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EVENT-RELATED BRAIN POTENTIALS AND SELECTIVE ATTENTION IN SCHIZOPHRENIA

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1. Introduction

Event-related brain potentials (ERPs) have been utilized frequently in research investigating the selective attention mechanisms in the human sensory information processing system. Sutton et al.[18] found a late positive ERP elicited from a relevent stimulus during a psychological task in normals at a latency of some 300 msec from the point of stimulus presentation. This component was designated P300. Hillyard et al.[3, 4] also conducted a series of experiments investigating ERPs during various psychological tasks in normals, and they have proposed that "stimulus set" as termed by Broadbent[1] be indexed by the N100-P200 component, and "response set"[A] by the P300 component, respectively. ERPs are assumed to be good physiological indicators of selective attention.

In this study, Broadbent's, Sutton's and Hillyard's hypotheses derived from normal controls is applied to schizophrenics. The purpose of the study is to distinguish schzophrenics' attentional deficits and their hemispheric dysfunction in auditory information processing from those of normal controls by means of recorded ERPs. In the experiment we employed the dichotic detection task, in which the subjects were requested to detect the target stimuli

A) Two sets of selective attention, i.e., "stimulus set" and "response set" are defined by Broadbent as follows:
"---In the case of perceptual selection, we may for the moment treat them as equivalent to stimulus set and response set. Filtering or stimulus set is the selection of certain items for analysis and response, on the basis of some common characteristics possessed by the desired stimuli. Pigeon-holing or response set is the selection of certain classes of response (category states) as having a high priority for occurrence even if the evidence in their favour is not especially high."
(Decision and Stress by D.E. Broadbent, Academic Press, New York, 1971, p 177)

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from the non-target stimuli presented to one ear, and to count them silently. In this paper the characteristics of the N100-P200 and P300 components of schizophrenics' ERPs are discussed with reference to their disorders in the two stages of selective attention, that is, "stimulus set" and "response set" as defined by Broadbent.

2. Methods

Subjects

Ten schizophrenic patients (4 males, 6 females) were selected randomly from a group of patients diagnosed as schizophrenia at the Neuro-Psychiatric Outpatient Clinic, Tokyo University Hospital. All ten subjects met the criteria for "Schizophrenic Disorders" according to the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, of the American Psychiatric Association (DSM-III). Subjects' ages ranged from 22 to 45 years (mean age: 29 years), and mean age at onset of illness was 24 years. Nine of the ten subjects were under psychotropic drug medication (Table 1). All of the subjects were right-handed.

Ten right-handed volunteers (5 males, 5 females, mean age: 29 years) served as normal controls. They had no history of neurological or psychiatric disorders.

Procedure

In the experiment, tape-recorded stimuli were presented through headphones to subjects seated in a sound-proof room at the Research Institute of Logopedics and Phoniatrics, Faculty of Medicine, University of Tokyo.

Experiment 1. ERP Recording During Binaural Listening

Preceding the dichotic detection task, the subjects were instructed to listen to sound stimuli presented binaurally, and their electroencephalograms (EEGs) were recorded under this condition. Throughout this session, the subjects were requested to relax with eyes closed. The stimuli consisted of 1 kHz tone bursts of 150 msec duration, presented at interstimulus intervals of 2 sec. Tone intensities were approximately 70 dBSL.

Experiment 2. ERP Recording During the Dichotic Detection Task

After Experiment 1, the subjects were asked to perform the

Table 1 Schizophrenic subjects

CASE NO.	CASE	SEX	AGE	AGE at ONSET	MEDICATION	DSM-III
1	Y.S.	F	29	17	none	Disorganized
2	K.M.	M	23	20	CPZ50mg TTX10mg THP2mg	Disorganized
3	T.K.	M	27	23	CPZ100mg THP4mg PMZ25mg	Residual
4	K.T.	F	27	26	CPZ200mg HPD2.25mg THP6mg PMZ25mg NZP5mg	Residual
5	S.S.	F	23	19	PPZ6mg THP6mg DZP6mg	Undifferentiated
6	K.K.	M	38	35	CPZ75mg HPD3mg THP6mg PMZ75mg DZP6mg NZP5mg	Disorganized
7	T.O.	F	31	30	CPZ125mg HPD3mg THP4mg PMZ62.5mg DZP4mg PB40mg	Paranoid
8	N.H.	F	22	18	HPD3mg PZ2mg THP5mg	Paranoid
9	M.O.	M	29	22	CPZ75mg HPD2.25mg THP6mg CZX6mg Li_2CO_3 600mg	Disorganized
10	E.F.	F	43	28	CPZ100mg LPZ25mg HPD9mg THP6mg	Disorganized

CPZ: chlorpromazine TTX: thiothizene THP: trihexyphenidyl
PMZ: promethazine HPD: haloperidol NZP: nitrazepam
PPZ: perphenazine DZP: diazepam PB: phenobarbital
PZ: pimozide CXZ: cloxazolam Li_2CO_3: lithium carbonate

dichotic detection task. The subjects were instructed to distinguish the "target stimuli" from the "non-target stimuli" presented to one ear, counting the "target stimuli" silently. At the conclusion of each series of stimulus presentation, the subjects were asked to give the total number of "target stimuli" counted. EEGs were recorded during this dichotic detection task.

The stimuli consisted of four non-verbal sounds, which are shown schematically in Fig 1. As shown in the figure, each stimulus consisted of a frequency modulation sound (FM sound) which lasted 50 msec and a frequency constant sound (tone burst) which lasted

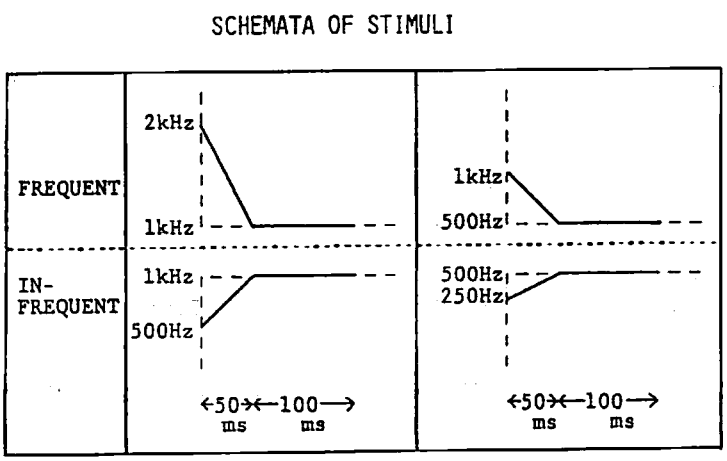

Fig. 1 Schematic representations of the stimuli employed in the experiment (ordinate: frequency, abscissa: time course, See text.)

100 msec. Total duration of each stimulus was 150 msec. The four stimuli were paired based on equal constant frequency, that is, "1 kHz" pair, shown on the left, and "500 Hz" pair, shown on the right of Fig. 1. Each pair of stimuli was presented to each individual ear during a session. Two sounds in the upper part of Fig. 1 were presented more frequently with a priori probability of 0.8, then the two sounds in the lower part with a priori probability of 0.2. Infrequent stimulus i.e., "target stimulus" of each pair of sounds was required to be detected. Inter-stimulus intervals were 2 sec. Tone intensities were approximately 70 dBSL. The attended ear to which the target stimulus was presented was abbreviated "left" or "right."

As shown in Table 2, Experiment 2 consisted of four sessions (two target stimuli ("500 Hz," "1 kHz") x two sides of attend ear ("left," "right")).

Figure 2 illustrates the condition in which a target stimulus of "1 kHz" was presented to the right ear of a subject (session 4 in Table 2).

EEG recording

EEGs were derived from the T3, T4 and Cz regions, monopolarly using linked ear lobes (A1 + A2) as reference. Ag/AgCl electrodes were employed. EEGs were then amplified using DC preamplifiers (YHP, 8811A) and recorded on FM analog tapes with stimulus signals

Table 2 Experimental sessions (Numbers in the table indicate the sequence of the experimental sessions.)

SEQUENCE OF EXPERIMENTAL SESSIONS

relevant stimulus / attended ear	"500Hz"	"1KHz"
right	1	4
left	3	2

(data-recorder: TEAC, R-252) for subsequent off-line analyses.

Data analysis

After the experiment, EEGs without artifacts were selected and digitized at the rate of sampling frequency of 250 Hz/CH.

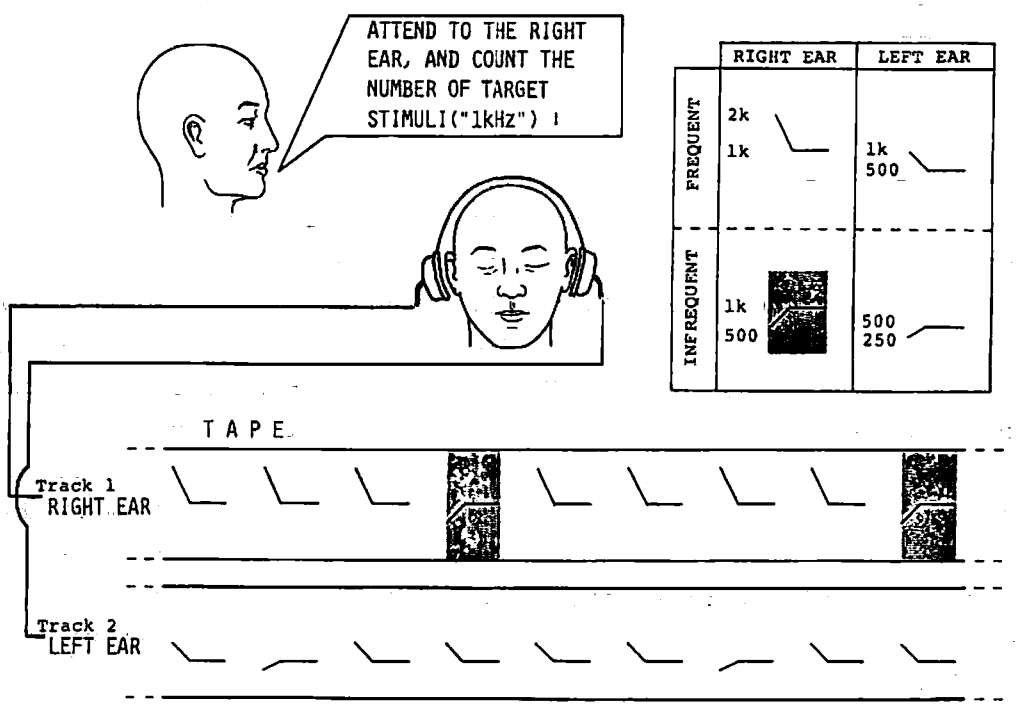

Fig. 2 Illustration of one experimental session. (The subject is asked to detect the target stimuli, "1 kHz," presented to the right ear, and to count them silently. At the conclusion of the stimulus presentation, the subject is asked to give the total number of target stimuli. EEG is recorded during the session.)

EEGs were averaged using a laboratory mini-computer (DEC, LSI-11/2). The averaging epoch began 500 msec before stimulus onset and lasted for 1500 msec thereafter. A total of 64 or 128 data was averaged.

Each of the ERP components was labeled as follows: N100 as the most negative peak in the 60 - 180 msec after stimulus onset, P200 as the most positive peak in 120 - 250 msec, P300 as the most positive peak in 250 - 510 msec. Each peak amplitude of the ERP components was scaled using a mean voltage of 500 msec duration prior to stimulus presentation as zero level. The interval between stimulus onset and the appearance of each peak of the ERPs were designated as the peak latency of each.

3. Results

Figure 3 illustrates the representative averaged ERP patterns of schizophrenic and normal control subjects. The amplitudes of the N100-P200 components and the P300 component in schizophrenics were smaller than those in normal controls, and P300 waveforms in schizophrenics were not so sharply defined as those in normal controls.

The N100-P200 component

Table 3 shows the mean and standard deviation of each component's amplitude of ERPs derived from the Cz region of both schizophrenics and normal controls, which were elicited from three different stimuli, that is, (1) ERPs elicited from sounds presented binaurally, designated as "binaural," (2) ERPs elicited from irrelevant stimuli during the dichotic detection task, designated as "irrelevant," (3) ERPs elicited from relevant stimuli during the dichotic detection task, designated as "relevant." Mean amplitude of the N100-P200 component of each ERP of schizophrenics was significantly smaller than that of normal controls ("binaural": $t = 2.822$, $p < 0.02$; "irrelevent": $t = 3.74$, $p < 0.005$; "relevant": $t = 2.67$, $p < 0.05$).

Figure 4 shows the changes of the N100-P200 amplitude due to presence or absence of task in both schizophrenics and normal controls. The dichotic detection task tended to produce a larger N100-P200 amplitude than the without-task condition in schizophrenics ($t = 1.94$, $p < 0.1$), but the same task produced no differ-

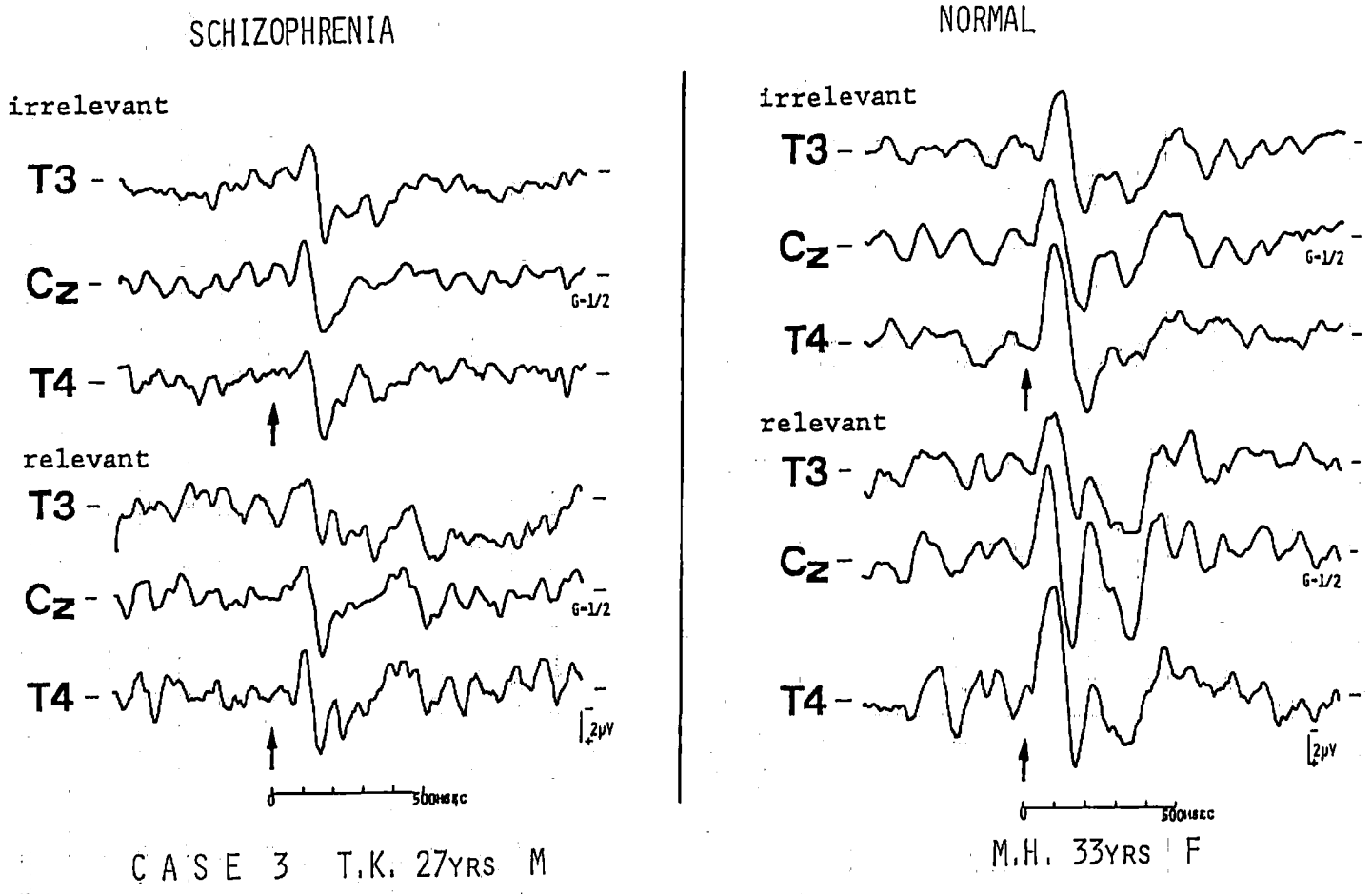

Fig. 3 Representative ERP waveforms of schizophrenics and normal controls. (The terms "T3", "Cz" and "T4" indicate the EEG recording sites. Arrows indicate the starting points of stimulus presentation. Upper three traces are ERPs elicited from the "irrelevant stimuli," and lower three are ERPs elicited from the "relevant stimuli.")

Table 3 The means and standard deviations of the amplitudes of each ERP component derived from the Cz region in both schizophrenics and normal controls. (In this table, the terms "binaural," "dichotic," "irrelevant," and "relevant" indicate the ERP recording conditions. See text.)

MEAN AMPLITUDE AND S.D. OF N100, N100-P200, P300 (Cz)

		binaural	dichotic	
			irrelevant	relevant
N100	S	3.2 ± 1.6	3.8 ± 1.6	4.1 ± 1.3
	N	6.1 ± 2.4 **	6.1 ± 1.7 **	6.6 ± 2.2 **
N100-P200	S	7.3 ± 2.2	8.0 ± 2.1	8.9 ± 1.4
	N	13.1 ± 5.8 *	12.8 ± 3.4 ***	12.4 ± 3.7 *
P300	S		1.7 ± 1.1	3.6 ± 2.7
	N		4.3 ± 2.1 **	8.0 ± 2.1 ***

* p<0.05
** p<0.01
*** p<0.005
(t Test)

S: schizophrenia (n=10)
N: normal (n=9)

ence in normal controls.

Table 4 shows the mean and standard deviation of each peak latency of ERPs derived from the Cz region, elicited from the above-mentioned three stimuli in both groups. There was no real difference in N100 and P200 peak latencies between schizophrenics and normal controls.

The P300 component

Figure 5 compares the P300 amplitudes elicited from "relevant" stimuli from the Cz region between schizophrenics and normal controls. The mean amplitude of the P300 component in schizophrenics was 3.6μV, and that in normal controls was 3.0μV. The mean amplitude of schizophrenics was significantly smaller than that of the normal controls ($t = 3.93$, $p<0.005$).

As shown in Table 4, the mean peak latency interval of the P300 component in schizophrenics was significantly longer than that of normal controls ($t = 3.94$, $p<0.005$).

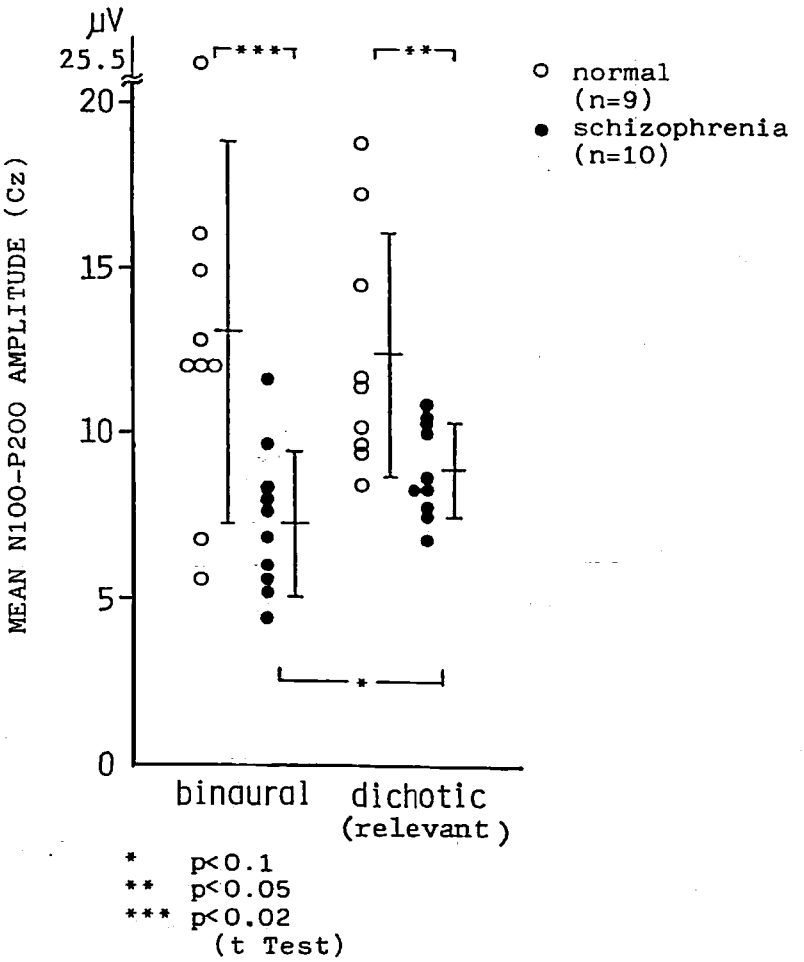

Fig. 4 The N100-P200 amplitudes (derived from the Cz region) of schizophrenics and normal controls in the task and without-task conditions. (See text.)

Figure 6 shows the mean amplitude of the P300 component of ERPs derived from the Cz region in schizophrenics, elicited from two relevant stimuli, "500 Hz" and "1 kHz." The figure compares the data obtained from "attend to the right ear" as opposed to "attend to the left ear." In the "1 kHz" situation, the amplitude of the P300 component elicited from relevant stimuli applied to the right ear failed to show a marked difference from the irrelevant stimuli, while there was a significant difference between the relevant and irrelevant stimuli while attending to the left ear.

Figure 7 shows the amplitudes of the P300 component elicited from the relevant stimuli as compared to the irrelevant stimuli in

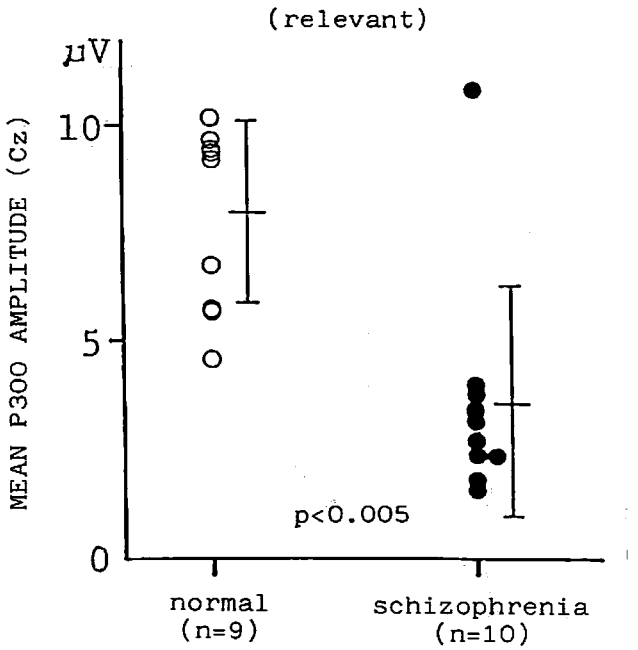

Fig. 5 The P300 amplitudes (derived from the Cz region) of schizophrenics and normal controls. (See text.)

normal controls. The data shows significant difference between the relevant and the irrelevant stimuli under all conditions, including "500 Hz" and "1 kHz" target stimuli, as well as sidedness of attended ear.

Comparison of the N100-P200 amplitude of ERPs derived from the T3 and T4 regions

Figure 8 shows the mean amplitudes of the N100-P200 components of the ERPs from the T3 and T4 regions of schizophrenics as well as normal controls, elicited from the relevant and irrelevant stimuli. The figure compares the data obtained from "attend to the right ear" as opposed to "attend to the left ear." The mean amplitudes of the N100-P200 components derived from both the T3 and T4 regions of schizophrenics were significantly smaller than those of normal controls (T3: $t = 2.91$, $p<0.02$; T4: $t = 2.39$, $p<0.05$) when relevant stimuli were applied to the right ear. No significant difference was found between normal controls and

Table 4 The means and standard deviations of the latencies of each ERP component derived from the Cz region in both schizophrenics and normal controls. (In this table, the terms "binaural," "dichotic," "irrelevant," and "relevant" indicate the ERP recording conditions. See text.)

MEAN PEAK LATENCY AND S.D. OF N100, P200, P300 (Cz)

		binaural	dichotic irrelevant	dichotic relevant
N100	S	98 ± 8	102 ± 13	101 ± 11
	N	100 ± 15	102 ± 10	98 ± 11
P200	S	170 ± 22	182 ± 13	184 ± 12
	N	176 ± 15	189 ± 13	182 ± 17
P300	S		381 ± 55 **	392 ± 45 ***
	N		322 ± 22 **	332 ± 16 ***

** $p<0.01$
*** $p<0.005$
(t Test)

S: schizophrenia (n=10)
N: normal (n=9)

schizophrenics when the same stimuli were applied to the left ear. Irrelevant stimuli produced a significantly smaller amplitude in the N100-P200 component derived from the T3 region of schizophrenics than in that of normal controls ("right": $t = 3.31$, $p<0.01$; "left": $t = 2.60$, $p<0.05$), while there was no significant difference between the amplitude of the N100-P200 component derived from the T4 region of schizophrenics and that of normal controls. The sidedness of the attended ear had no influence on the results.

In binaural listening, without-task situation, the amplitude of the N100-P200 component derived from the T3 and T4 regions of schizophrenics was significantly smaller than that of normal controls (T3: $t = 3.05$, $p<0.01$; T4: $t = 3.07$, $p<0.01$).

Relationship between P300 amplitude and correct response percentage

This experimental group of schizophrenics and normal controls was also subjected to a similar experiment employing the same

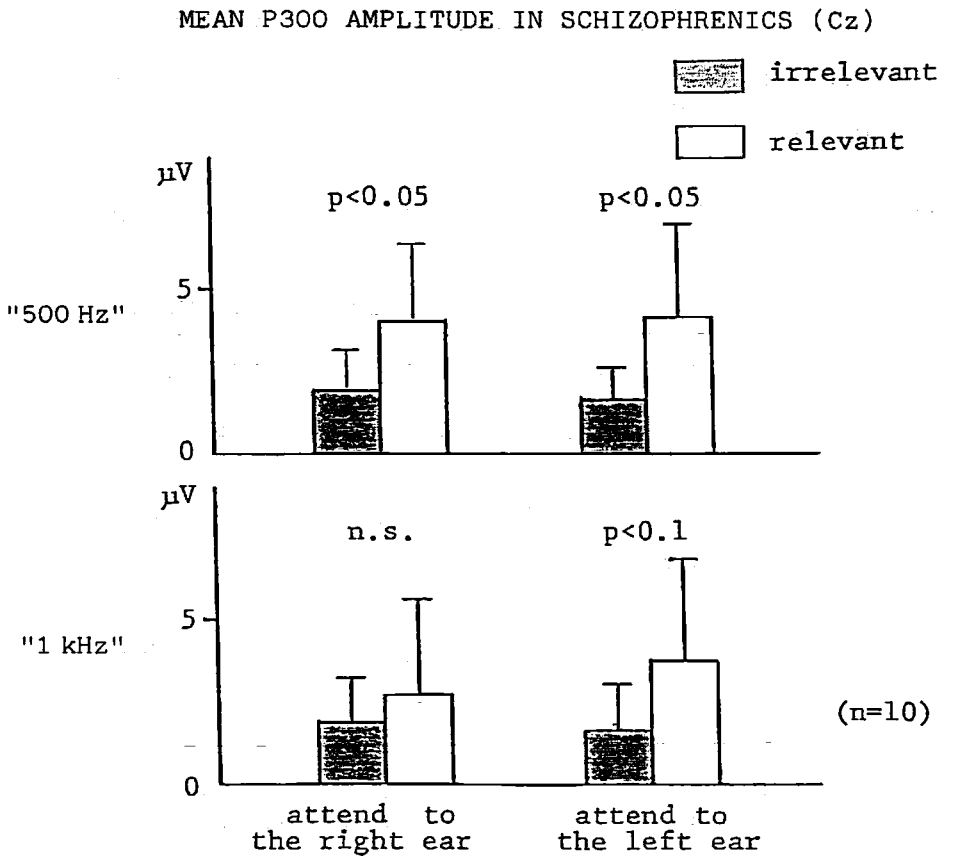

Fig. 6 The P300 amplitudes elicited from the "irrelevant stimuli" and the "relevant stimuli" in schizophrenics. (See text.)

stimuli ("500 Hz" and "1 kHz," relevant and irrelevant), requiring subjects to press a response key upon presentation of the "target stimuli," instead of counting the "target stimuli" silently. This experiment yielded each subject's reaction time for relevant stimuli and correct response percentage. Then, the relationship between the amplitude of the P300 component and correct response percentage was examined.

Figure 9 illustrates the relationship between the amplitude of the P300 component and correct response percentage of relevant stimuli ("500 Hz" and "1 kHz") for both schizophrenics and normal control groups. In "1 kHz" stimulus presentation, a positive correlation was found between correct response percentage and the amplitude of the P300 component in both schizophrenic and normal control groups. However, increase in amplitude of the P300 component was greater for normal controls than for schizophrenics.

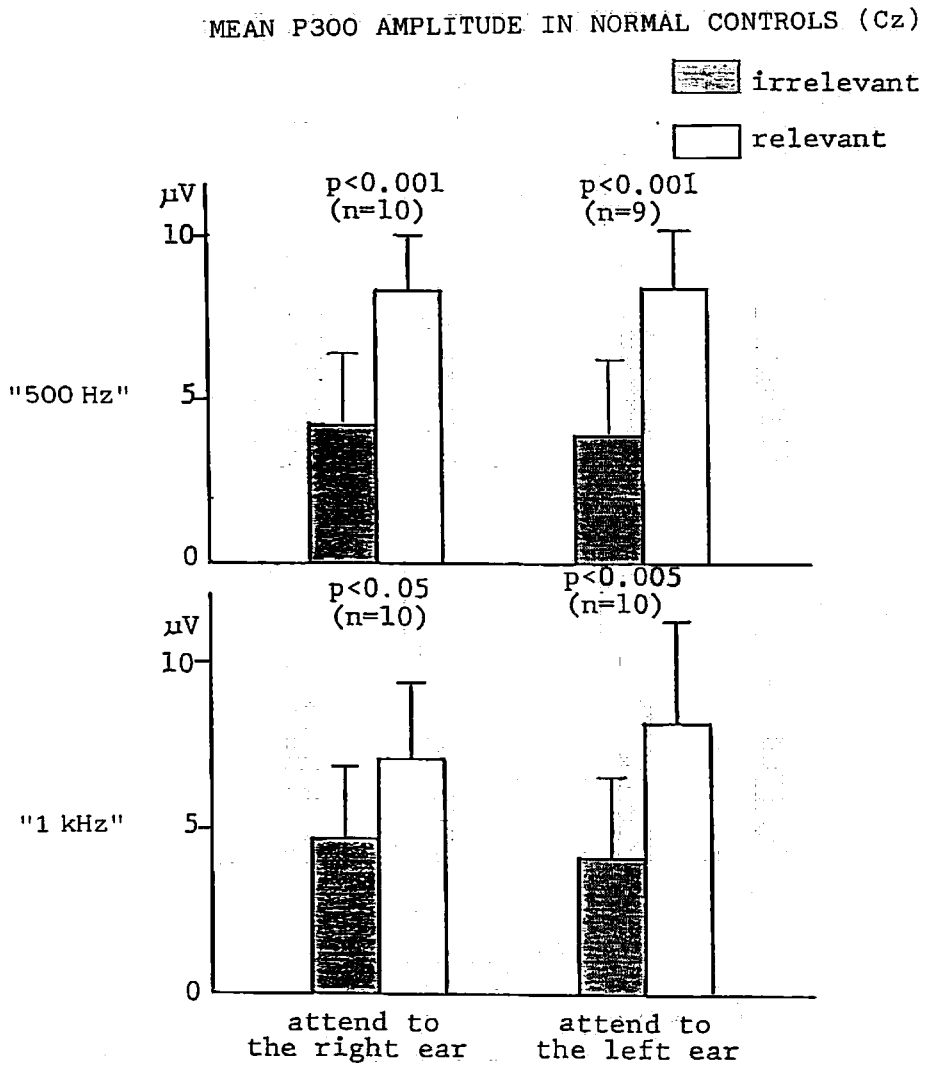

Fig. 7 The P300 amplitudes elicited from the "irrelevant stimuli" and the "relevant stimuli" in normal controls. (See text.)

4. Discussion

Attentional deficits in schizophrenics

Broadbent[1] proposed two stages of selective attention in the human sensory information processing system, i.e., "stimulus set" and "response set." Hemsley[2] reviewed the experimental psychology research on schizophrenics' attentional deficits applying Broadbent's hypothesis with normals. He demonstrated that schizophrenics had disturbances in both sets of selective attention, but that most of the studies on attentional defects of schizophrenics had not differentiated between these two sets.

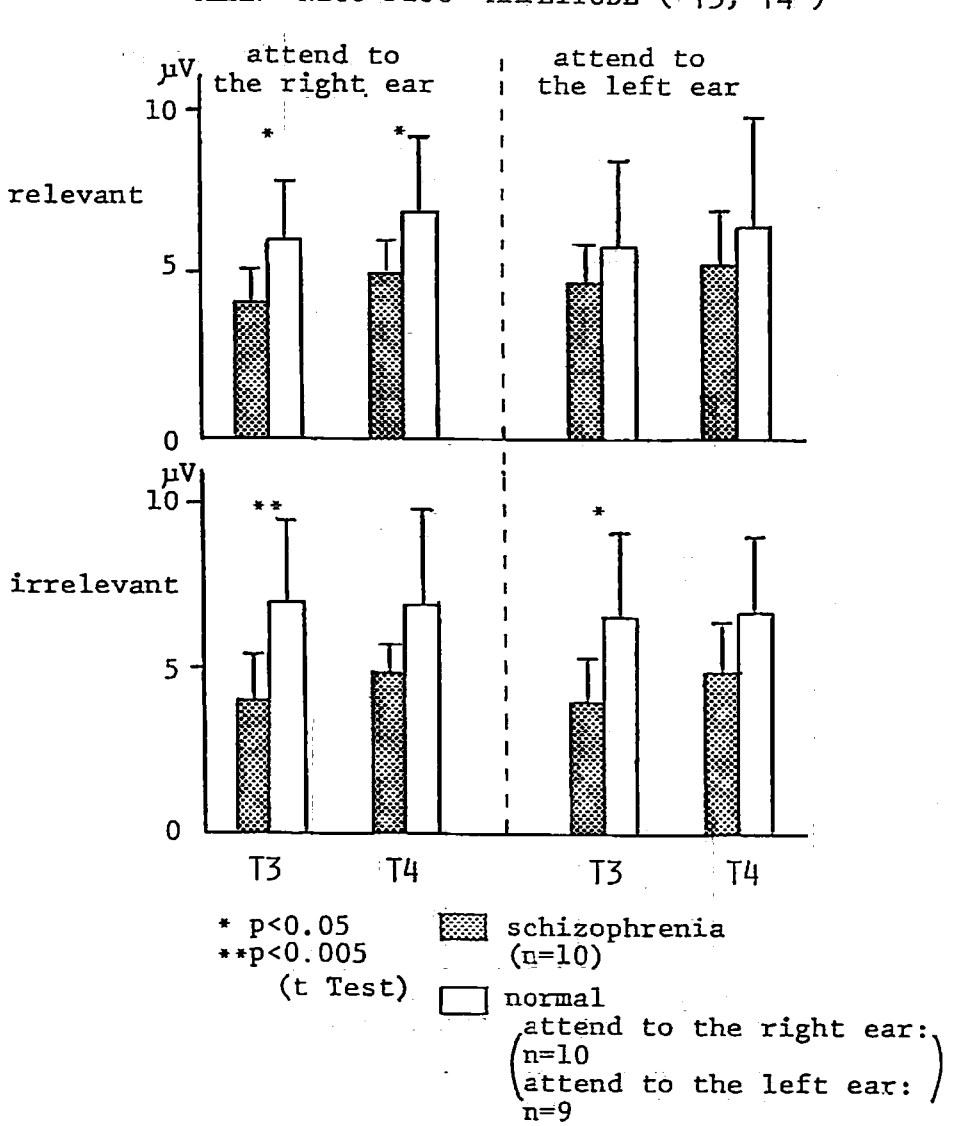

Fig. 8 The N100-P200 amplitudes derived from the T3 and T4 regions in schizophrenics and normal controls. (See text.)

Hillyard et al.[3,4] proposed that Broadbent's two sets of selective attention be indexed by the different ERP components, based on their ERP research studies on normals.

In the following discussion, the results of the experiment will be discussed with reference to the two sets of selective attention defined by Broadbent.

(1) "Stimulus set" and the N100-P200 component

Hillyard et al.[3,4] and Picton and Hillyard[12] have proposed

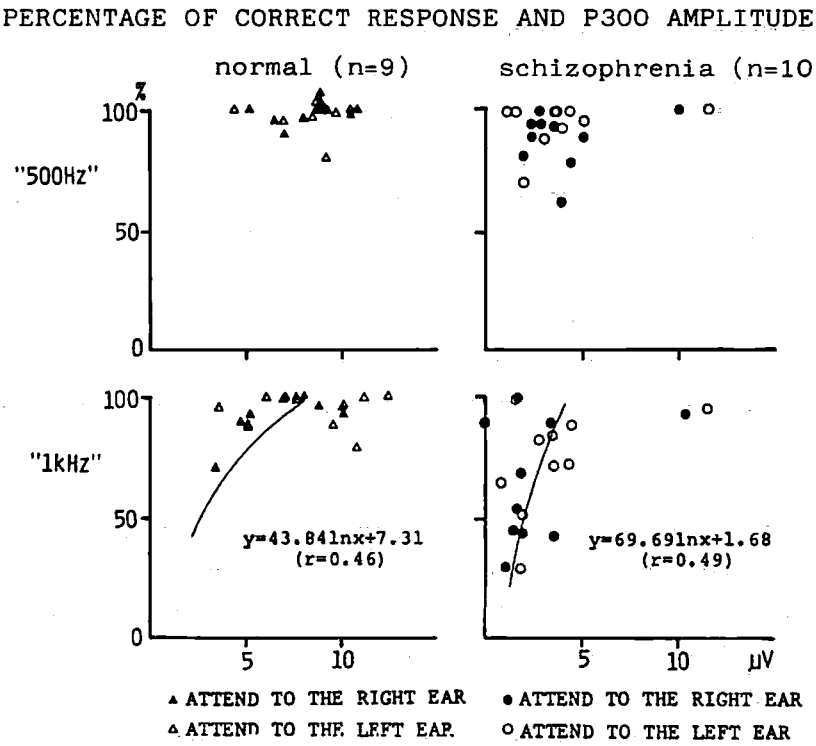

Fig. 9 The relationship between correct response percentage and the P300 amplitude in schizophrenics and normal controls. (See text.)

that the N100-P200 component reflects Broadbent's "stimulus set" (or "filtering"), or Treisman's[20] "input selection" in sensory information processing. The present results showing that the amplitude of the N100-P200 component of schizophrenics was smaller than that of normal controls are in consensus with the results of previous reports.[7, 15] Our results suggest that schizophrenics have some disturbance in the "stimulus set" of selective attention. Moreover, this also supports the "filter" deficit theory proposed by McGhie[9] and Payne et al.[11]

Only in schizophrenics did the dichotic detection task tend to produce a larger amplitude of the N100-P200 component than in the without-task condition. This was not observed in normal controls. This condition may be interpreted as the result of increased attention level while engaged in tasks. It also probably corresponds to the fact that the number-reading task, that is, tracking and reading silently a number on a pendulum, can normal-

ize certain kinds of eye-tracking impairments in schizophrenics (Shagass et al.,[16] Holzman et al[6]).

(2) "Response set" and the P300 component

Sutton et al.[18,19] first reported the P300 component of ERPs in normals, and they proposed that the P300 component is an endogeneous (rather than evoked) potential that is emitted when relevant or salient information is recognized by the subjects.

Hillyard et al. proposed that the P300 component reflects processes where newly-input stimulus is compared with stored memory representation of relevant information. This process has been termed "response set" or "pigeon-holing" by Broadbent and "target selection" by Treisman.[20]

Our results concerning the P300 component in normal controls support the above hypothesis. They also show that the amplitude of the P300component in schizophrenics is smaller than in normal controls. This suggests that schizophrenics also have a disturbance in the "response set" of selective attention. The increase in amplitude of the P300 component was greater for normal controls than for that of schizophrenics. Further study on the implications of this condition is more necessary than study on the implications of the disturbance in "response set" of selective attention in schizophrenics.

Ruchkin et al.[14] have demonstrated that "guessing tasks" increase the amplitude of the P300 component, but that "detection tasks" reduce it. The dichotic detection task in the present experiment also appears to bear the characteristics of a "guessing task" in normal controls, since normal control subjects are more likely to guess the appearance of target stimuli than schizophrenic subjects. Schizophrenic subjects seemed to merely detect targets. It may remain, in the case of schizophrenics, a simple "detection task." This difference in approach to the task between schizophrenic and normal control subjects may account for the large difference in the amplitude of the P300 component between the two groups.

As mentioned above, abnormal ERPs in schizophrenics are thought to be a physiological reflection of disturbance in selective attention. Therefore, ERP research studies are considered useful in clarifying schizophrenics' attentional deficits in their sensory information processing systems.

Hemispheric asymmetries of ERPs in schizophrenics

Hiramatsu et al.[5] reported observing abnormal auditory evoked response waveforms in some schizophrenic patients, i.e., the N100 component of the auditory evoked responses (AEPs) of the left mid-temporal region of schizophrenics with persistent auditory hallucinations showed a double-peaked pattern, and the phase of AEP from the left mid-temporal region and that from the right mid-temporal region were reversed. Regarding the left to right asymmetry, Roemer et al.[13] also reported that in schizophrenic subjects the left hemisphere showed AEPs with unstable waveforms.

In the present experiment, the following results were obtained. When relevant stimuli were applied to the right ear, schizophrenics produced smaller amplitude of the N100-P200 component at the T3 and T4 regions than normal controls. No difference was found between normal controls and schizophrenics when stimuli were applied to the left ear. Irrelevant stimuli produced smaller amplitude of the N100-P200 component at the T3 region in schizophrenics than in normal controls, while the amplitude of the N100-P200 component at the T4 region showed no difference between normal controls and schizophrenics. The sidedness of the attended ear had no effect on the above result. In addition, the relevant stimuli applied to the right ear failed to produce a larger amplitude of the P300 component at the Cz region than the irrelevant stimuli, while the relevant stimuli applied to the left ear produced a larger amplitude than the irrelevant stimuli.

During the dichotic detection task, the hemispheric functions contralateral to the side of the ear to which relevant stimuli are presented are those which are mainly activated (Milner et al.,[10] Kimura[8]). The above results, therefore, suggest that when schizophrenics are engaged in psychological tasks, their selective attention is distracted more strongly in the left hemisphere than in the right.

ERP studies are considered to be one means of clarifying the asymmetry of hemispheric dysfunction in schizophrenics.

Effects of psychotropic drugs

Shagass et al.[17] reviewed the literature concerning the effects of psychotropic drugs on ERPs and reported that minor tranquilizers

and sedatives, producing a state of drowsiness in subjects, reduced the ERP amplitude. They also reported that anti-psychotic medication tends to improve deviant ERPs toward "normal."

Among the schizophrenic subjects, one subject who was receiving no medication showed almost the same ERP amplitude as the mean amplitude of ERPs of schizophrenics who were receiving medication. Hence, the effect of medication appears to have had no influence on the results of this study. However, this factor needs further investigation.

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