of the HD subjects show a striking similarity to the findings reported from studies with chronic schizophrenics, psychotic children, and children at high risk to manifest schizophrenia (Saletu et al., 1971; Itil et al., 1974). The latency values for the HD subjects were shorter in comparison to all other subjects and the HD subjects also had lower amplitude values. Based on the associated Z scores, none of these measures were significantly different than the scores of the entire group. It is worth mentioning, however, that the average Z score of the latency measures for the HD group was .54, while the average Z score for the amplitude values was .24. This is in agreement with Itil et al. (1974), who found significant differences in latency measures between high risk subjects and normal controls, but no significant differences in amplitude measurements. These authors have suggested that: "...short latencies may indicate a potential for becoming schizophrenic, while the amplitudes are only affected when the disease is clinically manifest in later life." (1974, p. 898). Along these same lines, it is of interest to note that the shortest latency values occur at the earliest AER com-

ponents and get increasingly longer, and less deviant, across the 500-msec. AER period. Once again, in the context of an arousal hypothesis, the earliest latency values would be expected to be most susceptible to fluctuations in arousal.

D. The HD Subjects (EEG)

Excluding the two subjects who were found to be deviant on the psychophysiological measures, three tentative EEG patterns, i.e., relationships between Z scores on power and Z scores on the CV, were identified. The first pattern (subjects 101401, 200602) has negative Z score values on both the power and CV measures. This pattern most clearly reflects the general findings of the study which have been dubbed paradoxical. The paradoxical nature of the findings are highlighted with these two subjects, since the lowered levels of slow wave activity (delta and theta) and also the lowered levels of fast wave activity (beta₁ and beta₂) would lend support to a lowered level of arousal hypothesis, while the negative values at the CVs would lend support to an increased level of arousal hypothesis.

The second pattern (subjects 200102, 701502) is characterized by positive Z scores on both power and the CVs. The increased power, however, is primarily in the delta and theta band widths as opposed to the beta₁ and beta₂ band widths, and the subjects in this category would seem to be characterized by lower levels of arousal. This interpretation is somewhat problematic, however, since there were increases in beta₁ and beta₂ for both subjects, and for sub-

ject 200102, the increase at β_2 was significant. An alternative interpretation is to consider the EEG patterns of these two subjects as paradoxical. This latter interpretation finds some support from two separate sources. Itil et al. (1974) have stated that their high risk subjects had increased delta, theta, β_1 and β_2 activity, and also had lowered (not significantly) CVs in relation to the normal control subjects. Itil et al. interpret these findings in support of a fluctuating level of arousal hypothesis with increases and decreases over short time periods. Lifshitz and Gradijan (1974) report that some chronic schizophrenics also produce more power at delta and theta, and β_1 and β_2 than do normal controls. They do not, however, argue for a fluctuating state of arousal hypothesis, but, instead, state that increased slow wave activity, under certain conditions, may indicate increased levels of arousal. What is common to both the Itil et al. and the Lifshitz and Gradijan study is the finding of a lowered CV. (In the Lifshitz and Gradijan study, this finding was significant.) With respect to the two subjects under examination, the CV was associated with positive Z scores and the notion of an increased level of cortical arousal seems difficult to support. Since no group differences were found between conditions, the notion of a fluctuating state of arousal hypothesis seems somewhat problematic and the paradoxical nature of the findings seems to stand out.

The third pattern (subjects 100301, 700701) is characterized by minus Z scores on power and positive Z scores on the CVs. The decreased power at both delta and theta as well as at β_1 and β_2 , along with the positive Z scores on the CV measures, suggests a

lowered level of cortical arousal.

E. Summary and Conclusions

What is perhaps most noteworthy in the present study is not only the statistical differences between the groups and the differential support of the four hypotheses but, instead, is the identification of a group of eight HD subjects and the specification of certain neurophysiological characteristics of the HR and HD subjects which are strikingly similar to the EEG and AER findings from adult schizophrenics, psychotic children, and other children at high risk to manifest schizophrenia.

Of the two EEG measures, the CV is a more powerful predictor variable than the frequency characteristics, and is in agreement with the results reported from previous studies. The frequency findings of the HR subjects were not in accord with the general findings of other studies. The most striking difference was the finding that the HR subjects in the present study produced significantly less, not more, high frequency low voltage activity, i.e., β_2 . These seemingly contradictory findings, i.e., a lowered CV and frequency characteristics which do not suggest heightened arousal, have led to the usage of the term paradoxical. The term has as its referents the vast amount of work in the area of rapid eye movement (REM) sleep. REM sleep is characterized by an EEG pattern which is similar to a waking EEG and, at the same time, the subject is asleep and, by some indicators, in quite a "deep" sleep. With reference to the present study, the paradoxical findings (or effect) are not nearly as dramatic nor as

well understood as the REM phenomena. The HR subjects do, however, seem to be at both high and low levels of arousal simultaneously. An examination across conditions does not support a fluctuating state of arousal hypothesis, and the AER findings do not support either an increased or decreased arousal hypothesis. Thus, the paradoxical nature of the results were emphasized.

The results of the AER analysis of the HD subjects is more in accord with an increased level of arousal hypothesis. An examination of the EEG findings of these subjects, however, emphasizes the paradoxical effect. This effect is most clearly demonstrated in subjects 101401, 200602, 200102, and 701502. The specification of three EEG patterns in the HD subjects brings to mind the concept of "spectrum of schizophrenia" as well as Claridge's notion of arousal based on two functionally related systems. The subjects in the HD group (including the two subjects with "mixed" EEG patterns who were found to be deviant on the psychophysiological task) may all eventually manifest schizophrenia, but each may have different underlying systems which are dysfunctional. Another very similar way of viewing these subjects is to think that each subject may suffer from both increased and decreased arousal, depending on which system is dysfunctional. It is interesting to speculate and try and make sense, or find specific "meaning" for the results of the present study. At the current stage of high risk research, however, it seems more prudent to have less speculation and to focus on the "more tangible" aspects of the results. By taking this approach, it may be possible to suggest future research strategies which could extend

some of the findings which seem to cut across the various studies of chronic schizophrenia, psychotic children and children at high risk to manifest schizophrenia. By limiting speculations, it may be possible to accomplish this latter task without adding further generalities to an area of research which seems to have more than its share of generalities and vague concepts at the present time.

F. Suggestions for Future Research

A disordered level of arousal hypothesis has received widespread support and is worthy of future investigative efforts. One such approach may simply be the employment of self-rating scales to get some notion of a subject's own perception of his/her level of arousal and/or anxiety. Another approach which can be particularly sensitive to disordered levels of arousal is the investigation of the sleep patterns of these subjects, particularly their REM sleep. Ellman (1977), for example, has made a number of suggestions along these lines, with particular emphasis on REM deprivation and investigation of the REM rebound phenomena. Another approach of interest would be the investigation of the AER in these children under a variety of situations which would be differentially sensitive to arousal. For example, if, as Shagass has suggested (1969), certain inferences can be made about inhibitory processes based on the configuration of the AER wave form (particularly increases or decreases in amplitude), then it would be of real interest to study the AER of these children when stimuli have different values and/or when stimuli are omitted. Perhaps the most propitious research at this time, however, is to follow the sub-

jects in the present study over time. It is important to know, for example, if the eight HD subjects do, in fact, remain "deviant". Are the neuroelectric patterns delineated in the HD subjects good predictors of schizophrenia? Will changes in the frequency characteristics of the EEG be forthcoming, and will these changes be in line with the frequency characteristics so often observed in chronic schizophrenics? More importantly, will these changes take place only in those subjects who do manifest schizophrenia? One of the prime personality characteristics of the high risk researcher must be the ability to delay gratification. There must, by definition, be a considerable delay between certain ideas gleaned from research and the eventual testing of these ideas through observation of those children who are predicted to manifest schizophrenia.

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