CHAPTER 1

INTRODUCTION

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INTRODUCTION

The present investigation which is a study of the P300 component of the event-related potential (ERP) in schizophrenia, falls within the domain of cognitive psychophysiology as applied to psychopathology.

1.1 EVENT-RELATED POTENTIALS AND THE P300

Event-related potentials (ERPs) are changes in the ongoing EEG that take place at the occurrence/absence of an event. Such small bioelectrical changes in the brain are picked up by electrodes placed on different locations on the scalp. The changes are studied with the help of sophisticated amplifiers that can augment these potentials several thousand times; frequency filters, that permit only relevant frequencies, and thereby reduce artifacts; and computers, that may be programmed to average these changes over several repeated trials so that random changes may cancel out.

Figure 1., depicts how the brain reacts electrophysiologically to the occurrence of an infrequent target tone (the subject was required to press a button when high-pitched tones occurred), and to a frequent, nontarget (low-pitched) tone.
As may be observed, the response may be characterized by positive (in this case, an ascending peak) or negative (in this case, a descending trough) deflections of the potential, and also by the time after which such a deflection takes place. In the instance depicted, an N100 (a negative deflection that occurs about 100 milliseconds after onset), a P200 (a positive peak that occurs about 200 milliseconds after onset), and a P300 (positive peak that occurs about 300 milliseconds after the event) component are apparent.

Figure 1: The ERPs to rare (dark line) & frequent tones (light line) obtained from a normal subject in the present study.
Interest in the study of ERPs are due to a wide variety of reasons. In the first place it is a noninvasive technique by which internal happenings of the brain may be indexed. It has always been a cherished goal in psychology to study how the human brain ticks, and to lay bare the processes that make possible the versatile cognitive operations that the human mind is capable of. Event related potentials contributes to this endeavour by clarifying how the brain reacts, at least electrically to events. Brandeis and Lehmann (1986) state this succinctly:

"Event-related potentials open a time and space window onto the covert steps of brain information processing which needs not be accompanied by overt behaviour or private experiences. Event-related potentials are the only noninvasive method which resolves the dynamic patterns of events in the human brain down to the milli-seconds range." (p.151).

While early ERPs have proved extremely useful in the study of the afferent sensory systems, later potentials have an important significance in the understanding of several mental operations like attention, encoding and memory.

Since ERPs may be studied using scalp electrodes, placing several electrodes on different locations of the scalp helps to understand the topography (the extent to which the amplitude and latency of the particular potential changes with change of scalp location) of the potential. Advances in computer technology has brought further enhancement and applicability of research in topography. The computerized
brain electrical activity mapping (BEAM) technology (See Morstyn, Duffy & McCarley, 1983) pictures the electrical activity over the entire scalp in colour frames, in which low to high amplitudes are depicted by shades of different colours. Each frame, therefore, is a pictorial summary of an event-related potential over a fixed interval, say 4 milliseconds. Inspection of a frame is, therefore, informative of the way various locations of the scalp react to the same event, at the same point in time. Inspection of several such sequential frames reveals how this activity progresses over time at each given scalp location. Such an investigation on schizophrenics will be elaborated in the next chapter.

Among the endogenous ERPs, the P300 has evinced the greatest interest, and is easily the most widely researched potential in psychology today. The reasons are not far to seek. First and foremost, as the next chapter will detail more elaborately, the latency of the component has been shown to be sensitive to stimulus evaluation. This has generated a wave of enthusiasm, since this can literally enable us to understand when the brain "ticks." As a consequence, it is now within the realms of possibility to time mental phenomena, to clock how long the brain takes for easy and difficult tasks, to compare and to contrast individuals based upon the speed of evaluating simple events, to investigate mental disorders and neurological diseases in terms of what
effects these have on such cognitive evaluations of events, and so forth. The above use of event related potentials for the use of timing cognitive operations has been referred to as "mental chronometry" (See Kutas, McCarthy & Donchin, 1977).

As may be clear from all the above, the P300 derives much of its importance from the perspective of information processing theory. In such a context, it shares a parallel with reaction time, which, especially in early experimental psychology, was widely used as an invaluable index of mental operations. However, the P300 has other advantages. While the required evaluation of a stimulus may be assumed to have occurred once a correct response has been emitted in a reaction-time paradigm, a delay in emitting a correct response does not necessarily imply delayed evaluation. This is so, because a delayed reaction-time may result from a large number of factors after stimulus identification has taken place: delay in the choice of a response, a cautious strategy, the urge to recheck the accuracy of the evaluation, slowed down motor execution, a lack of cooperation on the subject's part to perform the response, and so forth. Since the P300 is an objective and a more direct index of brain activity, these problems are to a large extent, conveniently side-stepped. Thus, Duncan-Johnson (1981) exclaims, "The P300 component of the event-related potential is a unique tool in the study of human information processing" (p.207).
Speed of processing, at first glance, appears to be no more than one aspect of cognitive operations, however, research has shown that it has far-reaching implications. Several studies (Pfefferbaum & Ford, 1988) have shown for instance that the P300 latency in adulthood is directly correlated with age; the regression equation suggesting an increase of latency by 1.42 ms per year on a simple visual task requiring recognition of simple words. The above has also found widespread application in the evaluation of clinical dementia, where studies have unequivocally shown a significantly delayed P300 latency (See Goodin, Squires, and Starr, 1978; Pfefferbaum, Wenegrat, Ford, Roth, and Kopell, 1984).

The P300 was first discovered by Sutton, Braren, Zubin and John (1965). Under experimental conditions that manipulated the probability of occurrence of two stimuli, and also the degree to which the subject was certain that one stimuli would occur, they discovered the occurrence of a robust positive potential that peaked about 300 milliseconds after onset of the stimulus. They also found that the amplitude of the component increased significantly for stimuli that were rare, and also for the stimuli that were not anticipated as compared to stimuli that the subject knew would occur. While both these observations were on the amplitude of the component, it was not long before researchers realized that
if the amplitude depended upon factors like the surprise-value of the stimulus, then evaluation of the stimulus had taken place, and hence the latency of the peak could reflect the time taken for stimulus evaluation processes. This hypothesis was later confirmed by many researchers. Duncan-Johnson (1981), for instance, showed that the P300 latency was delayed further when the subject had to make discriminations between two closely resembling colours (reddish purple vs bluish purple) as compared with easier discriminations between red and blue.

It must be clarified that the P300 component is sometimes called the P3, since it is the third (after the P1 and P2), positive, potential. Also, though the P300 in the experiment of Sutton et al. (1965) emerged at about 300 ms., researchers (See Pritchard, 1981) have shown that, depending on the task, the component may occur as late as 800 ms., after stimulus onset. Also, later researchers have demonstrated the need to discriminate between the P300 and the Slow Wave, both of which are positive components that emerge at about the same time, and which, visually, may occur as a single broad peak. The two components however, have different topographical areas of influence, and may be separated statistically by principal-components analysis, and experimentally, under certain conditions like equivocation (Squires, Squires, & Hillyard, 1975; Ruchkin, Munson, &
Sutton, 1982). In instances where such a positive peak may represent the combined influence of peaks like the P300 and the Slow Wave, some authors who prefer a more precise terminology, favour the usage of the term "Late Positive Complex".

1.2 THE P300 COMPONENT IN SCHIZOPHRENICS

Studies of ERPs in psychiatric patients in general, and schizophrenics in particular derive from three basic thrusts. First, it is necessary to view this interest within the broad attempt to determine a biological basis for the aetiology, manifestation, and course of schizophrenia. This interest has spawned research that spans several disciplines: genetics, which has shown that the incidence of the disorder progressively increases with the degree of biological relatedness with patients; virology, in which there is ongoing research to determine whether the disease could be caused by a slow virus; neuropathology and neuroradiology, from which some evidence has accrued to indicate that in at least a subsection of schizophrenics, structural brain pathology is evident (For details, see Mirsky & Duncan, 1986).

With advances in biotechnology, this approach has seen further development. Stratta, Rossi, Gallucci, Amicarelli, Passariello, and Casacchia, (1989) using magnetic resonance
imaging techniques, showed that schizophrenics manifested brain ventricular enlargement and smaller ratios between corpus callosum and brain. And, Buchsbaum, Haier, Cappelletti, Ball and Hazlett (1984), used positron-emission tomography (PET Scan) to show that some schizophrenics were characterized by deviant local brain metabolism.

The research using ERPs potentials in schizophrenics and other psychiatric patients are part of the same thrust, but may be differentiated from several of the structural approaches outlined above, since ERPs are indices of the functional aspect, rather than the structural aspect of the brain. And, since it has become obvious today that structural and functional abnormalities do not bear a one-to-one relation with each other, research in ERPs complement structural approaches.

Secondly, interest in the study of ERPs in schizophrenics, as also with other biological approaches, has been sustained by the growing dissatisfaction with the conventional symptomatic criteria of the disease. The symptomatic approach, based on phenomenology, has failed to render an adequate demarcation of the various subtypes of the illness, as also to predict the course, or to identify persons at risk for the illness so that prevention strategies may be implemented. The above has led to a determined search for a "biological marker" of the illness. The scope of such a
search has spread to the event-related potentials. Saitoh, Niwa, Hiramatsu, Kameyama, Rymar, and Itoh (1984) for instance, after contrasting schizophrenics and siblings of schizophrenics with a group of normals, concludes that abnormalities of the amplitude of the P300 and the late positive complex may reflect a genetic predisposition in schizophrenia.

There is an additional factor that has generated interest in research in ERPs in schizophrenics. From very early conceptualizations of the disease (Bleuler, 1911), several theorists and clinicians have held that an underlying cognitive deficit is basic to schizophrenics, which in turn contributes to the manifestation of several other symptoms, like hallucinations and delusions. Over the decades, there has been little agreement about the exact nature of this deficit. Bleuler (1911), postulated a "loosening of associations" in thinking, McGhie and Chapman (1961) favoured a disorder of attention, Koh and his associates (See Koh, 1978) have offered evidence in favour of an impairment of short-term memory, and Nuechterlein and Dawson (1984) have suggested a reduction of capacity to process information under demanding conditions. Within the outlines of information processing theory, therefore, ERPs is considered an important technique to help identify the exact locus of the deficit. In other words, it is believed that when
cognitive operations are conceptualized as a series of sequential stages of information flow, ERPs could help identify the precise stage/process of abnormality in schizophrenics. The relevant studies in this context will be detailed in the next chapter.

In sum, the search for a biological determinant in schizophrenia, the glaring inadequacies of the prevailing approach based on phenomenology, and the increasing evidence suggesting an underlying cognitive deficit in schizophrenics, combine to make ERP research in schizophrenia an area of wide interest and importance today.

1.3 ISSUES THAT REQUIRE FURTHER STUDY

While a more detailed discussion of relevant literature will follow in the next chapter, a brief analysis of some issues that require further study and a justification of the present investigation will be presented below.

The research on the P300 component in normals has been vast, however, studies in psychiatric patients have been scarce. Despite this, useful results have been obtained. One consistent finding that has emerged is the decrement in P300 amplitude in schizophrenia. This has been found on several different tasks: auditory (Pfefferbaum, Wenegrat, Ford, Roth & Kopell, 1984; Roth & Cannon, 1972; Verleger &
Cohen, 1978), visual (Baribeau-Braun, Picton & Gosselin, 1983; Brecher & Begleiter, 1983), somatosensory (Shagass, Straumanis, Roemer & Amadeo, 1977). Several authors have also shown that these results are not due to antipsychotic medication (Baribeau-Braun et al., 1983; Pass, Klorman, Salzman, Klein, & Kaskey, 1980; Roth & Cannon, 1972), or due to latency variability in schizophrenics (Roth, Pfefferbaum, Horvath, Berger & Kopell, 1980).

The above studies, however, have also brought into sharp focus, an additional factor that could be contributing to the decrement in P300 amplitude. Schizophrenics have been found to be characterized by a significantly greater degree of errors on the tasks used to elicit the P300 component (Baribeau-Braun et al., 1983; Brecher & Begleiter, 1983; Josiassen, Shagass, Roemer & Straumanis, 1985; Pass et al., 1980). Consequently, it becomes important to confirm that the decrement in P300 amplitude is actually due to the diagnostic status and not due to atypical potentials elicited by the erroneous responses. Several studies have failed to control this variable, and the present investigation will address this issue by ensuring that only ERP epochs to correct responses are analysed.

In addition, it is important to determine whether the decrement in P300 amplitude is specific to schizophrenics and whether it is more characteristic of specific subtypes.
The authors are not aware of any reported research to evaluate the influence of the subtypes of schizophrenia on the P300 component. Of particular interest to ERP research are the Negative schizophrenics who have been hypothesized to have brain abnormalities, such as cortical atrophy and dialated ventricles (See Andreasen, Olsen, Dennert, Smith, 1982; Crow, 1980). The present investigation will study the P300 in both Negative and Positive subtypes of schizophrenia, and also in a control group of patients with major depressive illness.

Another issue of crucial interest is whether schizophrenics in general or a specific subtype of schizophrenia have an impairment of P300 latency. The P300 latency is believed to index stimulus-evaluation processes, and patients of dementia have been found to manifest a delayed P300 latency (See Goodin et al., 1978; Pfefferbaum et al., 1984b). There is much research to suggest that schizophrenics actually have an information processing deficit (See Nuechterlein & Dawson, 1984). The precise nature of this deficit is still being evaluated. It would be interesting to give schizophrenics stimuli that require different varieties of processing, in order to determine whether they are deficient in processing of a specific variety.
This issue, in part, has been addressed by past research, and results have shown, with some degree of consistency, that schizophrenics do not manifest a P300 latency deficit (See Pritchard, 1986). However, the tasks used for the purpose have been simple, perceptual discriminations (high versus low-pitched tones; the visual stimulus 1.00 versus 0.00). While it is of value to rule out a deficit in latency on these tasks, it is also important to determine whether schizophrenics are capable of more complex processing, like semantic classification of single stimuli into superordinate categories. This is of particular relevance, since schizophrenics have been found to do poorly on psychological tests that measure abstraction, such as the Object-Sorting Test and the Proverbs Test (Magaro, 1980; Oltmanns & Neale, 1978).

The identification of an ERP delay will, more directly, indicate a malfunctioning of the brain, and may also serve to help understand other cognitive deficits and psychopathology. Besides, it is often more difficult to interpret a performance deficit on a complex psychological test, since the deficit may be influenced by several other factors like inadequate cooperation, defensiveness, poor motivation and the like. For the above reasons, the present investigation will test schizophrenics on simple tasks as well as on a task that requires abstraction.