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INTERVENTIVE EFFORTS AND INTRA-INDIVIDUAL VARIATIONS OF P300 AMPLITUDES IN SCHIZOPHRENICS

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INTRODUCTION

Previous findings to the effect that psychological and psychophysiological abnormalities in schizophrenia can be somewhat improved through psychological interventive efforts are intriguing and may lend themselves to therapeutic developments for schizophrenic patients. For example, Holzman et al.4) reported that saccadic movements in eye-tracking tasks were reduced by altering verbal instructions. Kashima et al.5) and Goldberg et al.3) reported that poor performance levels on theWisconsin Card Sorting Test were ameliorated with employment of a verbal coaching procedure.

Concerning the P300-amplitude reduction widely found in schizophrenia, there has been no study reported so far that has tapped the issue of whether psychological interventions can influence the P300 abnormalities in schizophrenia. In the present preliminary study, we investigated possible effects of psychological interventions upon the P300 in schizophrenic patients, specifically by coaching schizophrenic subjects while they were engaged in performing rather difficult auditory target-detection tasks.

SUBJECTS

The subjects consisted of seven medicated DSM-III schizophrenic patients (5 males, 2 females). The age of the patients ranged from 25 to 51 years (mean age : 34.4 years). At the time of the investigation, six patients had remained without positive symptoms for at least one month (two patients one month, four patients several years). The single remaining

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patient had had a delusional idea. Their scaled-expanded BPRS1) scores were distributed within a range from 4 to 23 (mean score:16.6).

METHODS

We employed a three-tone discrimination task for the P300-evoking paradigm, which consisted of a series of 200 tone bursts of 150 msec duration delivered at 2 sec intervals. The series included tones at 950 Hz, 1000 Hz, and 1053 Hz in random sequence. The 1000 Hz tone occurred with a probability of 0.66, and the 950 Hz and 1053 Hz tones each occurred at one of 0.17. The tones were delivered at 50dBSL binaurally through headphones.

The subjects went through six runs. In all runs, the subjects were required to press a lever upon detection of the targets as accurately and quickly as possible. The targets were one of the two infrequent tones. The designation of the target tones was not changed through all six runs in each subject, and it was counter-balanced across the subjects.

In the third and fourth runs, a buzzer sound ("coaching buzzer") was delivered 1100 msec after each designated target tone to indicate the target occurrence (the "intervention" runs). The coaching buzzer sounds were delivered after recording of EEG-segments for averaging, as well as reaction-time measurements to the target tones. Therefore, the delivery of buzzer sounds had no influence on EEGs, performance levels, or reaction times.

EEGs were derived from the Pz region with Ag/AgCl electrodes referred to linked earlobe electrodes (with a band-pass filter of 0.15 - 300 Hz). Trials in which EEG-amplitudes exceeded 100uV were automatically excluded from the averaging. The EEG data were then digitized on-line with a sampling frequency of 500 Hz from 128 msec preceding stimulus-onset to 896 msec post-stimulus. Individual data for each type of stimulus were averaged separately. Data with incorrect responses (omission errors or commission errors) were excluded from the averaging. These averaged waveforms were smoothed with a digital filter (moving average method; width of data window: 50 points) to minimize any alpha activity in the record. The baseline was determined as the mean voltage over the 128 msec period before the stimulus onset.

RESULTS

The data were analyzed in the following two ways. Firstly, the data for all the subjects were analyzed as a whole; secondly, analyses were conducted separately for two patient sub-groups obtained after breaking down the subjects based on the P300-amplitudes in the first and second runs.

The six runs were divided into three blocks, with the first

and second runs designated as the "pre-intervention" block, the third and fourth runs as the "mid-intervention" block, and the fifth and sixth runs as the "post-intervention" block.The data analyses were performed by comparing the three blocks.

(1) Results of the data analyses for the subjects as a whole

Table 1 and Figure 1 show the results obtained through the analyses for all the subjects as a whole. As shown in Table 1, the performance levels tended to improve in the "mid-" and "post-intervention" blocks as compared to the "pre-intervention" block; however, the reaction times showed no significant difference among the three blocks. In the upper half of Figure 1, two comparisons of the grand-averaged ERP waveforms for the target stimuli derived from the Pz region in the three blocks are shown, each comparing two waveforms out of the three. The lower half of the figure demonstrates the results of the paired t-test between the corresponding two waveforms. The paired t-test revealed no significant difference in these ERP waveforms.

(2) Results of separate analyses for the two sub-groups

The criterion we employed for dividing the subjects into two sub-groups was whether the P300-peak amplitudes in the first and second runs exceeded 5 uV or not. The group of subjects with P300 amplitudes of greater than 5 uV was designated as the "large P300 group", with the other group (P300 less than 5 uV) being designated as the "small P300 group". The small P300 group consisted of three patients and the large P300 group four patients.

In the small P300 group, performance levels were significantly improved in the "mid-" and "post-intervention" blocks, and reaction times tended to be shortened in the "mid-intervention" block as compared to the "pre-intervention" block (Table 2). Furthermore, P300 amplitudes increased significantly in the "mid-intervention" block compared to the "pre-intervention" block, and were sustained in the "post-intervention" block (Figure 2). All three subjects in this sub-group reported that they felt the task to be easier in the "mid-" and "post-intervention" blocks than the "pre-intervention"block. In the large P300 group, no significant difference was found in either the performance levels or the reaction times in comparisons among the "pre-", "mid-" and "post-intervention" blocks (Table 3). However, the P300 amplitudes decreased significantly in both the "mid-" and "post-intervention" blocks compared to the "pre-intervention" block (Figure 3). Concerning the subjective difficulties of the task, two out of four subjects in this group reported that their difficulties increased in both "mid-" and "post-intervention" blocks, and two subjects reported no subjective change.

Sub-group comparisons between the small and large P300 groups demonstrated no significant difference in the performance levels or the reaction times for the "pre-", "mid-", or

"post-intervention" blocks.

DISCUSSION

As far as the present authors have surveyed the related research, this report is the first to investigate the influence of psychological intervention on P300 abnormalities in schizophrenia.

It was found that a psychological intervention, coaching by means of buzzer-sounds delivered to help subjects performing an auditory discrimination task, is effective in augmenting the P300 amplitudes of schizophrenic patients, and that this effect was differential among subjects depending upon their original P300 amplitudes. Coaching was effective in augmenting P300s and improving performance levels in subjects with small original P300s. On the other hand, coaching produced P300 reduction in subjects with large original P300. These changes in P300s were consistent with the changes in task-difficulty judgments reported by the patients. Summing up the changes in the two sub-groups, the analyses for all subjects as a whole revealed no significant change before and after the intervention.

P300 amplitude reduction is a widely found electrophysiological abnormality in schizophrenia. Recently, however, some researchers have reported that as clinical symptoms improve with antipsychotic-drug medication, P300 amplitudes increase to some degree. Matsubayashi et al.6) reported that a P300-amplitude increase in patients whose symptoms had been improved with medication. Duncan et al.2) also reported similar results. Therefore, it can be suggested that P300 amplitudes do not necessarily remain unchanged in the same schizophrenic subjects when repeatedly measured, but rather vary somewhat due to therapeutic intervention.

The results of the present study suggest that P300 amplitudes in schizophrenic patients can be influenced not only through antipsychotic medication but also through psychological intervention. However, this does not mean that P300 amplitude reduction in schizophrenia is "normalized". It should be noted that, firstly, P300 amplitudes in the "mid-" and "post-intervention" blocks in the small P300 sub-group was much less when compared, for example, with that of the larger P300 sub-group in the "pre-intervention" block. Secondly, a P300 amplitude increase was observed in some of the subjects. The possibility of differences in clinical characteristics, including symptoms and behavior patterns, between the small and large P300 sub-groups attracted the attention of the present authors. However, no difference in clinical characteristics between the two sub-groups has been noted so far. It can be speculated that such a difference in P300 responses to intervention as reported in this study might be relevant to response differences to actual clinical psychological interventions (psychotherapy, behavior therapy, cognitive-behavioral therapy).

Reproduction of the results obtained here will enhance the clinical utility of P300 measurements. This may have value in the choice of psychological and behavioral therapeutic approaches and in the assessment of treatment efficacy. Moreover, it may shed light on the brain mechanisms involved in effective psychological and behavioral treatments.

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Table 1 Behavioral data for the subjects as a whole

	hit rate (percent)	reaction time (msec)
pre-intervention	50.0 ± 20.0	651 ± 89
mid-intervention	57.4 ± 20.0	622 ± 46
post-intervention	59.2 ± 22.3	642 ± 75

* p<0.1 (paired t-test)

Table 2 Behavioral data for the small P300 group

	hit rate (percent)	reaction time (msec)
pre-intervention	45.1 ± 24.4	664 ± 56
mid-intervention	62.7 ± 19.2	628 ± 38
post-intervention	65.2 ± 21.8	615 ± 65

** p<0.05 * p<0.1 (paired t-test)

Table 3 Behavioral data for the large P300 group

	hit rate (percent)	reaction time (msec)
pre-intervention	53.7 ± 16.8	642 ± 111
mid-intervention	53.3 ± 20.9	617 ± 53
post-intervention	54.8 ±.23.0	662 ± 79

n.s.

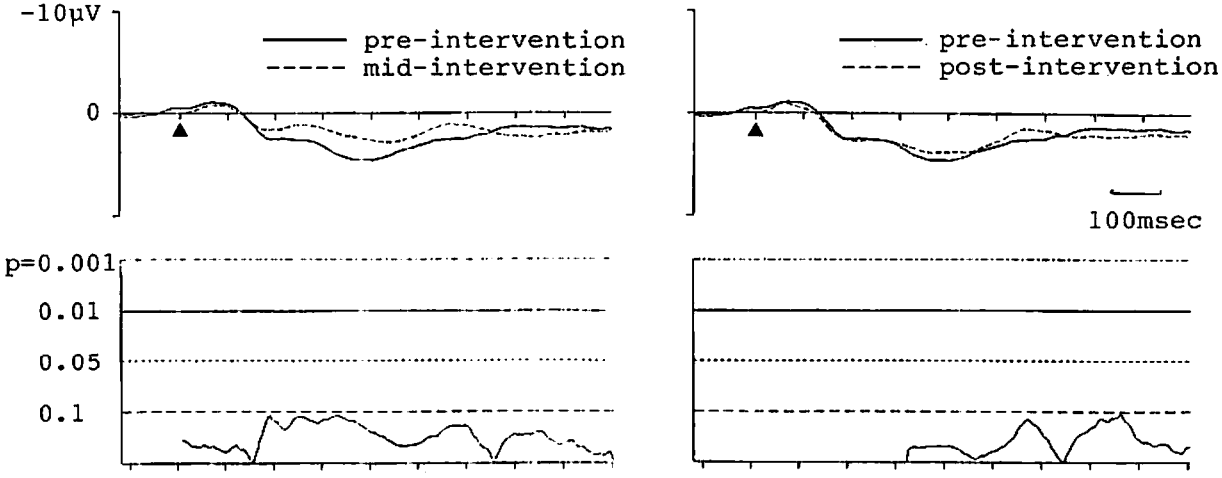

Fig. 1

ERP waveforms and results of t-test for all the subjects as a whole. The figure in the upper half show comparisons of the grand-averaged ERP waveforms for the target stimuli derived from the Pz region in the three blocks, each comparing two waveforms out of the three. Filled triangles indicate stimulus-onset. The lower half figures demonstrate the results of the paired t-test between the corresponding two waveforms.

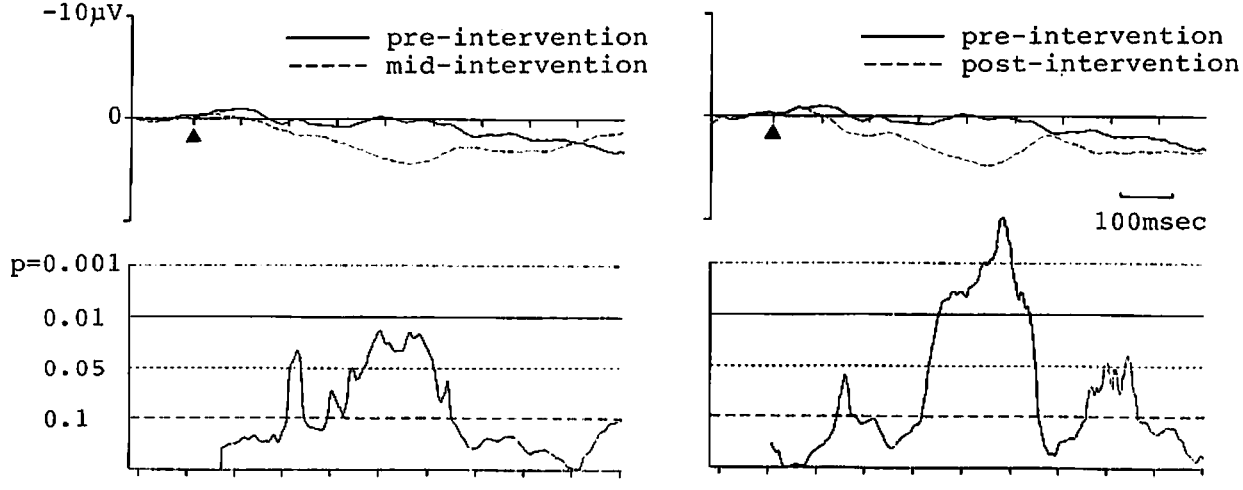

Fig. 2

ERP waveforms and results of t-test for the small P300 group. Detailed explanation is same as given in fig. 1.

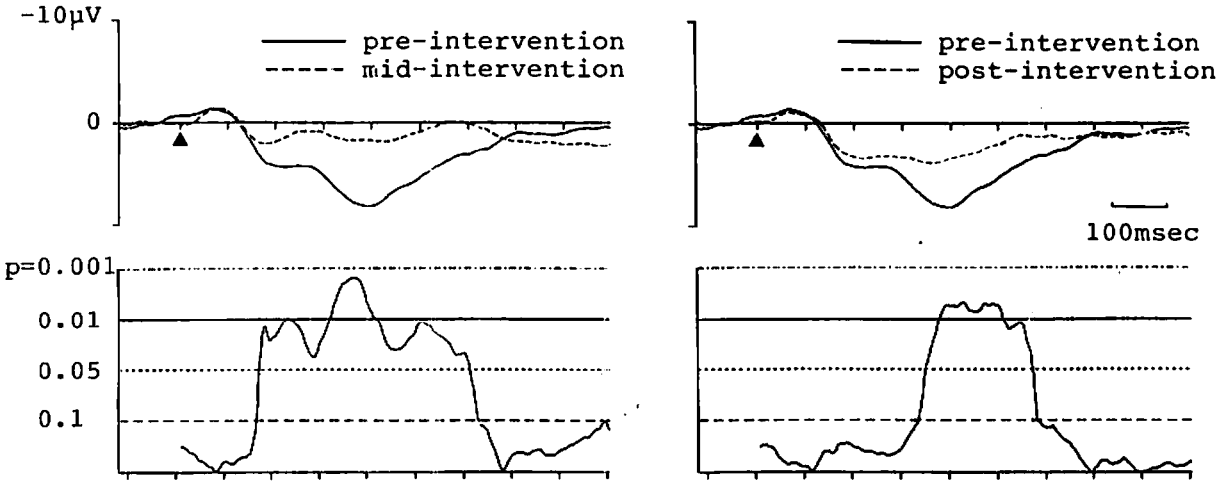

Fig. 3

ERP waveforms and results of t-test for the large P300 group. Detailed explanation is same as given in fig. 1.