Event-Related Brain Potentials: A Window on Information Processing in Schizophrenia

by Connie C. Duncan

Abstract

The application of the P300 component of the event-related brain potential to the study of attentional impairment in schizophrenia is discussed, and two recent studies are described. In one, the relative effects on P300 of stimulus modality and probability were evaluated. The data showed that the P300 is smaller in schizophrenic patients relative to normal controls for low-probability auditory stimuli. Next is described a preliminary report that evaluated whether this P300 reduction reflects a core deficit (trait marker) or clinical symptomatology (state marker). To pursue this question, a group of schizophrenic patients was studied on and off neuroleptic medication. The data showed that improvement in clinical state was highly correlated with increased visual P300 but was uncorrelated with auditory P300. These findings suggest that P300 elicited in the visual modality has the characteristics of a state marker of schizophrenia. In contrast, auditory P300 remains a candidate for a vulnerability trait marker of schizophrenia. The core deficit in schizophrenia thus appears to involve the auditory information-processing system, whereas fluctuations in clinical state may be reflected in the visual processing system.

During the past 15 years, the emerging methodology of event-related brain potentials has been applied to the study of the well-documented attentional impairment in schizophrenia (Mirsky and Duncan 1986). Beginning in 1972, a number of studies have shown that the amplitude of a specific component of the event-related brain potential—the P300—is reduced in schizophrenic patients. The amplitude of the P300 has been shown to be a sensitive index of attention deployment (Duncan-Johnson and Donchin 1977, 1982), so that its reduction in schizophrenic patients is consistent with the behavioral findings. Because the P300 is derived from cerebral electrical activity, it also offers the potential to study dynamic brain function. Thus, the P300 component is an attractive tool to investigate putative neurobiological mechanisms underlying the attention deficit in schizophrenia.

We have recently extended and broadened the finding of attenuated P300 in schizophrenic patients by evaluating the relative effects of stimulus modality and probability (Duncan et al. 1987b). Figure 1 shows the event-related potential waveforms elicited by auditory and visual stimuli at three levels of probability for a group of schizophrenic patients and a group of matched normal control subjects. As in previous studies, the P300 was smaller in the schizophrenic patients than the normal controls. However, this difference was significant only for low-probability stimuli in the auditory modality and was not found to be significant in the visual modality, suggesting that schizophrenic patients have a greater deficit in auditory than in visual processing. This finding may provide a clue to the underlying pathophysiology of the disorder and is reminiscent of the relative
The event-related potential waveforms shown were recorded from the vertex and averaged over subjects. They were elicited by auditory and visual stimuli presented at 3 levels of probability in a choice reaction time task. The data collected from the normal control (solid lines) and schizophrenic (dashed lines) subjects are superimposed. Stimulus onset is indicated by an "S" on the time scale. Positivity of the scalp electrodes with respect to the reference electrodes is plotted as a downward deflection. The P300 is the positive deflection that occurred at a peak latency of 300-400 ms following onset of the stimulus. It is apparent that the P300 was smaller and later for the schizophrenic patients than for the controls, a difference that was maximal for low-probability stimuli in the auditory modality. (Reproduced with permission from Duncan et al 1987b.)

Another issue of interest in the application of the P300 methodology to schizophrenia is whether the P300 reduction is a reflection of a core deficit, independent of clinical state, or whether it is a reflection of clinical symptomatology. Alternatively stated, is the P300 reduction a trait as contrasted with a state marker of the disorder (Duncan, in press)? A number of research strategies could be pursued to answer this question, but the most salient, perhaps, involves comparison of the same patients in different stages of their disorder (Roth et al 1986). There are virtually no data in the literature in which this comparison is reported. Approximations have been achieved experimen tally by comparing different groups of patients on and off neuroleptic medication, yielding conflicting results.

There is, however, no report of the same schizophrenic patients being studied on and off neuroleptic medication; nor is there a report of correlations between changes in P300 amplitude and clinical state in the same sample of patients. We recently reported such crucial, albeit preliminary, information on a group of seven schizophrenic patients which indicated that the trait-state issue may interact with differences in the modality of information to be processed (Duncan et al. 1987a).

Our findings indicate that the amplitude of P300 elicited in the visual modality has the characteristics of a state marker of schizophrenia. The degree of improvement in clinical state as a consequence of neuroleptic medication was found to be highly correlated with the increase in P300 amplitude. Patients who exhibited the greatest clinical improvement following the administration of neuroleptic treatment showed the greatest enhancement of P300 amplitude ($r = -0.88, p < 0.01$). Figure 2 presents the event-related potential waveforms recorded on and off medication for two patients, one who improved dramatically following neuroleptics ("Responder") and one who showed very little response to medication ("Non-responder"). In contrast, in the auditory modality, clinical response was uncorrelated with changes in P300 ($r = 0.13$). Data for one representative normal control subject tested on two occasions are also presented for comparison. In the normal control, it is clear that the visual P300 was very stable over time.

The increase in visual but not auditory P300 amplitude is consistent with the hypothesis that successful neuroleptic treatment enhances a patient's capacity to process visual but not auditory information. This hypothesis could
Figure 2. Event-related potential waveforms elicited by a visual stimulus in schizophrenic patients before and after medication and in a normal control subject tested twice

The event-related potential waveforms shown were recorded from midline frontal (Fz), central (Cz), and parietal (Pz) sites. They were elicited by a visual stimulus presented with a probability of .10 in a choice reaction time task. The left and center panels show data for two schizophrenic patients who were tested twice, once when they were unmedicated and once when they were stabilized on neuroleptic medication. On the left are shown the waveforms for a schizophrenic patient who improved dramatically following the administration of neuroleptics (“Responder”). In the center are shown the data for a patient who did not improve on neuroleptics (“Non-responder”). On the right are shown the waveforms for a normal control subject who was also tested twice. The Responder exhibited a substantial increase in P300 following the administration of neuroleptics. In contrast, the Non-responder’s waveforms showed no P300 on either test session. For the normal control, P300 was stable across tests. (Reproduced with permission from Duncan et al. 1987a.)

be tested experimentally. Nevertheless, the fact that clinical state was not correlated with auditory P300 amplitude suggests that it may still be a candidate for a vulnerability trait marker of schizophrenia. As reported above, our own data suggest that the auditory P300 appears to be significantly more sensitive to differences between schizophrenic and normal persons than is the visual P300 (Duncan et al. 1987b).

These results are preliminary and need to be replicated on a larger sample of patients. Nevertheless, they raise questions about prior reports of the independence of P300 amplitude and medication status (e.g., Roth et al. 1981). Previous studies did not take into account the modality of the stimuli used to elicit P300 or the clinical response of the patients to treatment. Our data show that mere treatment with neuroleptic medication alone, unaccompanied by symptomatic change, is insufficient to alter visual P300 amplitude. It is conceivable that the core deficit in schizophrenia is more closely related to auditory information processing and that fluctuations in clinical symptomatic state are reflected in visual processing. In any case, it will be important to understand these modality differences in processing in schizophrenia.
In addition to being a potential trait marker of schizophrenia, the P300 technique can also be applied to understanding the symptoms of schizophrenia. Research using P300 could help to identify specific stages or aspects of information processing that are responsible for impaired attention (e.g., Duncan-Johnson et al. 1984). Moreover, since the technique is dynamic and noninvasive, it is especially attractive as a means of studying the biological bases of the disorder—for example, as an index of drugs that affect brain areas implicated in the schizophrenia (Duncan and Kaye 1987) or as a marker of neurochemical imbalances or structural abnormalities. The temporal resolution of P300 can support inferences about brain events on time scales not possible in studies using tissue assays or radioactivity.

The full power of this method would be attained by studying a large, diverse sample of schizophrenic patients; using paradigms that tap different aspects and modalities of information processing; studying the effects of the experimental variables on P300 as well as other components of the event-related potential; conducting long-term followup investigations of patients in different stages of their disorder and without the confounding effects of medication; identifying homogeneous clinical and biological subtypes of the disorder; and correlating event-related potentials with clinical state, specific symptomatology, behavioral responses, and measures of brain structure and function. To the extent that time and resources permit, I plan to conduct research on each of these aspects of the disorder and to extend the investigation to studies of first-degree relatives and other major psychiatric disorders (e.g., Duncan et al. 1986; Duncan and Rosenthal 1986). Such studies provide an opportunity to understand the nature of the information-processing deficit in schizophrenia and to illuminate the core pathophysiology of the disorder.

References

Duncan, C.C. Current issues in the application of P300 to research on schizophrenia. In: Straube, E., and Hahlweg, K., eds. Schizophrenia Models, Vulnerability and Intervention. New York: Springer-Verlag, in press


Roth, W.T., Duncan, C.C.; Pfefferbaum, A.; and Timst-Berthier, M. Applications of cognitive ERPs in psychiatric patients. In: McCallum, W.C.; Zappoli, R.; and Denoth, F., eds. Cerebral Psychophysiology. Studies in Event-Related Potentials. (EEG Sup-

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