early evoked potentials*

Charles Shagass

This paper is concerned with "early" sensory evoked potential (EP) phenomena and their role in clinical psychiatric research. The dividing point in time between early and late EP events is arbitrary; it will depend upon the nature of the stimulus and the sensitivity of recording procedures. In general, EP events occurring within 50 msec after stimulus application are considered "early," although this boundary may reasonably be moved to 100 msec or more under different conditions.

Later EP events have been studied more often than early ones in investigations of a psychological or psychiatric nature. This may be because the later EPs are far more sensitive to psychological maneuvers, such as manipulation of attention (Satterfield 1965). Nevertheless, the early EP events do offer some advantages for psychiatric research. Their underlying neurophysiology is better understood than that of the later potentials. Also, their relative insensitivity to psychological influence renders them less susceptible to change by uncontrolled factors; results are less likely to be either produced or obscured by stray thoughts.

Some Methodological Considerations

Recording Procedures

The early sensory evoked potentials consist of three or more components in only 50 msec—a higher frequency of response than is often recorded in EEG systems. Therefore, the main consideration in instrumentation is that the upper frequency cutoff of all elements of the system must be sufficiently high to allow the signal of interest to be recorded without distortion. We have found that an upper frequency cutoff of at least 500 Hz is required to record the initial peaks of the somatosensory evoked potential (SEP) without attenuation, and Desmedt et al. (1974) advocate 3 KHz. A higher frequency response (minimum, 3 KHz) is needed for the very early auditory evoked potentials (AEPs) described by Jewett, Romano, and Williston (1970). These early components are also far smaller than the later components. If the investigator wishes to record only the fast early potentials, he can improve the signal-to-noise ratio in two ways: (a) by setting the lower end of the frequency band-pass at a relatively high value (e.g., 10 Hz), to eliminate slower activity; (b) by averaging a larger number of trials, which can be accumulated in a short time because these EPs are attenuated very little at high rates of stimulation.

Contamination by Extracerebral Potentials

Bickford, Jacobson, and Cody (1964) drew attention to the fact that potentials recorded from the scalp may be originating in structures other than the brain, and that constant vigilance is required to deal with extracerebral contaminants. Myogenic contaminants may have short latencies, particularly with somatosensory and auditory stimuli (Cracco and Bickford 1968 and Goff et al., in press). With visual stimuli, the electroretinogram may be recorded along with early potentials. Measures that can be taken to diminish, or at least to identify, extracerebral contaminants include muscle tension and relaxation maneuvers and the monitoring
of presumed extracerebral sources, such as eye movements.

**Subject Factors**

Age and sex are both important. Because they may relate to EP characteristics differently in psychiatric patients than in normals, statistical designs that permit the interactions between age, sex, and diagnosis to be tested are desirable (Shagass, Overton, and Straumanis 1972 and 1974). The effects of current or recently administered drugs are a constant problem in psychiatric studies; serial recordings before and during drug administration may give some indication of the extent to which drugs influence results. It is noteworthy that "control" subjects may deny recent drug ingestion, because they do not consider alcohol or marijuana to be drugs. Additional factors that may influence EP characteristics are time of day (Heninger et al. 1969) and tobacco smoking (Hall et al. 1973).

**Measurement Procedures**

**Amplitude and Latency**

The compound EP is generally assumed to consist of a series of components that may overlap in time. Measurements of latency and amplitude are usually based upon visually discernible peaks. Since peak identification involves subjective judgments, we have attempted to objectify amplitude measurements by performing them automatically with a computer (Shagass 1972). Our procedure depends upon defining standard time epochs that contain events of interest; the average deviation of the data points about the mean of these epochs is computed. This technique is essentially the same as measuring the area under the curve; the average deviation values correlate to a level of about 0.9 with hand measurements made on clear signals. Our attempts to devise computer algorithms for measuring latencies have, so far, been successful only for initial SEP peaks (Shagass, Overton, and Straumanis 1972).

**Wave Shape Variability**

The extent to which wave shapes vary in time can be assessed in a variety of ways (Callaway and Halliday 1973). One popular method is to obtain product-moment correlation coefficients between corresponding data points in two or more EPs (Callaway, Jones, and Layne 1965).

**Intensity-Response Functions**

When several stimulus intensities are employed, one can obtain curves relating amplitude or latency to stimulus strength (Shagass and Schwartz 1963a). The linear slope of such curves can be computed as an index of the intensity-response function. This procedure has been used by Buchsbaum and Silverman (1968) in their EP test of Petrie's (1967) concept of "augmenting-reducing." Generally, the amplitude slope is highly correlated with the mean amplitude level across intensities, but covariance adjustment can be used to derive a slope value that is independent of mean level (Soskis and Shagass 1974).

**Recovery Functions**

After stimulation, the excitability of the sensory cortex may be altered for some time. Recovery function measurements attempt to depict the time course of such alterations in excitability before full recovery of responsiveness. Recovery can be measured by applying paired stimuli with varying interstimulus intervals. Figure 1 shows the normal amplitude recovery function, expressed as the ratio of the second to first response (R2:R1) of the negative-positive component of the SEP; note that there are several phases of recovery within the first 100 msec. When stimuli are close together, the second response overlaps the first, which can then be visualized only by subtraction methods (see figure 2). Also, adjustment of R2 for regression upon R1 is preferable to use of the R2:R1 ratio. In recent years we have used a modified SEP recovery function procedure, with the following features: (a) constant interstimulus interval (10 msec); (b) different intensities of initial (conditioning) stimuli in each sequence; (c) conditioning trains (nine stimuli) in addition to single conditioning stimuli; (d) test stimuli of constant intensity. Figure 2 shows sample tracings. In addition to measures of recovery after single stimuli or trains of varying intensity, the procedure yields intensity-response functions (based on RC, figure 2) and measures of wave shape variability (based on R1, figure 2). To measure variability, product-moment correlations be-
between corresponding data points of the five R1 SEPs were obtained for two epochs: 15 to 100 and 101 to 200 msec. The coefficients were Z-transformed to give a normally distributed "similarity index" (Zr), amenable to statistical analysis. Figure 3 shows sample tracings from two subjects; note that variability was different for the 15 to 100 and 101 to 200 msec epochs.

Description and Interpretation of Early Evoked Potentials

The notation used here to designate EP peaks will be that of polarity and the usual latency; for example, a scalp-negative peak commonly occurring at 20 msec will be designated as N20.

Figure 1. Normal somatosensory evoked potential (SEP) recovery function

Somatosensory Evoked Potentials (SEPs)

Much of the work with SEPs performed in our laboratory was done with bipolar recordings; these have the advantage of containing less "noise," and it is probable that they yield reasonably accurate quantitative relationships for recovery and intensity-response functions. Bipolar recordings do not, however, give an accurate picture of the true forms of potentials at each of the two scalp electrodes. The tracing obtained between lead 5 and the linked ears in figure 4 agrees well with the general description of the early SEP given by Allison et al. (in press). Peaks a to g can be designated as P15, N20, P25, P30, N35, P45, and N65. It will be seen that P30 is not visible in lead 6, which is anterior to the central sulcus.

Note.—Tracings at the left show SEPs to paired "conditioning" and "test" stimuli at varying intervals. Relative positivity at posterior lead gives upward deflection. Amplitudes were measured from T1 to P1 and from T2 to P2 to yield the recovery curve on the right. Recovery is expressed as the ratio of amplitudes, second divided by first SEP; corrections were made for overlapping effects of the first response.
The neural origin of early SEP components has been elegantly reviewed by Allison, et al. (in press). They integrated scalp EP data with results obtained from direct cortical recordings made in patients undergoing neurosurgery and in animal studies. Their main conclusions may be summarized as follows:

- **P15** is a potential generated by the ascending afferent volley in cerebral lemniscal pathways. It corresponds to the large positive potential recorded in or near the ventroposterolateral (VPL) nucleus of the thalamus. The evidence suggests that P15 is scalp recording of some combination of lemniscal inflow to VPL, synaptic events in VPL itself, and the ensuing thalamocortical volley. P15 has a very widespread, but slightly contralateral, scalp distribution, which is compatible with the assumption of a spatially extended deep source; in essence, it is a "far-field" potential.

- The potentials immediately following P15, and occurring over contralateral scalp—namely N20, P25, and P30—must reflect initial cortical activity, or the primary SEP. Direct cortical recordings suggest the existence of two separate generators in the postcentral gyrus. One generator is located in the posterior bank of the central sulcus; it gives rise to the N20-P30 SEP in the posterior electrode and the phase-reversed P20-N30 SEP in an anterior lead. The second generator is located in the anterior portion of the crown of the postcentral gyrus near the central sulcus; it produces the P25-N35 complex recorded from a restricted region of the crown of the postcentral gyrus. Because the P25-N35 generator is oriented upward, it may not be recorded unless leads are properly positioned. On the other hand, the N20-P30 generator in the posterior bank of the central sulcus is oriented anteroposteriorly and will be picked up from a relatively wide area. This explanation of the N20-P30 generator accounts for the fact that amplitudes are greatest over the posterior parietal area (figure 4). The presence of two functionally distinct regions of the primary somatic cortex has been demonstrated in the monkey.

- The origin of P45 remains unclear; it does not appear to reverse in polarity across the central sulcus; although it is a contralateral event, it is perhaps generated in a rather diffuse region of somatomotor cortex.

Uncertainty also surrounds the origins of N65 which, although found only in cortex contralateral to the stimulated nerve, also does not reverse in polarity.

**Figure 2.** SEP obtained in two averaging sequences with the modified recovery function procedure

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**Note.**—Test stimulus, 10 mA above threshold. Relative positivity at posterior electrode gives upward deflection. R1 is average with 50 stimuli of test intensity. RC is average response to 50 stimuli of conditioning intensity. R2 is response to 50 paired conditioning and 50 test stimuli (interstimulus interval, 10 msec) minus 50 RC. R10 is response to 50 trains composed of 9 conditioning stimuli and 1 test stimulus (interval between stimuli, 10 msec) minus 50 trains of 9 conditioning stimuli. Initial negative deflection (N20) is designated as peak 1. Note suppression of R2 and R10 with 10 mA conditioning stimuli and slight augmentation of R2 and R10 with threshold conditioning stimuli.
Auditory Evoked Potentials (AEPs)

The early AEP contains a large number of distinct events. Those occurring within the first 9 or 10 msec have been designated as P2, N2, P3, P4, P5, P6, P7, and P9 by Goff et al. (1976); they correspond to peaks I to VII of Picton et al. (1974) (figure 5). In addition, N2 is a consistent definite event between P2 (I) and P3 (II). Peaks P2 to P6 do not change during sleep (Amadeo and Shagass 1973a) and are little affected by thionental anesthesia (Goff et al., in press). These findings favor the view that P2 to P6 are lemniscal in origin; P7 and P9 were more affected by anesthesia (Goff et al. 1976). Buchwald and Huang (1975) performed a series of lesions in the cat to locate the generators of peaks corresponding to P2 to P6. Their results indicate the following sources: P2, acoustic nerve; P3, cochlear nucleus; P4, neurons of the superior olivary complex, activated by projections crossing the midline; P5, neurons of the ventral nucleus of the lateral lemniscus and preolivary region, activated equally by crossed and uncrossed projections; P6, neurons of the inferior colliculus, activated primarily by crossed projections.

Goff et al. (in press) consider potentials N15 and P20 to be myogenic, originating in the posterior ear musculature. They were not successful in their attempts to demonstrate that any of the scalp-recorded AEP components reflects the primary response in auditory cortex. P12 and P25 (Po and Pa, figure 5), which could be considered candidates, were both suppressed or abolished by barbiturate anesthesia, and P25 showed no phase reversal in depth recordings. However, P25 and P50 (P1, figure 5) are considered neurogenic, since they were recorded from the depth.

Visual Evoked Potentials (VEPs)

VEPs are sensitive to many stimulus characteristics, such as intensity, color, pattern, and contrast (Regan 1972). Ciganek's (1961) description of the VEP to flash has been generally adopted. His peaks I to IV can be described as N40, P53, N73, and P94. In our own VEP studies, possibly because of brighter stimuli, the first peaks were N32, P46, and N65 (Shagass and Schwartz 1965). Ciganek considered N40, P53, and N73 to be the primary response, but this formulation was disputed by Bergamini and Bergamasco (1967), who concluded that the low amplitude P20-P25 wave recorded by Cobb and Dawson (1960) was probably the true primary VEP. With pattern stimuli, possibly because of lower luminance, VEP latencies are generally longer. Jeffreys and Axford (1972a and 1972b) have described an initial component (CI) with a latency of 65–80 msec and a

Note.—Each SEP is average of 50 sweeps with stimulus 10 mA above threshold. Vertical lines in middle of tracings at 100 msec from stimulus. Zr values, based on product-moment correlation coefficients between corresponding data points in the records, are shown at bottom. Note lack of correspondence between the Zr values for the two epochs.
Figure 4. SEP to right (broken line) and left (continuous line) median nerve stimuli

Note.—Scalp leads referred to linked ear reference. Five μV square wave calibration signal precedes stimulus marker. Upward deflection reflects positivity at scalp. Note that early SEP occurs mainly in contralateral hemisphere.

second component (CII) at 90–100 msec; they adduced evidence that CI is of striate cortical origin and that CII is extrastriate. Both are greatly influenced by the retinal location of the stimulus, and are of different polarity according to whether the stimulus is in the upper or lower half-field. By stimulating the right or left visual field with the brief appearance of a checkerboard pattern, markedly lateralized VEPs can be demonstrated (Shagass, Amadeo, and Roemer 1976).

Psychiatric Correlates

SEP

Unpaired Stimuli

With several intensities of median nerve shock, early SEP amplitude and the intensity-response function slope were generally greater in psychiatric patients than in controls (Shagass and Schwartz 1963a and 1963c). Among patient groups, amplitudes were similar to normal only in those with dysthymic neuroses, characterized by anxiety, depression, and somatic complaints. The finding of generally greater early SEP amplitude in patients was not confirmed within the context of a subsequent recovery function study with only one stimulus intensity (Shagass 1968). Recently, however, Ikuta (1974) reported greater early SEP amplitudes in schizophrenics than in normals, and we have replicated some of the earlier intensity-response findings with the modified recovery function procedure. We found the early SEP (up to 100 msec) to be of significantly greater amplitude in patients with chronic undifferentiated, chronic paranoid, and schizoaffective subtypes of schizophrenia than in normals or in patients with acute or latent schizophrenic subtypes (Shagass, Overton, and Straumanis 1974). Mean intensity-response curves of age- and sex-matched chronic and acute schizophrenics and nonpatients are shown in figure 6.

Wave shape variability was assessed as in figure 3. During the 15–100 msec epoch, variability was lower in chronic schizophrenic patients than in normals, non-psychotic patients, or acute schizophrenics (Shagass 1973a and 1973c). Although variability is correlated
Figure 5. Identification of the auditory evoked potential (AEP) components

Note.—A: AEPs to 60 dB clicks presented monaurally at a rate of 1/sec. Each tracing represents the average of 1,024 responses from vertex-mastoid electrodes. Averaging was done using three separate time bases. B: Diagrammatic representation of AEP components plotted on logarithmic scales. Mean data for eight subjects.


with amplitude, differences between groups persisted after statistical adjustments were made for amplitude differences, indicating an independent variability factor. Trends toward less than normal variability in the 15-100 msec epoch were also found in major depressions of manic-depressive or psychotic depressive type, and in the schizoaffective subtype of schizophrenia, but differences did not reach statistical significance. The opposite trend was found in manic patients, who showed significantly greater early SEP variability than matched controls.

SEP modified recovery function test findings were also evaluated with respect to Brief Psychiatric Rating Scale (BPRS) ratings (Overall and Gorham 1962) in a heterogeneous sample of 67 schizophrenic patients (Shagass et al. 1974). Amplitudes during the first 100 msec of the SEP were lower, and wave shape variability was greater, in patients who rated high on depression and low on the other psychopathology scales, such as hallucinatory activity; conversely, higher amplitudes and lower variability were found in patients who rated low on depression and high on other scales. Figure 7 shows distributions of the wave shape similarity index during the 15-100 msec epoch in matched groups, divided at the median BPRS depression rating and the total of the ratings. Although SEP variability was lower during the first 100 msec in the more psychotic and chronic schizophrenics, variability after 100 msec was greater, a finding in accord with the results of studies employing other stimulus modalities (Callaway, Jones, and Layne 1965, Cohen 1973, and Lifshitz 1969). The SEP differences between more depressed, less psychotic schizophrenics and less depressed, more psychotic schizophrenics appear to provide a neurophysiological parallel of Overall and Klett's (1972) "schizo-depressive contrast function."

Recovery Functions

In three consecutive series, we found amplitude recovery of early SEP components, particularly N20-P30, to be generally reduced from normal in psychiatric patients (Shagass and Schwartz 1962a and 1963b and Shagass 1968). The initial phase of recovery, which takes place during the first 20 msec (figure 1), was attenuated or delayed in patients with schizophrenias, psychotic depressions, and personality disorders. In dysthymic neuroses, recovery was similar to normal in one series, and intermediate between that of nonpatients and the
Figure 6. Mean intensity-response curves obtained with modified SEP recovery function procedure

Note.—Measurements were obtained in age- and sex-matched chronic and acute schizophrenic patients and nonpatients, and are based on average deviation about the 15-30 msec epoch mean. Log transforms of amplitude are employed to normalize distributions.

other diagnostic groups in another series. In developing the modified recovery function procedure, we hoped to obtain greater diagnostic specificity; however, the measures of recovery with the modified procedure provided fewer significant results than those based on responses to single stimuli (Shagass, Overton, and Straumanis 1974 and Shagass et al. 1974). Following the observation that psychotic depreesives were among those patients displaying reduced N20-P30 SEP amplitude recovery, serial studies were conducted on a group of patients undergoing electroconvulsive therapy (Shagass and Schwartz 1962a). The results indicated that effective treatment of severe depressions tended to normalize SEP recovery, thus demonstrating that reduced recovery in depression is a state- rather than a trait-related phenomenon. These results in depression also indicate that reduced SEP recovery is not due to the patients' possibly lower intellectual level, as suggested by the findings of Wasman and Gluck (1975) in slow learners.

SEP latency recovery has been investigated in two series (Shagass 1968 and Shagass, Overton, and Straumanis 1974), yielding findings apparently opposite to those with amplitude recovery. With brief interstimulus intervals, the latency of the test response tends to be prolonged, and recovery from this prolongation occurred more rapidly in patients than in nonpatients. Augmented latency recovery was manifest only with the most intense of the conditioning stimuli employed in the modified procedure and was found particularly in chronic schizo-

Figure 7. Distribution of wave shape similarity index for 15 to 100 msec epoch in schizophrenics

BPRS RATINGS

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Note.—Schizophrenic patients were divided according to high and low BPRS ratings on depressive mood and the total of the other 15 ratings. Dotted line in center of each distribution indicates median value for the whole group. Similarity measures were low in patients with high ratings of depression, and high in patients with high total BPRS minus depression scores.
phrenic and manic-depressive, depressed patients.

Interpretation of the recovery function as a measure of cortical excitability has recently received some support from the work of Begleiter, Porjesz, and Yerre-Grubstein (1974), who studied SEP recovery during experimental alcoholization and withdrawal. They showed that SEP recovery increased during alcohol withdrawal. Conversely, it seems reasonable to infer that reduced recovery reflects inhibition of cortical excitability.

Some Psychoactive Drug Effects

The effects of psychoactive drugs on EPs have been recently reviewed (Shagass 1974). A few effects on early EPs will be considered here.

**Lithium.** Heninger (1969) reported that lithium carbonate (Li) increased N20-P30 SEP amplitude. We have confirmed and extended Heninger's findings with the modified recovery procedure (Shagass, Straumanis, and Overton 1973). In addition to amplitude increase during the 15-50 msec epoch, amplitude recovery was markedly augmented with threshold conditioning stimuli, while there was a tendency for relatively less recovery with high intensity conditioning stimuli. The combination of facilitation and suppression, depending upon conditioning stimulus intensity, suggested that lithium increases the dynamic range of cortical responsiveness (Shagass 1973a). When the data were further analyzed by digitally filtering the SEP into two frequency bands, 4-28 and 32-500 Hz, it was shown that SEP amplitude augmentation with Li took place entirely within the fast (32-500 Hz) band.

Heninger (in press) has recently reported additional evidence that Li affects mainly the P30 SEP component; he also found significant correlations between the SEP changes, increase in EEG 4-7 Hz activity, and slowing of psychomotor test performance (e.g., prolongation of reaction time). He drew attention to data in cat and monkey, which indicate that the main effect of Li is at the level of the first cortical synapses; changes were not observed at the thalamic level. Therefore, it appears that the early cortical SEP reflects a relatively specific neuro-psychological change brought about by a major psychoactive agent.

**Antidepressants.** In depressed patients with greater than normal early SEP amplitude, imipramine tended to produce amplitude reduction, although the opposite effect was found in normal subjects given therapeutic doses of this drug (Shagass, Schwartz, and Amadeo 1962). Recently, the effect of amitriptyline was studied with the modified SEP recovery procedure (Shagass, Straumanis, and Overton 1973). Amitriptyline reduced amplitude, and digital filtering showed that the amplitude reduction took place over the entire frequency range of the SEP. Although the amplitude changes with Li and amitriptyline were opposite during the 15-50 msec epoch, other effects of these two agents were different, rather than opposite.

**Antipsychotic drugs.** Saletu et al. (1971a and 1971b) found that both fluphenazine and thiothixene reduced amplitude of the N20-P30 SEP component in schizophrenic patients. However, when chlorpromazine, 50 mg, was given in a single dose to nonpatient volunteers, the opposite effect (i.e., amplitude increase) was found (Saletu, Saletu, and Itil 1972). This suggests a parallel to the opposite EP effects found with tricyclic antidepressants in depressed patients and normals (Shagass, Schwartz, and Amadeo 1962). Although there appears to be great variability in SEP change with antipsychotics, this may be of clinical significance, since the SEPs of the patients with favorable clinical response were altered by antipsychotic drugs, whereas those of patients who showed little or no clinical response displayed little SEP change (Saletu et al. 1971a, 1971b, and 1971c and Shagass 1973a).

**AEP**

The P50 peak is virtually the only early AEP event that has been studied in psychiatric patients. Saletu, Itil, and Saletu (1971) found that P50 latency was shorter in chronic schizophrenics than in nonpatients; faster latencies were observed in those patients with evidence of thought disorder. They also found lower amplitudes between P50 and N100 in the schizophrenics, but this difference was contributed mainly by N100. Itil et al. (1974) have studied the AEP in children, 10-12 years old, at high risk for schizophrenia (schizophrenic parent). AEP latencies in the high risk children were generally shorter than those of controls; although most differences did not achieve statistical significance, one peak occurring before 40 msec did so. No amplitude differences were found. The authors drew attention to the similarity between AEP latency results in high risk children, psychotic children, and chronic schizophrenics.
Heninger (1976) found that Li increased early AEP as well as SEP amplitudes, but that the ion did not modify VEP.

**VEP**

Flash VEP amplitudes were found to be greater and latencies shorter than those of nonpatients in a heterogeneous group of psychiatric patients (Shagass and Schwartz 1965 and Shagass, Schwartz, and Krishnamoorti 1965). Schizophrenic patients tended to have faster P45 latencies than other subjects, while their VEP amplitudes were lower than those of nonpsychotic patients. These findings were not replicated by Speck, Dim, and Mercer (1966) and Floris et al. (1967), whose patient populations were composed mainly of schizophrenics. Vasconetto, Floris, and Morocutti (1971) found VEP differences between schizophrenic patients and normals, consisting of lower amplitude P100 and shortened latency of N150 in the patients; they also found that patients with endogenous depression had greater amplitudes of N70 and N150 than normals. Since Rodin, Grisell, and Gottlieb (1968) had shown that their early results in schizophrenics (Rodin et al. 1964) were greatly influenced by failure to immobilize the pupil, it is possible that variable VEP findings in psychiatric patients may reflect failure to control for this factor.

Perris (1974) compared the maximum amplitude occurring between the first three VEP peaks (i.e., to N70) in right and left occipital recordings. Patients with psychotic types of depression showed greater asymmetry, with reduced amplitude on the left side, than patients with neurotic depressions or schizophrenias. Following treatment with antidepressant drugs, the asymmetries tended to be reversed. Perris' results suggest relative impairment of left hemisphere function in psychotic depressions.

Our study of VEP recovery yielded largely negative results, although we did find delayed recovery of N32 latency in patients, particularly in nonpsychotic categories. Speck, Dim, and Mercer (1966) reported reduced recovery of N70 in schizophrenic patients, and Heninger and Speck (1966) showed that reduction of psychopathology with antipsychotic drugs was correlated with normalization of N70 recovery. Floris et al. (1967, 1968, and 1969) also found that VEP amplitude recovery was significantly reduced in schizophrenic patients.

Vasconetto, Floris, and Morocutti (1971) later showed that recovery of N70 was reduced also in both neurotically and psychotically depressed patients, but the reduction was less in the psychotically depressed. Ishikawa (1968) compared VEP recovery in schizophrenics and normals and found that those schizophrenic patients with abnormally delayed recovery were characterized by hallucinations.

**A Hypothesis About Chronic Schizophrenia**

I have recently attempted to formulate a hypothesis based on analysis of the available EP findings in chronic schizophrenia (Shagass 1976). In chronic patients, as contrasted with schizophrenics of other subtypes, and with normals, all late EP events tend to be attenuated and more variable. In contrast, early EP events tend to be of greater amplitude and less variable, or to have a shorter latency. I have proposed that these differences from normal in early EP events reflect impaired functioning of filtering mechanisms, designed to regulate sensory input so that later processing of sensory information may be carried out effectively. The attenuated, and more variable, later EP events would reflect defective functioning of information processing mechanisms, resulting from inadequate filtering of the initial input. Although the exact nature of the filtering mechanism that may be impaired in chronic schizophrenia is not known, EP changes similar to those found in chronic schizophrenic patients can be brought about by experimentally reducing the level of activation in septal region and mesencephalic reticular formation (Schwartz and Shagass 1963 and Shagass and Ando 1970). There are also similarities between the deviations from normal in EPs of chronic schizophrenics and the changes that take place in sleep (Shagass and Trusty 1966 and Amadeo and Shagass 1973b), and EEG frequency is lower than normal in chronic schizophrenics (Shagass 1976). These facts led to the hypothesis that subcortical mechanisms involved in regulating sensory input are underactivated in chronic schizophrenia.

**Conclusion**

Investigation of early EP events has yielded a number of correlates of psychopathology and revealed changes with psychoactive drugs that may be pertinent to
understanding their central effects. Since the equivalents of early EP events in man can be readily identified in animals, positive results from clinical psychiatric studies can guide focused animal investigations on neurophysiological mechanisms in mental illness. The EP correlates promise to provide neurophysiological models, which could help to bridge the gap between clinical and neurochemical phenomena. Awareness of these possibilities should encourage more intensive psychiatric research on early EP phenomena.

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The Author

Charles Shagass, M.D., is Professor of Psychiatry, Temple University Medical Center, and Chief of Temple Clinical Services, Eastern Pennsylvania Psychiatric Institute, Philadelphia, Pa.