late event-related potentials and psychopathology*

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Introduction

Event-related potentials include not only the short duration evoked potentials (EPs) associated with sensory stimulation or motor response but also longer duration potentials such as the contingent negative variation, for which the eliciting events are more complex. For EPs there seems to be a relationship between the latency of the EP component and the degree of influence by more cognitive psychological variables such as attention. In general, the “early” sensory EP components occurring before 50 msec are least sensitive to these variables, components between 50 and 200 msec are affected to an intermediate extent, and the components after 200 msec are the most susceptible to psychological influence. Conversely, the earlier components are most dependent on stimulus modality and other physical parameters of the stimuli. Although early EP components might be better for reflecting the more enduring features of psychiatric disorders—a biological substrate for schizophrenia, for example—since they are less influenced by fluctuations in mental state, it is important to realize that psychiatric disorders are not known to alter sensation in its primary aspects. If there are characteristic psychological manifestations of these disorders, these manifestations would be more likely to influence the later components of the EP or other event-related potentials. Both sides of this argument are represented in psychopathology and event-related potential research today: Some investigators study the early EP components in hopes of finding a central biological deficit in schizophrenia or affective disorder, while others envision the late potentials as a tool in delineating the states of consciousness of people with unusual states of consciousness.

In the following sections, I will discuss some findings regarding the influence of psychopathology on late event-related potentials such as the contingent negative variation, the readiness potential, late negative waves, and late positive waves. In each case there will be a brief summary of parameters that are known to influence the phenomena. Studies reported in these sections have generally used nonpsychiatric volunteers as subjects. These sections will be followed by reports on psychopathological variations in these phenomena. Only a brief review is attempted here. Interested readers will find supplementary information in the books of Shagass (1972) and Callaway (1975), and in the proceedings of congresses on slow potentials of the brain (McCallum and Knott 1973, McCallum and Knott 1976, and Otto, in press). Earlier reviews of the contingent negative variation and psychopathology were written by Tecce (1971) and Dongier (1973).

The Contingent Negative Variation (CNV)

Description and Methodology

The CNV is a negative shift in electrical potential over the top of the head as compared to the potential of electrical reference electrodes placed on the ear lobes or other more remote locations of the body. The prototypic paradigm for CNV elicitation is a constant-foreperiod warned reaction time task. For example, Timsit-Berthier et al. (1973) used a click as a warning stimulus (S1) followed at a constant interval of 1.5 sec.
by a train of flashes (S2) which the subject turns off by pressing a button. Since the CNV has an amplitude of only 20 μV or less, it is advantageous to average 10 or 20 individual trials, using the method of signal averaging that is customary for other types of event-related potentials. Figure 1 illustrates the time course of this negative shift. The negativity begins to rise a few hundred msec after S1 and peaks shortly before S2. After S2, the CNV returns to baseline, sometimes overshooting with a positive wave. The return of the CNV to baseline is often referred to as CNV resolution.

In order to record a wave that evolves as slowly as the CNV, it is necessary to use an amplifier with adequate low frequency response. Amplifier time constants of 5 to 10 seconds are customary for CNV research. The most important artifact that must be excluded in CNV recording is produced by eye movement (Straumanis, Shagass, and Overton 1969). The cornea of the eye is about 100 mV more positive than the orbit, and movements of this dipole result in potential shifts over the scalp that can be much larger than brain event-related potentials. Thus, it is imperative to monitor eye movement during CNV trials by placing electrodes near the eyes. There are a number of ways to reduce eye movement contamination: instructing subjects to fix their gaze on some point, eliminating from the average those trials contaminated with eye movement, or compensating for the eye movement contribution to the CNV with a subtraction procedure (Roth 1973). Another artifact of more infrequent occurrence is skin potential artifact (Corby, Roth, and Kopell 1974 and Picton and Hillyard 1972). This artifact can be eliminated by using subdermal electrodes or breaking the skin with repeated needle pricks at the sites of placement of disc electrodes. It is less of a problem if references are at the ear lobes rather than at the mastoids (Picton and Hillyard 1972).

**Parameters Affecting CNV Amplitude**

Many of the CNV research findings up to 1970 were synthesized in an article by Tecce (1972), which proposed that CNV amplitude is jointly determined by the two processes of attention and arousal. The CNV is larger when more attention is focused on the task, this effect being partly a function of subjective motivation and involvement. If a distracting task is performed simultaneously with the main reaction time (RT) task, CNV amplitude is decreased and RT is increased (Tecce, Savignano-Bowman, and Kahle, in press). Factors that might be thought to increase attention, such as requiring a stronger or faster motor response or giving an S2 that is hard to detect (Low et al. 1967), increase CNV amplitude. Subjects can control their own CNV amplitude to a certain extent by adopting different attitudes. For example, by imagining that the motor response would require much effort, or that S2 was going to be difficult to detect, subjects increased their CNV amplitudes (McAdam et al. 1966).

Arousal was postulated to bear a curvilinear relationship to CNV amplitude. CNV amplitude is higher at moderate than at high levels of arousal, such as that produced by using electrical shocks as the S2 in highly emotional subjects (Knott and Irwin 1973), or at low levels of arousal, such as that found in drowsy sleep-deprived subjects (Naitoh, Johnson, and Lubin 1971).

One of the major problems with Tecce’s (1972) formulation is a difficulty in specifying exactly what it is that attention is directed toward while the CNV is being generated. There is evidence that CNVs are larger when subjects are instructed to concentrate on quick response instead of on accurate recognition of S2 (Loveless and Sanford 1974b). On the other hand, if attention is directed to preparation for the motor act, why is RT so poorly correlated with CNV amplitude (Näätänen and Gaillard 1974 and Rebert and Tecce...
1973)? If the attentional factor could be more adequately specified, a one-process explanation might suffice for explaining variations in CNV amplitude, with arousal simply being one of many factors that could influence this attentional process.

Recent research has emphasized that the CNV itself is not a unitary process and that CNVs produced with S1-S2 intervals of 1 to 2 seconds are an uncertain mixture of at least two waves—an initial negative shift that has a frontal scalp distribution and a final negative shift with a more central distribution. By using S1-S2 intervals of 4 seconds, the two components can be separated. The first component was initially thought to represent an orienting component (Loveless and Sanford 1974a) but in one experiment it increased in amplitude with the number of trials (Rohrbaugh, Syndulko, and Lindsley 1976). The second component occurs before the response and is related to the readiness potential, which will be discussed below. The second component is larger with faster RTs (Rohrbaugh, Syndulko, and Lindsley 1976). The relative contribution of these two waves to the changes in CNV amplitude wrought by attention and arousal is a matter for future investigation.

**CNV Amplitude and Psychopathology**

A number of investigators have found reduced CNV amplitude in psychotic patients. McCallum and Abraham (1973) found 30 to 50 percent reductions in medication-free schizophrenics who had the symptoms cited by Schneider (1959) as pathognomonic for schizophrenia, in CNV trials both with and without distracting tones. Schizophrenics without these symptoms did not differ significantly from the control group. Further studies related syndrome intensity as assessed by the Present State Examination (Wing, Cooper, and Sartorius 1974) to CNV amplitude (Abraham 1973 and Abraham, McCallum, and Gourlay 1976). Greater severity of both psychotic syndromes, such as the “auditory hallucination syndrome” and the “depressive delusion syndrome,” and neurotic syndromes, such as the “worry syndrome,” resulted in smaller CNVs. The only syndrome that resulted in higher CNV amplitudes was “obsessive neurosis.” At the end of hospital treatment, patients were retested. Even though they were clinically improved, the schizophrenic group that initially had small CNVs still had small CNVs on retesting. Timsit-Berthier et al. (1973) also found smaller CNVs in psychotics, a result these investigators attributed to great reductions in amplitudes in certain patients. The percentage of subjects with CNVs less than 5 μV was 8 percent in a control group, 10 percent in neurotics, 24 percent in schizophrenics, and 23 percent in patients with affective disorder. There was a test-retest correlation for CNV amplitudes of 0.55 for stable patients after 1 to 2 years, and of 0.48 for patients who were improved or worsened after the same time period (Timsit-Berthier and Gerono 1976). Many of these patients in the last two studies were receiving medication, but the investigators made no attempt to correlate medication level with CNV change.

Neurotics, psychopaths, and patients with psychosomatic disease have all been reported to differ in CNV amplitude from normal controls. The early anecdotal reports by Walter (1964 and 1966) that anxious patients did not form as stable or as large CNVs, and that obsessive patients continued to manifest CNVs even when S2 was omitted, stimulated research interest and led to more systematic studies. McCallum and Walter (1968) showed that neurotic patients with severe global anxiety for which they were receiving drug treatment had decreased CNV amplitude as compared to controls in trials both with and without distracting tones. McCallum (1973) also found lower CNV amplitudes in a group of psychopaths, but this finding could not be replicated by Dongier, Dubrovsky, and Engelsmann (in press) or Syndulko et al. (1975). The study of Syndulko et al. was done with particular care using drug-free psychopaths. Dongier et al. (1973) reported that psychosomatic patients, the majority of whom had asthma, pulmonary tuberculosis, or psoriasis, had average CNV amplitudes twice that of controls.

**Attention, Anxiety, and the CNV Amplitude**

CNV amplitude reduction appears to be more related to anxiety and cognitive disorganization than specific psychiatric syndromes. Anxious neurotic persons and certain groups of schizophrenics are likely to have increased arousal (Broen 1968 and Lader 1975), which according to the formulation of Knott and Irwin (1973) reduces CNV amplitude through a saturation or ceiling effect. People who are anxious have a tonic negative
cortical shift, and the CNV, which is a phasic increment in this negativity, is diminished because of a physiological ceiling on cortical polarization. This hypothesis cannot be tested directly at the present because of the unreliability of measuring standing cortical potentials at the scalp, but it gains some plausibility by analogy with other indicators of anxiety such as the heart rate, which shows diminishing reactivity to transient stressors as the basal level increases (Lacey 1956).

In addition, reduced focusing of attention or impaired maintenance of attentional set may be a cause of CNV decrease in both psychotics and neurotics. Some psychotics are susceptible to internal distraction from hallucinations and to external distraction from unstable perceptions or environmental events (McGhie, Chapman, and Lawson 1965). Distractions or interferences can explain many schizophrenic deficits (Callaway 1970). Similarly, decreased cooperativeness and motivation to perform the task may lead to inattention in psychotics. Anxious neurotics may also be more distractible and unable to focus attention; but, on the other hand, these patients are often overcooperative and overconcerned about performance.

The finding that after recovery psychotics continue to have reduced CNV amplitudes (Abraham, McCallum, and Gourlay 1976) is one that does not fit into the above formulations. Abraham, McCallum, and Gourlay’s finding suggests that the CNV provides an indication of enduring abnormal personality traits rather than just the subject’s mental state at the time of testing. It would be useful to have more information on the completeness of the recoveries of these patients, and what residual psychological deficits might remain that could lead to continued CNV reduction.

**Parameters Affecting CNV Duration**

In a simple RT task, the CNV resolves about 200 msec after S2, but in more complex paradigms that require longer processing of the information given by S2, CNV resolution can be delayed beyond 500 msec (Roth, Tinklenberg, and Kopell, in press). In general, the latency of CNV resolution is parallel with RT in that more difficult choice reaction time tasks produce longer CNVs and longer RTs. No motor response is actually necessary for CNV resolution. If a certain choice is defined as requiring no motor response, the CNV will resolve with the same latency that would have resulted had a button press been required (Roth et al. 1975).

Situations in which additional stimuli follow S2 can result in prolonged CNVs even when these stimuli are task-irrelevant (Weinberg 1972). Perhaps the subjects in this experiment maintained their attention in expectation of an event that might have turned out to have some significance. In another experiment, when the button press did not immediately turn off the train of flashes (S2) because the experimenter changed the experimental contingencies without informing the subjects, the CNV was prolonged in 6 of 10 subjects (Delanoï et al. 1975). Gauthier and Gottesmann (1976) managed to prolong the CNV without changing its amplitude by applying electrical labyrinthine stimulation before certain of the trials and at the same time requiring subjects to perform mental arithmetic in the S1-S2 interval. These last two experiments are difficult to interpret because of the psychological complexity of the experimental situations, but it is possible that both resulted in subject uncertainty about task performance that led to a prolongation of task-directed attention.

**CNV Duration and Psychopathology**

Timsit-Berthier et al. (1973) reported from Liége a higher incidence of prolonged CNVs in a group of 103 psychotics than in comparison groups of 121 neurotics and 92 controls. The CNVs were divided into four types on the basis of their mode of resolution (figure 2). In type I, the CNV returns to baseline within a few hundred msec after S2. In type II, the CNV begins to decline after S2 but does not reach baseline for several seconds. In type III, the CNV does not decline immediately and presents a “plateau” appearance. In type IV, the CNV rises further after S2 and presents a dome-shaped curve. Whereas type I is found in the majority of controls and neurotics, types III and IV are the predominant types in psychotics. Patients with affective psychoses had as high a percentage of type IV resolution (45 percent) as did schizophrenics (42 percent). Although many of the patients in this series were medicated, the same prolongation was seen in a subgroup of unmedicated patients (Timsit-Berthier 1973). Members of the original research group found similar results in different patient series in
Figure 2. Four different modes of CNV resolution

Type I

Type II

Type III

Type IV

Note.—EEG recording is as in figure 1. This figure is adapted, with permission, from figures 4 and 5 of Timsit-Berthier et al., *Electroencephalography and Clinical Neurophysiology*, 35:355-361, 1973.

Montreal (Dubrovsky and Dongier 1976). These investigators call the part of the CNV following S2 the post-imperative negative variation (PINV). A prolonged PINV, defined as one that fails to return to baseline within 2 seconds of S2, was found in 12 percent of 42 controls, 32 percent of 67 neurotics, and 59 percent of 46 psychotics. Over 90 percent of schizophrenics who had been sick less than 6 months had prolonged CNVs. There were no age or sex differences between ambulatory schizophrenics who had abnormal PINVs (65 percent) and those who did not (27 percent) (Chouinard et al. 1975).

A partial confirmation of these results has come from a British group. Although their earlier reports denied that schizophrenics had prolonged CNVs (Abraham 1973 and McCallum and Abraham 1973), more recent findings (Abraham, McCallum, and Gourlay 1976) give some support to the Liege and Montreal groups. Specifically, the curves reported by Abraham, McCallum, and Gourlay (1976) did not show the same morphological types that Timsit-Berthier et al. (1973) had reported, possibly because the British group used faster amplifier time constants, but the mean voltage measured in the range from S2+350 to S2+3,500 msec was significantly more negative for patients than for controls. The measure of prolongation used by Abraham, McCallum, and Gourlay has a high positive correlation with CNV amplitude ($p = 0.60$ according to a personal communication from Abraham), which is especially interesting in that patient-control differences would have implied an association between low amplitude and prolongation. Both the Belgian and British investigators believe that the length of the CNV normalizes as the patients recover (Abraham, McCallum, and Gourlay 1976 and Timsit-Berthier et al., in press).

Neurotic patients show intermediate degrees of prolongation between controls and psychotics. Timsit, Reul, and Timsit-Berthier (1974) scored blindly the Rorschach tests of neurotic patients with and without prolonged CNVs. The distinguishing feature between the two groups was that subjects with longer CNVs showed more anxiety in their Rorschach responding. There was no evidence of latent psychosis in the neurotics with prolonged CNVs. Neurotic patients characterized by psychiatrists as having a bad prognosis had a higher incidence of prolonged CNVs (Dubrovsky and Dongier 1976). The prognostic criteria were not reported. Phobic patients had larger and more prolonged CNVs when S2 was a picture of the feared object (Barbas, Dubrovsky, and Solyom, in press).

CNV Duration—Artifact or Prolonged Information Processing?

The investigators of CNV prolongation seem to be highly aware of possible contamination of records by eye movement artifact and have taken measures to...
eliminate this contamination. However, better documentation of the elimination of eye movement artifact could be routinely provided by giving the eye lead measurements from the trials that are accepted for averaging. The use of a single mastoid reference (Timsit-Berthier et al. 1973) is a mistake in two ways. First, horizontal eye movements affect the EEG without being noticeable in the eye electrodes, which are placed above and below the eye. Second, the mastoid is prone to contamination by cephalic skin potential artifact (Picton and Hilliard 1972). Eliminating trials contaminated with palmar skin conductance response is an insufficient control, since the two types of skin responses are different, albeit related. By injecting atropine under the electrodes in certain subjects and observing a maintenance of CNV prolongation, Timsit-Berthier et al. (in press) have provided strong evidence that prolonged CNVs can occur without skin potential changes.

The records of some patients cannot be interpreted because of the large amount of artifact they contain. There is a dilemma in that exclusion of this group produces an often unreported sampling bias while inclusion adds noise to the data. The magnitude of this problem is indicated by Dongier, Dubrovsky, and Engelsmann (in press) who reported that 55 percent of patient records and 23 percent of control records were judged "unreadable" by two independent assessors.

Even though the CNV paradigm used by these investigators was an RT paradigm, they did not report RT or other response characteristics. If patients respond more slowly, their CNV would be expected to be prolonged. Although Timsit-Berthier et al. (1973) do not tell us exactly what the patients were instructed about the task, they do state that "a good motor performance was never encouraged." Abraham, McCallum, and Gourlay (1976), on the other hand, encouraged fast responses. One of the most consistent behavioral findings in schizophrenic patients is that their RTs are longer than those of normals and, under the conditions used by the British group, one would expect about a 300 msec delay on the average (Shakow 1963). Even if S2 were a uniform stimulus, an RT difference of 300 msec could cause considerable differences between patients and controls in the amount of CNV resolution occurring before S2+350 msec. In all of these studies on CNV and psychosis, however, S2 is a train of flashes that does not end until the response is made, so that slower responses mean longer S2s. In general, sustained stimuli are associated with prolonged negativity (Jarvilehto and Fruhstorfer 1973 and Kohler and Held 1949), which could contribute to the differences between patients and controls. Late positive waves that might well occur with latencies of 300-400 msec after S2 in this type of paradigm might also influence resolution measurements. As I shall describe below, these positive deflections are generally of lower amplitude in patients. (I will ignore here the controversy over whether CNV resolution and late positive waves are part of the same process.)

If we assume that CNV resolution failed to occur until seconds after the button was pressed in many of the psychotic patients of Timsit-Berthier et al., we might venture to postulate that the concentration of attention associated with CNV negativity fails to be dissipated at the time the response is made. There is evidence both from clinical and experimental observations that schizophrenics cannot shift attentional sets as rapidly as normals. Schizophrenic thinking is often stereotyped and repetitive. In a reaction time task, schizophrenics responded less rapidly to a stimulus that occurred in a different sensory modality from its predecessor

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**Figure 3. The readiness potential**

![Figure 3](https://example.com/figure3.png)

**Note.**—A response-synchronized average was computed from a subject who was told to press a button every 4 to 5 seconds. The EEG recording is as in figure 1. Electromyographic (EMG) activity from the extensor pollicis longus is also shown. This figure is adapted, with permission, from figure 2 of Timsit-Berthier, Delaunoy, and Rousseau, *Electroencephalography and Clinical Neurophysiology*, 35:363-367, 1973.
However, the difference between schizophrenics and controls for modality shifts was only 22 msec, which although significant is smaller than the CNV prolongation effect by a factor of more than 100.

The duration of the RP after the initiation of response can be influenced by the type of response. Slow or sustained motor contractions result in delayed RP resolution (Hazemann, Metral, and Lille, in press).

**The Readiness Potential (RP)**

*Description and Methodology*

Voluntary movements associated with evoked potentials are called average movement potentials. Subjects are requested to make a movement repetitively, such as a button press every 4 or 5 seconds, and an average is computed with the physical consequences of the movement or the electromyogram of the muscles involved as the synchronizing event. Figure 3 illustrates that this EP includes activity both before and after the onset of movement. After the movement, there is a positive return. The negative shift that precedes the movement is called the readiness potential (RP) or Bereitschaftspotential and is slightly greater over the cortex contralateral to the movement in right-handed people (Kutas and Donchin 1974). Like the CNV, the readiness potential can be severely contaminated with eye movement artifact, and measures similar to those used for dealing with this problem in the CNV must be taken (Gerbrandt, Goff, and Smith 1973).

**Parameters Affecting the RP and Its Resolution**

Although the RP has a slightly different distribution from the CNV under most circumstances (Kutas and Donchin, in press, and McCallum, in press), there are a number of similarities between the two responses. In both cases, the amplitude of the negativity increases with the force required to make the response (Kutas and Donchin 1974 and Low and McSherry 1968), and both can be increased by creating a situation where more attention is directed to the response (McAdam and Seales 1969). In all likelihood, the second components of the CNV and the RP are identical (Rohrbaugh, Syndulko, and Lindsley 1976). The RP decreases markedly with age beginning in the fourth decade of life (Deecke, Englitz, and Schmitt, in press), a result similar to that reported by Loveless and Sanford (1974a) for the CNV.

The prolonged RP is free from some of the ambiguity of interpretation that the prolonged CNV presents. The prolonged RP, by the fact that its synchronizing event is the onset of the response, can be clearly defined as a postresponse event, while it is uncertain how much of the negativity after S2 in the CNV paradigm is prereponse or postresponse. However, there are response factors other than the time of response onset that may be important in understanding the RP. Prolongation could correlate with slow or sustained muscular contractions as it did in control subjects (Hazemann, Metral, and Lille, in press). Patients may space their button presses differently from controls and create different conditions of temporal recovery (Roth et al. 1976a). In addition, because of the similarities of the CNV and RP, any of the psychological factors that are adduced to explain the variations of the former might also be applied to the latter. For example, inertia of attentional set might underlie RP as well as CNV prolongation.

**RP and Psychopathology**

Timsit-Berthier, Delaunoy, and Rousseau (1973) have reported prolongation of the negativity of the RP in 75 percent of psychotic patients as compared to 30 percent of neurotics and 12 percent of controls. In the psychotic patients there was a significant association between CNVs of types III and IV and prolonged RPs. These authors did not provide information as to whether prolonged motor potentials were as prevalent in schizophrenics as in patients with affective disorders. Dongier, Dubrovsky, and García-Rill (1974) found prolonged RPs, defined as lasting more than 500 msec after the button press, in 43 percent of psychotics, 32 percent of neurotics, and 19 percent of controls. The only clinical distinction among the patients reported was that prolonged RPs were found in 60 percent of acute psychotics but in only 6 percent of chronic psychotics.
Late Negative Waves After Unpaired Stimuli

Timsit-Berthier, Delaunoy, and Rousseau (1973) and Timsit-Berthier (1975) have also studied late negative potentials that follow the S1 or S2 of the CNV paradigm when there is no temporal contingency between S1 and S2. In the first paradigm, single clicks were delivered at random intervals and no motor response was required. In the second paradigm, 1-second trains of light flickering at 18 Hz were delivered at random intervals without requiring a response. The third paradigm was like the second except that a button press, which terminated the train of light flashes, was required. In the fourth paradigm single clicks were responded to with a button press.

EPs to stimuli in each of the paradigms were analyzed in terms of the morphology of the EP. Type A was defined as having no significant deflections after 250 msec, type B as being dominated by positive waves after 250 msec, type C as being dominated by a negative wave lasting about a second, and type D as having a negative wave that lasted over a second. The exact definitions of modes C and D depend on the specific paradigm.

Psychotic, neurotic, and control patients were tested in each paradigm. The first paradigm failed to distinguish the three groups, while all of the other paradigms did. In each case, psychotics had higher percentages of the D morphology.

Interpretation of these results must take into account several event-related components. Type B is apparently a composite of late positive waves that outweigh negative components. These waves are the ones referred to in evoked potential literature as P200 (P2) and P300 (P3). The negative potentials of types C and D may be the negativity associated with stimuli of long duration (Järvilehto and Fruhstorfer 1973 and Kohler and Held 1949), with the early component of the CNV (Rohbaugh, Syndulko, and Lindsley 1976), or with task-relevant nontarget stimuli (Roth et al. 1976a). In paradigms 3 and 4, for which a button press was executed, a negativity such as that associated with prolonged RPs may be playing a role. Except for P300, which will be discussed below, very little is known about the psychological parameters influencing these waves. Their latency and polarity suggest that they fall into a class of phenomena influenced by attention, and their prolongation may be interpreted as a failure of resolution of attention.

Late Positive Waves (LPWs)

Description and Methodology

Positive waves with latencies over 200 msec are elicited in paradigms in which there is uncertainty about the nature or time of occurrence of stimuli. These waves occur to stimuli of all modalities. In one paradigm, for example, tone pips of three pitches are presented in a stimulus train with a constant 1-second interval between stimuli. The sequence of tones is random with the probability of the middle tone being set at 0.7 and of each of the other two tones at 0.15. When the subject's attention is directed to the tone pips by having him press a button in response to infrequent target pips, both infrequent target and infrequent nontarget pips elicit a positive wave with a latency around 350 msec. This component is often labeled P300. Figure 4 illustrates the EPs to frequent and infrequent tone pips under these circumstances.

Several paradigm features are useful in emphasizing LPWs. First, if auditory stimuli are used it is possible to suppress the earlier modality-specific component of the EP by embedding the rare class of stimulus in a stimulus train with interstimulus intervals (ISIs) of 1 second or less. This reduces the amplitude of the P190 (positive with a mean latency of 190 msec) component so that it is not confused with later positive deflections. Second, it is best to avoid a paradigm in which the subject can guess exactly when an uncertain target stimulus may or may not appear, such as in a fixed-foreperiod choice RT task. Such paradigms result in a CNV whose return to baseline can confuse the measurement of P300 (Roth et al. 1976a). Third, a motor response may produce its own EP concomitants that can confuse the interpretation of late positivity. Some investigators have tried to circumvent this problem by engaging subjects in counting or guessing tasks. RT can give so much information about cognitive processing speed, however, it is useful to include some experimental trials for which a quick motor response is required.

The same artifacts that can influence the CNV—eye movement and skin potential—can produce late positive
Figure 4. Late positive waves under three different conditions in a single subject

Note.—Each of three EEG leads (Fz, Cz, and Pz) is referenced to linked ear lobe leads. Positivity at the scalp is up. The line at the beginning of the tracing marks stimulus onset. N1 (N100) and P2 (P200) deflections predominate in the averages for the frequent stimuli, and N1 (N100) and P3 (P300) deflections in the averages for the infrequent stimuli.
shifts. The methods for controlling these artifacts are the same for late positive waves as for the CNV.

**Parameters Affecting Late Positive Wave Amplitude and Latency**

The amplitude of the LPW is a function of subjective probability of the stimulus event, the task-relevance of the event, and whether or not a task-relevant event is a target for some task. The subjective probability of the stimulus event bears a relationship to LPW amplitude that can be expressed in terms of information theory (Ruchkin and Sutton, in press). LPW amplitude monotonically increases with the amount of information received, which is equal to the subject's *a priori* uncertainty of event occurrence minus the subject's *a posteriori* uncertainty about having correctly perceived the event. In this case, the rarer the event, the larger the LPW. If the event is near threshold, however, the subject may be uncertain whether it occurred. Under these circumstances, the LPW is reduced by the amount of *a posteriori* uncertainty.

Making the stimuli task-relevant usually increases LPW amplitude. Subjects may be asked to guess which stimulus will come next, to count silently the number of stimuli in a certain class, or to press a button when targets occur. Yet even when stimuli are not defined by the experimenter as task-relevant, LPWs may occur (Roth 1973 and Squires, Squires, and Hillyard 1975). The effects of task-relevance are usually thought of as being mediated by directing the subject's attention. When attention is directed to a certain stimulus channel, target stimuli will elicit larger LPWs than nontarget stimuli (Squires, Squires, and Hillyard 1975). It is likely that task relevance interacts with subjective probability in the sense that subjects who are able to ignore the stimuli may not accurately register stimulus occurrence or may not form an accurate idea of stimulus probability.

In general, the latency of LPWs depends on how long it takes the subject to evaluate the stimulus for the purpose of the task. Less discriminable stimuli result in later LPWs (Squires, Donchin, and Squires, submitted for publication). If a visually presented word is to be evaluated for synonymity, the LPW is later than if the word is only to be recognized as a target word (Kutas and Donchin 1976).

Although I have summarized the LPW as if it were a unitary entity, there is considerable controversy about whether or not there are several distinct LPWs. Much of the evidence for distinctness comes from consideration of LPW scalp distributions. While most of the waves encompassed by current theories are maximal in the parietal lead and decline in amplitude anteriorly and posteriorly, under certain circumstances an LPW is elicited that is maximal in frontal and central leads (Roth, in press).

**Late Positive Waves and Psychopathology**

Roth and Cannon (1972) compared 21 schizophrenic patients, most of whom were on medication, with age- and race-matched controls on a paradigm that elicited LPWs. Stimuli were tone pips or white noise bursts given in trains with a constant 1-second interstimulus interval. The ratio of the frequent to the infrequent stimulus type was 1:15. Subjects were instructed to sit quietly and ignore the stimuli. During the first half of the 11-minute run, control subjects had much larger LPWs to the infrequent stimuli than did the schizophrenics. The LPW findings were uncorrelated with drug dose and with behavioral ratings. EP latencies did not distinguish the groups.

A paradigm quite similar to the one used by Roth and Cannon (1972) was used by Timsit-Berthier and Gerono (1976). Tones of two different frequencies were presented in a train with an ISI of 5 seconds. The two tone types were randomly presented in a ratio of 1:5.7, and subjects were required to count the infrequent stimuli. A group of nine psychotics had much smaller LPWs to the infrequent stimuli than did the schizophrenics. These LPWs had a mean latency around 220 msec. A positive wave at 150 msec was also smaller in the schizophrenics. The LPW findings were uncorrelated with drug dose and with behavioral ratings. EP latencies did not distinguish the groups.

A paradigm quite similar to the one used by Roth and Cannon (1972) was used by Timsit-Berthier and Gerono (1976). Tones of two different frequencies were presented in a train with an ISI of 5 seconds. The two tone types were randomly presented in a ratio of 1:5.7, and subjects were required to count the infrequent stimuli. A group of nine psychotics had much smaller LPWs to the infrequent stimulus type than did matched controls, both at a vertex and at an occipital lead. This study has been reported only in a preliminary form, and details as to the medication status and diagnoses of the patients are yet to be specified.

Reduced LPW amplitudes in patients are not restricted to paradigms using auditory stimuli. Shagass et al. (in press) tested 32 schizophrenic patients who had been off medication for at least 6 days and compared them with 16 controls. Stimuli of three modalities were
presented in random order at intervals varying randomly between 1.5 and 2.0 sec. The sequential probability of stimulus type was 0.5. The auditory stimuli were clicks, the visual stimuli were patterns flashed on a television screen, and the somatosensory stimuli were electric pulses delivered to the median nerve at the wrist. Subjects were told to sit quietly during the run and gaze at a point on the television screen. Homologous LPWs in each of the three modalities were reduced in amplitude in the schizophrenics as compared to the controls. These peaks had mean latencies of 360 msec in the auditory mode, 300 msec in the visual, and 280 in the somatosensory. Other waves were also reduced in the schizophrenics: N130 and P180 in the somatosensory mode, and N100 and P200 in the auditory mode. The amplitudes of the LPWs were small because of the relatively high stimulus probabilities and the lack of stimulus task relevance, and it is a sign of the robustness of the findings that they are statistically significant for LPWs of such small amplitudes.

A task of considerably more psychological complexity was employed by Levit, Sutton, and Zubin (1973) in a comparison of 10 schizophrenics, 10 psychotic depressives, and 10 controls. All groups were matched for age, sex, race, socioeconomic status, and educational level; and the two patient groups, which consisted only of patients medicated with chlorpromazine, were matched for drug dosage. Patients had to guess whether light flashes or noise bursts would be presented on successive trials. There were two conditions: one in which the subjects were told before each trial which stimulus modality was next (the certain condition), and another in which the subjects were not told (the uncertain condition). Trials were categorized for purposes of signal averaging on the bases of certainty vs. uncertainty of guess, correctness vs. incorrectness of guess, and shift vs. repetition of stimulus modality. In the uncertain condition the sequential probability of either modality was 0.5. Results were given in terms of amplitude from N110 to the peak of the LPW at about 330 msec, although in the discussion the authors state that the same group differences were found for the LPW measure separately. Both schizophrenics and depressives had smaller N110-P300 amplitudes than controls in the uncertain condition. Mean schizophrenic amplitudes were about half the mean control amplitudes. The groups did not differ when trials were divided by the correctness of the guess, but schizophrenics tended to have larger amplitudes in the ipsimodal trials, while depressives and controls tended to have larger amplitudes in the cross-modal trials.

**Interpretation**

Since both subjective probability and task-relevance influence LPW amplitude, it is pertinent to ask which of these factors is playing the larger role in reducing the LPWs of patients. In all the experiments reviewed, the stimuli were well above threshold so that information delivery was a function only of *a priori* subjective probability of stimulus occurrence. Although one might assume that schizophrenics would be less likely to form the correct expectancies because of inattention or other cognitive deficiencies, RT experiments show that under certain circumstances schizophrenics form expectancies as strong as or stronger than those of the controls. For example, Waldbaum, Sutton, and Kerr (1975) had schizophrenics react to auditory and visual stimuli identical to those used by Levit, Sutton, and Zubin (1973). The subject pressed one of two keys labeled “sound” and “light,” depending on the guess the subject made about the next stimulus in the sequence, and then lifted his finger as quickly as possible when either stimulus was actually delivered. In the certain condition subjects were told what to expect on the next trial and in the uncertain condition they were not. Schizophrenics benefited when they knew what to expect even more than controls in terms of more decrease in RT in the certain condition. Furthermore, schizophrenics were slowed more than normals when the sensory modality of a stimulus was different from that of the previous trial (cross-modal stimuli). This is an exaggeration of the expectancy effect in normals that gives undue weight to the immediately prior stimulus in forming expectancies about the subsequent stimulus. From these RT results, larger LPWs might be anticipated in schizophrenics, since rare stimuli would be even less probable subjectively.

Unless we make an ad hoc assumption that LPW generation itself is altered in patients, we are left with the possibility that the task-relevance instructions failed to direct the patients in the same way they did the controls. Perhaps through lack of motivation or distracting factors in the psychotic state of consciousness, subjects failed to attend to the stimuli. Some of
the discrepancies between the results of the RT and the non-RT guessing paradigm may be due to the fact that the stimuli in the non-RT version are essentially irrelevant to the task. LPWs to these stimuli reflect a concern with whether the guess had been right or wrong, a concern that might have been more pressing in the controls than in the patients. The same considerations apply whether the essence of task relevance is the selection of stimulus channels or reaction to a target stimulus.

In the experiments of Roth and Cannon (1972) and Shagass et al. (in press) the stimuli were defined by the experimenters as task irrelevant. LPWs in the controls are evidence that people react to rare events automatically, as is the case for autonomic reactions to orienting stimuli. As would be expected for an orienting response, LPW amplitude declines over the course of the experimental run (Roth and Cannon 1972). The Roth and Cannon experiment shows especially clearly that a difference between schizophrenics and normals persists even when the subjects' instructions bias against the difference. Even though controls can usually follow instructions better than patients, the schizophrenics apparently do better at performing the assigned task of ignoring the stimuli.

These studies shed little light on what patient characteristics are associated with LPW reduction. Certainly schizophrenia and affective disorder are not the only conditions that reduce LPWs: Both marihuana and ethanol intoxication do the same thing (Roth et al. 1973 and Roth, Tinklenberg, and Kopell, in press). A state of reduced interest in the outside world—be it due to schizophrenic autism, depressive preoccupation, or the indifference and blunted reactivity of intoxication—may be the common factor in these various instances of LPW attenuation.

**General Conclusions**

There is great opportunity for refinement and extension in the studies that I have reviewed. In many series of patients, less than optimum classification and symptom assessment were used, medication doses were not even mentioned, and control groups were inadequately matched on variables such as intelligence, socioeconomic status, or even age, sex, and race. In general, the quality of research in the area of EPs and psychopathology is poorer than in experiments designed to answer questions of theoretical interest to psychology. Some of these deficits can be blamed on the exigencies of the psychiatric hospital, some on the newness of the researchers to the area of evoked potentials, and some on a desire to make the big discoveries first and let the subtle refinements follow.

Clearly, there are differences between patients and controls on many EP measures; only the converse would be surprising. It is a rare behavioral test that would fail to distinguish the patients from the controls in these series. Shakow (1963) slyly suggested that the amazing thing about biochemical and physiological studies of schizophrenia is that many fail to find differences between patients and controls. His own RT tests can separate patient and control groups with a high degree of accuracy. It is not surprising that event-related potentials most influenced by behavior should be sensitive to psychopathology. A more pertinent question is whether they have anything to add to behavioral assessment. For this reason, the trend in the pure psychological study of event-related potentials to assess behavior concomitantly with EEG recording is recommended to investigators of the CNV and other late waves in patient populations.

To some, the psychological interpretation of EP differences between patients and controls is a disappointment. Biological insights into synaptic mechanisms that might help the biochemists and animal neurophysiologists could be more helpful than studying potentials that are swayed by fluctuations in attention and arousal—psychological factors that are hardly the essence of schizophrenia or depressive disease. This is a powerful argument, but we must bear in mind that the very definitions of these diseases are psychological. We call people schizophrenics because they hear voices talking to them when no one is there and yet have unimpaired memory and intelligence. Perhaps auditory EPs that could be affected by internal voices might be more to the point than the nonspecific phenomena now under scrutiny.

In actual psychiatric practice, clinical decisions are made on the basis of what the patient says, how he talks and behaves, and historical information provided by witnesses. No formal psychological test or behavioral test has ever become widely accepted as an important part of clinical psychiatric decision making. The closest psychophysiology has come to clinical usefulness is the sedation threshold (Shagass 1957). Yet most psychiatric
residents have never heard of it and may never see it used.

What then are the requirements for a psychophysiological test that would be clinically useful? First, it must be sensitive enough so that it does more than distinguish the severe psychotic from well-adjusted controls. It should be so sensitive that it can be shown superior to clinical observations or less expensive behavioral tests. Second, it must be specific enough to distinguish characteristics of patients that are important for clinical decisions with an acceptably small number of false positives and false negatives. Some examples of important clinical decisions in today’s psychiatry are choosing the appropriate drug treatment, assessing treatment efficacy, deciding whether a patient can successfully live outside the hospital without harming himself or others, estimating the length of hospitalization or treatment needed, and deciding whether electroconvulsive therapy is indicated.

The need for better tests is apparent. Although clinical assessment may be the only method for making these decisions today, many of them turn out to be wrong at great cost to the patient and to society. Psychophysiological tests are potentially more objective, unbiased, and cheaper than the human clinician, and could be of special help in evaluating the mute or uncooperative patient or patients whose verbal report cannot be relied upon. These goals seem worthwhile though remote. We can be heartened by the fact that we seem to be in a phase of rapid expansion of knowledge about event-related potentials that promises a clarification of the uncertainties faced in interpreting the results that were reviewed here.

References


Dubrovsky, B., and Dongier, M. Evaluation of event-related slow potentials in selected groups of psychiatric...


Shagass, C.; Straumanis, J.J.; Roemer, R.A.; and Amadeo, M. Evoked potentials of schizophrenics in several sensory modalities. *Biological Psychiatry*, in press.


Squires, N.K.; Donchin, E.; and Squires, K.C. Bisensory stimulation: Inferring decision-related process from P₃₀₀ component. Submitted for publication.


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