Ann. Bull. RILP (1985) No. 19, 261-274

# EVENT-RELATED POTENTIAL CORRELATES OF PSYCHOTROPIC DRUG ACTION ON ATTENTIONAL AND COGNITIVE IMPAIRMENTS IN SCHIZOPHRENIA

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

Summary

The purpose of this study was to investigate the effects of antipsychotic drugs on the cognitive deficits of schizophrenic patients. Amplitudes of ERPs, as well as attention-related negative components recorded during syllable discrimination tasks were utilized as indices for estimation of cognitive functioning. Ten DSM-III unmedicated schizophrenics, as well as 11 normal controls, were used. A series of tests were administered to the unmedicated schizophrenics; they were then given antipsychotic medication and retested. The following results were obtained: 1) The stimuli presented to the attended ear produced larger amplitudes of the N100 component and smaller amplitudes of the P200 component, when compared to the stimuli presented to the non-attended ear in the controls. Schizophrenics failed to demonstrate this channel effect for the N100 and P200 components, and the amplitude of the attention-related negative component was smaller than that of the normal controls before medication. However, this channel effect became recognizable during the course of the medication. 2) The Late Positive Components (LPCs) elicited by the target stimuli were greater in comparison to those of the non-target stimuli in the controls; however, this target effect was not observed in the case of the schizophrenics even after the medication. These results suggest that the deficit of channel selective attention in schizophrenics is improved by antipsychotic drugs; however, the deficits in cognitive functioning, such as 'context updating', remain unimproved.

## I Introduction

It is considered that cognitive and attentional deficits are basic symptoms in schizophrenia. Attentional mechanisms are considered to be under monoamine control (Oades, 1982[1]). Accordingly, it is useful to investigate the effect of antipsychotic drugs, which have antimonoaminergic effects, on schizophrenic cognitive and attentional functioning in order to examine the 'monoamine hypothesis' of schizophrenia.

Event-Related Potentials (ERPs) are considered to be physiological indices which reflect cognitive and attentional functioning. Näätänen et al. (1978)[2] and Hansen and Hillyard (1980)[3] recorded ERPs during tasks that required a subject to detect and count target stimuli in the attended ear. They reported that an endogenous prolonged negative component with a

*Department of Neuropsychiatry, Faculty of Medicine, University of Tokyo, Tokyo, Japan

peak latency of 200 msec was observed when the ERPs elicited by stimuli in an unattended ear were subtracted from those elicited by stimuli in an attended ear. This negative component is called 'processing negativity' (Nätäänen et al., 1978) or 'Nd' (Hansen and Hillyard, 1980). Attentional functioning can be estimated by measuring this attention-related negative component. Furthermore, the P300 component, which is elicited by infrequent and task relevant stimuli, is considered to reflect cognitive functioning such as 'context updating' (Donchin et al., 1978[4]).

The purpose of this study was to investigate the effects of antipsychotic drugs on the cognitive and attentional deficits of schizophrenic patients, utilizing ERPs as indices for the estimation of cognitive and attentional functioning.

Many recent studies utilizing neuropsychological tests have been carried out on schizophrenics. These studies have suggested that 1) schizophrenics demonstrate a left hemispheric dysfunction and that 2) schizophrenics display a disturbance in the integration of both hemispheres. Our previous studies also revealed these dysfunctions by using the N100, P200 and P300 components of ERPs recorded during dichotic detection tasks (Saitoh et al., 1981[5]) and during syllable discrimination tasks (Kameyama et al., 1984[6]).

This study is also aimed at investigating the relationship between attentional deficits and hemispheric functioning in schizophrenics through an analysis of abnormalities in the attention-related negative component of ERPs recorded in the bitemporal regions during syllable discrimination tasks.

## II Method

### II-1 Subjects

The subjects consisted of ten unmedicated schizophrenic patients (4 males, 6 females) randomly selected from a group of schizophrenic patients under treatment at the Neuropsychiatric Outpatient Clinic, Tokyo University Hospital. All patients met the diagnostic criteria of DSM-III (American Psychiatric Association, 1980[7]) for schizophrenic disorders. The ages of the patients ranged from 20 to 48 years (mean age: 33 years). None of the patients had received any psychotropic drugs for at least 10 months prior to the experiments which were conducted during the first visit before medication (first series of tests). After 2 to 6 months of medication, the same experiments were conducted (second series of tests). The patients received from 1-22 mg (mean: 5mg/day) of haloperidol during the second series of tests. Total BPRS scores were 48.5 during the first series of tests and 37.2 during the second series, showing a significant difference ($t[18]=2.71$, $p<0.05$). The mean scores on item 4 (conceptual disorganization), item 10 (hostility), item 11 (suspiciousness), and item 12 (hallucinatory behavior) were significantly higher during the first series of tests ($t[18]=1.85$, $p<0.1$; $t[18]=2.16$, $p<0.05$; $t[18]=2.34$, $p<0.05$; $t[18]=1.80$, $p<0.1$; respectively). It

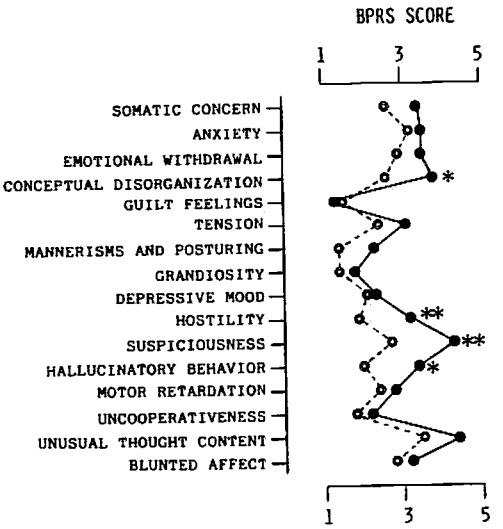


Fig. 1. Comparison of the BPRS profiles of schizophrenics between 1st test(●——●) and 2nd test(◎- - - -◎). **p<0.05; *p<0.1.

seems that the positive schizophrenic symptoms were significantly improved during the second series of tests (Fig. 1).

Eleven normal people (7 males, 4 females) served as the control group. The ages of the controls ranged from 21 to 41 years (mean age : 30 years).

All of the patients and controls were right-handed and were found to be free from any hearing disabilities.

II-2 Procedure

ERPs were recorded during syllable discrimination tasks similar to those employed by Hink et al. (1978)[8]. Four different CV syllables produced by a male voice were presented to one ear, with the same four syllables by a female voice being presented to the other ear monoaurally through headphones. Subjects were required to attend to one ear, counting the total number of times a particular syllable ('target syllable') was heard in each run.

The auditory stimuli, procedure, and recording system were the same as reported in Hiramatsu et al. (1984)[9]. Brief explanations for the above items are given below.

Four CV-syllables (/ba/, /da/, /ga/, /za/) uttered by a male voice were presented to one ear, with the same four CV-syllables by a female voice being presented to the other ear monoaurally through headphones. Each of the eight stimuli was presented

randomly with an equal a priori probability of 0.125. The duration of the stimuli was 150 msec. The intensity of the stimuli was approximately 60 dBSL. The interstimulus intervals ranged from 800 to 1000 msec.

The subjects were seated in an anechoic room with eyes closed. They were informed that a male voice would be presented to one ear, then a female voice would be presented to the other. They were required to count silently the number of occurrences of a particular syllable (/ga/) they heard in a given ear in each run. All of the subjects performed 4 runs, that is, one target syllable X two voices (male or female) X two attended channels (left or right ear). The number of the target stimuli for each run was set within the range of 40-45. After the conclusion of each run, the subjects were asked to give the number of the target stimuli detected.

During the runs, EEGs were recorded monopolarly with Ag-AgCl electrodes placed at the Cz, T3 and T4 regions, utilizing linked earlobe electroles as references. The EEGs without artifacts were passed through a bandpass filter set at 1.5-25 Hz (-6dB/oct) and averaged separately for the left and right ears into four categories: 1) target syllables in the attended ear (N=64); 2) non-target syllables in the attended ear (N=192); 3) target syllables in the non-attended ear (N=64); and 4) non-target syllables in the non-attended ear (N=192). The sampling periods were 20 msec before and 600 msec after the stimulus onset.

Each of the ERP components was defined as follows: N100 was the most negative peak in the 56-156 msec period after the stimulus onset; P200 was the most positive peak in the 40-120 msec period after the N100 peak; the late positive component was the positive deflection in the 50-330 msec period after the P200 peak. The peak amplitudes and latencies of the N100 and P200 components, as well as the averaged amplitude of the late positive component (LPC), were measured. Furthermore, in order to examine the attention-related negative component, the ERPs elicited by stimuli in an unattended ear (that is, categories 3+4) are subtracted from those elicited by stimuli in an attended ear (that is, categories 1+2). The most negative peak of this difference wave in the 56-256 msec period after the stimulus onset was designated as PDW. The peak amplitude and latency of the PDW were designated as PADW and PLDW, respectively. The PADW, PLDW and the averaged amplitude of the difference wave in the 56-256 msec period after the stimulus onset (AADW) were measured. Each amplitude of the ERP components was measured with respect to a zero level, which was defined as the mean amplitude during a 20 msec pre- and post-stimulus period.

II-3 Statistical analysis

The data was analyzed utilizing the ANOVA program of the SPSS (Statistical Package for the Social Sciences). The ERPs derived from the Cz region were analyzed employing the amplitudes of the N100 and P200 components, as well as the LPC, as dependent

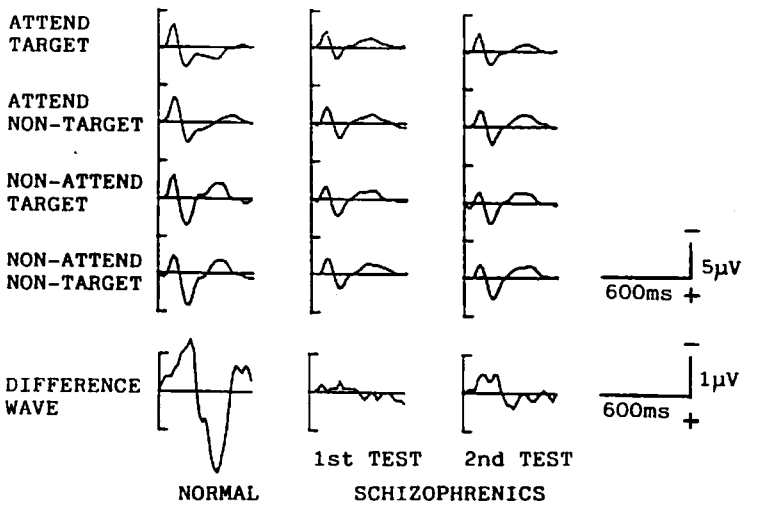


Fig. 2. Grand averaged ERPs of normal subjects, unmedicated schizophrenics (1st test) and medicated schizophrenics (2nd test). "Attend Target": target stimuli presented to the attended ear; "Attend Non-target": non-target stimuli presented to the attended ear; "Non-attend Target": the same syllables as the target stimuli presented to the non-attended ear; "Non-attend Non-target": syllables different from the target stimuli presented to the non-attended ear.

variables. SEX (Male/Female), SYLLABLE (Target/Non-target), CHANNEL (Attend/Non-attend), and EAR (the side on which the stimulus was presented: Left/Right) were employed as independent variables, with the following as covariants:

1) normal controls: age; academic level
2) schizophrenics, first series of tests: age; academic level
3) schizophrenics, second series of tests: age; academic level; dosage of haloperidol.

To examine the group difference in the attention-related negative components, t-tests were conducted for the PADW, PLDW and AADW derived from the T3, T4 and Cz regions.

## III Results

Figure 2 shows the averaged ERP and difference wave patterns (both for Cz) of all the normal controls and the first and second series of tests for the schizophrenics. The waveform of the P300 component, which was elicited by the target stimuli in the normal controls, could not be clearly identified in the schizophrenics during either the first or second series of tests.

The amplitudes and latencies of the N100 and P200 components derived from the Cz region are presented in Table 1, and the LPC derived from the Cz region is presented in Table 2. The PADW, PLDW and AADW derived from the Cz, T3, and T4 regions are presented in Table 3.

Table 1. Mean amplitudes (μV) of the N100 and P200 components derived from the Cz region.

| | | Attend | Non-attend |
|---|---|---|---|
| N100 | Normal controls | 3.87±1.49 | 3.29±1.54 |
| | Schiz. 1st Test | 2.78±1.72 | 2.49±1.54 |
| | Schiz. 2nd Test | 2.78±1.78 | 2.23±1.04 |
| P200 | Normal controls | 3.38±1.90 | 4.47±2.30 |
| | Schiz. 1st Test | 2.46±1.73 | 2.79±1.57 |
| | Schiz. 2nd Test | 2.55±1.41 | 3.26±2.01 |

Table 2. Mean LPC (μV) derived from the Cz region.

| | Attend Target | Attend Non-target | Non-attend Target | Non-attend Non-target |
|---|---|---|---|---|
| Normal controls | 0.52±1.17 | -0.10±0.71 | -0.50±0.96 | -0.45±0.54 |
| Schiz. 1st Test | -0.40±0.87 | -0.39±0.50 | -0.32±0.84 | -0.54±0.64 |
| Schiz. 2nd Test | -0.37±0.71 | -0.55±0.51 | -0.65±0.89 | -0.59±0.64 |

Table 3. Peak amplitude (PADW), peak latency (PLDW ) and averaged amplitude (AADW) of the difference wave

| | | PADW (μv) | PLDW(msec) | AADW (μV) |
|---|---|---|---|---|
| T3 | Normal controls | 1.53±0.87 | 179.6±43.2 | 0.54±0.61 |
| | Schiz. 1st Test | 0.82±0.78 | 151.0±70.2 | -0.09±0.50 |
| | Schiz. 2nd Test | 0.89±0.60 | 163.6±54.1 | 0.11±0.43 |
| T4 | Normal controls | 1.29±0.76 | 148.5±52.0 | 0.40±0.49 |
| | Schiz. 1st Test | 1.12±0.98 | 148.4±74.8 | 0.12±0.80 |
| | Schiz. 2nd Test | 1.04±0.74 | 143.6±62.3 | 0.17±0.62 |
| Cz | Normal controls | 2.33±1.59 | 168.4±48.5 | 0.77±0.84 |
| | Schiz. 1st Test | 1.38±0.91 | 149.8±62.3 | 0.20±0.70 |
| | Schiz. 2nd Test | 1.63±1.36 | 156.6±69.4 | 0.39±0.92 |

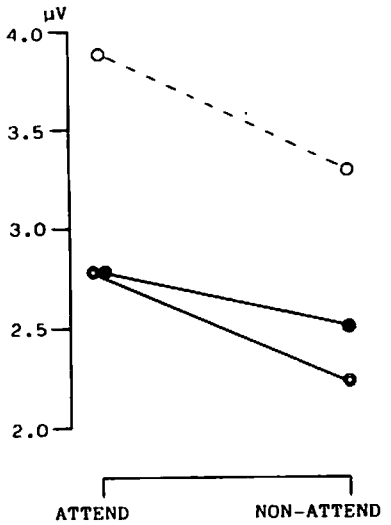


Fig. 3. Mean amplitudes of the N100 component at the Cz region. o- -o, normals (n=11x4); ●—●, schizophrenics, 1st test (n=10x4); ◎—◎, schizophrenics, 2nd test (n=10x4).

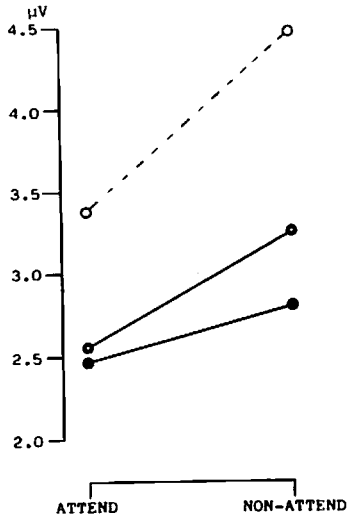


Fig. 4. Mean amplitudes of the P200 component at the Cz region. o- -o, normals (n=11x4); ●—●, schizophrenics, 1st test (n=10x4); ◎—◎, schizophrenics, 2nd test (n=10x4).

III-1 The amplitude of the N100 component derived from the Cz region

The ANOVA revealed that the main effect of CHANNEL on the amplitudes of the Cz-N100 tended to be significant in the controls ($F[1,70]=2.927$, $p<0.1$). That is, the amplitudes of the Cz-N100 elicited by the stimuli presented to the attended ear were greater than those for the non-attended ear in the controls (Fig. 3).

This channel effect was not significant in the first series of tests for the schizophrenics ($F[1,62]=0.578$, n. s.); however, this channel effect tended to be significant in the second series of tests for the schizophrenics ($F[1,61]=3.038$, $p<0.1$) (Fig. 3).

III-2 The amplitude of the P200 component derived from the Cz region

The ANOVA revealed that the main effect of CHANNEL on the amplitudes of the Cz-P200 was significant in the controls ($F[1,70]=5.372$, $p<0.05$). That is, the amplitudes of the Cz-P200 elicited by the stimuli presented to the attended ear were less than those presented to the non-attended ear in the controls (Fig. 4).

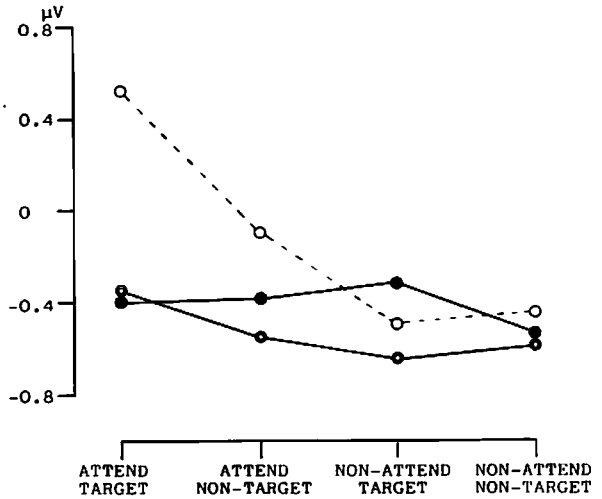


Fig. 5. Mean LPCs at the Cz region. o---o, normals (n=11x2); ●——●, schizophrenics, 1st test (n=10x2); ⊗——⊗, schizophrenics, 2nd test (n=10x2).

This channel effect was not significant in the first series of tests for the schizophrenics ($F[1,62]=0.837$, n. s.); however, this channel effect tended to be significant in the second series of tests for the schizophrenics ($F[1,61]=3.359$, $p<0.1$) (Fig. 4).

III-3 The averaged amplitudes of the late positive components derived from the Cz region (Cz-LPCs)

ANOVA revealed that the main effect of CHANNEL on the Cz-LPCs was significant ($F[1,70]=12.374$, $p<0.01$), and that the effect of CHANNEL X SYLLABLE on the Cz-LPCs tended to be significant ($F[1,70]=3.052$, $p<0.1$) in the controls. Furthermore, in the controls, the effect of SYLLABLE on the Cz-LPCs elicited by the stimuli presented to the attended ear was significant ($F[1,34]=4.301$, $p<0.05$). However, this SYLLABLE effect was not observed for the non-attended ear ($F[1,34]=0.050$, n. s.). That is, the Cz-LPCs elicited by the stimuli presented to the attended ear were greater than those to the non-attended ear, and the target syllables in the attended ear (that is, the target stimuli) produced the largest Cz-LPC values in the controls (Fig. 5).

Neither a CHANNEL effect nor an interaction for CHANNEL X SYLLABLE was observed in the first series of tests for the schizophrenics (CHANNEL: $F[1,62]=0.059$, n. s.; CHANNEL X SYLLABLE: $F[1,62]= 0.577$, n. s.), as well as in the second series of tests for the schizophrenics (CHANNEL: $F[1,61]=1.095$, n. s.; CHANNEL X SYLLABLE: $F[1,61]=0.662$, n. s.). That is, the augmentation in the detection of target stimuli was not observed either in the first or the second series of tests of the schizophrenics.

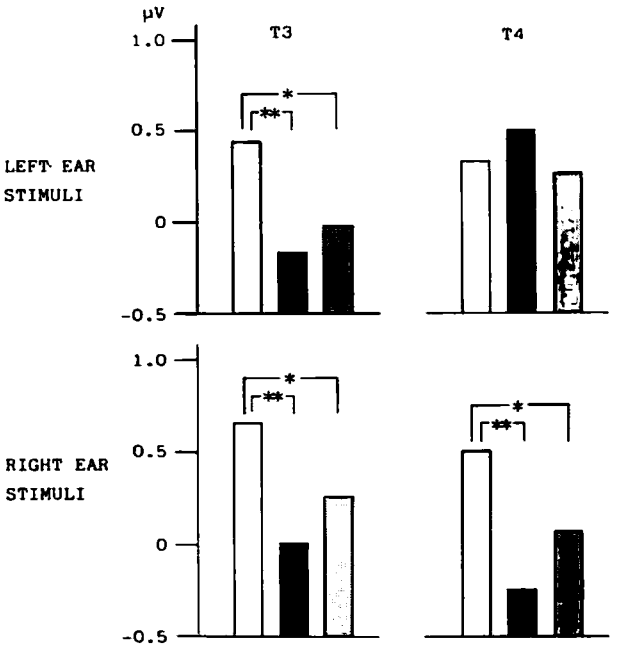


Fig. 6. Averaged amplitudes of the difference waves derived from the T3 and T4 regions. ▭ normals; ▬ schizophrenics, 1st test; ▭ schizophrenics, 2nd test. **p<0.05; *p<0.1.

III-4 Difference wave derived from the Cz, T3 and T4 regions

In order to examine the attention-related negative component, the most negative peak amplitudes (PADW) and latencies (PLDW) of the difference waves, as well as the averaged amplitudes (AADW) of the difference wave were compared among the three groups.

The PADWs and the AADWs derived from the Cz and T3 regions in the first series of tests for the schizophrenics were significantly less than those noted for the controls (Cz-PADW: $t[40]=2.35$, $p<0.05$; Cz-AADW: $t[40]=2.41$, $p<0.05$; T3-PADW: $t[40]=2.79$, $p<0.01$; T3-AADW: $t[40]=3.66$, $p<0.01$). The PADW and the AADW derived from the T3 region in the second series of tests of the schizophrenics were also significantly less than those of the controls (T3-PADW: $t[40]=2.74$, $p<0.01$; T3-AADW: $t[40]=2.64$, $p<0.05$). Although there was a significant difference in results from the Cz between the schizophrenics' first series of tests and the control group, there was no significant difference between the second series of tests and the control group (Cz-PADW: $t[40]=1.53$, n. s.; Cz-AADW: $t[40]=1.43$, n. s.). The PLDWs derived from the T3 and Cz regions were not significantly different among the three groups, nor were the PADW, PLDW, and AADW derived from the T4 region.

In order to investigate the relationship between attentional deficits and hemispheric functioning in the schizophrenics, the AADWs derived from the T3 and T4 regions elicited by the right or left ear stimuli were compared among the three groups.

When the stimuli were presented to the right ear, the AADWs derived from the T3 and T4 regions in the first series of tests of the schizophrenics were significantly less than those of the controls (T3-AADW: $t[19]=2.73$, $p<0.05$; T4-AADW: $t[19]=3.12$, $p<0.01$), and those in the second series of tests of the schizophrenics tended to be significantly less than those of the controls (T3-AADW: $t[19]=1.95$, $p<0.1$; T4-AADW: $t[19]=1.73$, $p<0.1$).

On the other hand, when the stimuli were presented to the left ear, the AADW derived from the T3 region in the first series of tests of the schizophrenics was significantly less than those of the controls ($t[19]=2.40$, $p<0.05$), and those in the second series of tests of the schizophrenics tended to be significantly less than those of the controls ($t[19]=1.83$, $p<0.1$); however, the AADW derived from the T4 region was not significantly different among the three groups (Fig. 6).

## IV Discussion

### IV-1 ERPs and attentional and cognitive functioning in schizophrenics

The N100 amplitude was increased for stimuli in the attended ear, while the P200 amplitude was reduced for the same stimuli in the controls. Furthermore, the P300 component was observed only in the controls when they had detected the target stimuli. These results support those of our previous study (Hiramatsu et al., 1984[9]).

The P300 component is considered to reflect cognitive functioning such as 'context updating' (Donchin et al., 1978[4]).

By subtracting the ERPs elicited by the stimuli in an unattended channel from those elicited by the stimuli in an attended channel, it was revealed that the attention-related endogenous negative component overlapped with the exogenous N100 and P200 components. This also produced an increase in the N100 amplitude, along with a decrease in the P200 amplitude, for the attended channel in this study.

The unmedicated schizophrenics (that is, the schizophrenics in the first series of tests) failed to demonstrate a channel effect for the N100 and P200 components, and the amplitude of the attention-related negative component was less than that of the controls. The channel selection effect was not observed in the case of the schizophrenics before medication. This channel effect, however, became recognizable during the course of the medication.

The LPCs elicited by the target stimuli were not greater in comparison to those of the non-target stimuli in the first or

second series of tests of the schizophrenics. Therefore, even after medication, the target effect was not observed in the schizophrenics, although it was noticed in the control group.

These results support our previous study (Kameyama et al., 1984[6]) by revealing the ERP change during the course of medication. In the previous study, ten unmedicated schizophrenics, as well as a different group of 12 medicated schizophrenics were studied.

The results of the present study suggest that the deficit in channel selective attention of schizophrenics is improved by antipsychotic drugs; however, the deficits in cognitive functioning, such as 'context updating' remain unimproved. Orzack et al. (1967)[10] and Spohn et al. (1977)[11] reported that schizophrenics performed poorly on an attention test (Continuous Performance Test) before medication; showed significant improvement during the course of medication; but that they showed no similar improvement on a cognitive test (Digit Symbol Substitution Test). Killian et al. (1984)[12] assessed the effects of antipsychotic drugs on selected cognitive tests in schizophrenic patients and reported that medication did not affect performance on these tests in any manner. The results of these psychological tests support the results of this study.

IV-2 Selective attention and hemispheric dysfunction in schizophrenics

The averaged amplitudes of the difference wave derived from the T3 and T4 regions in the schizophrenics were less than those of the controls when the stimuli were presented to the right ear. On the other hand, when the stimuli were presented to the left ear, the averaged amplitude of the difference wave derived from the T3 region in the schizophrenics was less than that of the controls, while the amplitude derived from the T4 region showed no difference between the controls and the schizophrenics. These abnormalities were more prominent in the first series of tests than in the second for the schizophrenics.

Hiramatsu et al. (1984)[9] reported that the some mechanism is at work in syllable discrimination tasks such as in the dichotic listening tests reported by Kimura (1967)[13]. This mechanism can be said to activate the transmission of the sound presented to the contralateral ear and inhibit the sound presented to the ipsilateral ear. Hence, it can be suggested that the deficits in channel selective attention in unmedicated schizophrenics may be related to the left hemispheric dysfunction, that is, the left hemispheric hypofunction.

Furthermore, positive schizophrenic symptoms were more prominent during the first series of tests than in the second for the schizophrenics. It can also be suggested that the deficits in channel selective attention, as well as the left hemispheric dysfunction of schizophrenia are related to these positive symptoms.

IV-3 Attentional and cognitive functioning and monoamine

The deficit in selective attention in the unmedicated schizophrenics was improved during the course of the antipsychotic drug (haloperidol) medication. The use of haloperidol suppresses Tourette's syndrome and also introduces symptoms of inattentiveness (Goldstone and Lhamon, 1976[14]). In a study by Oke and Adams (1978)[15], rats that received intracisternal 6-Hydoxydopamine (6-OHDA) made many errors when irrelevant stimuli were introduced. These animal experiments suggest that attention is modulated by dopamine activity. Hence, we can speculate that the deficit in selective attention in schizophrenics is related to a hyperdopaminergic activity in the brain. We can also speculate that antipsychotic drugs alleviate this deficit by antidopaminergic action.

On the other hand, since the P300 was not elicited after antipsychotic medication, the dysfunction in cognitive functions, such as 'context updating', was not improved.

The positive schizophrenic symptoms were significantly improved during the second series of tests, whereas the negative schizophrenic symptoms were not improved. Hence, the positive symptoms can be considered related to the abnormalities of the N100 and P200 components, whereas the negative symptoms can be considered related to the abnormalities of the P300 component.

Angrist et al. (1980[16], 1982[17]) have reported that the positive symptoms of schizophrenia were increased by the administration of amphetamines, but negative symptoms were not changed in chronic inpatients. On the other hand, negative symptoms were significantly improved by administering amphetamines to stable outpatients. They concluded that the negative symptoms of their chronic patients were not improved because they had irreversible organic dysfunctions, whereas those of their stable outpatients were reversible and could improve. From these results, they pointed out the possibility that dopaminergic hypofunction contributes some elements to the schizophrenic defect state.

Since the subjects of this study were all stable outpatients, according to the hypothesis of Angrist et al., we can speculate that their negative symptoms and the abnormalities of the P300 component are related to the organic dysfunctions of the dopaminergic system.

In our previous study (Kameyama et al. 1984[6]), we reported that the dosages of the antipsychotic drugs correlated negatively with the amplitudes of the Late Positive Components. Myslobodsky and Mintz (1983)[18] reported that in hemi-Parkinsonian patients, there were lower amplitudes of the P300 components derived from the damaged hemisphere and that this abnormality could be improved by administration of L-DOPA. These facts suggest that drugs which have antidopaminergic effects diminish the amplitudes of the P300 component.

However, in our schizophrenics the P300 component was not clearly elicited during the first series of tests (given to unmedicated schizophrenics). This may suggest that the lack of P300 cannot be explained only by supposing an abnormality in the dopaminergic system.

In a recent study, an abnormality of the noradrenergic system was pointed out for schizophrenics (Van Kammen and Antelman, 1984[19]; Hornykiewicz, 1982[20]). Furthermore, Segal and Bloom (1976)[21] speculated that noradrenaline influences attentional mechanisms. Hence, the relationship between the abnormality of the P300 component in schizophrenics and the abnormality of monoaminergic systems must be elucidated by other experiments that investigate the effects of antidopaminergic, antiadrenergic, and antiserotonergic drugs on ERPs.

References


1. Oades, R. D. (1982). Attention and Schizophrenia. Pitman: London.
2. Näätänen, R., Gaillard, A, W. K., and Mantysalo, S. (1978). Early selective-attention effect on evoked potential reinterpreted. Acta Psychologica, 42, 313-329.
3. Hansen, J. C. and Hillyard, S. A. (1980). Endogenous brain potentials associated with selective auditory attention. Electroencephalography and clinical Neurophysiology, 49, 277-290.
4. Donchin, E., Ritter, W., and McCallum, W. C. (1978). Cognitive psychophysiology: The endogenous components of the ERPs. In Callaway, E., Tueting, P., and Kolow S. H. (Eds), Event Related Brain Potentials in Man. Academic Press: New York. 349-411.
5. Saitoh, O., Kameyama, T., Hiramatsu, K., Niwa, S. and Itoh K. (1981). Event-related brain potentials and selective attention in schizophrenia. Ann. Bull. RILP, 15, 109-127.
6. Kameyama, T., Hiramatsu, K., Niwa, S., Saitoh, O., Rymar K., and Itoh, K. (1984). Selective attentional functioning as reflected in ERPs during syllable discrimination tasks (II). Correlations between cognitive deficits and abnormal ERP findings in schizophrenics. Ann. Bull. RILP, 18, 267-294.
7. American Psychiatric Association. (1980). Diagnostic and Statistical Manual of Mental Disorders, 3rd Ed. Washington.
8. Hink, R. F., Hillyard, S. A., and Benson, P. J. (1978) Event-related brain potentials and selective attention to acoustic and phonetic cues. Biological Psychology, 6, 1-16.
9. Hiramatsu, K., Kameyama, T., Niwa, S., Saitoh, O., Rymar K., and Itoh K. (1984). Selective attentional functioning as reflected in ERPs during syllable discrimination tasks (I). An introduction to the method and results for normal control subjects. Ann. Bull. RILP, 18, 245-266.
10. Orzack, M. H., Kornetsky, C., and Freeman H. (1967). The effects of daily administration of carphenazine on attention in the schizophrenic patient. Psychopharmacology 11, 31-38.
11. Spohn, H. E., Lacoursiere, R. B., Thompson, K., and Coyne L. C. (1977). Phenothiazine effects on psychological and psycho-

physiological dysfunction in chronic schizophrenics. Archives of General Psychiatry, 34, 633-644.
12. Killian, G. A., Holzman, P. S., Davis, J. M., and Gibbons, R. (1984). Effects of psychotropic medication on selective cognitive and perceptual measures. Journal of Abnormal Psychology, 93, 58-70.
13. Kimura, D. (1967). Functional asymmetry of the brain in dichotic listening. Cortex, 3, 163-178.
14. Goldstone, S. and Lhamon, W. T. (1976). The effects of haloperidol upon temporal information processing by patients with Tourette's syndrome. Psychopharmacology, 50, 7-10.
15. Oke, A. F. and Adams R. N. (1978). Selective attention disfunction in adult rats neonatally treated 6-hydoxydopamine. Pharmacology, Biochemistry and Behavior, 9, 429-432.
16. Angrist, B., Rotrosen, J. and Gershon, S. (1980). Differential effects of amphetamine and neuroleptics on negative vs. positive symptoms in schizophrenia. Psychopharmacology 72, 17-19.
17. Angrist, B., Peselow, E., Rubinstein M., Corwin, J., and Rotrosen, J. (1982). Partial improvement in negative schizophrenic symptoms after amphetamine. Psychoparmacology, 78, 128-130.
18. Myslobodsky, M. S. and Mints, M. (1983). Hemisphere laterality vs hemi-interdependence: an answer from analysis of dopamine hemideficiency syndrome. In Flor-Henry, P. and Gruzelier, J. (Eds), Laterality and Psychopathology. Elsevier: Amsterdam. 539-555.
19. Van Kammen, D. P. and Antelman, S. (1984). Minireview. Impaired noradrenergic transmission in schizophrenia? Life Sciences 34, 1403-1413.
20. Hornykiewicz, O. (1982). Brain catecholamines in schizophrenia—a good case for noradrenaline. Nature, 299, 484-486.
21. Segal, M. and Bloom, F. E. (1976). The action of norepinephrine in the rats' hippocampus III: Hippocampal cellular response to locus coeruleus stimulation in the awake rat. Brain Research, 107, 499-511.