In, "Schizophrenia and Youth", eds. C. Eggers,
Springer-Verlag: Heidelberg, pp 119-123, (1991).

Signs of Differential Stimulus Processing Problems: A Comment on Event-Related Potentials in Young Schizophrenic and Autistic Subjects

R. D. OADES and D. ZERBIN

A number of event-related potentials (ERPs) can be recorded within a second after presentation of a stimulus. If the stimulus is unusual or meaningful, these ERPs represent some important stages in the processing of the information received, for instance matching it with internal representations of similar features.

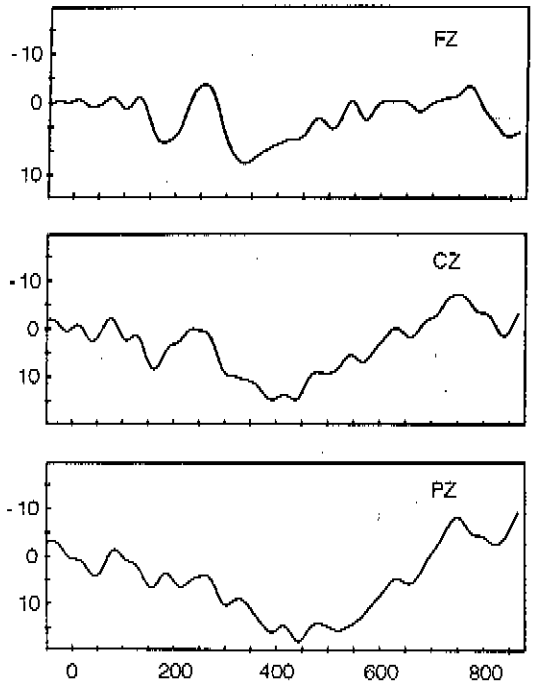
Reports of ERPs in patients with psychiatric illness, as in other fields of study, have too often emphasized one weakness and tried to show that is (to a greater or lesser degree) specific to the syndrome studied. In schizophrenia a reduced P3 amplitude is a case in point. A common alternative strategy is to divide the material studied into two and to show dichotomy of some characteristic (examples in schizophrenia are high vs low dopamine activity, positive vs negative symptoms). In any series of admissions, however, it is clear that although extremes occur, many patients exhibit intermediate levels of a given characteristic and display more than than just one impairment.

Our first purpose here is to suggest that oversimplifications are belied by the range of schizophrenic "states" that are presented in the clinic and that the number of stages of information processing shown by ERPs can and do illustrate a range of items in which a schizophrenic can have problems.

Young schizophrenics – the subject of this volume – have been under-studied in biological psychiatry. This is unfortunate, as the information that could be gained might not only beneficially influence treatment at an early stage of the illness but also, in the absence of years of pharmacological treatment and negative environments, improve our understanding of the basic components of the illness.

One experimental paradigm we use is the three-tone choice reaction time task (ACRT) (Pfefferbaum et al. 1984). Subjects must discriminate between two rare tones [target (T) = 1.4, non-target (NT) = 2.0 KHz, $p = 14\%$ each] and a common standard (S, 0.8 KHz) presented in a Bernouilli sequence. We record topographically from 16 sites (linked ear reference, $<2\,k\Omega$ resistance), first during a passive presentation of the tones and then after instructions to respond as quickly as possible to the target (active condition).

In this paradigm we examine several difference waves to demonstrate the differential processing accorded to various stimulus features. For example, NT–S (subtraction of ERPs) represents mismatch negativity (MMN; Näätänen 1988) and T–S represents a difference negativity (Nd; Hackley et al. 1987) in the 60–360 ms latency range. An advantage of our paradigm is that we can also



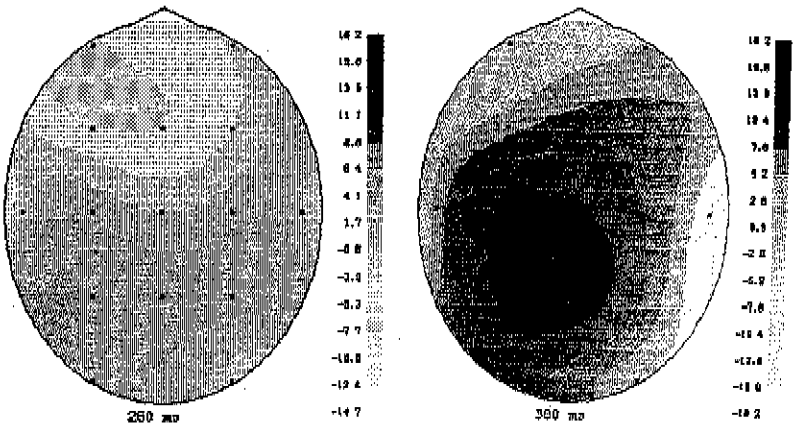
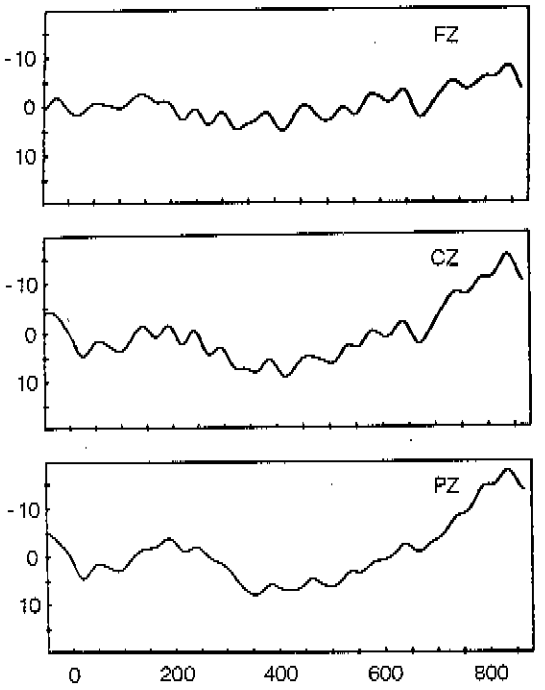


Fig. 1a. Differential processing waveforms (T–"T") recorded from Fz, Cz and Pz are shown above, topographic maps at 260 and 380 ms recorded from 15 sites below. Recordings in a from a 15-year-old right-handed healthy male, and in b from a 16-year-old right-handed paranoid schizophrenic (adoptee without family history of psychiatric illness, DSM-III-R 295.33, marked negative and positive symptoms, rating of 68 on Brief Psychiatric Rating Scale, treated with 763 chlorpromazine equivalents per day)



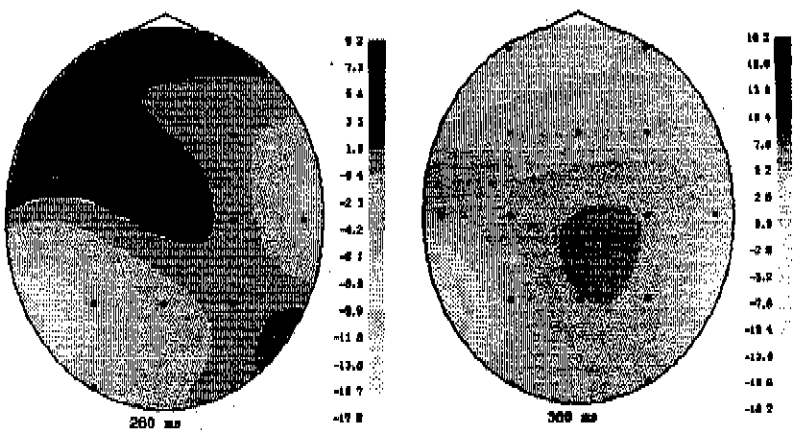


Fig. 1b.

look at T–NT and T–"T", which control, respectively, for the rarity of the tone and its physical features (both of which can modify the ERP).

Figure 1a shows a normal development of wave peaks reflecting cognitive processing of the T–"T" difference. Negative peaks are seen frontally at ca. 120 and 260 ms (differential processing negativity recalling N1 and N2),

positive peaks frontocentrally at 180 and parietally from 380 ms (recalling P2 and P3).

A recording from a paranoid schizophrenic (Fig. 1b) shows a number of differences. Early negativity is extended both temporally and topographically (100–200 ms). Negative and positive waves with onsets from 200–300 ms are missing, and positive peaks with onset at 320 and 490 ms are both shallow and shifted centromedially.

The presence of shallow late positivity recalls numerous reports of decreased P3 amplitude in schizophrenia and has been interpreted in terms of impaired evaluation of the meaningfulness of a stimulus. But the absence of the second negative wave is of particular interest. Possibly it is the same component that appears to peak around 380 ms with a delay of ca. 120 ms. Brecher et al. (1987) and Grillon et al. (1990) have reported delayed N2 waves in adult schizophrenics (mean age >30 years). Negative waves with this sort of latency (e.g. N2, MMN) have been associated with stimulus match-mismatch functions, storage of information in the sensory-buffer and the switching of attention (Breton et

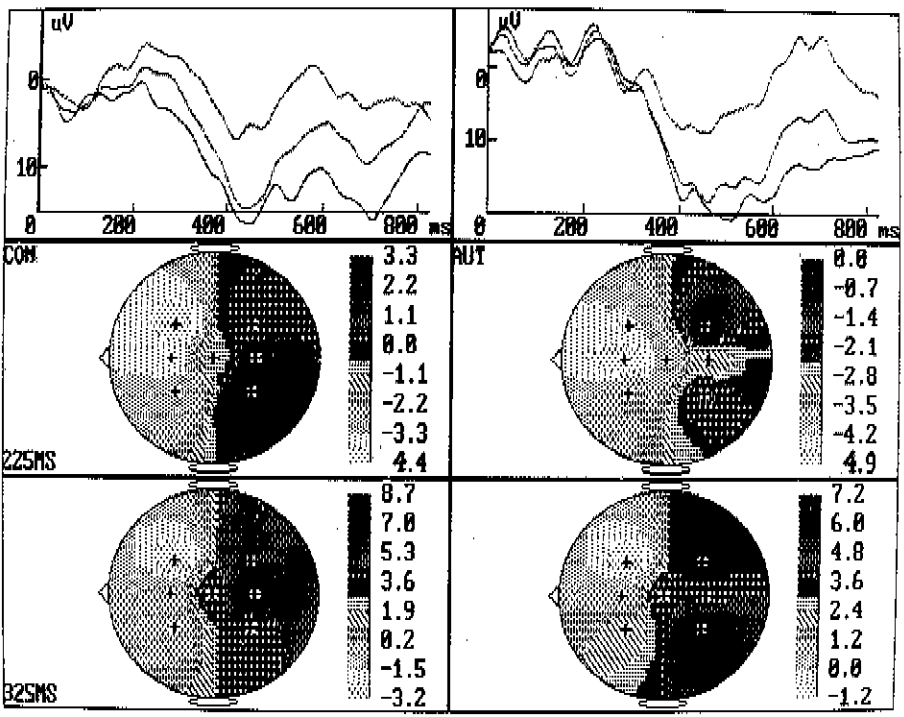


Fig. 2. Differential processing waveform (T–"T") recorded from Fz, Cz and Pz is shown above the topographic maps at 225 and 325 ms (grand means from seven sites). Tones: 50 dbSL, S = 1 KHz p 0.72, NT = 2 KHz, T = 0.5 KHz. *Left*, recordings were made from 7 healthy children matched for age and gender with *right* six male and one female unmedicated autistic children (mean age 11.3 years). All subjects were right-handed

al. 1988; Näätänen 1988). In connection with these interpretations it is interesting to note that particular emphasis has been given to the role of dopamine in switching processes in the normal brain (Oades 1985) and the impaired function of dopamine in schizophrenics, and to the dysfunction of match-mismatch processes in the processing of information by schizophrenics (Gray et al. 1991).

How specific is this impairment of mid-latency differential processing negativity? It may be present in some paranoid schizophrenic or schizoaffective patients, but we have not seen it in young disorganized schizophrenics or compulsive neurotics (unpublished data). In Fig. 2 we see that a similar component in a group of subjects with childhood autism (DSM diagnosis) seems normal, even though we have previously drawn attention to an impaired processing negativity of shorter latency (175 ms) and P3 at 425 ms in this group compared to healthy controls (Oades et al. 1988, 1990).

We conclude that it is worth taking a closer look at the differential processing of stimuli in schizophrenics and its relation to symptoms and the response to antidopaminergic medication. Improved definition of cognitive problems in these terms could also help to focus the efforts of the therapist.

Acknowledgments. We are grateful to Professor Eggers (University of Essen, FRG) and to Professor Geffen (Flinders University, Adelaide, South Australia) and Dr. L. Stern (Regency Park Centre, Adelaide, South Australia) for their support in the schizophrenia and autism projects respectively.

References

Brecher M, Porjesz B, Begleiter H (1987) The N2 component of the event-related potential in schizophrenic patients. EEG Clin Neurophysiol 66:369–375

Breton F, Ritter W, Simson R, Vaughan HG (1988) The N2 component elicited by stimulus matches and multiple targets. Biol Psychol 27:23–44

Gray JA, Feldon J, Rawlins JNP, Hemsley DR, Smith AD (1991) The neuropsychology of schizophrenia. Behav Brain Sci 14:1–84

Grillon C, Courchesne E, Ameli R, Geyer MA, Braff L (1990) Increased distractibility in schizophrenic patients: electrophysiologic and behavioral evidence. Arch Gen Psychiatry 47:171–179

Hackley SA, Woldorff M, Hillyard SA (1987) Combined use of microreflexes and event-related brain potentials as measures of auditory selective attention. Psychophysiology 24:632–647

Näätänen R (1988) Implications of ERP data for psychological theories of attention. Biol Psychol 26:117–163

Oades RD (1985) The role of noradrenaline in tuning and dopamine in switching between signals in the CNS. Neurosci Biobehav Rev 9:261–283

Oades RD, Walker MK, Geffen LB, Stern LM (1988) Event-related potentials in autistic and healthy children on an auditory choice reaction time task. Int J Psychophysiol 6:25–37

Oades RD, Stern LM, Walker MK, Clark CR, Kapoor V (1990) Event-related potentials and monoamines in autistic children on a clinical trial of fenfluramine. Int J Psychophysiol 8:197–212

Pfefferbaum A, Ford J et al. (1984) Clinical application of the P3 component of event-related potentials. EEG Clin Neurophysiol 59:85–103