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CORRELATIONS OF EVENT-RELATED POTENTIALS WITH SCHIZOPHRENIC DEFICITS IN INFORMATION PROCESSING AND HEMISPHERIC DYSFUNCTION*

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Summary

In order to obtain further insight into hemispheric dysfunction in schizophrenics, two experiments were conducted employing Event-Related Potential (ERP) recording during dichotic detection tasks as well as syllable discrimination tasks. ERP results derived from the T3 and T4 regions are reported. Based on results in the two experiments, it is concluded that schizophrenics display a dysfunction of the left hemisphere, as well as a dysfunction in the integration mechanism of both hemispheres. It is also speculated that the left-hemisphere dysfunction in schizophrenics is particularly correlated with positive psychotic symptoms.

Introduction

Schizophrenics have long been noted as demonstrating various psychological deficits (Hunt and Cofer, 1944), among which, disturbances in attentional functioning have caught the attention of many investigators (e.g. Oades, 1982). Here, attentional function refers to not only the selection of relevant stimuli, but also, to the evaluation of stimuli and the selection of appropriate responses. The former corresponds to "stimulus set," the latter to "response set," as defined by Broadbent (1958, 1971). Hemsley and his colleagues (Hemsley and Zawada, 1976; Hemsley and Richardson, 1980) reported that disturbances in response set distinguished schizophrenics from depressives.

Measurements of Event-Related Potentials (ERPs) have been utilized in studies on attentional functioning. Hink, Hillyard and Benson (1978) recorded ERPs during syllable discrimination tasks and found that the N1 component in normal subjects was enhanced for all stimuli in the attended ear, while the P3 component was enhanced only for "target" stimuli in that ear. They concluded that the N1 and P3 waves provide converging physiological evidence for the existence of multiple levels of selective attention as proposed by Broadbent. Although many controversies still exist, the following is assumed at the present time: The N1 component correlates with the stimulus set, while the P3 component is related to the response set.

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Accordingly, the present authors decided to investigate schizophrenic deficits in attentional functioning in terms of ERPs, particularly during psychological tasks necessitating the activation of the two sets in selective attention. More specifically, dichotic detection tasks as employed by Springer (1971) and syllable discrimination tasks as employed by Hink et al. were considered well suitable to such an investigation.

In addition, ERP studies employing the tasks mentioned above seem to provide further evidence for hemispheric dysfunction in schizophrenics, since such dysfunction has been suggested partly on the basis of previous results by other investigators obtained with dichotic listening tasks (e.g., Colburn and Lishman, 1979).

Hence, we conducted two experiments with schizophrenics, measuring ERPs during dichotic detection tasks and syllable discrimination tasks, respectively. In the present report, the results concerning ERPs recorded in the temporal regions will be described. Correlations of ERPs derived from the Cz region with the two sets involved in selective attention will be presented elsewhere (Saitoh, Hiramatsu, Niwa, Kameyama and Itoh, 1983; Hiramatsu, Kameyama, Niwa, Saitoh, Rymar and Itoh, 1983).

Experiment I

Method

Subjects

Ten schizophrenics (4 males, 6 females) who met the diagnostic criteria for schizophrenic disorders in DSM-III, as well as 10 normal subjects (5 males, 5 females) participated in Experiment I. The ages of the schizophrenics ranged from 22 to 43 years (mean, 29.2), with those of the normal subjects ranging from 21 to 42 years (mean, 29.3). Nine out of the ten schizophrenics had been undergoing psychotropic drug therapy. All subjects were right-handed and free from any hearing disabilities.

Procedure

Dichotic detection tasks were employed in Experiment I. The stimuli consisted of the four non-verbal sounds shown schematically in Fig. 1. Each stimulus consisted of a frequency modulation sound which lasted 50 msec, and a frequency constant sound which lasted 100 msec. The total duration of each stimulus was 150 msec. The four stimuli were paired on the basis of equal constant frequency. That is, the "1 kHz" pair, shown on the left, and the "500 Hz" pair, shown on the right of Fig. 1. Each pair of stimuli was presented through headphones simultaneously to both ears during a session. The two sounds in the upper part of Fig. 1 were presented more frequently, with an a priori probability of 0.8, than the two sounds in the lower part of Fig. 1, which were presented with an a priori probability of 0.2. The infrequent stimuli, that is, the "target stimuli" of each pair of sounds, were required to be detected. The interstimulus intervals were of 2 sec duration. The tone intensities were approximately 70 dBSL.

Experiment I consisted of four sessions: two target stimuli (1 kHz, 500 Hz) × two attended ears (left, right). In each session, the subjects were required to detect the target stimuli and to count them silently. At the conclusion of the stimulus presentation, the subjects were asked to give the total number of target stimuli. EEGs were recorded during the sessions.

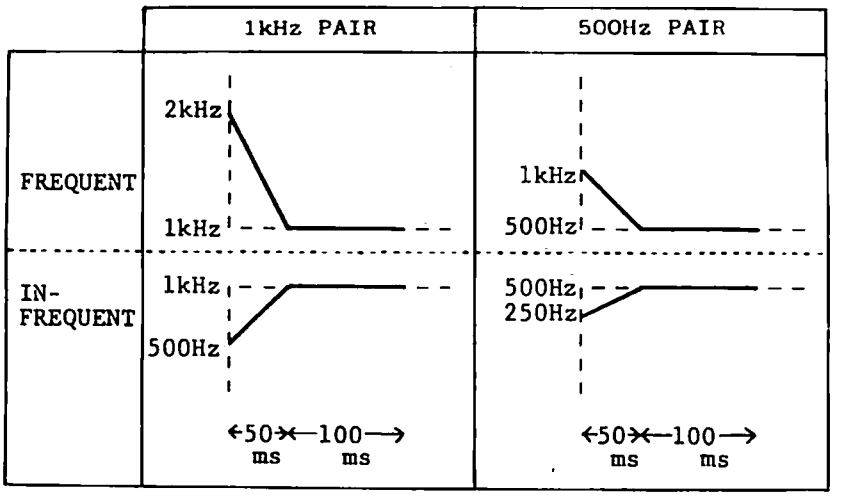

Fig. 1 *Schemata of stimuli*

EEG recording and data analysis

EEGs were recorded at the Cz, T3 and T4 regions monopolarly, utilizing linked earlobe electrodes as references (electrodes: Ag/AgCl). The EEGs were then amplified using DC preamplifiers (bandpass down 6 dB at 1.5 and 300 Hz) (YHP, 8811A) and recorded on FM analog tapes along with the stimulus signals (data recorder: TEAC, R-252). After the experiment, the EEGs without artifacts were passed through a bandpass filter set at 1.5 to 25 Hz and digitized at a sampling frequency of 250 Hz/CH. Subsequently, the EEGs were averaged using a laboratory mini-computer (DEC, LSI-11/2). The averaging period began 20 msec before the stimulus onset and lasted for 620 msec thereafter. A total of 56 or 112 EEGs were averaged for each ERP, and printed out by an X-Y plotter.

The method for measuring the ERP components is illustrated in Fig. 2. Each of the ERP components was labelled 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 (LPC including the P300 component) was the averaged amplitude of the ERP in the 50–330 msec period after the P200 peak. The amplitudes and latencies of the N100 and P200 components and the LPC were measured employing the mini-computer and printed out by a line-printer. Each amplitude of the ERP components was measured with respect to a 20 msec pre- and post-stimulus baseline at the zero level.

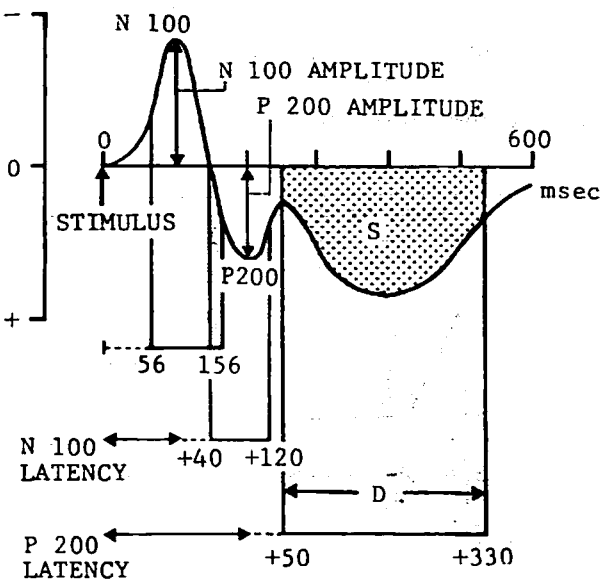

Fig. 2 *Illustration of the method for measuring ERP components*

Results

The N100, P200 and late positive components of the schizophrenics were compared with those of the normal controls. There was no significant difference in the latencies of each component between the schizophrenics and the normal controls. Below, the results concerning the amplitudes of each ERP component will be presented. Hereafter, ERPs elicited by sounds which included target stimuli presented to either ear will be abbreviated as "ERPs to target stimuli": those elicited by sounds which included no target stimuli as "ERPs to non-target stimuli." In addition, N100 components derived from the T3 and T4 regions will be designated as "T3-N100" and "T4-N100," respectively. P200 components derived from the T3 and T4 regions will also be designated as "T3-P200" and "T4-P200," respectively.

1. N100 component

Fig. 3 shows the mean amplitudes of T3-N100 and T4-N100 to the target stimuli presented to the right as well as left ear in both groups. When the target stimuli were presented to the left ear, the mean amplitudes of T3-N100 and T4-N100 were significantly smaller in the schizophrenics than in the normal controls (T3: $t = 2.42$, $p < 0.02$; T4: $t = 2.97$, $p < 0.005$). Target stimuli presented to the right ear produced a significantly smaller T3-N100 amplitude in the schizophrenics than in the normal controls ($t = 3.10$, $p < 0.005$). However, there was no significant difference in the amplitudes of T4-N100 to target stimuli presented to the right ear between the two groups. In examining the intra-group differences between T3-N100 and

T4-N100 to target stimuli presented to one ear, it was found that in schizophrenics target stimuli presented to the right ear tended to produce a smaller T3-N100 amplitude than T4-N100 amplitude ($t = 1.76$, $p < 0.1$).

The "laterality index (LI)" concerning the amplitudes of the N100 component was calculated according to the following formula:

$$LI = \frac{T3N100AMP - T4N100AMP}{T3N100AMP + T4N100AMP} \times 100,$$

where T3N100AMP = the T3-N100 amplitude; and T4N100AMP = the T4-N100 amplitude.

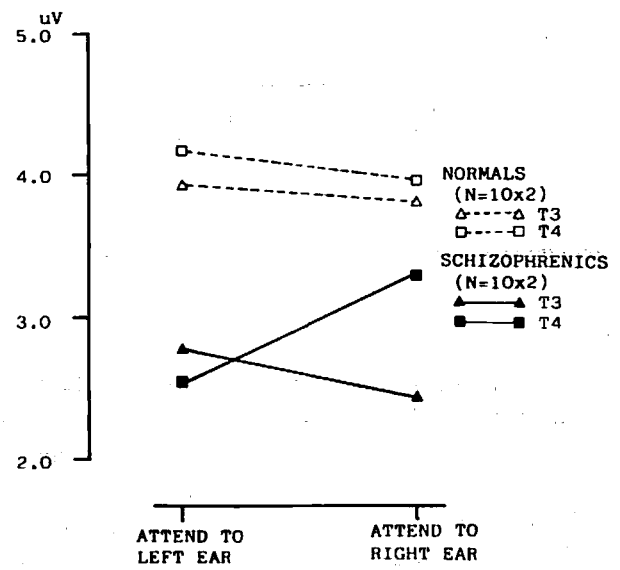

Fig. 3 *Mean amplitudes of T3-N100 and T4-N100 for the target stimuli*

Fig. 4 shows LIs for target stimuli presented to the right as well as left ear in both groups. When attending to the left ear, the normal controls displayed a minus value for LI, which indicates that the T4-N100 amplitude was greater than the T3-N100 amplitude. On the other hand, the schizophrenics displayed a plus value for LI, which indicates that the T4-N100 amplitude was smaller than the T3-N100 amplitude for them. When attending to the right ear, the normal controls displayed a plus value for LI, which indicates that the T3-N100 amplitude was greater than the T4-N100 amplitude for them. On the other hand, the schizophrenics displayed a minus value for LI, which indicates that the T3-N100 amplitude was smaller than the T4-N100 amplitude for them. The LI pattern for the schizophrenics was the reverse of that for the normal controls.

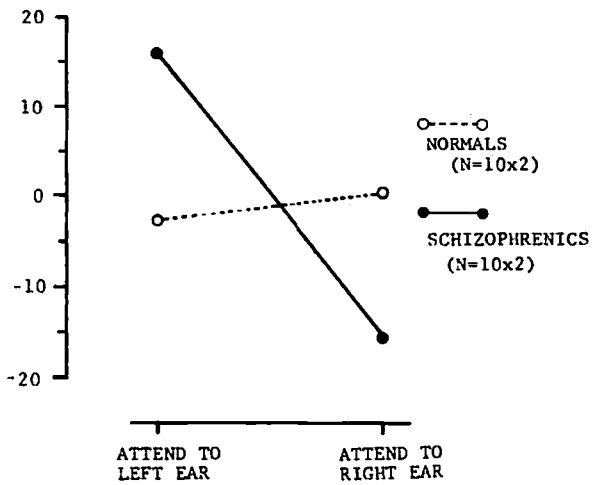

Fig. 4 *Laterality index (LI) of the amplitude of the N100 component for the target stimuli*

2. P200 component

Fig. 5 shows the mean amplitudes of T3-P200 and T4-P200 for non-target stimuli presented to the right and left ears. Non-target stimuli presented to the left ear tended to produce a smaller T3-P200 amplitude in the schizophrenics than in the normal controls ($t = 1.89$, $p < 0.1$). However, there was no significant difference in the T4-P200 amplitude for non-target stimuli presented to the left ear between the two groups. On the other hand, when non-target stimuli were presented to the right ear, the mean T3-P200 and T4-P200 amplitudes were significantly smaller in the schizophrenics than in the normal controls (T3: $t = 2.96$, $p < 0.005$; T4: $t = 3.09$, $p < 0.005$). In examining the intragroup differences between T3-P200 and T4-P200 for non-target stimuli presented to one ear, it was found that in the schizophrenics non-target stimuli tended to produce a smaller T3-P200 amplitude than T4-P200 amplitude, regardless of the side of the attended ear ($t = 1.86$, $p < 0.1$).

3. The late positive component (LPC)

Fig. 6 shows the mean LPCs derived from the Cz region for target stimuli presented to the right as well as left ear in both groups. Target stimuli presented to the left ear produced no significant difference in LPCs between the schizophrenics and normal controls; while, target stimuli presented to the right ear produced a significant difference in LPCs between the two groups. Specifically, the schizophrenics displayed a smaller LPC values than the normal controls ($t = 2.20$, $p < 0.05$).

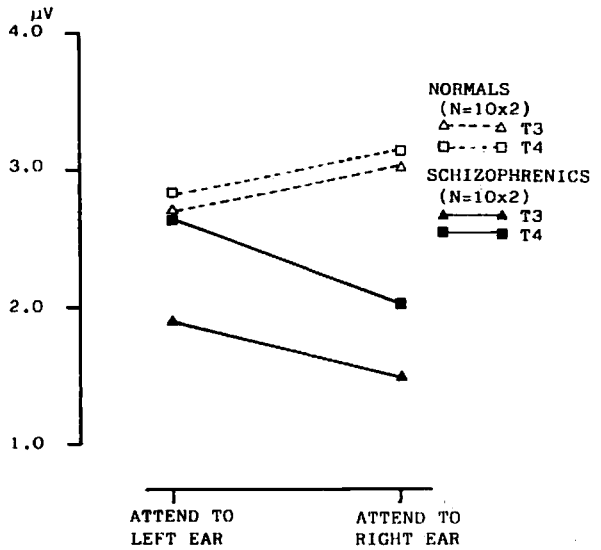

Fig. 5 *Mean amplitudes of T3-P200 and T4-P200 for the non-target stimuli*

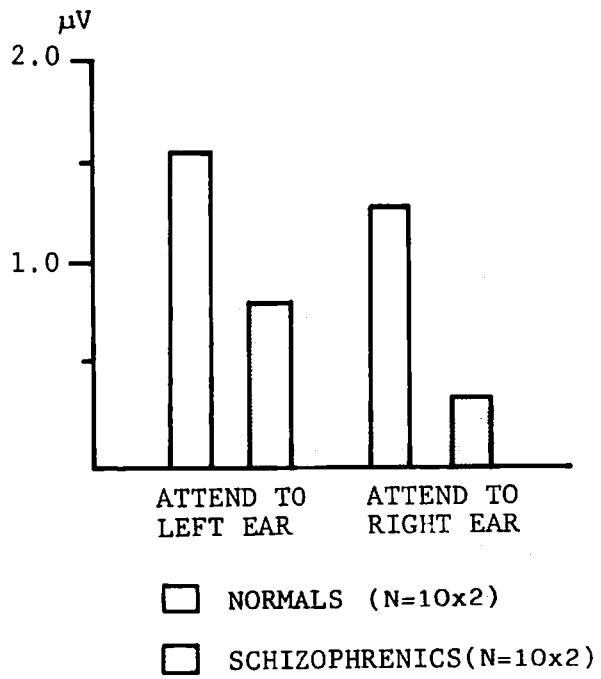

Fig. 6 *Mean value of LPCs derived from the Cz region for the target stimuli*

Experiment II

Method

Subjects

Twenty-two schizophrenics (11 males and 11 females; ages 19–39 years; mean, 29.1), as well as twenty normal controls (10 males and 10 females; ages 20–38 years; mean, 29.1), participated in Experiment II. All of the schizophrenics met the diagnostic criteria for schizophrenic disorders in DSM-III. Ten out of the 22 schizophrenics (5 males, 5 females) had not received any drugs for at least 4 weeks prior to the experiments, while the remaining 12 schizophrenics (6 males, 6 females) were under medication at the time of the experiments. All subjects were right-handed and free from any hearing disabilities.

Auditory Stimuli

Syllable discrimination tasks were employed in Experiment II. Four CV-syllables (/ba/, /da/, /ga/, /za/) 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 through headphones monaurally. The four CV-syllables by the male voice and the female voice were digitized and stored in a mini-computer (DEC, LSI-11/2) and were modified in waveshape into a duration of 150 msec. Each of the eight stimuli was presented randomly with an equal a priori probability of 0.125. The syllables by the male voice were placed in one channel (ear) and those by the female voice in another channel and presented through stereo-headphones (TEAC, HP102) monaurally, with an intensity of approximately 60 dBSL. The interstimulus intervals ranged between 800–1,000 msec.

Procedure

The subjects were seated in an anechoic room with eyes closed. They were informed that a male voice would be presented to one ear, and a female voice to the other ear, and were required to silently count the number of occurrences of a particular target syllable in a given ear in each run. All of the subjects performed 16 runs; that is, four target syllables × two voices (male or female) × two attended channels (left or right ear). The order of the 16 runs was randomized for all subjects, with the number of the target syllables for each run being set between 18–26. After the conclusion of each run, the subjects were asked to give the number of target stimuli detected.

EEG Recording and Data Analysis

Similar methods for the EEG recording and data analysis were employed in Experiment II as in Experiment I.

Results

1. T3-N100 and T4-N100 amplitudes

Judging from the results of an ANOVA conducted on the data, a main effect for "CHANNEL (Attend/Non-attend)" factor (abbr. channel effect) on the T3-N100 and T4-N100 amplitudes was observed in the normals [$F(1,303) = 7.28$, $p < 0.01$], but not in the schizophrenics [$F(1,335) = 0.36$, n.s.]. Furthermore, in the normals interaction effect of "REGION(T3/T4)" X "EAR(Left/Right)" on the amplitude of the N100 component was significant [$F(1,303) = 8.78$, $p < 0.01$]. This result signifies that both T3-N100 and T4-N100 amplitudes were larger when the stimuli were presented to the ear contralateral to the EEG-source side than when presented to the ipsilateral ear (see Fig. 7). However, in the schizophrenics, this interaction was not significant [$F(1,335) = 0.05$, n.s.]. Instead, the main effect of "REGION" tended to be significant in the schizophrenics [$F(1,335) = 3.47$, $p < 0.1$]. That is, T4 produced smaller amplitudes for the N100 component, as compared to T3.

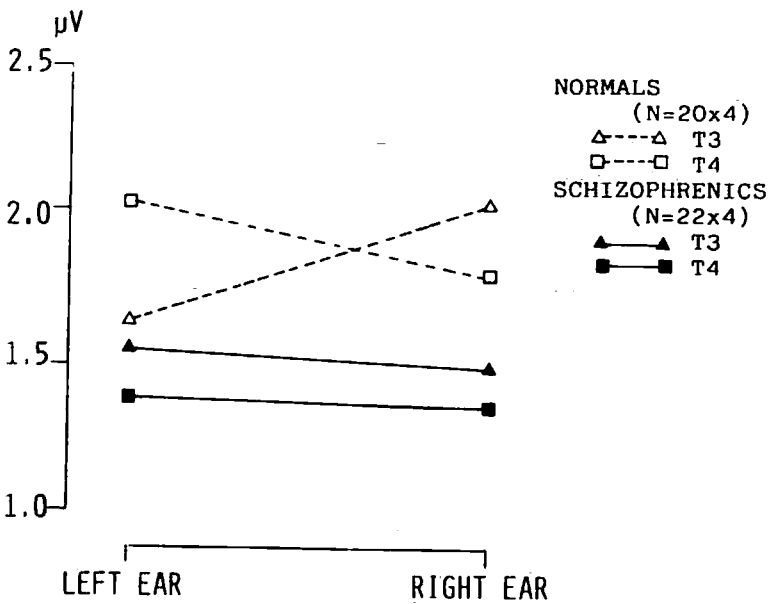

Fig. 7 *Mean amplitudes of T3-N100 and T4-N100*

2. T3-P200 and T4-P200 amplitudes

The channel effect on the T3-P200 and T4-P200 amplitudes was significant in the normals, as well as in the schizophrenics [$F(1,303) = 26.44$, $p < 0.01$; $F(1,335) = 5.16$, $p < 0.05$, respectively]. An interaction of "REGION" X "EAR" on the T3-P200 and T4-P200 amplitudes was not observed in either the normals or the schizophrenics. In the normals, the amplitudes showed an effect for "REGION" [$F(1,303) = 15.87$, $p < 0.01$]: that is, the T4-P200 amplitudes were always larger

than the T3-P200 amplitude, irrespective of the side of the stimulus presentation (left ear or right ear). However, this region effect was not observed in the schizophrenics [$F(1,335) = 0.11$, n.s.], and the T4-P200 amplitudes were nearly equal to the T3-P200 amplitudes (see Fig. 8).

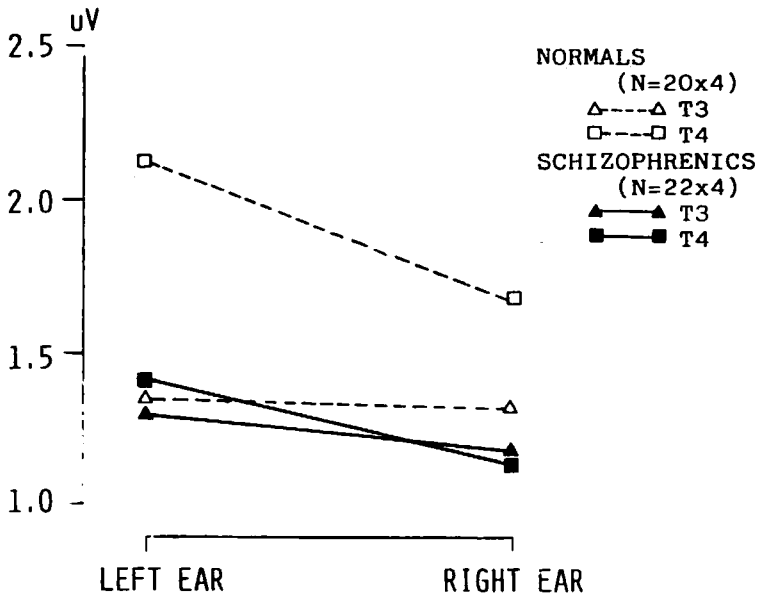

Fig. 8 *Mean amplitudes of T3-P200 and T4-P200*

3. T3-LPCs and T4-LPCs

In the normals, an effect for "CHANNEL" and an interaction for "CHANNEL" X "SYLLABLE(Target/Non-target)" were observed [$F(1,303) = 61.18$, $p < 0.01$; $F(1,303) = 8.37$, $p < 0.01$, respectively]. Furthermore, an interaction of "CHANNEL" X "SYLLABLE" X "REGION" was observed [$F(1,303) = 3.51$, $p < 0.1$]. That is, the effect of the interaction of "CHANNEL" X "SYLLABLE" was more prominent in T3 than in T4 (see Fig. 9). In the schizophrenics, an effect for "CHANNEL" was observed [$F(1,335) = 11.19$, $p < 0.01$], but an interaction for "CHANNEL" X "SYLLABLE" was not observed [$F(1,335) = 0.05$, n.s.]. The interaction of "REGION" X "EAR" was significant in the normals, as well as in the schizophrenics [$F(1,303) = 41.82$, $p < 0.01$; $F(1,335) = 23.48$, $p < 0.01$, respectively].

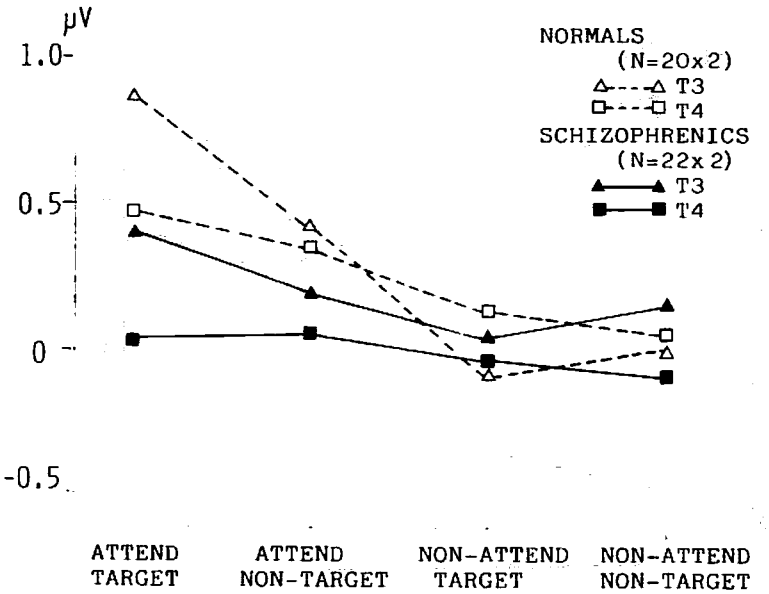

Fig. 9 *Mean value of T3-LPCs and T4-LPCs*

4. The effect of medication on the latencies of the N100 and P200 components

In the next step, the effect of medication was examined. Judging from the results of the ANOVA, the effect of the "MED(Medicated/Non-medicated)" factor, and the effect of the interaction of "MED" × "REGION" on the latencies of the N100 and P200 components were both significant [N100: $F(1,319) = 22.29$, $p < 0.01$; $F(1,319) = 7.13$, $p < 0.01$; P200: $F(1,319) = 6.45$, $p < 0.05$; $F(1,319) = 7.13$, $p < 0.01$, respectively]. As is shown in Fig. 10, the latency of T3-N100 for the non-medicated group was shorter than that of the medicated group, while the latency of T4-N100 was nearly equal in both groups. The latency of T3-N100 for the non-medicated group was also shorter than that of T4-N100 for the non-medicated group.

Fig. 11 illustrates findings for the P200 component similar to those described above for the N100 component. The latencies of the N100 and P200 components derived from the T3 and T4 regions in the medicated schizophrenics were found to be nearly equal to those of the corresponding components in the normals.

Discussion

In Experiment I, the target stimuli presented to the right ear tended to produce a smaller T3-N100 amplitude than T4-N100 amplitude; and the non-target stimuli presented to either ear tended to produce a smaller T3-P200 amplitude than T4-P200 amplitude in the schizophrenics. Furthermore, in Experiment I, the target stimuli presented to the right ear produced a significantly smaller LPC in the schizophrenics than in the normal controls; while, the target stimuli presented to the left

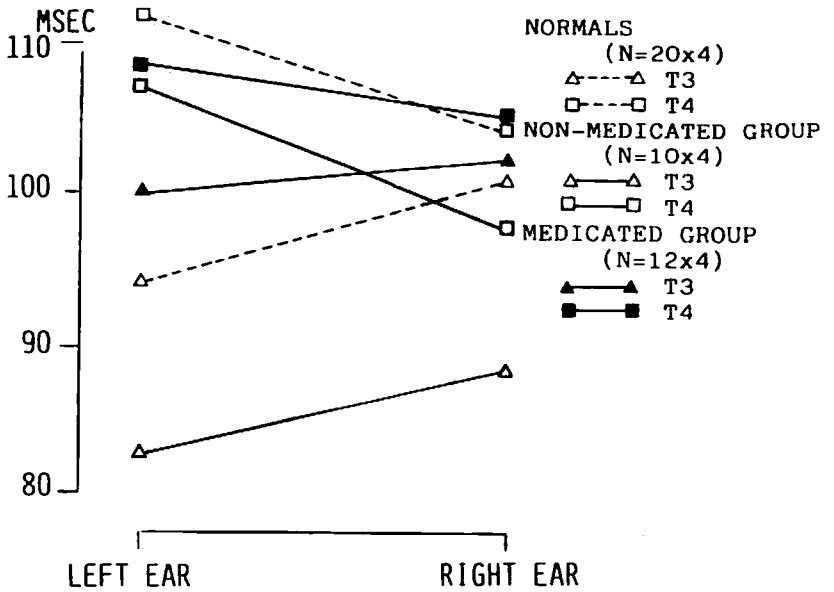

Fig. 10 *Mean latencies of T3-N100 and T4-N100*

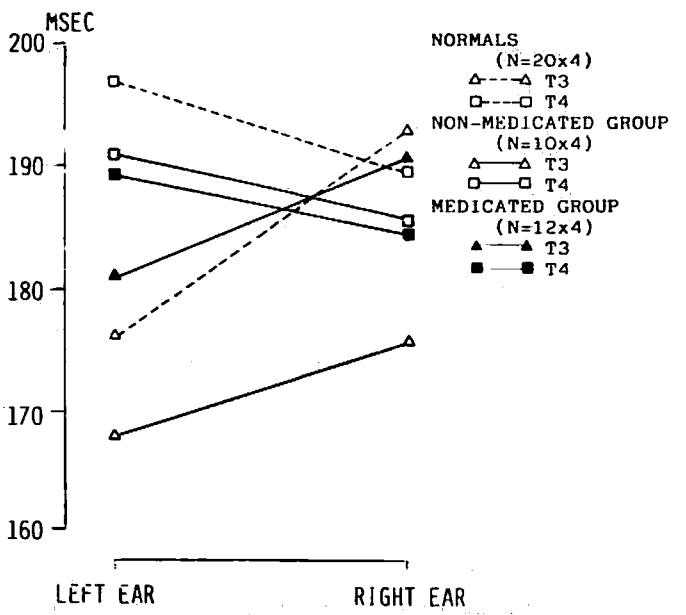

Fig. 11 *Mean latencies of T3-P200 and T4-P200*

ear produced no such significant difference in LPCs between the schizophrenics and the normal controls.

According to Kimura (1973) and Milner, Taylor and Sperry (1968), the contralateral hemisphere (in contrast to the ipsilateral hemisphere) of the attended ear is predominantly activated during dichotic detection tasks. Hence, our results seem to suggest that schizophrenics demonstrate a dysfunction in the left hemisphere.

However, one result of Experiment II seems to call for cautious consideration of the relationship between hemispheric dysfunction and psychotic symptoms. That is, the non-medicated group of schizophrenics in our study demonstrated shorter latencies for the N100 and P200 components exclusively in the T3 region when compared to those of the normal controls. However, the medicated group of schizophrenics displayed latencies for the N100 and P200 components nearly equal to those of the normal controls even in the T3 region.

Schizophrenics have been reported as displaying shorter latencies for the N100 and P200 components (Saletu, Itil and Saletu, 1971; Sakalis, Curry, Mould and Lader, 1972; Roth and Cannon, 1972). However, few reports have mentioned asymmetries in latencies.

Seven out of our 10 non-medicated patients were in an active phase at the time of the experiment. Therefore, it can be speculated that schizophrenics demonstrate shorter ERP latencies in the T3 region during their active phase. Hence, hemispheric dysfunction of the left hemisphere in schizophrenics may be a phenomenon closely related to positive psychotic symptoms.

Furthermore, it can also be speculated that neuroleptics normalize the shortened latencies in the T3 region. A lateralized effect of neuroleptics has also been suggested by Mintz, Tomer and Myslobodsky (1982).

In addition, the result concerning LIs obtained in Experiment I may also be relevant to disturbances in the integration mechanism of both hemispheres in schizophrenics. In Experiment I, the LI pattern for the schizophrenics was the reverse of that of the normal controls. This result can not be explained simply in terms of lateralized hemispheric dysfunction. The integration mechanism of both hemispheres, which in the case of normal subjects assures that an appropriate set is attended to by one ear, is disturbed in schizophrenics. This disturbance seems to be reflected in the reversed pattern of LIs.

Some results in Experiment II also seem to be relevant to disturbances in the integration mechanism of both hemispheres in schizophrenics. In Experiment II, the schizophrenics displayed smaller amplitudes for the N100 component in the T4 region as compared to those in the T3 region. In addition, the schizophrenics failed to demonstrate an enhancement in the amplitude of the N100 component at electrode sites contralateral to the ear of the stimulus presentation. The schizophrenics also failed to show an asymmetry in the P200 amplitudes between the T3 and T4 regions. All these results seem to indicate that schizophrenics have some difficulties in the integration mechanism of both hemispheres.

Based on the results in Experiments I and II, it can be concluded that schizophrenics seem to have two kinds of hemispheric dysfunction; one being a dysfunction of the left hemisphere, with the other being a dysfunction in the integration mechanism of both hemispheres. It can also be suggested that left-hemisphere dysfunction in schizophrenics may be related to positive psychotic symptoms.

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