AINO JOURNAL, Vol. 2, 2003, pp. 23 – 28

Original Paper

The Wisconsin card sorting test performance and the P300 of event-related potentials in schizophrenia

Akira IWANAMI *Aino Institute of Medical Technology*
Akio KOYAMA *Aino Institute of Medical Technology*

Abstract

Both a poor performance on the Wisconsin Card Sorting Test (WCST) and abnormalities in P300 are the most frequently replicated biological findings in schizophrenic patients. The relationships between the computer version of WCST performance and the P300 amplitude and latency were examined in 36 schizophrenic patients. Event-related potentials were recorded during two auditory tasks, which were a standard oddball task and a distraction task similar to that of Grillon et al. (1990). Several of the WCST performance measures correlated significantly with P 300 latency for the target stimuli in both tasks. When dividing the patients into the good WCST group and the poor WCST group, there was a significant difference in the P300 latency for the target stimuli in the distraction task and an altered P300 distribution for the target stimuli in the oddball task for the novel stimuli in the distraction task between the two groups. These findings indicated that impaired frontal lobe function might cause a delay in information processing in schizophrenia.

Key words: P300, ERP, WCST, schizophrenia

Introduction

The Wisconsin Card Sorting Test (WCST) is a neuropsychological test that reflects abstraction and reasoning, rule learning, responsiveness to verbal feedback and reinforcement, and shifting capacity (Grant and Berg, 1948; Milner, 1963). It has shown some specific sensitivity to frontal lobe lesions. Impairment on this test in schizophrenic patients has been suggested to support the notion of frontal lobe dysfunction in this disease (Berman et al., 1986; Weinberger et al., 1986). Recently, some investigators tried to use this test for cognitive training in schizophrenic patients (Goldberg and Weinberger, 1994; Kern et al., 1997).

Event-related potentials (ERPs) are objective indices of human information processing, and provide a reliable method for evaluating the impairment of information processing in patients with mental disorders (Coull et al., 1988; Frodl-Bauch, 1999; O'Donnell et al., 1999). Many ERP studies in schizophrenia have focused on the abnormalities of the P300 component, which is an endogenous positive potential that occurs at an approximate latency of 300 ms after the presentation of task-relevant or novel stimuli embedded among irrelevant stimuli (Donchin and Coles, 1988). Most previous studies have demonstrated a reduction in the P300 amplitude and a delay of the P300 latency in schizophrenic patients, compared with those of normal controls (Prichard, 1986; Ford, 1999).

However, the relationship between WCST performance and P300 abnormality has not been fully reported. In the present study, we examined the relationship between WCST performance and P300 measures in schizophrenic patients using two auditory tasks.

Methods

Subjects

The study sample consisted of 36 physically healthy outpatients (17 males and 19 females)

who gave written informed consent before participating in this study. The patients were diagnosed as schizophrenia according to the DSM-IV (American Psychiatric Association, 1994) on the basis of a structured psychiatric interview, the Schedule for Affective Disorders and Schizophrenia (Spitzer and Endicott, 1978), and medical records. None of the subjects had a history of electroconvulsive shock treatment, alcohol or other drug abuse and dependence, or a neurological illness affecting the central nervous system.

Their mean age was 32.6 years (SD 12.0), the mean age at onset 22.3 years (SD 6.4), the mean duration of illness 10.3 years (SD 5.6), and the mean duration of education 13.6 years (SD 4.0). All subjects, except one, were treated with neuroleptics, and their mean daily dosage of chlorpromazine equivalent was 498 mg (SD 627). The mean total score of the Brief Psychiatric Rating Scale (Overall and Gorham, 1962) was 33.2 (SD 7.9), which indicated that the symptoms of the patients were mild. All patients and normal controls were right-handed according to the Edinburgh Inventory of Handedness (Oldfield, 1971).

WCST

A computer version of WCST (WCST computer version-2) was used in the present study (Heaton RK, 1993). This test administers and scores the WCST based on Heaton's system. Responses are entered using a standard keyboard. The keyboard option utilizes 4 predefined alphanumetric keys to which colored keytops representing the 4 stimulus cards are affixed. Patients were asked to sit directly in front of the computer and to press the key which they regard as the correct response.

In this test, the subjects are required to sort a series of cards (maximum 128) to 1 of 4 key cards that vary in shape, color, and number of shapes. The subject must discover the correct matching rule using feedback after each response. After 10 consecutive correct responses, the rule changes without warning.

Dependent measures for the WCST included the number of categories completed, the numbers of trials administered, correct response rate (%), perseverative error rate (%), reaction time for correct response, trials to complete first category. The WCST performances of the subjects are shown in Table 1. They are substantially impaired compared with the normal findings reported by Heaton et al. (1993).

Table 1 The WCST performance of the subjects

	mean	SD
categories completed	4.0	2.4
trials administered	112.3	16.1
% correct response	47.1	31.1
% perseverative response	2.4	2.2
reaction time for correct response (sec.)	2.2	2.7
trials to complete first category	37.1	44.9

ERP recordings

Event-related potentials were recorded during two auditory tasks, which were a standard oddball task and a distraction task similar to that of Grillon et al. (1990), in a sound-proof room. Subjects were presented with a series of 270 auditory stimuli with a fixed interstimulus interval of 1500 ms. In the oddball task, 85% of the stimuli were tones of 1 KHz, and the other 15% tones of 2 KHz. In the distraction task, 70% of the stimuli were tones of 1 KHz, 15% tones of 2 KHz, and the other 15% white noise (novel stimuli). Stimuli were presented in a Bernoulli sequence. The stimulus intensity was 75 dBSPL, and the tone duration 50ms, with a rise/fall time of 10ms. The subjects were instructed to press a button as quickly as possible for the infrequent high-pitch tones in both tasks.

According to the international 10–20 system, the scalp electroencephalogram (EEG) was recorded with Ag/Ag-Cl disc electrodes at Fz, Cz, and Pz monopolarly, referred to linked earlobes. The bandpass was set at 0.15–120 Hz. Vertical and horizontal electrooculograms (EOG) were recorded from electrodes placed below and at the outer canthus of the right eye. EEG samples were acquired every 2.5 ms from 40 ms before to 600 ms after the stimulus onset. Trials contaminated by peak to peak potentials of over 100 μV or accompanied by EOG of over 75 μV were eliminated from the averaging.

The responses to frequent and rare tones and novel stimuli with correct reactions were averaged separately. ERPs for target stimuli in both tasks and for target and novel stimuli in the distraction task were analyzed. P300 was defined as the most positive peak between 250 and 500 ms poststimulus. Amplitudes were measured with respect to an average voltage during the 40 ms prestimulus.

Results

Correlations between the WCST performance and the P300 measures

Pearson-product moment correlation coefficiencies were calculated between the WCST performance and the P300 measures.

(1) P300 for target stimuli in the oddball task
Reaction time for a correct response correlated significantly with P300 latency at Pz ($r=0.357$, $df=35$, $p<0.05$).

(2) P300 for target stimuli in the distraction task
The number of categories completed correlated significantly with P300 latency at Pz ($r=-0.331$, $df=35$, $p<0.05$). The numbers of trials administered correlated significantly with P 300 latency at Fz ($r=-0.390$, $df=35$, $p<0.05$), Cz ($r=-0.355$, $df=35$, $p<0.05$) and Pz ($r=-0.347$, $df=35$, $p<0.05$). The perseverative error rate correlated significantly with P300 latency at Fz ($r=-0.351$, $df=35$, $p<0.05$), and Cz ($r=0.408$, $df=35$, $p<0.05$).

(3) P300 for novel stimuli in the distraction task
No significant correlation was found between the WCST performance and the P300 measures for novel stimuli in the distraction task.

Table 2 Clinical measures of the good and poor WCST group

	Poor WCST group	good WCST group	
number of subjects	15	21	
age (years)	39.5 (13.0)	27.7 (8.6)	*
age at onset (years)	24.0 (8.4)	21.5 (37.3)	
duration of illness (years)	15.5 (12.6)	6.2 (7.7)	*
duration of education (years)	14.2 (5.0)	13.0 (2.9)	
daily dosage (mg)	700 (828)	353 (393)	
BPRS total score	34.4 (6.6)	32.4 (8.8)	

* $p<0.01$

Comparison of the good WCST group and the poor WCST group

According to the definition of Seidman et al. (1991), 21 patients who archived more than 4 categories were defined as the good WCST group, and 15 patients who archived less than 4 were as the poor WCST group. The poor WCST group was older ($t=3.284$, $df=34$, $p<0.01$) and had longer duration of illness ($t=2.749$, $df=34$, $p<0.01$) than the good WCST group. The two groups did not differ significantly in other clinical measures (Table 2).

Table 3 shows the means and standard deviations of P300 amplitude and latency between the two groups. Repeated measures of analysis of variance (ANOVA) were performed for the P300 amplitude and latency, with the electrode site as a within-subjects variable and the group as a between-subjects variable. For the P300 amplitude for the target stimuli in the oddball task, there was an electrode site effect ($F[2,34]=9.658$, $p<0.001$), and an interaction effect between group and electrode site ($F[2,34]=3.343$, $p<0.005$). For the P300 amplitude for the novel stimuli in the distraction task, there was an electrode site effect ($F[2,34]=11.932$, $p<0.0001$), and an interaction effect between the group and

Table 3 ERP measures in the good and poor WCST group

oddball task (target)

	P300 latency			P300 amplitude		
	Fz	Cz	Pz	Fz	Cz	Pz
good WCST group	357.8 (33.8)	349.9 (38.7)	359.8 (44.3)	6.6 (5.1)	6.7 (5.0)	7.6 (4.6)
poor WCST group	337.3 (26.4)	333.0 (26.3)	339.1 (27.1)	7.3 (4.5)	9.5 (4.3)	11.0 (5.1)

distraction task (novel)

	P300 latency			P300 amplitude		
	Fz	Cz	Pz	Fz	Cz	Pz
good WCST group	340.8 (38.3)	342.2 (34.3)	346.9 (22.5)	9.3 (4.9)	9.6 (6.1)	10.5 (6.6)
poor WCST group	344.2 (32.1)	337.5 (33.9)	336.0 (33.5)	6.8 (5.1)	8.9 (5.4)	10.3 (5.1)

distraction task (target)

	P300 latency			P300 amplitude		
	Fz	Cz	Pz	Fz	Cz	Pz
good WCST group	366.6 (37.8)	363.3 (41.3)	380.3 (44.8)	4.2 (2.7)	4.7 (2.0)	6.2 (2.4)
poor WCST group	340.6 (30.4)	338.1 (29.5)	342.2 (41.5)	4.1 (4.9)	5.5 (4.7)	7.1 (4.9)

electrode site ($F[2,34]=3.250$, $p<0.005$). For the P300 latency for the target stimuli in the distraction task, there was a group effect ($F[1, 34]=7.927$, $p<0.01$). For the P300 amplitude for the target stimuli in the distraction task, there was an electrode site effect ($F[2, 34]=16.486$, $p<0.0001$).

Correlations between the WCST and the P300 measures and clinical variables

No significant correlation was found between the WCST and the P300 measures and clinical variables.

Discussion

Both the poor performance on the WCST and the abnormalities of P300 are the most frequently replicated biological findings in schizophrenic patients. However, the relationship between the two findings has not been fully revealed. From the findings of the present study, the impaired performance of WCST was associated with the delay in the P300 latency and the altered distribution of P300.

Although several studies reported a delayed P300 latency in medicated and unmedicated schizophrenic patients (Blackwood et al., 1987; Faux et al., 1993; Roxborough et al., 1993; Shajahan et al., 1997), there are some conflicting findings. Some studies (O'Donnell et al., 1995; Salisbury et al., 1998) reported no differences in P300 latencies between schizophrenic patients and normal controls, others (Pfefferbaum et al., 1989) reported a P300 delay in only medicated subjects. However, it is suggested that P300 latency is delayed in schizophrenic patients with severe dysfunction from the findings of previous studies, although it is uncertain whether every schizophrenic patient, with various biological backgrounds, show abnormalities in the P300 latency.

From the findings of the present study, there was a close relation between P300 delay and impaired frontal lobe function in schizophrenic patients. Kutas et al. (1977) first reported that P300 latency represented the stimulus evaluation time. Later, McCarthy and Donchin (1981) and Duncan-Johnson and Donchin (1982) interpreted it as the time subsumed by stimulus perception and identification/classification. Accordingly, the P 300 latency may be associated with the speed of information processing in the brain. Considering that the WCST performance reflects frontal lobe function, the findings of the present study indicated that impaired frontal lobe function might cause a delay in information processing.

Previous studies have not fully clarified the relationship between the WCST performance and the P300 latency. Roxborough et al. (1993) reported the relationship between neurophychological and P300 abnormalities in schizophrenia. They showed a significant correlation between the P300 latency and the performance of verbal fluency test, which is sensitive to left frontal function, but there was no significant correlation between the P300 latency and the categories completed in WCST in schizophrenia. Kindermann et al. (2000) reported that in elderly depressed patients a longer P300 latency was associated with poorer performance on the measures of executive functions except WCST perseverative errors. However, they did not use other measures of the WCST performance. These two studies described above did not find a significant relationship between the P300 latency and the WCST performance, but they were consistent in that delayed P300 latency reflected the impairment of the executive function. The different findings observed in the present study may have arisen from the differences in the clinical background of the subjects, the methods of administering the WCST, and the measures of WCST.

The P300 amplitude for target stimuli in the oddball task and for target and novel stimuli in the distraction task did not correlate significantly with the WCST performance. P 300 comprises two main subcomponents. P 300 for target stimuli reflects mainly P3b, and P300 for novel stimuli P3a. Although both P3 b and P3a have different cognitive significance, they are common in their amplitudes being associated with the inhibitory processes in information processing (Iwanami et al., 1998). The findings of the present study may indicate that this inhibitory process, which is associated with thought disorder in schizophrenic patients (Iwanami et al., 2000), is not regulated in the frontal lobe.

There are some limitations to the present study. Considering the possible heterogeneity of the pathophysiology of schizophrenia, the sample size should be larger. Longitudinal studies need be performed to assess the clinical significance of the cognitive deficits in

schizophrenia. In addition to the WCST, other neuropsychological batteries are necessary to clarify the nature of the abnormality of P300 in schizophrenia. Future studies should overcome these limitations.

Acknowledgement

This work was supported by the Ministry of Education, Culture, Sports, Science and Technology of Japan.

References

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders, 4th edition. Washington D.C.: American Psychiatric Association.

Berman KF, Zec RF, Weinberger DR (1986) Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. II. Role of neuroleptic treatment, attention, and mental effort. Arch Gen Psychiatry 43 : 126–35.

Blackwood DH, Whalley LJ, Christie JE, Blackburn IM, St Clair DM, McInnes A (1987) Changes in auditory P 3 event-related potential in schizophrenia and depression. Brit J Psychiatry 150 : 154–160.

Coull JT (1998) Neural correlates of attention and arousal: insights from electrophysiology, functional neuroimaging and psychopharmacology. Prog in Neurobiol 55 : 343–61.

Donchin E, Coles MGH (1988) Is the P300 component a manifestation of context updating? Behav Brain Sci 11 : 357–374.

Faux SF, McCarley RW, Nestor PG, Shenton ME, Pollak SD, Penhune V, Mondrow E, Marcy B, Peterson A, Horvath T (1993) P300 topographic asymmetries are present in unmedicated schizophrenics. Electroencephalogr Clin Neurophysiol 88 : 32–41.

Ford JM (1999) Schizophrenia: the broken P300 and beyond. Psychophysiology 36 : 667–82.

Frodl-Bauch T, Bottlender R, Hegerl U (1999) Neurochemical substrates and neuroanatomical generators of the event-related P300. Neuropsychobiology 40 : 86–94.

Grillon C, Courchesne E, Ameli R, Geyer MA, Braff DL (1990) Increased distractibility in schizophrenic patients. Electrophysiologic and behavioral evidence. Arch Gen Psychiatry 47 : 171–179.

Goldberg TE, Weinberger DR (1994) Schizophrenia, training paradigms, and the Wisconsin Card Sorting Test redux. Schizophr Res 11 : 291–6.

Grant MF, Berg EA (1948) A behavioral analysis of degree of reinforcement and ease of shifting to new responses in Weigl-type card sorting problem. J Experimental Psychology 38 : 404–411.

Heaton RK (1993) WCST computer version-2. Odessa, FL: Psychology Assessment Resources, Inc.

Heaton RK, Chelune GJ, Talley JL, Kay GG, Curtiss G (1993) Wisconsin Card Sorting Test manual: Revised and expanded. Odessa, FL: Psychology Assessment Resources, Inc.

Iwanami A, Isono H, Okajima Y, Noda Y, Kamijima K (1998) Event-related potentials during a selective attention task with short interstimulus intervals in patients with schizophrenia. J Psychiatry Neurosci 23 : 45–50.

Iwanami A, Okajima Y, Isono H, Kasai K, Hata A, Nakagome K, Fukuda M, Kamijima K (2000) Event-related potentials and thought disorder in schizophrenia. Schizophr Res 42 : 187–91.

Kern RS, Wallace CJ, Hellman SG, Womack LM, Green MF (1996) A training procedure for remediating WCST deficits in chronic psychotic patients: an adaptation of errorless learning principles. J Psychiatr Res 30 : 283–94.

Kindermann SS, Kalayam B, Brown GG, Burdick KE, Alexopoulos GS (2000) Executive functions and P 300 latency in elderly depressed patients and control subjects. Am J Geriatric Psychiatry 8 : 57–65.

Kutas M, McCarthy G, Donchin E (1977) Augmenting mental chronometry: the P300 as a measure of stimulus evaluation time. Science 197 : 792–795.

McCarthy G, Donchin E (1981) A metric for thought: a comparison of P300 latency and reaction time. Science 211 : 77–80.

Milner B (1963) Effects of different brain lesions on card sorting. Arch Neurol 9 : 90–100.

O'Donnell BF, Faux SF, McCarley RW, Kimble MO, Salisbury DF, Nestor PG, Kikinis R, Jolesz FA, Shenton ME (1995) Increased rate of P300 latency prolongation with age in schizophrenia. Electrophysiological evidence for a neurodegenerative process. Arch Gen Psychiatry 52 : 544–549.

O'Donnell BF, McCarley RW, Potts GF, Salisbury DF, Nestor PG, Hirayasu Y, Niznikiewicz MA, Barnard J, Shen ZJ, Weinstein DM, Bookstein FL, Shenton ME (1999) Identification of neural circuits underlying P 300 abnormalities in schizophrenia. Psychophysiology 36 : 388–98.

Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9 : 97–113.

Overall JE, Gorham DR (1962) The brief psychiatric rating scale. Psychol Rep 10 : 799–812.

Pfefferbaum A, Ford JM, White PM, Roth RT (1989) P3 in schizophrenia is affected by stimulus modality, response requirements, medication status, and negative symptoms. Arch Gen Psychiatry 46 : 1035–1044.

Pritchard WS. Cognitive event-related potentials in schizophrenics. Psychol Bull 1986 ; 100 : 43–66.

Roxborough H, Muir WJ, Blackwood DH, Walker MT, Blackburn IM (1993) Neuropsychological and P300 abnormalities in schizophrenics and their relatives. Psychol Med 23 : 305–314.

Salisbury DF, Shenton ME, Sherwood AR, Fischer IA, Yurgelun-Todd DA, Tohen M, McCarley RW (1998) First-episode schizophrenic psychosis differs from first-episode affective psychosis and controls in P 300 amplitude over left temporal lobe. Arch Gen Psychiatry 55 : 173–180.

Seidman LJ, Talbot NL, Kalinowski AG, McCarley RW, Faraone SV, Kremen WS, Pepple JR, Tsuang MT (1991) Neuropsychological probes of fronto-limbic system dysfunction in schizophrenia. Olfactory identification and Wisconsin Card Sorting performance. Schizophr Res 6 : 55–65.

Shajahan PM, O'Carroll RE, Glabus MF, Ebmeier KP, Blackwood DH (1997) Correlation of auditory 'oddball' P300 with verbal memory deficits in schizophrenia. Psychol Med 27 : 579–586.

Spitzer RL and Endicott J (1978) Schedule for affective disorders and schizophrenia : Lifetime version. New York, NY : Biometric Research, New York State Psychiatric Association.

Squires NK, Squires KC, Hillyard SA (1975) Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. Electroencephalogr Clin Neurophysiol 38 : 387–401.

Weinberger DR, Berman KF, Zec RF (1986) Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. I. Regional cerebral blood flow evidence. Arch Gen Psychiatry 43 : 114–24.