Brit. J. Psychiat. (1983), **142,** 152–155

Visual Evoked Potentials in Schizophrenia

Intensity Effects and Hemispheric Asymmetry

J. F. CONNOLLY, J. H. GRUZELIER, R. MANCHANDA and S. R. HIRSCH

Summary: Visual evoked potentials (VEP) to different flash intensities were recorded at a central site (Cz) plus at homologous temporal and occipital locations in normal and unmedicated schizophrenic subjects. Schizophrenic patients showed an hemisphere asymmetry of the P100-N120 peak-trough amplitude with smaller left but larger right hemisphere amplitudes than normal. Further, two subgroups of patients were found with abnormalities lateralized to the left hemisphere. One group was found to have abnormal P100 amplitude-intensity patterns at the left temporal site while the other group showed deviant N120 amplitude-intensity patterns at the left occipital location. The clinical significance of these results can be seen in the higher nuclear schizophrenia (PSE-CATEGO) scores in the left temporal subgroup and the higher hypomania and situational anxiety scores in the left occipital group. Patients also showed slower than normal P100 and N120 peak latencies.

It is well known that the amplitude of the visual evoked potential (VEP) to flash stimuli does not necessarily increase monotonically with increments in stimulus intensity (e.g. Tepas and Armington, 1962). Subjects whose VEP amplitude increases with stimulus intensity have been labelled Augmenters, while those whose amplitudes fail to increase have been called Reducers. This terminology arose after a relationship was found between VEP amplitude and Petrie's (1967) finding that subjects could be classified as Augmenters (A) or Reducers (R) according to whether they characteristically over or underestimated stimulus size in the tests of kinesthetic figural after effect (Buchsbaum and Silverman, 1968). Since that time, the VEP augmenting-reducing phenomenon has been linked to among other things, acute schizophrenia (Landau *et al*, 1975), the paranoid dimension in schizophrenia (Schooler *et al*, 1976), manic-depressive illness and treatment outcome (Buchsbaum *et al*, 1971) and MAO levels in unipolar and bipolar depression (Buchsbaum *et al*, 1973).

Recently, however, it has been demonstrated that the basis of the VEP augmenting-reducing paradigm is unsound being the result of artefacts produced by methodological shortcomings (Connolly and Gruzelier, 1982a) and misconceptions concerning the stability of the phenomenon (Connolly, 1980). Furthermore, these problems of method have been shown to be exacerbated in schizophrenic patients due to abnormalities in VEP, notably in their peak latencies, which fail to meet the assumptions of the customary VEP augmenting-reducing methods (Connolly and Gruzelier, 1982b). Thus, the relationship between VEP augmenting-reducing and psychopathology must be considered unproven such that the VEP amplitude and latency characteristics of schizophrenic patients in response to changes in stimulus intensity remain an open question. As a consequence this paper reports VEP amplitude and latency data in response to changes in stimulus intensity without reference to the concept of augmenting/reducing.

The second major issue which this paper addresses is the question of whether any VEP abnormalities found in schizophrenia are lateralized to one or other brain hemisphere. Since the original work of Flor-Henry (1969) much research has concentrated on lateralized abnormalities in psychiatric diseases (see Gruzelier, 1981). Thus VEP amplitude-intensity data was collected from lateral sites over temporal and occipital regions as well as the conventional midline site.

This experiment's objective therefore was to assess the features of VEP amplitude-intensity patterns in schizophrenia and further, to determine if VEP hemisphere symmetry in normal subjects also characterized unmedicated schizophrenic patients.

Methods and Subjects

Twenty-two healthy volunteers (11 men and 11 women) and 16 unmedicated schizophrenic patients (11 men and 5 women) were tested. Patients received

no psychoactive medication for at least three months prior to testing and were characterized by one or more florid symptoms (delusions, hallucinations or thought disorder). All 16 patients were diagnosed schizophrenic by two psychiatrists and subsequently received treatment in line with this diagnosis. However, diagnoses were also assessed using the CATEGO criteria of the Present State Examination (PSE) (Wing *et al,* 1974). Twelve patients received diagnoses of Nuclear Schizophrenia (NS), two of Nuclear Schizophrenia/Psychotic Depression (NSPD) and two of ? Paranoid Psychosis/? Affective Psychosis (DP?/AP?). Groups were age-matched; control subjects had a mean of 30.0 years and patients of 31.2 years.

Details of the psychophysiological methods and procedures used are presented in Connolly and Gruzelier (1982a and b). Briefly, subjects were exposed to 6 flash intensities (0.31, 0.65, 1.25, 2.5, 5 and 10 ft lamberts) of 500 msec in duration and an interstimulus interval of 500 msec. EEG was sampled at 250 Hz and was recorded with a bandpass of 1–75 Hz (half-amplitude) using AG/AG C1 electrodes positioned at Cz, T3, T4, 01 and 02 and referenced to linked ears. Subjects were grounded with an electrode on the right arm. Vertical and horizontal eye movements (EOG) were recorded (Connolly and Kleinman, 1978). EOG was not found to be correlated with stimulus intensity and no subject lost more than 15 per cent of the 360 stimulus presentations due to eye movements.

Peak-to-trough amplitudes for the P100-N120 and N120-P200 waveforms were measured as were the amplitudes of the P100, N120 and P200 peaks (measured from the prestimulus baseline to peak). Latency of each of these three peaks from stimulus onset was also measured.

Results were analysed with analysis of variance (ANOVA) for repeated measures and the Newman-Keuls test. Stimulus intensity and electrode location were within-subject factors while the between-subject factor was the normal/schizophrenic distinction.

Results

The results have been divided into two major sections concerned with amplitudes and latencies respectively.

Amplitudes

The abnormalities found in the VEP amplitudes of schizophrenic patients were primarily concerned with amplitude/intensity patterns at left hemisphere recording sites and hemispheric imbalances.

A Diagnosis×Hemisphere interaction ($P < 0.0515$) for P100-N120 amplitudes was found which as Fig 1 shows was attributable to the hemisphere asymmetry

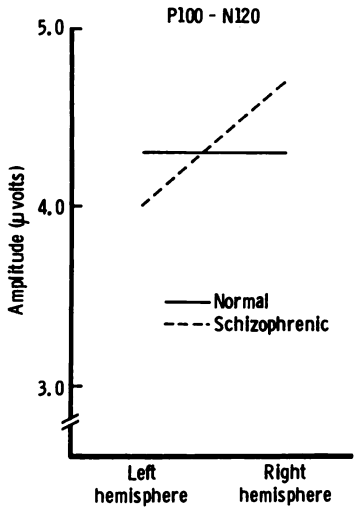

FIG 1.—P100-N120 peak-trough amplitudes of left and right hemisphere sites for control and schizophrenic samples.

of schizophrenic patients with smaller left but larger right hemisphere amplitudes than normal.

Post hoc examination of the P100 amplitude data revealed that normal controls and schizophrenic patients differed in amplitude-intensity patterns at the temporal sites. While only 1/22 of the normal controls showed increasing amplitude-intensity pattern at the left temporal site, 6/16 of the schizophrenic sample did so. At the right temporal location 3/22 of the controls showed an *increasing* pattern in contrast to schizophrenic patients, all of whom showed a *decreasing* pattern. A Fisher Exact Probability test indicated that these amplitude-intensity pattern distributions were significantly different ($P < 0.033$).

The possible clinical significance of this result can be judged by the difference in CATEGO syndromes between the 6 patients showing increasing amplitude-intensity patterns and the 10 patients failing to do so. The 6 patients had higher scores for Nuclear Schizophrenia ($P < 0.05$) ($\bar{x} = 2.83$, SD = 0.41 vs $\bar{x} = 1.40$, SD = 1.27). Five of the six had scores of 3, while only three of the 10 did so.

Post hoc analyses of N120 amplitudes revealed group differences in the hemisphere asymmetry at occipital sites. More patients showed increasing amplitudes to stimulus intensity increments on the left than right side which was opposite to the pattern found in the controls ($P < 0.05$); however, this effect applied to just 4 patients and 5 controls.

Nevertheless as with P100 amplitudes, CATEGO differences were found for patients showing increasing amplitude intensity patterns at the left occipital site;

https://doi.org/10.1192/bjp.142.2.152 Published online by Cambridge University Press

they were characterized by higher scores for Hypomania ($P < 0.05$) ($\bar{x} = 0.80$, SD = 1.30 vs $\bar{x} = 0.00$, SD = 0.00) and Situational Anxiety ($P < 0.05$) ($\bar{x} = 0.18$, SD = 1.64 vs $\bar{x} = 0.18$, SD = 0.60). It should be noted that only one of the patients exhibiting left occipital abnormalities was included in the 6 patients showing the left temporal abnormalities. Three of these patients received NS diagnoses and one DP?/AP?.

Latencies

As with the amplitude data, the latency abnormalities found in the schizophrenic patients centered on the P100 and N120 peaks. The ANOVA revealed Diagnosis effects due to delays of the P100 ($P < 0.02$) and N120 ($P < 0.009$) peaks in the patients (Fig 2). Although the trend was in the same direction, the P200 latencies for the patients were not significantly slower than normal.

Discussion

This experiment has presented data supportive of a left hemisphere abnormality in at least a substantial subgroup of schizophrenic patients together with a more generalized hemispheric imbalance. It has also demonstrated the necessity of recording event-related brain potentials (ERP) from several sites; no findings of any note would have been uncovered by the VEP paradigm used here if topography of the response had not been investigated. In fact, without the topographic analysis the important anterior-posterior dimension would not have been revealed. Related to this is the equally necessary procedure of not only assessing clinical state at the time of testing but also searching for clinical syndromes related to the biological subgroupings obtained. Even in a group of carefully defined schizophrenic patients it would be ill-advised to ignore the possibility of subgrouping and treat the group as a unit throughout all analyses.

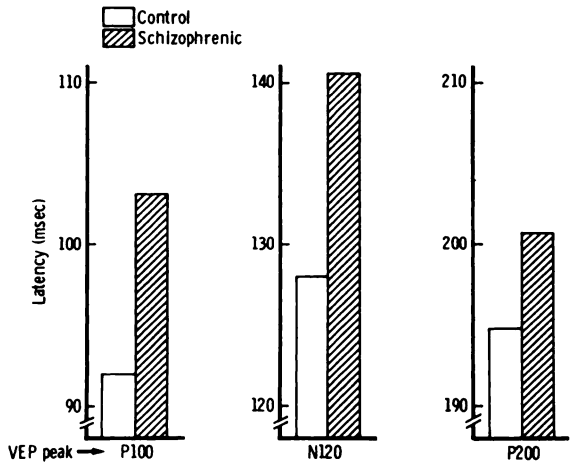

FIG 2.—P100, N120 and P200 peak latencies for control and schizophrenic samples.

The abnormal *increase* in the amplitude of the P100 peak of the VEP at the left temporal site in a subgroup of six patients is noteworthy. What is particularly important is that this biologically-based phenomenon was related to the clinically-based judgement of the severity of the nuclear schizophrenia syndrome. Further support for a left hemisphere abnormality was found in a further four patients at a more posterior site for the N120 peak. Again, this VEP abnormality was found to be related to the severity of syndromes concerned with hypomania and situational anxiety. These results support, in general terms, the left hemisphere abnormalities found in schizophrenia using evoked potential measures (Shagass *et al*, 1979). These results also emphasize the importance of multiple EEG recording sites situated not only laterally but along anterior-posterior lines. Thus, these findings have found left hemisphere VEP abnormalities in 62.5 per cent of a clinically well-defined schizophrenic group. These patients were further divided into those characterized by a nuclear schizophrenia syndrome accompanied by a left temporal abnormality and those typified by more affective features together with a left occipital perturbation.

The asymmetry of the P100-N120 amplitude in the schizophrenic group highlights another major factor in biological research in this area. Firstly, this asymmetry was found in the schizophrenic patients generally. Secondly, the asymmetary could not be attributed solely to a reduced left hemisphere amplitude as the right hemisphere was abnormally increased. Thus, the VEP and a number of amplitude measures of it are capable of producing very different sorts of information. While the schizophrenic group displayed a P100-N120 amplitude asymmetry, the subgroups showed further abnormalities localized to the left hemisphere. Thus the VEP has revealed 'layers' of abnormalities ranging from a general imbalance or asymmetry between the hemispheres to abnormalities associated with clinical syndrome localized to temporal and occipital areas.

The abnormally slow latencies of the schizophrenic group were restricted to the first two peaks (P100 and N120) of the VEP. Evoked potential latency abnormalities have not been consistently demonstrated in schizophrenic patients (see Buchsbaum, 1977). However, in this experiment the latency abnormalities were characteristic of the schizophrenic group rather than subgroups.

In conclusion, sophisticated assessment of simple VEP to light flashes in a schizophrenic patient sample

has revealed abnormalities, some of which are associated with particular clinical syndromes.

Acknowledgements

The authors wish to thank Messrs. C. Sharpe and R. Bond for assistance with computer software and statistical programs.

References

BUCHSBAUM, M. (1977) The middle evoked response components in schizophrenia. *Schizophrenia Bulletin*, **3**, 93–104.

—— GOODWIN, F., MURPHY, D & BORGE, G. (1971) AER in affective disorders. *American Journal of Psychiatry*, **128**, 19–25.

—— LANDAU, S., MURPHY , D. & GOODWIN, F. (1973) Average evoked response in bipolar and unipolar affective disorders: Relationship to sex, age of onset, and monamine oxidase. *Biological Psychiatry*, **7**, 199–212.

—— & SILVERMAN, J. (1968) Stimulus intensity control and the cortical evoked response. *Psychosomatic Medicine*, **30**, 12–22.

CONNOLLY, J. (1980) The influence of passive and task conditions on intensity-related changes in exogenous visual event-related potentials (ERPs). *International Symposium on the Psychological Significance of Event-Related Potentials*, Zeist.

—— & GRUZELIER, J. (1982a) Amplitude and latency changes in the visual evoked potential (VEP) to different stimulus intensities. *Psychophysiology*, in press.

—— —— (1982b) A critical examination of augmenting/reducing methodology in schizophrenic patients and controls. In *Advances in Biological Psychiatry*, vol. 9 (ed. Langnau). Basel: Karger.

—— & KLEINMAN, K. M. (1978) A single channel method for recording vertical and lateral eye movements. *Electroencephalography and Clinical Neurophysiology*, **45**, 128–29.

FLOR-HENRY, P. (1969) Psychosis and temporal lobe epilepsy: a controlled investigation. *Epilepsia*, **10**, 363–95.

GRUZELIER, J. H. (1981) Cerebral laterality and psychopathology: fact and fiction. *Psychological Medicine*, **11**, 219–227.

LANDAU, S. G., BUCHSBAUM, M. S. CARPENTER, W., STRAUSS, J. & SACKS, M. (1975) Schizophrenia and stimulus intensity control. *Archives of General Psychiatry*, **32**, 1239–45.

PETRIE, A. (1967) *Individuality in Pain and Suffering*. Chicago: University of Chicago Press.

SCHOOLER, C., BUCHSBAUM, M. S. & CARPENTER, W. T., JR.(1976) Evoked response and kinesthetic measures of augmenting/reducing in schizophrenics: replications and extensions. *Journal of Nervous and Mental Disease*, **163**, 221–32.

SHAGASS, C., ROEMER, R., STRAUMANIS, J. & AMADEO, M. (1979) Evoked potential evidence of lateralized hemispheric dysfunction in the psychoses. In J. H. Gruzelier and P. Flor-Henry (Eds). *Hemisphere Asymmetries of Function in Psychopathology*, Amsterdam: Elsevier-North Holland.

TEPAS, D. I. & ARMINGTON, J. C. (1962) Properties of evoked visual potentials. *Vision Research*, **2**, 449–61.

WING, J. K., COOPER, J. E. & SARTORIUS, N. (1974) *The measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press.

J. F. Connolly, PH.D., *Wellcome Research Fellow in Mental Health*

J. H. Gruzelier, PH.D, *Senior Lecturer in Psychology*

R. Manchanda, M.D., *Lecturer in Psychiatry*

S. R. Hirsch, M.PHIL., F.R.C.PSYCH., *Professor of Psychiatry*

Department of Psychiatry, Charing Cross Hospital Medical School, 22–24 St Dunstans Road, London W6 8RP

(Received 5 July 1982)