Ann.Bull.RILP(1985)No.19, 275-282

DECOUPLING OF STIMULUS AND RESPONSE PROCESSES SEEMS RESPONSIBLE FOR SLOW REACTION TIMES IN SCHIZOPHRENICS WITH MILD SYMPTOMATOLOGY

Ken-Ichi Hiramatsu*, Masaru Akimoto*, Masato Fukuda*, Osamu Saitoh*, Tomomichi Kameyama*, Shin-Ichi Niwa*, Kiyoyuki Yamazaki*,** and Kenji Itoh

Summary

Event-related potentials (ERPs) and reaction times (RTs) during a 3-tone auditory detection task were recorded from schizophrenics with mild symptomatology and normals. The P3 component latencies of single trials were assessed using an adaptive correlating filter technique. Performance levels and P3 latencies were almost identical in both groups. However, RTs in schizophrenics occurred approximately 100 msec later than those recorded in normals. Correlations between P3 latency and RT were lower in schizophrenics than in normals. The slow RTs in schizophrenics can be explained by a delay in the response process and decoupling between the stimlus and response processes originating from a deficit in a higher organizing system.

I. Introduction

The slowness in response characteristics of schizophrenics during reaction time (RT) tasks is one of the most common findings that reflect their deficiency in information processing[1]. Behavioral measures, however, have not yet clearly identified specific stages in information processing responsible for slow RTs in schizophrenics[2-4].

It has been suggested that the P3 latency of event-related potentials is associated with the time taken for situation-evaluation or context-updating[5-6]. Thus, the measurement of P3 latencies recorded during psychological tasks might provide a useful tool for identifying specific deficits in the information-processing of schizophrenics. Roth et al.[7], among other investigators, reported that schizophrenics had prolonged P3 peak latencies in averaged ERPs elicited by unexpected stimuli to which no behavioral responses were required. However, determining peak latencies from averaged ERPs is problematic because the variability of component latency from trial to trial results in a peak latency that may not be representative. This problem can be solved by computing P3 latency for every trial. An examination of the relationship between single-trial P3 latencies and RTs may be fruitful for elucidating the mechanism producing slow RTs in

* Department of Neuropsychiatry, Faculty of Medicine, University of Tokyo, Tokyo, Japan
** Present adress: Institute of Medical Electronics, Faculty of Medicine, University of Tokyo, Tokyo, Japan

schizophrenics. Since Kutas et al.8), many investigators[9-14] have employed the adaptive correlating filter (ACF)[15] technique for measuring P3 latencies in single-trial ERPs recorded from normal subjects. Recently, Pfefferbaum et al.[16] reported that P3 latencies and RTs were prolonged in schizophrenics but single-trial P3/RT correlations were not significantly reduced.

The purpose of the present study was to obtain information about the mechanism responsible for slow RTs in schizophrenics by comparing the relationship between P3 latency and RT for schizophrenics with that for normal controls using P3 latencies measured in single-trials.

II. Method

II-1. Subjects

Male schizophrenics (N=9) and normal male volunteers (N=9) in their twenties and thirties were subjects in this study. They were group-matched for age (28.2 and 28.6 years, respectively) and educational background (15.2 and 16.0 school years, respectively). All subjects were judged as mixed (3 normals) or right handed (the others) employing Kameyama et al.'s Questionnaire[17]. All schizophrenics met the diagnostic criteria for schizophrenic disorders in DSM-III[18]. The subtypes of the schizophrenic disorders of these subjects were as follows: residual type, 6; paranoid type 2; disorganized type 1. The patients included in this study were selected from a larger group on the basis of accurate performance in a preliminary test using experimental paradigm to be described. Total BPRS[19] scores of these patients ranged from 22 to 38 (means; 30.1), with their GAS[20] scores being distributed as follows: 51-60, 2 patients; 61-70, 6; 71-80, 1. Eight patients had been treated on comparatively low doses of neuroleptics. The dosages were converted into equivalent dosages of chlorpromazine according to Lehmann's conversion table[21]. The mean dosage for 8 patients was 222.5 (±182.5) mg. One patient was not treated on neuroleptics at the time of the investigation. Thus, the symptomatology of the patients in this study is, on the whole, comparatively mild.

II-2. Procedure

A 3-tone auditory detection task was employed consisting of a series of 300 tone bursts with 150 msec duration, delivered at 2 sec intervals. The series included tones at 970Hz, 1000Hz and 1030Hz in random sequence. The 1000Hz tone occurred 4/6 of the time (frequent), and each of the 970Hz and 1030Hz tones occurred 1/6 of the time (infrequent). Tones were delivered at 50 dBSL binaurally through headphones. Subjects were required to detect one of the two types of infrequent tones as the target in one session, pressing a response lever upon detection of the targets. Hence in total, each subject performed two sessions for the two different targets. In sessions when the target was the 970Hz tone, they were required to press the lever to the right, with

the thumb and index fingers of the right hand; similarly to the left for the 1030Hz targets. Speed as well as accuracy were emphasized equally in the instructions. Data for the two sessions were pooled and analyzed together.

II-3. Data recording and analysis

EEGs derived from the Pz region referred to linked earlobe electrodes (time constant, 0.3 sec) were recorded on FM analog tapes. EEG data without artifacts were then digitized off-line with a sampling frequency of 500Hz. Digitized data for each type of stimulus, from 128 msec preceding stimulus-onset to 896 msec post-stimulus, were edited separately. These data were smoothed with a digital filter (moving average method; width of data window, 50 points) to minimize any alpha activity in the record. As the first step to obtaining single-trial ERPs, conventional stimulus-synchronized average (SSA) ERPs were obtained. In the second step, single-trial P3 latencies for the targets were determined using the ACF technique. The initial template was obtained from the SSA waveform for the targets, by taking 125 msec of activity before and after the P3 peak to give a total template duration of 250 msec. The template was moved in 2 msec increments across a 400 msec segment of data from each trial, beginning at a time corresponding to 200 msec before P3 peak latency in the SSA waveform. Cross-correlation coefficients between the template and single-trial data were calculated at each position. The latency at which the maximum correlation coefficient occurred was considered to be the latency of P3 for that single-trial. The single-trial EEG data were then reaveraged by aligning each trial at its P3 latency (latency synchronized average, LSA). This LSA waveform served as the new template, and the point-by-point cross-correlation procedure was repeated. In the third step, estimated P3 latencies for trials in which the maximum correlation coefficient with the template was below 0.8, were excluded. Data acquisition and analysis were performed by a DEC VAX-11/780 computer. Details of ACF employed in this study have been described elsewhere[22].

III. Results

Table 1 shows the behavioral data for both groups. Omission error rates in schizophrenics tended to be greater than those of normals [$t=1.95$, $p=0.06$ (two-tailed)]; however, commission error rates as well as total error rates did not differ significantly between the groups.

The percentage of single-trials in which the target was correctly detected and which also had a maximum correlation coefficinet above 0.8 (referred to as correct single-trials) was 79.0% in the schizophrenics and 90.3% in the normal controls. Thus, the schizophrenic group produced significantly more trials, in which a P3 compoment was not clearly identifiable [$t=4.49$, $p<0.001$ (two-tailed)], even though they performed the tasks correctly.

Means and standard deviations of P3 latencies for correct

single-trials were almost equal in both groups (Table 2). That is, P3 latencies were neither delayed nor distributed more widely in schizophrenics as compared with the normal controls.

However, the mean RT in schizophrenics was greater than that of normal controls [t=13.14, p<0.001 (two-tailed)]. RTs exceeded P3 latencies by approximately 100 msec in the normals, and 200 msec in the schizophrenics.

Fig. 1 shows the correlation coefficients between RTs and P3 latencies for all correct trials in each subject of both groups. The mean correlation coefficients for each group are also shown in Fig. 1. Both groups showed low but significant positive correlations (r=0.35, in the normal controls; r=0.24, in the schizophrenics). The correlation coefficient in the normal controls was greater than that of the schizophrenics [t=2.17, p<0.04 (two-tailed)]. When broken down into each subject, 7 out of 9 normal controls showed significant correlations, while only 4 out of 9 schizophrenics displayed significant correlations.

Table 1.

Performance levels for both groups.
Figures indicate mean percentages (S.D.).

	Omission error	Commission error IF-NT	Commission error F-NT	Total error
Normal Controls (N= 9 X 2)	7.4 (7.7)	5.1 (4.0)	1.6 (2.8)	3.1 (2.4)
Schizophrenics (N= 9 X 2)	13.3 (10.3)	1.0 (1.2)	0.7 (1.0)	2.8 (1.8)

* (Omission error)

IF-NT: Infrequent non-target, F-NT: Frequent non-target, * : p<0.1 (t-test, two-tailed).

Table 2.

Means (S.D.) of P300 latencies and reaction times for correct single-trials in both groups.

	P300 (msec)	RT (msec)	P300 - RT (msec)
Normal controls (729 trials)	406 (76)	505 (113)	99 (112)
Schizophrenics (593 trials)	414 (88)	607 (157)	193 (160)

* (RT) * (P300 - RT)

* : p<0.001 (t-test, two-tailed).

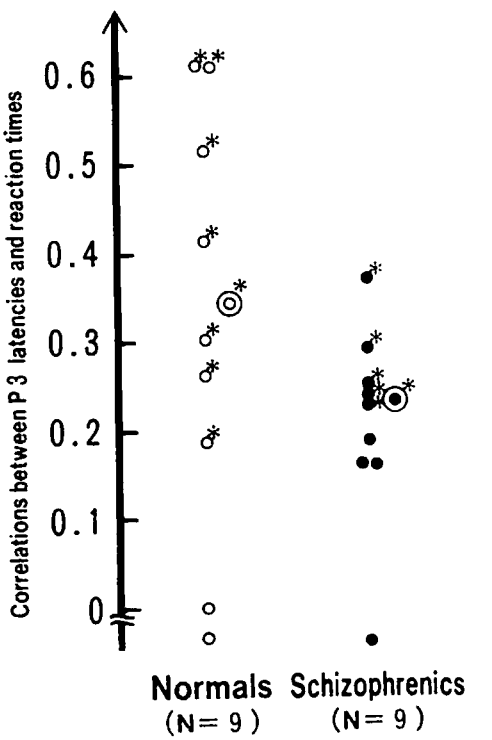

Fig. 1. Pearson's correlation coefficients between the P300 latencies and the reaction times for all normal controls and schizophrenics. Mean coefficient values are represented by ⊙ for the normal controls, and ● for the schizophrenics. * p<0.05.

IV. Discussion

The schizophrenic subjects employed in the present study seemed to have performed the required tasks as accurately as the normal controls. However, schizophrenics produced more trials in which a P3 was not clearly identified, even though they performed the tasks correctly. Possible explanations for this difference are that either schizophrenics had failed more frequently to fully evaluate stimulus characteristics, or schizophrenics had been unsuccessful more frequently in context-updating after full evaluations compared with normal controls. In any case, the absence of P3 from a greater proportion of trials than normals may be one of the reasons for the common finding that schizophrenics display smaller P3 amplitudes in SSA waveforms.

The P3 latency for correct single-trials was not delayed in schizophrenics, but the RT in schizophrenics was more prolonged than that of normals. Furtermore, single-trial P3/RT correlations were reduced in schizophrenics.

Kutas 8) and other investigators 9-14) who measured single-trial P3 latency in normals employing ACF technique reported that the P3 latency provides an estimate of stimulus evaluation time, independent of response processing time. Thus, it is suggested that the stimulus processing time represented by P3 latency is neither delayed nor widely distributed in the schizophrenics used in the present study.

No prolongation of P3 latency in schizophrenics is inconsistent with the result of Pfefferbaum et al. 16). This may be due to differences in experimental paradigm and the sample bias. Schizophrenic patients in the present study were outpatients with mild symptomatology, while Pfefferbaum et al.'s schizophrenic patients were inpatients with impaired performance on the MMS (mini mental state) examination; almost half of their patients would have been classified as 'demented' by the MMS criterion. The auditory stimuli used in the Pfefferbaum et al.'s study were 1000 Hz (frequent), 500 Hz and 2000 Hz (infrequent). Thus, 3-tone paradigm of 30 Hz discrimination in the present study was more difficult than that of their study. However, if this difference in experimental paradigm would be the main source for the discrepancy of P3 latency between the two studies, it could not be well explainable that schizophrenics displayed the prolongation of P3 latency in the easier paradigm with no prolongation in the more difficult paradigm. Thus, the sample bias seems the main source for the discrepancy betweeen the two studies. That is, Pfefferbaum et al.' patients seem to be more 'cognitively impaired', so that they displayed the prolongation of P3 in contrast to our patients with mild symptomatology.

In spite of no prolongation of P3 latency, schizophrenics displayed slow RTs and low correlations between P3 latencies and RTs. This suggests that slow reaction times for the schizophrenics in the present study are not due to a delay in the stimulus process but due to a delay in the response process, and that the

stimulus and response processes are more loosely coupled in schizophrenics than in normal controls.

What is an appropriate explanation for the delay in the response process as well as the decoupling between the stimulus process and response process in schizophrenics? The delay in RTs of schizophrenics are not thought as result of effects of neuroleptics administered to the schizophrenic subjects; the reasons for this being, 1) no significant correlation was found between RTs and neuroleptic dosages in the schizophrenics, 2) neuroleptics have been reported not to prolong RTs in schizophrenics[23-24].

We measured schizophrenics' RTs employing a 2-tone discrimination paradigm in another study[25], there was no significant difference in RTs between schizophrenics and normal controls. Therefore, schizophrenics do not necessarily display a delay in the response process. As the stimulus difficulty in the 2-tone discrimination paradigm was less than that of the present study, with the response difficulty being equal, it seems possible that the coupling between the stimulus and response processes becomes looser in schizophrenics as the stimulus difficulty increases, thus producing a delay in the response process.

As for normal subjects, Pfefferbaum et al.[14] have suggested that, in difficult and unfamiliar sensory discrimination tasks, subjects may be less confident, with some doubts remaining after the full evaluation of a stimulus, leading to hesitation before pressing a button, thereby decoupling P3 latencies from RTs. According to this suggestion, the schizophrenics in the present study are considered to have hesitated more than the normal controls. This hesitation seems consistent with the tendency for schizophrenics to make more omission errors. While, Baribeau-Braun et al.[26] have discussed, based upon their study on ERPs of schizophrenics, that the slowness and inefficiency of schizophrenic information-processing could result from an inability to organize the processes, that is the stimulus-set as well as response-set as defined by Broadbent, in an optimal manner. As far as normal psychological processes are concerned, "hesitation" fits the explanation of the decoupling; however, in the case of schizophrenics, some deficits in allocation of processing resources should also be taken into account, as Baribeau-Braun et al. have suggested. In other words, a possible organizing system which effectively controls the stimulus process and response process may be disturbed to a greater extent in schizophrenics as stimulus discrimination become more difficult. This decoupling between the stimulus process and the response process may be the reponsible factor for slow RTs in schizophrenics, at least in those with such a mild symptomatology as displayed by the patients in the present study. Such a functional "splitting" between different processes that are coupled in normal conditions might be suggested as a common cerebral basis for "splitting of the mind".

This study was presented at the 6th Meeting of the Japanese Society of Biological Psychiatry (March 23-24, 1984)[27].

We thank Ms. Chika Aoki, Mr. Yozo Katsuragawa and Mr. Toru Nakajima who assisted us greatly in conducting this study. We gratefully appreciate critical comments of Former Professor H. Utena, Department of Neuropsychiatry, Faculty of Medicine, University of Tokyo, on the previous manuscript of this paper, to whom we owe the idea of "functional splitting" for understanding pathophysiology of schizophrenia. Our special thanks are due to Former Professor K. Gambo, Geophysical Institute, Faculty of Science, University of Tokyo, for his kind advice regarding mathematical methods for data-analyses, and to Dr. G. Barrett, Medical Research Council, Institute of Neurology, National Hospital (London), for his kind correction of the previous manuscript.

References

1. K.H. Nuechterlein (1977). Reaction time and attention in schizophrenia: A critical evaluation of the data and theories. Schizophrenia Bulletin 3, 373-428.
2. S.D. Koh, R. Szoc and R.A. Peterson (1977). Short-term memory scanning in schizophrenic young adults. Journal of Abnormal Psycology 86, 451-460.
3. J. Wishner, M.K. Stein and A.L. Peastrel (1978). Stages of information processing in schizophrenia: Sternberg's paradigm. Journal of Psychiatric Research 14, 35-45.
4. P.N. Russell, C.E. Consedine and R.G. Knight (1980). Visual and Memory search by process schizophrenics. Journal of Abnormal Psychology 89, 109-114.
5. E. Donchin, W. Ritter and W.C. McCallum (1978). Cognitive psychophysiology: The endogenous components of the ERP. In E. Callaway, P. Tueting and S.H. Koslow (Eds.), Event-Related Potentials in Man. Academic Press: New York. 349-411.
6. A. Magliero, T.R. Bashore, M.G.H. Coles and E. Donchin (1984). On the dependence of P300 latency on stimulus evaluation processes. Psychophysiology 21, 171-186.
7. W.T. Roth, T.B. Horvath, A. Pfefferbaum, J.R. Tinklenberg, J. Mezzich and B.S. Kopell (1979). Late event-related potentials and schizophrenia. In H. Begleiter (Ed.), Evoked Brain Potentials and Behavior. Plenum Press: New York. 499-515.
8. M. Kutas, G. McCarthy and E. Donchin (1977). Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. Science 197, 792-795.
9. E. Donchin (1981). Surprise! ..... Surprise? Psychophysiology 18, 493-513.
10. C.C. Duncan-Johnson (1981). P300 latency: A new metric of information processing. Psychophysiology 18, 207-215.
11. G. McCarthy and E. Donchin (1981). A metric for thought: A comparison of P300 latency and reaction time. Science 211, 77-79.
12. C.C. Duncan-Johnson and E. Donchin (1982). The P300 component of the event-related brain potential as an index of informa-

tion processing. Biological Psychology 14, 1-52.
13. J.M. Ford, A. Pfefferbaum, J.R. Tinklenberg and B.S. Kopell (1982). Effects of perceptual and cognitive difficulty on P3 and RT in young and old adults. Electroencephalography and clinical Neurophysiology 54, 311-321.
14. A. Pfefferbaum, J. Ford, R. Johnson, B. Wenegrat and B.S. Kopell(1983). Manipulation of P3 latency: Speed vs. accuracy instructions. Electroencephalography and clinical Neurophysiology 55, 188-197.
15. C.D. Woody (1967). Characterization of an adaptive filter for the analysis of variable latency neuroelectric signals. Medical and Biological Engineering 5, 539-553.
16. A. Pfefferbaum, B.G. Wenegrat, J.M. Ford, W.T. Roth and B.S. Kopell (1984). Clinical application of the P3 component of event-related potentials. II. Dementia, depression and schizophrenia. Electroencephalography and clinical Neurophysiology 59, 104-124.
17. T. Kameyama, S. Niwa, K. Hiramatsu and O. Saitoh (1983). Hand preference and eye dominance patterns in Japanese schizophrenics. In P. Flor-Henry and J. Gruzelier (Eds.), Laterality and Psychopathology. Elsevier: Amsterdam. 163-180.
18. American Psychiatric Association (1980). Diagnostic and Statistical Manual of Mental Disorders, 3rd Ed. Washington.
19. J. Overall and D. Gorham (1962). The brief psychiatric rating scale. Psychological Report 10, 799-812.
20. J. Endicott, R.L. Spitzer, J.L. Fleiss and J. Cohen (1976). The global assessment scale. Archives of General Psychiatry 33, 766-771.
21. H.E. Lehmann (1975). Psychopharmacological treatment of schizophrenia. Schizophrenia Bulletin 1, 27-45.
22. K. Yamazaki, M. Akimoto, K. Hiramatsu, S. Niwa, T. Kameyama, O. Saitoh, K. Rymar and K. Itoh (1984). Assessment of P300 latencies for indivisual EEG responses employing an adaptive correlating filter. Folia Psychiatric et Neurologica Japonica 38, 465-471.
23. G. Brooks and L. Weaver (1961). Some relations between psychiatric and psychomotor behaviour changes associated with tranquilizing medications. Comprehensive Psychiatry 2, 203-210.
24. J.M. Held, R.L. Cromwell, E.J. Frank Jr. and W.E. Fann (1970). Effect of phenothiazines on reaction time in schizophrenics. Journal of Psychiatric Research 7, 209-213.
25. T. Kameyama, S. Niwa, K. Hiramatsu, O. Saitoh and H. Utena (1984). Analysis of choice reaction times for dichotic discrimination tasks in schizophrenics. Ann. Rep. Pharmacopsychiat. Res. Found. (Eng. abst.) 15, 98-106.
26. J. Baribeau-Braun T.W. Picton and J.-Y. Gosselin (1983). A neurophysiological evaluation of abnormal information processing. Science 219, 874-876.
27. K. Hiramatsu, M. Akimoto, O. Saitoh, T. Kameyama, S. Niwa, K. Yamazaki and K. Itoh (1984). What stage in information processing is responsible for slow reaction times in schizophrenics? Folia Psychiatrica et Neurologica Japonica 38, 339.