Reprinted from the Archives of General Psychiatry
December 1967, Volume 17

Cortical Evoked Potentials and Psychopathology

A Critical Review

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THE ESTABLISHMENT of brain-evoked potentials as a valid technique for tapping cerebral responses to specific stimuli has created frenzied attempts to relate it to many areas of research, not always appropriately. Many researchers have been investigating the possibility that the averaged evoked response might elucidate and differentiate mechanisms involved in psychopathology, and as a result, a wealth of evidence has been amassed relating various aspects of psychopathology to the cortical evoked response.

In this paper, no attempt has been made to present an exhaustive review of the literature. Our purpose is to give a critical review of selected experiments from the current literature, attempting to integrate and compare them, and emphasizing the need for further controls in experimental design wherever necessary.

In 1960 Shagass and Schwartz began to study evoked potentials in psychiatric patients, hoping to provide psychiatrically relevant measures of cerebral responsiveness. Most of their work has dealt with the somatosensory potential evoked by electrical stimulation over the ulnar nerve at the wrist. So far they have studied two measures of responsiveness based on amplitude: (1) the intensity-response gradient and (2) the recovery cycle, determined by the method of paired "conditioning" and "test" stimuli, using supramaximal intensities. Shagass and Schwartz[1-5] found that in a heterogeneous psychiatric population, two characteristics of the response differed significantly from normal. Evoked potentials in patients were of greater amplitude and their recovery, as measured by comparing responses to conditioning and test stimuli, was less during the first 20 msec of the recovery cycle. In a later experiment, Shagass and Schwartz[6] attempted to determine whether similar relationships prevail for cerebral responses evoked through the visual modality. They found that nonpatients differed significantly from the entire heterogeneous psychiatric patient group in having a smaller amplitude of one of the initial components, faster recovery of the initial latency, and more "ringing." Thus, it may be said that the general trend of the findings was in accord with expectations from their previous studies of somatosensory responses. It should be noted that these findings are in direct contradiction to those of Rodin,[7] who found the amplitudes of the visual evoked potentials to be lower in chronic schizophrenics than in nonpatients.

Toxic disturbances of perception in delirium tremens have been thought to play a significant role in the formation of hallucinations. As a result, Gross et al[8] undertook the study of evoked responses to clicks during episodes of delirium tremens. They hypothesized that patients in delirium tremens would manifest an acute disturbance of the response to acoustic stimuli, and that there would be a correlation between this disturbance and the formation of auditory hallucinations. In this experiment average evoked potentials to 700 clicks were obtained for all four patients. All subjects were tested over a period of several days subsequent to admission in the hospital. The most interesting findings are those which show the striking relationship between hallucinatory activity and the amplitudes of the auditory evoked response. Since the clinical course of these patients was studied rather carefully, it was

Submitted for publication June 26, 1967.
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found that the evoked potentials recorded when hallucinations were present were consistently lower than those recorded when hallucinations were not present. Furthermore, it was observed that as the patients improved their evoked responses recovered. It is not known how many of these findings are due to a specific blood-alcohol level, or to such manifestations of withdrawal as tremulousness. In a subsequent study Gross et al[9] established that alcohol affects the auditory evoked response in man. They found that amplitudes were significantly reduced, with maximal effect observed at 15 to 30 minutes after ingestion. In the dosage used there was no significant change in the latencies.

Callaway et al[10] conducted an experiment on evoked responses and segmental set in schizophrenics. The differences in potentials evoked by two trivially different tones were used to assess degree of preoccupation with ordinarily disregarded details. In this study "set" refers to the operational strategy adopted by an individual for categorizing sensory inputs and for directing action. Schizophrenics establish multiple enduring minor sets.

The tendency to form multiple, broken, disarticulated approaches is referred to as "segmental set." Three groups of subjects were used as follows: 32 schizophrenic patients, 25 nonpatients, and 20 miscellaneous nonschizophrenic patients. Four pairs of averaged evoked responses were collected from each subject. Each pair of evoked responses consisted of an averaged evoked response to forty 1,000-cps tones and to forty 600-cps tones. The tones were presented in a random pattern at a comfortable sound level of about 70 db above standard reference. The interval between tones varied from 0.75 to 3.0 seconds. The digital output of average transients from the computer was used to compute a Pearson product-moment correlation coefficient between the values at the 200 ordinates of the evoked response averaged for all 160 high tones, and comparable values for the low-tone evoked responses. The authors predicted that schizophrenics would manifest a reduced similarity between averaged responses evoked by the two tones. The mean correlations of coefficients were 0.873 for the schizophrenic patients, 0.942 for the nonschizophrenic patients, and 0.952 for the nonpatients. The prediction was confirmed. The results of this study are somewhat unclear, since all but six patients had received phenothiazine drugs in the recent past or were on moderate doses of phenothiazines at the time of testing. Furthermore, it should be noted that the reduced similarity between the forms of the pair of evoked responses found in the schizophrenic patients may be accounted for by greater variability of the responses. The authors should have obtained the averaged evoked response to the same tone on two different occasions for all groups. If no differences could be found between evoked responses across the various groups, it seems that a stronger case would be made for the segmental set explanation.

Jones et al[11] used the averaged auditory evoked response recorded from scalp electrodes as a neurophysiological measure of perceptual performance in schizophrenic patients. In this study the authors used a correlation coefficient as an index of the difference between an averaged evoked response to a series of 600-cps tones and a response to several 1,000-cps tones. The technique is exactly the same as the one reported in the study described above. They postulated that nonpatients would have almost identical averaged evoked responses to two physically different tones, since no specific psychological distinction could be made between the tones. However, the schizophrenics preoccupied with "trivial" details of their environment and having difficulty separating relevant and irrelevant stimuli do give some attention to the small physical distinction between the tones. As a result, the authors hypothesized that their two averaged evoked responses would be quite different. These predictions were confirmed. In a recent study by Jones et al[12] the identical technique, as described above, was utilized. In this study 18 newly admitted schizophrenic patients were studied. The clinical state of each patient was assessed in two ways: daily, with three nurses rating each patient, using nurses' ratings of ward behavior, and weekly, in clinical interviews done by the authors. It should be noted that no data are presented on the interjudge reliability of these clinical ratings. The general results indicate that disordered speech and high levels of anxiety tend to be associated

with lower two-tone evoked response correlations. Effective general functioning is associated with high evoked response correlations. Patients characterized by incoherent delusional talk tended to have low evoked response correlations, whereas those with coherent organized delusions tended to have high evoked response correlations. The authors conclude that the two-tone evoked response correlation is sensitive to clinical change and may be of value in the assessment of change during the course of schizophrenia. It appears to reflect the current state psychological functioning rather than some underlying factor or permanent characteristic of schizophrenic patients. It should be noted that in this study the majority of patients received 20 to 60 mg of trifluoperazine daily, 1 to 4 mg of benztropine daily, and barbiturates. Three patients had electroshock therapy during the course of the study. The authors do not make explicit the relationship between the course of improvement and dosage of drug given, as a result the relationship between drug dosage and evoked response is unknown. Furthermore, it is quite possible that the lower correlations in the schizophrenic patients may be due to a greater state-specific variability in level of functioning. This greater variability of evoked responses in schizophrenics is reported independently in the following study.

Speck et al[13] investigated the input-output relationships for psychiatric patients and nonpatient groups using flashes of light as discrete units of information. The patient group consisted of 71 psychiatric patients with varied diagnosis; the control group consisted of 41 nonpatients. Several series of light flashes were presented, both singly and in pairs, to the closed eyes of all reclining subjects. The patients showed a decrease of amplitude in response to paired flashes as compared to single flashes, whereas the nonpatients showed an increase. There was no significant difference in the mean latencies between the schizophrenic group and the nonpatient group. Recovery functions were calculated for all subjects. This function is obtained by using two stimuli of equal intensity separated by graded time intervals. The comparison between the amplitudes of the responses as a function of time yielded the recovery function curve. It is generally considered that this function is related to the excitability of a local neuronal population. The nonpatients showed a supernormal phase in their recovery function curve at 35 msec, followed by a subnormal response and again a supernormal response at 100 msec. The patients had a subnormal response at 35 msec, which continued until the 100 msec range was reached, where it also became supernormal. In this study the nonpatient group showed significantly less variability. It is quite conceivable that this finding could account for the results obtained by Callaway et al.[1] Seven of the patients were classified as depressives and were, on the average, older than the schizophrenic and nonpatient groups. The authors found that the latencies of response obtained from the depressive patients were longer than the latencies from schizophrenic patients and nonpatients. It should be noted that in comparing the amplitudes of the responses given by the depressive patients to those of the other two groups, the authors used a two-tailed test in their statistical analysis; the results were not significant. However, in comparing the latencies of responses given by depressives to those of schizophrenic and nonpatients, the authors used a one-tailed test of significance and the results reached the 5% level of significance. On the basis of this finding the authors invoke a cybernetic model, and conclude that the information-transmitting channels may be slowed in depressive patients.

Conclusion

In conclusion, it seems quite premature to assess the applicability of the evoked response to psychopathology for clinical purposes. So far the results obtained are often divergent and tenuous. Unfortunately, the complex nature of the subject matter of psychopathology does not easily lend itself to rigorously controlled experimentation.

Classification of patients is a major problem. The significance of differences between "patients" and "nonpatients," apart from reflecting the effects of hospitalization per se, is difficult to assess. On the other hand, studies of specific patient samples in which the psychiatric classification is based upon

clinical diagnosis without explicit criteria and without interjudge reliability is also a serious limitation of interpretation. The inherent difficulties involved in experimentally dealing with psychopathological problems, where therapeutic treatment must necessarily continue, makes carefully controlled investigation almost impossible. For this reason, in many studies the effects of treatment (eg, drugs, psychotherapy, electroshock, etc) remain unknown and uncontrolled—clouding the possibility of a clear interpretation of the results. In certain cases in which drugs are administered, blood level and biochemical analyses would seem to be important, but are omitted. Furthermore, the specific effects of drugs on the evoked responses of normals is frequently overlooked or not investigated. In the last analysis, due to the many flaws and problems in the methodological framework, great caution is suggested in interpreting the results obtained in this fast growing area of research.

Summary

At present, no clear conclusions can be drawn about the utilization of evoked potentials as a criterion for differentiating psychological disturbance from "normal" functioning. Due to the complexity of the problems investigated, many variables were found to be uncontrolled by the experimental designs. It remains for future research, with refinements in techniques and methodology, to determine to what extent this approach will be of value to studies of psychopathology.

Generic and Trade Names of Drugs

Trifluoperazine (HCl)—*Stelazine (HCl)*.
Benzotropine—*Cogentin*.

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