CHAPTER

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CHAPTER 2

REVIEW OF LITERATURE

Before examining the literature regarding the P300 in schizophrenics and other psychiatric conditions, the variables that significantly influence the P300 component in normals, will be discussed. This will provide a better context within which the impairment of schizophrenics may be understood.

2.1 THE P300 AMPLITUDE

The P300 amplitude in normals.

The variable that has most widely been studied with respect to the P300 amplitude has been stimulus-probability. Most commonly, two stimuli (tones of different frequencies) one frequent and the other infrequent (say 20% of the times) are presented to the subject in a random sequence. What has been invariably observed is that the amplitude of the P300 component elicited by the infrequent stimulus is markedly greater than that of the frequent stimulus (See Pritchard, 1981). In a detailed study, Duncan-Johnson and Donchin (1977) have shown this to hold true for apriori probabilities ranging from 0.10 to 0.90. Figure 2, depicts the results.
Figure 2. Event-related potential waveforms, recorded from the parietal (Pz) lead and averaged over subjects, elicited by the high and low tones at nine levels of a priori stimulus probability. The data collected in the "Count high" (solid lines) and "Ignore" (dotted lines) tasks are superimposed. Stimulus occurrence is indicated by a black bar on the time scale. Positivity at the scalp electrode, with respect to the reference electrodes, is shown as a downward deflection in this and subsequent figures. (From Duncan-Johnson & Donchin, 1977.)
A second important factor that influences P300 amplitude is **task-relevance**. For stimuli that are equiprobable, the P300 amplitude shows a significant increase to stimuli that are targetted (vs. ignored), as accomplished by specific instructions to count/press a button on the occurrence of a particular stimulus. The study by Donchin and Cohen (1967) is a good illustration of this. The task involved a visual display in which an aperiodic flash of light was superimposed on a background of a circle or square that alternated randomly. In one session, subjects were required to ignore the background alternations and respond to the flash, and in another they were asked to respond to the background alternations while ignoring the flashes. The results showed that it was the targetted stimulus that elicited the P300 component. This effect is also seen (See Figure 2) in the study of Duncan-Johnson and Donchin (1977) where for each level of probability, subjects either ignored the infrequent tone or counted its occurrence.

The importance of the two factors mentioned above have been repeatedly confirmed by a wide variety of studies. Researchers interested in obtaining a prominent P300 component, combine these factors in an "odd-ball" paradigm, where the subject is instructed to respond only to the infrequent stimulus, and ignore occurrences of the other probable stimulus. Recently, attempts have been made to quantify the
nature of the interaction of these two factors, and Johnson (1988) holds that they are related in a multiplicative way, and may be summarized by the formula:

$$P_{300 \text{ amplitude}} = f[T(1/P + M)];$$

where "T" represents Information Transmission (function of task relevance and equivocation); "P" represents subjective probability, and "M" represents stimulus meaning (influenced by variables such as stimulus complexity and stimulus value).

While the auditory, tone paradigm has been the most commonly employed task in the P300 literature, research has shown that the results hold true for stimuli of other modalities as well. Several visual tasks have been used: numbers (Brecher & Begleiter, 1983); geometric designs (Ritter et al, 1983), and words (Kutas et al, 1977; Ritter et al, 1983; Lovrich Novich & Vaughan, 1988). Desmedt, Robertson, Brunko, and Debecker (1977) also demonstrated that the P300 component was as easily elicited in a somatosensory task, wherein four fingers were randomly stimulated and the subject was required to count the number of times a specified digit was stimulated.

What has also been demonstrated is that, in paradigms where the presented stimuli fall under a frequent category and a rare category, the P300 component is evoked by the rare category. Kutas et al (1977) and Ritter et al (1983) used different male and female names as stimuli. Though each name
appeared only once, the category of female names occurred infrequently. The subjects were required to press a button when female names occurred. It was observed that the task generated a P300 component.

The research on the P300 is vast, and the influence of other factors including guess-outcome, incentives, memory have been evaluated, however, these studies will not be detailed at length. Verleger (1988), Johnson (1988) and Pritchard (1981) have given an extensive review of these.

While the results demonstrating the influence of task-relevance, subjective probability and equivocation on the amplitude of the P300 component are reliable, the precise significance of the P300 in terms of information processing and psychological theory have been embroiled in controversy. An extensive debate as recent as a year ago, is illustrative. Donchin and his associates (See Donchin and Coles, 1988) propound the "context-updating" model, and assert that,

"the P300 is elicited by processes associated with the maintenance of our model of the context of the environment. The association of the P300 with novelty, ..its strong dependence on a limited-capacity system, and its strong dependence on the relevance of the eliciting event to the task lead to the suggestion that the processing it manifests is invoked whenever there is a need to revise the organism's model of the context. We are assuming that the larger the amplitude of the P300, the larger the change in the model (p.370)."

Verleger (1988) however argues that the empirical data better fit the "context closure" hypothesis, and assert that the
P300 is evoked by events that are awaited when subjects deal with repetitive, highly structured tasks.

The P300 amplitude in schizophrenia and depression.

While research on the P300 component in normals is extensive, research in schizophrenics and other psychiatric patients is much less prevalent. Roth and Cannon (1972) were the first to test schizophrenics. Using a sequence of a frequent and a rare tone (occurred 15% of the times), schizophrenics and normals were required to respond to the rare tone. The results showed that the amplitude of the P300 in schizophrenics was significantly reduced relative to that of normals. The reduction in P300 amplitude in schizophrenics has subsequently been confirmed by several other authors across a wide variety of conditions, so as to leave little room for doubt regarding the results.

Roth and his associates (Roth, Pfefferbaum, Horvath, Berger & Kopell, 1980b) replicated the results in a similar, auditory, tone task but under conditions of a persistent white noise background. It was also found that P300 amplitudes in schizophrenics was reduced to rare bursts of white noise, as it was to rare tones (Roth, Horvath, Pfefferbaum & Kopell, 1980a). Brecher and Begleiter (1983) used a visual paradigm that comprised of two equiprobable stimuli (1.00 and 0.00). Schizophrenics and controls were asked to respond to
one stimulus (1.00) under each of three different conditions: without incentive, with a monetary incentive for correct responses, and with an incentive if the response occurred within a specified time-limit. Schizophrenics were shown to be characterised by an impaired P300 amplitude on each of the three conditions.

The decrement in P300 amplitude in schizophrenics has also been demonstrated in the somatosensory modality by Shagass et al (1977) and Josiassen et al, (1985). Strandburg, Marsh, Brown, Asaranow and Guthrie (1984) determined that the deficit that characterized adult schizophrenics was also present in children who were schizophrenics, when they were compared with age-matched, normal children. Since information processing research has shown schizophrenics to be particularly impaired on demanding tasks of selective attention like dichotic listening, and sustained attention, like on the continuous performance test (CPT), some authors have used versions of these tasks to elicit the P300 (Hiramatsu, Kameyama, Saitoh, Niwa, Rymer & Itoh, 1984; Pass et al, 1980). Again, the results indicate a decreased amplitude of the P300 component in schizophrenics.

Some researchers have tried to determine whether some variables that are known to augment the P300 amplitude in normals, have a comparable effect in schizophrenics. It has been shown, for instance, that uncertainty results in an
augmented P300 amplitude in normals (Sutton et al, 1965; Ruchskin, Munson and Sutton, 1982). Typically, the presentation of the stimuli is so designed (for instance, by means of a preceding cue stimulus) that on some trials the subject is certain that the targetted response will follow while on others he is uncertain. The P300 component evoked by targets that followed uncertainty is then compared with that evoked by targets that followed certainty. Levit, Sutton and Zubin (1973) and Verleger and Cohen (1978) used such a paradigm and found that uncertainty does not augment the P300 amplitude in schizophrenics as significantly as it does in normals. In the same vein, Brecher and Begleiter (1983) showed that, whereas in normals the introduction of incentives for correct responses augmented the amplitude of the P300, it did not do so in schizophrenics.

There have been a few studies that have attempted to determine whether the abnormality reliably seen in schizophrenics, is also observed in groups at high-risk for schizophrenia. The interest in such a group stems from various reasons. First, an impairment found in the actively symptomatic group is sometimes difficult to interpret, since the deficit may not be primarily related to the disease process itself, but may be a consequence of medication, hospitalization and so forth. Secondly, if an impairment is shown to have pre-existed the symptomatic phase of the illness it
could be investigated as a possible "marker" of the disease. The frantic search for a marker in schizophrenia has gone on for decades, since it would have far reaching implications in prevention, classification into subtypes, diagnosis, course and so forth. Typically, first or second degree relatives of known schizophrenics, or individuals judged to be high on Anhedonia/Perceptual Aberration (traits, psychometrically known to be indices of vulnerability) form the high-risk population.

Saitoh et al (1984) tested schizophrenics, siblings of schizophrenics, and normals using an auditory task that required syllable discriminations. It was shown that like the schizophrenics, their siblings also were characterized by a reduced P300 amplitude. They also found that the characteristic augmenting of the late-positive complex to attended targets (as compared to the ERP to those non-attended targets presented to a ear which they were instructed to ignore) was not seen in schizophrenics and their siblings. The authors concluded that abnormalities of the late-positive complex that includes the P300, could reflect a genetic predisposition in schizophrenia. Simons compared anhedonic subjects and normals on a task that elicited the P300 component to neutral (low interest) slides and to slides depicting nudes (high interest). While normals showed an increase in the P300 amplitude to high interest slides, the anhedonics did
not. Similarly, Josiassen et al. (1985) demonstrated a decreased P300 amplitude in groups of schizophrenics and anhedonics on a somatosensory task.

The findings of a study by Friedman, Erlenmeyer-Kimling and Vaughan (1985) however, is not in consensus with that of the ones earlier reported. They assessed children of schizophrenic parents, children of parents with affective disorder, and children of normal parents. Using an auditory tone paradigm, they did not find a significant difference between the three groups with respect to P300 amplitude and the slow wave. They concluded that the cognitive components by themselves cannot be used to predict the development of schizophrenia. The discordant results may indicate either unreliability with respect to the finding, or indicate that the impairment of the P300 component is manifest only at an age later than teenage (The sample of Friedman and Erlenmeyer-Kimling, 1985, comprised mostly of children in their teens).

The postulation of the impairment in the P300 amplitude as a marker of schizophrenia, must also show that the particular deficit is specific to schizophrenia and not present in other psychiatric conditions. Unfortunately, many studies that have researched schizophrenics have compared them only with normals, and have failed to use a psychiatric control group as well.
The psychiatric control group most often tested are depressives, however, differences in diagnostic criteria, make comparisons difficult. The results have proven to be equivocal. Levit et al. (1973) for instance, found that the amplitude of the P300 component was not reduced in depressives. Patterson, Michalewski, and Starr (1988) evaluated demented, depressed, old and young normals on an odd-ball tone paradigm, and found that P300 amplitude did not differentiate the groups. On the other hand, Pfefferbaum et al. (1984b) in a more detailed study compared demented, schizophrenics, depressed and normal subjects on both auditory and visual tasks. The results showed that while the impairment in P300 amplitude was relatively pervasive in schizophrenics, only drug-free depressed subjects showed the deficit and only on the auditory task. Two studies (Baribeau-Braun and Lesevre, 1982; Thier, Axmann & Giedke, 1986) that have used a sample of more severely depressed subjects found reduced amplitudes in depressives relative to normals. In general, therefore, the research tends to indicate that abnormalities of the amplitude of the P300 component is not specific to schizophrenics, but is elicited also in more severely depressed individuals, especially on more complex tasks.

In sum, decreased P300 amplitude has been reported in schizophrenics by several researchers and across a wide variety of paradigms. There is also an indication that
persons at risk for schizophrenia may also share the deficit. However, in depressives, the evidence for decreased P300 amplitude is not as consistent or convincing.

**Interpretations regarding decreased P300 amplitudes in Schizophrenics.**

While many researchers have studied the P300 amplitude in normals and schizophrenics, only a few have attempted to speculate on the reason for such a finding. Roth et al. (1980b) suggest the following explanation. Since the P300 amplitude seems dependent upon information being taken in from the external environment, and since schizophrenics, according to some circles (See Bleuler, 1911), are prone to autism (characterised by internally, rather than externally generated stimulation), the decreased P300 amplitudes in schizophrenics merely indicate their being less influenced by information-input from an external locus.

There has been speculation that the deficit in P300 amplitude in schizophrenics may reflect underlying neuroanatomical pathology. This derives from converging evidence that the P300 is generated, at least in part, in the limbic system, primarily in the hippocampus and immediately surrounding cortex, along with the amygdala. Occasional investigations using depth electrodes support the limbic generation of the P300 (Halgren et al, 1980; Wood, Allison,
Goff, Williamson, & Spencer, 1980). On this basis, the deficit in the P300 may reflect pathology of the limbic system in schizophrenics. It is interesting to note that some support to this contention is available from postmortem studies, where shrinkage of the hippocampus, amygdala, and parahippocampal gyrus have been observed in schizophrenic brains, relative to those of controls (Bogerts, Meertz, & Schonfeldt-Bausch, 1985).

Several researchers have tried to determine whether the reduced amplitude of the P300 in schizophrenics may be an artifact due to an inadequately controlled variable, rather than due to the diagnostic status of the individual. Three variables have been considered: medication, latency jitter and error-rates. Each of these will be briefly considered below.

Neuroleptic medication that almost all schizophrenics receive today are known to have some influence on cortical arousal and neural activation. It is of value, therefore, to determine whether they have specific effects on the P300 component. There have been several ways in which the influence of medication has been experimentally controlled. Some authors (Brecher and Begleiter, 1983; Brecher et al, 1987; Levit et al, 1977; Saitoh et al, 1984) have included groups/subgroups of unmedicated schizophrenics (medication withdrawn for 2-4 weeks prior to evaluation) and demonstrated that P300
amplitude is reduced in both medicated and unmedicated schizophrenics. Others (Roth and Cannon, 1972; Roth et al, 1980b) have shown that the dosage of neuroleptic medication does not correlate with the ERP measures under consideration.

Since the amplitude of a component is conventionally calculated from the averaged wave form of the ERP, a reduced amplitude may result from an increased variability of the latencies of individual peaks (latency jitter), that together make up the average. The possibility of this being true in the case of schizophrenics, gains credence especially since schizophrenics have been found to have longer and more variable reaction times than normals. Roth et al. (1980b) evaluated this by computing the amplitudes after using an adaptive filter which decreases latency-jitter, and found that the decreased amplitudes persist in schizophrenics. Also studies (Roth et al, 1980b) that have separated short reaction-time trials from long reaction-time trials and have then separately derived ERPs to each, have found decreased P300 amplitudes in schizophrenics in both instances.

A more serious criticism against the studies regarding P300 amplitude concerns error-rates of schizophrenics on the tasks used to generate the P300 component. The criticism may be summarised as follows: If schizophrenics make a significantly greater degree of errors on the task, and if the event-related potentials to errors are different from that to
correct responses, then the reduced amplitudes of the P300 component may be due to the errors and not on account of the diagnostic status of the subjects.

With respect to error-rates, there is convincing empirical evidence for a higher rate of errors in schizophrenics. The evidence stems from both information processing literature and data from P300 studies themselves. A look at the type of tasks used to elicit the P300 component is informative. Since even the simple tasks require target detection from among a sequence of nontargets, the tasks resemble continuous performance tests, where sustained attention is required. The empirical data on the continuous performance tests is relatively unequivocal, and indicates deficits in schizophrenics at early and late stages of the illness (See Neuchterlein and Dawson, 1984). Besides, the vast majority of studies (Baribeau-Braun et al, 1983; Brecher and Begleiter, 1983; Pass et al, 1980; Pfefferbaum et al, 1984; Saitoh et al, 1984) that evaluated the P300 component in schizophrenics have also observed that on the same tasks, schizophrenics are characterized by higher error rates. Josiassen et al (1985) have found a striking 23% of errors in schizophrenics, whereas anhedonic and normal subjects secured only 3.0 and 0.5% errors respectively. In the study of Verleger and Cohen (1978) of fourteen chronic schizophrenic patients, six patients were not significantly motivated to
perform the instructions adequately (press the button quickly after each stimulus) and had to be dropped from the study.

The argument that erroneous trials may elicit a potential, different from that generated by correct responses, also appears justified. As has been explained in the early part of the review, the necessity to attend and respond to a target significantly increases the P300 amplitude. Consequently, to the extent that errors of omission and commission reflect stimuli inadequately evaluated, the P300 component will be attenuated. Surprisingly, several studies have failed to control this important variable, thus raising doubts about an otherwise, well documented result. A notable exception is the study of Pfefferbaum et al (1984b) who ensured that the averaged ERP was constituted by only the potentials to correct responses. Schizophrenics were demonstrated to be still impaired on the P300 amplitude. In the present investigation, as will be detailed in the next chapter, care will be exercised to document erroneous responses and omit them from the analysis of the P300 component.

2.2 AMPLITUDE OF OTHER MIDDLE LATENCY COMPONENTS IN SCHIZOPHRENIA AND DEPRESSION

While the current investigation is chiefly concerned with the P300 component, in order that the above results be understood in perspective, a brief comment on the research regarding the amplitudes of relevant middle latency compo-
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ponents is warranted. Depending on the type of experimental tasks designed to elicit the P300 component, other components like the P100, N100, P200 and N200 may also emerge. Besides, other experimental tasks like the presentation of clicks, tones, flashes have also been used to generate these components. It is of interest to determine whether or not decreased amplitudes are unique to the P300 component.

Mukundan (1986) using both auditory and visual tasks, found diminished amplitudes of the P100 component in schizophrenics. Brecher and Begleiter (1983), Baribeau-Braun et al. (1983), and Pfefferbaum et al. (1980a), found similar results with respect to the N100 component. However, the results regarding decreased amplitudes on these components does not appear to be as robust, pervasive and incontrovertible as the results regarding the P300. Hiramatsu et al. (1984), found that decreased N100 amplitudes in schizophrenics was evident only on the left hemisphere electrodes, and Roth et al. (1980a), after experimentally manipulating the inter-stimulus intervals between tones, found that decreased amplitudes of the N100 component in schizophrenics occurred only in conditions of high inter-stimulus intervals. Besides, there has been some isolated negative results, as for instance, Pfefferbaum et al. (1980b), who found increased, rather than decreased P100 and P200 amplitudes in schizophrenics.
In depressives, the results are again unclear. While some studies have reported an augmentation of middle latency components (Borge, 1973; Shagass, Roemer, Straumanis, & Amadeo, 1980), others have reported an attenuation (Giedke, Thier and Bolz, 1981; Knott and Lapierre, 1987). Khanna, Mukundan, and Channabasavanna (1989), observed that the increased amplitude of the P100 and N100 components was restricted to visual tasks and the left electrodes.

2.3 THE LATENCY OF THE P300 COMPONENT

The P300 latency in Normals.

With respect to the latency of the P300 component, there appears to be a consensus that it reflects stimulus evaluation processes. While the P300 was so named because it emerged at about 300 milliseconds after stimulus onset (Sutton et al, 1965), researchers have shown that based on the experimental paradigm, the component may be delayed until 600 to 800 milliseconds (See Pritchard, 1981).

Studies with normals have varied perceptual discriminability of the target stimuli and have shown that the P300 latency is prolonged when discriminability is more difficult. For example, Duncan-Johnson (1981) determined that the P300 peak emerged at 475 milliseconds when a red-blue discrimination had to be made, and at 530 milliseconds when a reddish-
purple versus bluish-purple discrimination had to be made. Polich (1987) compared three pairs of auditory stimuli: Tones of 1000Hz vs 2000Hz; 1000Hz tone at 40 dB vs 1000Hz at 60 dB; and 1000Hz tone at 40 dB vs 1000Hz at 45 dB. Results showed that the P300 peaked at 305, 315, and 355 ms, respectively.

The semantic evaluation of verbal stimuli which has great importance in information processing, especially as applied to the understanding of language, has also been studied by a few researchers. Kutas et al. (1977), and Ritter et al. (1983), contrasted the P300 peak generated by fixed names (for example, David vs Nancy) and variable names (different male and female names). Subjects were asked to press a button to the stimulus Nancy in the first session, and to any female name in the second. The authors demonstrated that, as hypothesized, when each stimulus had to be evaluated and categorized as in the second session, the P300 peak was significantly delayed.

In addition to the above variables, frequent stimuli relative to rare stimuli, and auditory (tone) relative to visual (flash) generate quicker P300 peaks (Duncan-Johnson, 1981; Polich, 1987).
The P300 latency in schizophrenia and depression.

Unlike the results regarding the P300 amplitude, most studies that evaluated the P300 latency have not discovered any deficit in schizophrenics or subjects of other diagnoses. Impairment of latency on the classical, two-tone, odd-ball paradigm, for instance, has not been documented in schizophrenics. Since schizophrenics are known to process information less efficiently under conditions of distraction, Hiramatsu et al. (1984), used a task in which auditory stimuli was given to both ears, with the subject being required to count targets of a particular ear. While the schizophrenics showed an amplitude deficit, they did not manifest a latency deficit. Similar results were secured by Roth et al. (1980a), on each of two auditory tasks, one of which involved a discrimination between two tones, while the other required a more difficult discrimination between four auditory stimuli. Brecher and Begleiter (1983) who used visual stimuli also did not find a significant deficit in schizophrenics. One study which obtained different finding is the one by Pfefferbaum et al. (1984). Testing demented, schizophrenic, depressed and normal individuals, on an auditory task that required the identification of a target from two other auditory stimuli, the authors found latency deficits in the demented and in the schizophrenics.
While several studies have reported a delay in reaction time in depressed individuals, a P300 latency deficit has not been reported. Patterson et al. (1988), Giedke et al (1981), Baribeau-Braun and Lesevre (1983), and Pfefferbaum et al. (1984), have studied psychiatrically depressed individuals but found no deficits on the P300 latency.

The clinical group that has shown an impairment of the P300 latency consistently over several studies and different paradigms, is the demented group. Goodin et al. (1978), and Squires et al. (1979), tested subjects diagnosed as dementia and contrasted them with age-matched normals on a simple auditory task requiring the discrimination between two tones. The authors found significant delay in the P300 peak in the demented. Syndulko et al. (1982), found that delayed P300 latency as a sole criteria was able to identify 83% of demented individuals. A study that evaluated patients of Huntington's disease on both cognitive as well as event-related potentials, found impaired P300 latencies in the patients and also a significant positive correlation between the degree of cognitive deficits and the P300 latency (Homberg, Hefter, Granseyer, Strauss, Lange, & Hennerici, 1986). On account of the above findings some authors (Goodin et al, 1978; Squires et al, 1979) suggest that deficits of the P300 latency may be used as a diagnostic indicator for dementia.
In addition to those diagnosed as clinically demented, research has reliably demonstrated a positive correlation between age (among adults) and the P300 latency (Goodin et al., 1977; Pfefferbaum et al., 1984a). Pfefferbaum and Ford (1988) have estimated an increment of 1.42 ms in P300 latency per year on a simple visual word task, and an increment of 1.79 ms per year on a similar word task when the stimulus is embedded in visual noise.

In sum, a prolongation in P300 latency, indicating a delay in the ability to evaluate information, has been consistently observed with cases of dementia. P300 latency has also been found to positively correlate with age among adults. However, most studies that have evaluated schizophrenics and depressives have not found significantly delayed P300 latencies on either auditory or visual tasks, under normal conditions or conditions under distraction.

It must be pointed out, nevertheless, that all reported studies have used tasks wherein schizophrenics were required to make discriminations that were essentially perceptual in nature. Tasks requiring semantic evaluation of verbal stimuli (ordering stimuli into their superordinate categories, like animals, furniture, and so forth) have not been used. The neglect of this area is particularly conspicuous, since there is empirical research to suggest that schizophrenics are deficient in abstraction (See Oltmanns & Neale,
1978; Pishkin and Bourne, 1981). In fact, researchers as early back as Goldstein and Scheerer (1941), and Gorham (1956), have highlighted this deficit in schizophrenics, and particularly in a subtype (chronic schizophrenics) that, according to today's nosology, would be similar to "Negative schizophrenics." It would be interesting to determine if performance deficits on the proverbs test and on other sorting tasks that have been consistently observed in schizophrenics would be corroborated by evidence of brain dysfunction, as would be suggested by event-related potentials. This will be relevant since such behavioural deficits are often influenced by factors like amotivation and lack of cooperation which are known to characterize schizophrenics. Thus, it appears premature to conclude that schizophrenics do not manifest latency deficits on the P300 component until semantic evaluation processes are also investigated. The current investigation has attempted to address this issue by including a Category Task, the details of which will be given in the following chapter.

2.4 LATENCY OF OTHER MIDDLE LATENCY COMPONENTS

A brief mention about findings regarding related middle latency components is appropriate. Experiments designed to elicit the P300 potential, like the auditory "odd-ball" paradigm, also produce N100 and P200 components. With
respect to the N100, while some studies (as described earlier in the Chapter) reveal a reduced amplitude in schizophrenics, none have reported a difference in N100 latency between schizophrenics and normals. This result holds true for a wide variety of conditions: auditory (Patterson et al., 1988; Roth et al., 1980), visual (Brecher & Begleiter, 1983), dichotic listening paradigms (Baribeau-Braun et al., 1983; Hiramatsu et al., 1984).

The results regarding the latency of the P200 component seem equivocal. Several ERP studies that have investigated the P300 have not commented upon the P200 component, possibly implying that no abnormality in latency was detected. A few studies state explicitly that no differences emerged between schizophrenics and normals on the P200 latency (Brecher & Begleiter 1983; Patterson et al., 1988). However, as an interesting exception, Pfefferbaum et al. (1984), found shorter P200 latencies in both schizophrenics and demented subjects. Roth et al. (1980b), in a task that required subjects to discriminate between a frequent and a rare tone, found similar results in schizophrenics but only in response to frequent tones.
2.5 TOPOGRAPHY OF THE P300

The topography of the P300 component, has not generated much interest. No lateralization effects have been typically observed. Most studies, both with normals and with pathological groups have used the midline electrodes (Fz,Cz,Pz) in the measurement of the potential and have confirmed that the P300 is prominent at central(Cz), and particularly so at the parietal(Pz) site (See Pritchard, 1981; 1986). Consequently, typically, only values at Pz have been used for statistical analyses.

One study that deserves mention is that of Morstyn et al. (1983), who employed the BEAM technology (as detailed in the introduction) to generate 128 frames, each frame summarizing 4 milliseconds of electrical activity over the entire scalp. Employing the conventional tone paradigm to generate the P300 component, Morstyn and his associates found evidence for a left hemisphere deficit in schizophrenics that became most obvious during the 296-396ms epoch. Further, unlike the normals, an asymmetric development of the component was seen in schizophrenics that led ultimately to significant deficits particularly over the temporal lobe areas.

More recently, data from several electrode sites is proving useful, since the data lends itself better to multivariate statistical methods, like factor analysis, by which
the components (factors) and their respective influences may be empirically verified (See Donchin & Heffley, 1978). Also, topography is proving important to differentiate between the P300 and the Slow Wave components. While the peaks of these two components overlap, their respective influences over locations of the scalp, particularly at Fz, appear different (See Ruchkin et al., 1982; Squires et al., 1975).

2.6 THE P300 COMPONENT AND INFORMATION PROCESSING

As has been mentioned in the introduction of the thesis, the P300 component derives much importance on account of its utility in information processing theory and research. Within the realms of research on the P300 potential, a distinction may be made between investigations whose immediate purpose was to study the P300 component per-se, and investigations that used the P300 as a tool in order to address other questions. The former focus engenders research on the correlates and the factors that influence the P300 component. Once these factors are known, it may be possible to use the potential to evaluate other hypotheses, or to further the knowledge regarding the stages and processes of information processing.

An illustration of the latter approach is Duncan-Johnson's work (1981) on the Stroop test. From the early years of experimental psychology, it is known that an incon-
gruence between the semantic **content** and the **form** of a verbal stimulus, results in delayed reaction-times. For instance, when subjects are required to name the colour of the ink of written material, they take longer on incongruent words (the word **BLUE** written in red ink) than on congruent words (the word **BLUE** written in blue ink). Whether the delay is due to a longer evaluation process resulting in a delayed identification of the colour, or whether it is due to a delay in the choice of the response after stimulus-identification has taken place, has been an issue of heated discussion. Since the latency of the P300 is known to be an index of stimulus evaluation, the author decided that the combined use of the P300 and reaction-time measures could solve the dilemma. If a delay of P300 occurred to incongruent, relative to congruent stimuli, a stimulus-evaluation difficulty was suggested. However, if a reaction-time delay occurred in the absence of a P300 delay, a difficulty with the choice of response was suggested. The results of the experiment (See Figure 3) using congruent, neutral (the word **TOWN** written in blue/red), and incongruent stimuli, clearly favoured the latter explanation.
Figure 3: Mean P300 latencies & reaction times of the Stroop colour-word test as a function of stimulus category. (Compiled from Duncan-Johnson, 1981).
In the same vein, Hink and Hillyard (1978) studied ERPs during syllable discrimination in a dichotic listening paradigm, and found that the N100 component in normals was enhanced to all stimuli in the attended ear, while the P300 component was enhanced only to target stimuli in that ear. He concluded that the N100 and the P300 represented physiological evidence for different levels of selective attention, and resembled the concepts of "stimulus-set" and "response-set" as propounded by Broadbent (1971).

There are isolated instances of such an approach in the literature of the P300 in schizophrenics. Saitoh et al. (1984), used four syllables in a dichotic listening paradigm and required schizophrenics, siblings of schizophrenics and normals to attend to a particular syllable that occurred only in a predesignated ear. Since the N100 amplitude is known to increase to all stimuli in the attended ear relative to the same stimuli in the unattended ear, any absence of such an enhancement would suggest an inability to maintain an appropriate "stimulus-set". On the other hand the P300 amplitude is known to increase to targetted stimuli relative to untargetted stimuli in the same ear. Hence any absence of such an enhancement would suggest an inability to maintain an appropriate "response-set". The results of the study showed schizophrenics to be deficient on both levels of selective attention; siblings of schizophrenics to be deficient only on
"response-set" and normals to be adequate on both levels. More of such research is definitely indicated.

The combined assessment of reaction-time and evoked potential measures provides scope to clarify several such issues within the framework of information processing. Some authors (Duncan-Johnson, 1981; Kutas et al., 1977; Michalewski, Prasher, & Starr, 1986), have productively used such an approach in research with normals, and the extension of this in research in psychiatry is a promising area. One such application is in the area of psychomotor retardation. Both major depressives and schizophrenics with negative symptoms are known to exhibit a marked degree of retardation on cognitive and behavioural indices. In terms of thinking, it manifests in "negative thought disorder," or poverty of speech and poverty of content of speech (See Andreasen and Olsen, 1982). They also manifest significant delays in terms of reaction-time and response time, on numerous test measures.

However, while neuropsychological and computerised tomography studies offer some evidence to suggest underlying brain impairment in schizophrenics, no significant evidence is present in depressives. The question that emerges is whether the locus of the factors responsible for the retardation are different in the two groups. In schizophrenics who show cognitive deficits, a delay at the cortical level in processing verbal and especially semantic stimuli, may lead to the
consequent retardation in thinking and poverty of ideas; and for depressives who do not manifest such deficits, the delay may be at a more peripheral motor level. If such is true, then both schizophrenics and depressives should manifest deficits in reaction-time, but only the Negative schizophrenics should manifest deficits of the P300 latency. The present study, as will be explained in the following chapter, will attempt to investigate this issue.

2.7 EVENT-RELATED POTENTIALS AND CLINICAL VARIABLES

In any research in psychiatry the diagnosis of the subject is an important factor, but is not the only relevant variable. Several other clinical factors like the degree and type of symptomatology at the time of testing, medication, family history of psychiatric illness, duration of illness, past history of electroconvulsive therapy, are important aspects. It would be useful to ascertain whether ERP measures are in any way related to these clinical variables.

Some studies have attempted to evaluate the above issues. The relevance of the clinical status of the subject to event-related potentials, for instance, has been illustrated by Van den Bosch and Rozendaal (1988) who evaluated schizophrenics soon after admission and retested them a month later, on the contingent negative variation (CNV) potential. The results showed significant differences between the two
evaluations. More pertinent to the present study, is the work of Homberg et al. (1986), who found that the P300 amplitude correlated more on depression and psychosis measures, while the P300 latency correlated with neuropsychological deficits in a group of subjects with Huntington's disease. Roth et al. (1980a), found a significant negative correlation (-0.63) between the measures of formal thought disorder and the P300 amplitude to rare tones.

Of all the clinical variables, the diagnosis of schizophrenia needs particular mention. Subjects may bear the same diagnosis, schizophrenia, but have widely differing symptomatology. The heterogeneity within the group is so striking that some authors refer to schizophrenia as the "group of schizophrenias." Of particular relevance is the distinction between schizophrenics with positive and those with negative symptoms. The validity of the distinction is, in an important way, based on empirical findings that show a higher preponderance of cognitive impairment and structural brain pathology (as determined by CT scan and autopsy studies) in schizophrenics with negative symptoms (See Crow, 1980; Andreasen, Olsen, Dennert, & Smith, 1982). Of late, there is growing evidence of a strong relationship between CT scan abnormalities and neuropsychological deficits (Donnelly, Weinberger, Waldman, & Wyatt, 1980; Keilp Sweeney, Jacobsen, Solomon, Louis, Deck, Frances & Mann, 1988). Hence, since
event-related potentials is a relatively direct evaluation of brain functioning, and since the P300 in particular, is believed to index the cognitive appraisal of the stimulus, it appears imperative that the distinction between positive and negative schizophrenics be retained. Previous investigations appear to have overlooked this important aspect, and seem to have assumed homogeneity purely on the basis of the same diagnosis. Hence, the present study will include two separate groups of schizophrenics: positive and negative.