

## The Utility of the Wisconsin Card Sorting Test in Differential Diagnosis of Cognitive Disorders in Iranian Psychiatric Patients and Healthy Subjects

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**Objective:** The Wisconsin Test Card Sorting Test (WCST) is a neuropsychological test that has been suggested as a more specific test for frontal lobes dysfunctions. This study was designed to determine whether WCST is able to differentiate between Iranian psychiatric patients with cognitive disorders and normal subjects, and whether WCST scores are related to severity of symptoms in depressive and schizophrenic patients.

**Method:** Participants were four groups: schizophrenics with positive symptoms (n=25); schizophrenics with negative symptoms (n=25); major depressives (n=25); and normal subjects (n=25). All subjects were tested individually using WCST. To analyze the data, various descriptive statistics, ANOVA, t-test and multiple regression analysis were used.

**Results:** Regarding the number of categories ( $P<0.001$ ) and the rate of perseverative errors ( $P<0.01$ ), according to the results, the normal subjects performed significantly better than patient groups on WCST, although the differences between patient groups were not significant. Our results also showed that greater positive or depressive symptoms were not associated with poorer scores on WCST performance. Only the level of severity of negative symptoms predicted scores on perseverative errors.

**Conclusion:** It is concluded that WCST can differentiate Iranian psychiatric patients with cognitive disorders from normal subjects, but it is not able to clearly differentiate schizophrenic patients with negative symptoms from those with positive symptoms and depressives. Only severity of negative symptoms affects WCST performance

**Keywords:** Cognition, Depression, Frontal lobe, Schizophrenia

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Although using neuropsychological tests for differential diagnosis of psychiatric disorders is not new, few studies have been used to investigate the diagnostic strength of such tests in Iran. In recent decades, many researches have used the Wisconsin Card Sorting Test (WCST) to investigate cognitive disorders in different patient groups (1-6). The WCST was developed to assess abstraction ability in normal subjects, but it is now used as a neuropsychological instrument (7-9). The test assesses the ability to form abstract concepts, and shift and maintain the set. Bearing in mind the very high expenses involved in the execution of experiments on psychiatric patients, valid psychological tests can be used as appropriate alternatives to help specialists to achieve differential diagnosis of psychiatric patients. As such the aim of this research is to study the utility of differential diagnosis of WCST in Iranian schizophrenic and major depressive patients and healthy subjects.

WCST has been suggested as a more specific test for frontal lobes dysfunctions (10). The frontal lobe patients achieve fewer categories and make more perseverative errors than controls, and they tend to make more perseverative errors than non-perseverative

ones (11). Physiological activation of a cortical network was examined during WCST performance in normal subjects. The WCST activation in the dorsolateral prefrontal cortex remained significant even after training and practicing the test (12). It was reported that volume of the dorsolateral prefrontal, as measured by magnetic resonance imaging (MRI), was significantly correlated with the number of perseverative errors in WCST in normal young and old people (13).

Different psychiatric populations show cognitive disorders. Brain-imaging studies have found abnormalities of the structure or dysfunctions of the frontal lobes in many schizophrenic patients (14, 15). Prefrontal gray matter abnormalities in schizophrenic patients may be associated with some symptoms including difficulties with set-shifting and decreased mental flexibility. According to Crow's hypothesis (16), there are two types of schizophrenia: type I and type II schizophrenia. Type I syndrome is characterized by positive symptoms and is presumed to be due to a deficit in dopamine transmission, but type II syndrome is characterized by negative symptoms and is related to structural brain changes. It is expected that type II

schizophrenic patients show impairment on tests sensitive to frontal lobe dysfunctions like WCST, but type I schizophrenics show no problems or at least better performance on such tests (17, 18). Cognitive dysfunctions have also been studied in depressive patients. It has been shown that (19) the findings of cognitive functions (using WCST) in schizophrenics and alcohol dependents were similar, and the scores of both groups were lower than the scores in the depressed and control groups (20). Frodl et al. (21) did not find a significant association between frontal lobe volumes and WCST in patients with depression. Cavedini et al. also rejected the existence of specific frontal lobe dysfunction in major depressive disorders (22). The frontal cerebral blood fluency (CBF) did not increase in postmenopausal women with moderate/severe symptoms of depression during WCST performance (23).

On the other hand, some studies (24) reported a significant correlation between positive symptoms and performance on WCST in schizophrenic patients; and a new study (25) found that frontal lobe executive functioning was abnormal in patients with depression. In two different studies (26, 27), schizophrenic patients and depressives, who exhibited comparable deficits, performed worse than normal controls in WCST.

Some researches showed that depression may affect neuropsychological test performances (28, 29). It is important to determine whether impaired executive functions in psychiatric patients are a result of organic dysfunction or the severity of clinical symptoms. The neuropsychologists must judge whether cognitive deficit reflect only the neuropsychological conditions. It is possible that frontal lobes' cognitive disorders in psychiatric patients are not related to kinds of symptoms and diagnosis, instead, they could be explained by some other factors like severity of symptoms.

Based on the results from previous studies cited above, this study was designed to determine whether WCST, as a neuropsychological instrument, would be able to differentiate between Iranian schizophrenic patients with positive symptoms, schizophrenic patients with negative symptoms, major depressives and normal subjects. In addition, we aimed to determine whether WCST scores are related to severity of symptoms in depressive and schizophrenic patients.

## Materials and Method

Fifty patients with a diagnosis of schizophrenia, 25 major depressives and 25 normal subjects participated in the study. The clinical participants were recruited from patients who attended "Ebne Sina" and "Razi" psychiatric hospitals in Shiraz, Iran, using convenience sampling method according to which those who were accessible served as the subjects of the study. The group of normal subjects was selected mainly from hospital staff. The groups were matched by age, gender and educational level. The mean age of patients was 35.80 (SD=5.78) years and the mean age of normal

subjects was 33.04 (SD=6.07). Premorbid intelligence was estimated by performing the Scale for Verbal Intelligence (30). Although normal subjects had a better mean, but the differences between groups were not significant. For all patient groups, the illness duration since the onset of first psychotic symptoms did not precede more than 5 years. All the patients were receiving antipsychotic medication and were clinically stable. Patients were included in the study if they met primary diagnosis of Schizophrenia or major depression. Patients met DSM-IV criteria for schizophrenia and major depression on the basis of a standardized diagnostic interview. They were inpatients with current episode of schizophrenia or major depression at psychiatric centers in Shiraz. To enter the study, 50 schizophrenic patients were sub-typed into schizophrenic patients with positive symptoms (n=25) and schizophrenic patients with negative symptoms (n=25), using The Scale for the Assessment of Negative Symptoms (SANS) and The Scale for the Assessment of Positive Symptoms (SAPS) (31). They were determined on the basis of a semi-structured screening interview using SANS and SAPS. Symptom ratings also incorporated information from the patient's families and case managers. Beck Depression Inventory-II (BDI-II) (32) was used to determine levels of depressive symptomatology. Only those participants who met the score >29 of the BDI-II were selected. Patients were excluded if they currently had another psychological disorders met with DSM-IV Axis I and II. All non clinical participants were screened to rule out the presence of clinical conditions. Neither the healthy control subjects nor their first-degree relatives had a history of neurological or mental illness. All subjects were informed of the nature of the investigation and the procedures involved, and informed consent was obtained. Table 1 contains demographic and clinical characteristics of subjects.

**WCST:** All patients underwent the Wisconsin Card Sort Test (7). WCST consists of 128 response cards and 4 stimulus cards. The test is based on 64 cards which are normally used in two successive trials. The shapes on the cards are different in color (red, green, blue or yellow), form (circles, stars, squares or crosses) and number (1, 2, 3, 4). During the administration of the test, four stimulus cards with the following characteristics are placed before the subject: one red triangle, two green stars, three yellow crosses, and four blue circles. The subjects must sort the cards according to color, form, and number. The participant decides whether the cards are to be matched by color, form or number. He/she is not told how to match the cards; however, he/she is told whether a particular match is right or wrong.

Participants try different rules to find a correct method for sorting the cards. During the course of the test, the matching rules are changed. Once the subject has made a specified number of consecutive sorts according to the initial "correct" principle (usually color),

Table 1. Demographic and clinical characteristics of subjects

Variables		Negative Schizophrenia (n=25)	Positive Schizophrenia (n=25)	Major Depression (n=25)	Normal Subject (n=25)
<b>Sex</b>	Male	18	17	16	18
	Female	7	8	9	7
<b>Age</b>	M	35.02	35.80	32.80	33.04
	SD	6.01	5.78	5.29	6.07
<b>VIS<sup>1</sup></b>	M	93.92	96.72	92.72	98.48
	SD	11.44	11.50	12.63	6.88
<b>SAPS<sup>2</sup></b>	M	29.36	58.966	---	---
	SD	10.59	20.36	---	---
<b>SANS<sup>3</sup></b>	M	59.84	24.67	---	---
	SD	15.33	9.67	---	---
<b>BDI-II<sup>4</sup></b>	M	---	---	38/56	---
	SD	---	---	10.92	---

1. Verbal Intelligence Scale  
 2. Scale for Assessment of Positive Symptoms  
 3. Scale for Assessment of Negative Symptoms  
 4. Beck Depression Inventory -II

In this study, the test is scored in terms of the number of categories, perseverative errors and sum of errors. If a subject responds correctly to color (form or number) 10 consecutive times, he/she achieves one category. It means a category is the number of runs of 10 correct responses. Perseveration is the uncontrollable repetition of a particular response, despite the absence of a stimulus. But not all perseverative responses are errors. Perseverative errors are the number of errors where the participant has used the same rule for their choice as the previous choice. Sum of errors is the total number of errors.

*Scale for Assessment of Negative Symptoms (SANS) and Scale for Assessment of Positive Symptoms (SAPS)* were used to measure the positive and negative symptoms of schizophrenia (31). The positive symptoms are mainly hallucinations, delusions, disorganized speech and thought, agitated motor control and disorganized behavior. Negative symptoms include alogia, affective blunting, avolition, anhedonia and attentional impairment. SANS and SAPS consist of 20 and 30 items respectively. Each item was rated on a scale of 0 (absent) to 5 (severe). The psychometric properties of a Persian-language version of SANS and SAPS was examined in an Iranian sample, Acceptable internal consistency reliability for SANS ( $\alpha = 0.78$ ) and SAPS ( $\alpha = 0.77$ ) have been reported (33).

*Beck Depression Inventory-II (BDI-II)* measures the severity of self-reported depression (32). Its item content corresponds to criteria for the diagnosis of depressive disorders as specified in the DSM-IV. It is composed of 21 items that are structured on a 4-point scale ranging from 0 (symptom not present) to 3 (symptom strongly present). The BDI-II total scores ranging from 0 to 13 represent normal to minimal depression; total scores from 14 to 19 are mild; total

scores from 20 to 28 are moderate; and total scores from 29 to 63 are severe. An acceptable Internal consistency reliability ( $\alpha=0.92$ ) has been reported for the total BDI-II scale for clinical patients (36).

The psychometric properties of a Persian-language version BDI-II was examined in an Iranian sample (34). The BDI-II-Persian had high internal consistency ( $\alpha=0.87$ ) and acceptable test-retest reliability ( $r=0.74$ ). Another study in Iran (35) reported acceptable validity and reliability for a Persian-language version of BDI-II in a sample of major depressive patients. language version of BDI-II in a sample of major depressive patients.

*Verbal Intelligence Scale:* The scale assesses premorbid intelligence. It is an Iranian intelligence scale and consists of 50 Persian-words. The subject reads the words. The items are structured on a 2-point scale including 0 (wrong) or 1 (correct). The scale had high internal consistency ( $\alpha=0.79$ ) and acceptable test-retest reliability ( $r=0.90$ ). The instrument strongly correlated with the Standard Progressive Matrices ( $r=0.36$ ) (34).

All statistical analyses were performed using SPSS for Windows (version 16). The collected data were analyzed statistically using various descriptive statistics, ANOVA, t-test and multiple regression analysis.

## Results

Table 2 contains the mean scores and standard deviations of the number of categories, perseverative errors and sum of errors on WCST for different groups. One Way Analysis of Variance (ANOVA) was performed to find out whether or not different groups differ from one another on WCST. Table 3 shows that on the number of categories ( $P<0.001$ ), perseverative errors ( $P<0.01$ ) and sum of errors ( $P<0.001$ ), the

differences between groups were significant. A post hoc test (Shefe) showed that all patient groups performed significantly worse than normal subjects on WCST. The differences between schizophrenic patients and depressives in the variable perseverative errors was not significant, but the depressive patients had significantly ( $P<0.01$ ) more categories than two schizophrenic patient groups with negative and positive symptoms. Additionally, Schizophrenic patients with positive symptoms showed significantly ( $P<0.05$ ) more errors in the variable sum of errors than depressives, but the difference between depressives and schizophrenic patients with negative symptoms in this variable was not significant.

To determine the relative effects of severity of clinical symptoms on the WCST scores, a series of multiple regression analyses were performed on the WCST performance scores (number of categories completed, number of total errors, number of perseverative errors) as dependent variables for all patient groups. Negative, positive and depressive symptom scores were used as predictor or independent variables. The regression of the WCST total error and categories completed scores, using all the above independent variables yielded no significant predictor, but negative symptom score was the only predictor for the perseverative error scores, ( $R^2=0.46$ ,  $F=19.57$ ,  $p<0.001$ ). Greater negative symptom scores predicted significantly more perseverative errors score. No other variables were significant. In addition, each patient group was divided into two subgroups. In this classification procedure, we

had two subgroups of schizophrenic patients with low and high negative symptom scores, two subgroups with low and high positive symptom scores and two depressive subgroups with low and high depressive symptom scores.

A series of t-tests analysis were conducted to compare WCST performance in each three patient groups with low and high scores of symptoms.

It was indicated that only the differences between the two groups with low and high negative symptoms on perseverative errors were significant ( $p<0.01$ ). The patients with greater negative symptoms had more perseverative errors.

### Discussion

Our results showed that WCST could differentiate between Iranian psychiatric patients and normal subjects, but it was not able to clearly differentiate patient groups from one another.

Regarding perseverative errors, sum of errors and number of categories (forming different variables of WCST), all patient groups including the schizophrenics with negative and positive symptoms and the major depressives had significantly worse scores than normal subjects. This is consistent with some of the previous findings according to which schizophrenic patients and depressives performed worse than normal controls in WCST (12, 36).

Berman et al. assessed cognitive functions using WCST and some other neuropsychological tests and

**Table 2. Mean scores (standard deviations) of the number of categories, perseverative errors and sum of errors of different patient groups and normal subjects on WCST**

Subjects	n	Categories	Perseverative Errors	Sum of Errors
Negative Schizophrenia	25	1.56 (1.68)	45.08 (30.79)	80.36 (22.90)
Positive Schizophrenia	25	1.60 (1.60)	46.36 (31.38)	81 (23.55)
Depression	25	3.52 (2.40)	46.36 (31.43)	55 (30.01)
Normal Subjects	25	5.20 (1.52)	19.12 (14.67)	30.92 (20.62)
Total	100	2.97 (2.36)	36.75 (29.27)	61.82 (31.87)

**Table 3. A comparison of the number of categories, perseverative errors and sum of errors of different groups on WCST using ANOVA**

Source of Variance		Sum of Squares	Mean Square	df	F	p-value
Categories	Between Groups	228.510	76.170	3	22.541	0.001**
	Within Groups	324.400	3.379	96		
	Total	552.910		99		
Perseverative Errors	Between Groups	11816.350	3938.783	3	5.179	0.002*
	Within Groups	73014.400	760.567	96		
	Total	84830.750		99		
Total Errors	Between Groups	42823.160	14274.387	3	23.731	0.001**
	Within Groups	57745.600	601.517	96		
	Total	100568.760		99		

\*\* $P \leq 0.001$ , \*  $P \leq 0.01$

It indicated that these patients are not able to perform as well as normal subjects on WCST (12). The Lower performance on the WCST was not an effect of lower IQ in patient groups, because the differences between patient groups and normal subjects were not significant. The WCST was able to differentiate psychiatric patients from normal subjects. As previously explained, WCST has been suggested as a more specific test for frontal lobe dysfunctions and schizophrenic patients, it also showed abnormalities of the structure and dysfunctions of frontal lobes (20, 21). Therefore, a worse performance on WCST in these patients is not unexpected. Contrary to expectation, difference between the two schizophrenic groups was not significant. It is inconsistent with some previous findings (24, 30). The result contradicts with some findings maintaining that cognitive dysfunction is more prominent in chronic patients (5). To date, most previous studies have reported that schizophrenic patients with negative symptoms have impairment on some tests, sensitive to frontal lobe, like WCST (23, 24), although some others showed different results (30). According to Crow's hypothesis (16), it was expected that schizophrenic patients with negative subtype show impairment on tests sensitive to frontal lobe dysfunctions. The findings of present study are not consistent with the notion that only negative symptoms are associated with cognitive impairment on WCST. Instead, it appears that both types of symptoms are associated with performance deficits on this test. The findings are controversial. For instance, in a study, negative subtype schizophrenics performed more poorly than positive subtype schizophrenics in the WCST (3). It was reported that negative subtype schizophrenics may have greater impairments on neurocognitive functions associated with frontal and parietal lobe dysfunction than positive subtype schizophrenics. In another study, schizophrenic patients with intact WCST performance had a lower mean negative symptom score than schizophrenic patients with impaired WCST performance (37). In summation, WCST was not able to differentiate schizophrenic patients with negative and positive symptoms. The patients with major depression also did significantly worse than normal subjects in WCST. It is consistent with the findings of the study that explored the performance on WCST in patients with major depression and compared their results with those of patients with frontal lobe tumor. Frontal lobe executive functioning was abnormal in patients with depression (25). Other studies have also reported that depressive patients did significantly worse than normal subjects in cognitive tests (38, 39, 40). Recently, a review on cognitive impairments in depressives showed that cognitive impairments are common in young adults with major depression (41). Depressed patients also showed impairments of executive functions (42). Comparing the performance on WCST in patients with major depression and those of patients with frontal lobe tumor confirmed such findings (25). Our results were

consistent with previous findings, which confirmed that WCST was able to differentiate major depressive patients from normal subjects. An important finding is that WCST could not differentiate between patient groups clearly. Perseverative error is a core symptom of schizophrenia which has been proposed as a phenotypic marker of the illness (43), but a comparison between schizophrenics and depressives showed that only the number of achieved categories could make a distinction between them. Depressive patients had significantly more categories than the two schizophrenic patient groups. Regarding the sum of errors, only schizophrenics with positive symptoms had significantly more errors than depressives, but not schizophrenics with negative symptoms. It could be supposed that WCST differentiates, at least in part, schizophrenic patients with positive symptoms from depressives, although the difference between the two patient groups on sum of errors was not significant. That is, individuals with negative schizophrenia and major depression were similar in terms of both the perseverative errors and the sum of errors. In the other words, WCST was not able to differentiate between Iranian schizophrenic and depressive patients clearly. The observed poor performance on WCST by schizophrenic and depressive patients may be related to frontal lobe dysfunctions in both patient groups. Some variables like etiology, area of damage, time since injury and size of damage can play a role in WCST performance in patients with frontal lobe damage (44). The results of present study supported the idea that different frontal lobe regions could be affected in people with schizophrenia and major depression. It has been reported that dorsolateral frontal lobe was activated during WCST performance by schizophrenic patients (12), but severe major depressive disorder was related to frontal-subcortical dysfunction (29). It is also possible that both patient groups are on a cognitive dysfunction continuum (45), schizophrenics with more and depressives with less cognitive disorders. Another reason could be the relationship between cognitive dysfunctions and severity of clinical symptoms. It is important to define whether impaired executive functions associated with psychiatric patients are a result of organic dysfunction or the severity of clinical symptoms, like positive, negative or depressive symptoms. In a new study, the comparison of the patients with psychotic depression, nonpsychotic depression and healthy controls showed that depression groups revealed different response patterns, reflecting more severe deterioration and signs of possible organic dysfunction in patients with psychotic depression (29). That is, the severity of clinical symptoms can alter the test results. Contrary to these findings our results showed that greater positive or depressive symptoms were not associated with poorer scores on WCST performance. Only the level of negative symptoms severity predicted scores on perseverative errors. Patients with greater negative symptoms revealed more perseverative errors. Negative symptom score was a

predictor of perseverative errors, but not the categories or total error scores. According to Crow's hypothesis (16), type II syndrome is characterized by negative symptoms and is related to structural brain changes. Therefore, frontal lobes disorder could be a reason for both negative symptoms and cognitive disorders. Both t-test and regression analysis showed that negative symptoms are related to cognitive disorders. In both of these analyses, negative symptoms were inversely associated with perseverative errors. In summary, the results of our study suggested that WCST, as a diagnostic neuropsychological test sensitive to frontal lobes' dysfunctions, could differentiate Iranian psychiatric patients with cognitive disorders from normal subjects, but it was not able to differentiate such patients clearly. Depressives had better scores than schizophrenics on some variables of WCST. However, WCST was not able to differentiate between the two groups clearly. Despite the fact that WCST could not differentiate Iranian psychiatric patients clearly, it is a useful neuropsychological test for comparing psychiatric patients and healthy subjects. In addition, it was also able to reveal, at least in part, the differences between some patient groups. Our findings showed that only the level of negative symptoms severity predicted scores on perseverative errors. There was no relationship between positive or depressive symptoms and poorer scores on WCST performance. Because of possible cultural differences, future studies on cognitive functioning in psychiatric patients should investigate the strength of differential diagnosis of WCST and other neuropsychological instruments in more Iranian psychiatric patient groups like patients with bipolar depression, obsessive compulsive disorder, schizoaffective disorder and frontal lobe lesion.

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