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Original Article

Comparing the executive function of patients with schizophrenia, acute/chronic type I disorder (manic episode), and healthy controls on Wisconsin Card Sorting Test and Continuous Performance Test

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Abstract

Introduction: From among various cognitive deficits, deficits in executive processes have an effective role in limiting the patients' ability to retain, acquire, and re-learn the skills necessary for real-life performance. Thus, the present study aimed to compare the executive function of patients with schizophrenia, acute/chronic type I disorder, and the healthy group.

Methods: The present research was an analytical-comparative study. The statistical population consisted of all the outpatients and inpatients with acute/chronic schizophrenia and acute/chronic type I disorder (manic episode) visiting Shafa Psychiatric Hospital, Rasht, Iran. Using convenience sampling, 60 male subjects aging 18-49 years old were selected in 2014-2015. They were matched for the variables of sex, age, and education level. The Wisconsin Card Sorting Test, Continuous Performance Test, and Raven's Progressive Matrices were administered, and the data were analyzed using MANOVA and Tukey post-hoc test.

Results: A significant difference was observed between the acute/chronic schizophrenia group, acute/chronic type I disorder (manic episode), and healthy group on the two tests. Patients with schizophrenia had a weaker executive function and attention deficit compared to those with type I disorder and the healthy group ($P \leq 0.05$).

Conclusion: Both schizophrenia and type I disorder patients show deficits in executive function and attention. However, the former group manifests higher impairment in cognitive activities, concept formation, cognitive flexibility, and attention deficit.

Introduction

Today, approximately 450 million individuals around the world suffer from a mental or behavioral disorder. According to the 2011 statistics of World Health Organization (WHO), 33% of years lived with a disability is the result of mental disorders including depression, diseases related to alcohol consumption, schizophrenia, and type disorder (1). Schizophrenia afflicts about 1% of the population, usually starts before 25, and persists for life. It is accompanied by a wide range of cognitive impairments (2), and most patients suffering from this disease show more than one neurological-cognitive symptom, e.g. deficits in memory, attention, concentration, motor functions, and executive functions. These deficits are observed in over 70% of patients with schizophrenia (3) and cover all mental processes, from basic forms (e.g. attention and consciousness) to more complicated ones (e.g. abstract thinking and problem solving). The type disorder which is characterized by recurrent episodes of mania and depression, with complete remission in the intervals, is considered to be relatively more benign than schizophrenia (4, 5). Nevertheless, this presentation contrasts with a large number of patients who fail to achieve pre-morbid levels of mental-social performance over the course of treatment (6).

From among various cognitive deficits, deficits in executive processes have an effective role in limiting the patients' ability to retain, acquire, and re-learn the skills necessary for real-life performance (7). Executive functions generally comprise a group of cognitive skills which are responsible for planning, starting, sequencing, and monitoring complex goal-oriented behaviors (8). Lezak conceptualizes these functions in four distinct components: volition, planning, purposive action, and effective performance (9).

Impairment in visual memory, abstract reasoning, and inhibitory control has been reported in patients with schizophrenia (Hou et al. 2016; Lam et al., 2014; Mosiołek et al., 2016) and those with type disorder (Bora et al., 2010; Levy & Weiss, 2010) (10, 11, 12, 13, 14). It must be noted that working memory, cognitive flexibility, visual memory, abstract reasoning (Langer et

al., 2012; Vakhtin et al., 2014) (15, 16) and inhibitory control (meta-analysis conducted by Cieslik et al., 2015) (17) are mediated by the frontoparietal neural network. Deficits in this network are accompanied with a genetic risk for schizophrenia and type disorder (McDonald et al., 2004) (18). Neurological imaging studies have revealed certain malfunctionings in different levels of this network in the relatives of schizophrenic patients (Schmidt et al., 2015) (19).

Sustained attention deficit, which is measured by the Continuous Performance Test (CPT), is one of the numerous cognitive functioning deficits in schizophrenia (20), always observed in schizophrenic patients, and manifested independently of clinical symptoms (21). Wang et al. utilized CPT for measuring sustained attention in 112 patients with first-episode schizophrenia who had not taken tranquilizers. Schizophrenic patients had a poor performance in all CPT scales compared with 296 non-psychotic first-degree relatives and 452 healthy individuals (22).

Bozikas et al. (2005) investigated sustained attention in schizophrenic and type patients in remission. They administered CPT to 18 outpatients with schizophrenia, 19 type I disorder patients in remission, and 30 healthy controls matching in terms of age, sex, and education level. The scores of the three groups significantly differed. Patients with schizophrenia performed more poorly than the other groups, while the performance of the type group did not significantly differ from that of healthy controls. The schizophrenic outpatients showed deficits in sustained attention, whereas the type I disorder patients in remission showed no signs of deficit (23). Ryan et al. (2012) examined the executive functioning performance of patients with type disorder (BD), including depressed and hypomanic/mixed (HM/M-BD) patients, and healthy controls. Results revealed that the HM/M-BD group performed significantly worse than the healthy controls and BD group in terms of inhibitory control (24).

There exists growing evidence for the role of brain dysfunction in the etiology and pathogenesis of schizophrenia and type disorder (25). Brain diseases usually induce behavioral changes, including impairment in cognitive abilities and neuropsychiatric symptoms. Therefore, awareness of the features of these behavioral changes can help with the diagnosis, management, and longitudinal care of patients with neurocognitive diseases. A neuropsychological evaluation is a tool for collecting quantitative data on behavioral changes in patients with identified diseases or those who are at risk of brain dysfunction. It can identify behavioral and cognitive disorders and is useful in diagnostic evaluation, rehabilitation planning, or management plan development for clinicians (26).

Accordingly, the present study attempted to shed more light on the executive functioning deficit hypothesis in schizophrenia and type disorder. In other words, this study attempted to evaluate executive function in patients with schizophrenia and type disorder I and compare their performance with each other and with healthy controls. Moreover, in comparing the executive function of patients in acute and chronic phases of both groups with each other and with healthy controls, this study evaluated the effect of time in order to determine a clearer and more specific path for training and cognitive

rehabilitation for these patients.

Materials and Methods

The present analytical-comparative study compared the executive function of 5 groups. The statistical population consisted of all the outpatients and inpatients with acute/chronic schizophrenia and acute/chronic type I disorder visiting Shafa Psychiatric Hospital, Rasht, Iran. Based on Cohen's Table and using convenience sampling, 60 subjects (12 with acute schizophrenia, 12 with chronic schizophrenia, 12 with acute type I disorder, 12 with chronic type 1 disorder, and 12 healthy individuals) were selected in 2014-2015. Sample size was determined using the formula for comparing two population means, with the α level and statistical power of β-1 (27). Patients with "multiple-episode schizophrenia, currently in the acute episode" are those who had experienced one psychotic episode before and their psychotic symptoms have relapsed for multiple times. Patients with "first-episode schizophrenia, currently in the acute episode" are those who are experiencing acute psychotic symptoms for the first time and have never had any psychotic disorders before (28). Patients with "type I disorder, single manic episode" are type patients who are experiencing symptoms of mania for the first time, with no previous manic or depressive disorder. Patients with "type I disorder, recurrent, most recent episode: mania" are patients with type I disorder who had experienced mania before once or multiple times and are experiencing it now (29). In this study, we selected chronic schizophrenic and type patients who were experiencing a relapse in symptoms, had a history of multiple admissions, and 5 years or more had passed since the onset of their disease. In addition, we selected acute schizophrenia and type patients who were experiencing acute symptoms of disorder for the first time and less than 2 years had passed since the onset of their disease. The patients were matched for the variables of sex, age, and level of education in groups. Both groups of patients had definitive schizophrenia or type I disorder diagnosis based on DSM-V criteria and took serotonin, dopamine (serotonin-dopamine), risperidone, and olanzapine antagonist antipsychotic medications. The subjects' age ranged from 18 to 49 years, with no history diseases such as mental retardation, personality disorder, epilepsy, and drug and alcohol dependence in the past year, or other medical and psychiatric diseases inducing cognitive disorders. The Wisconsin Card Sorting Test, Continuous Performance Test, and Raven's Progressive Matrices were administered to all the subjects individually. In accordance with ethical considerations, written consent forms were obtained from all the subjects, and they were informed they could withdraw from the study at any time. Furthermore, all the data were anonymous, and the subjects were told that they would receive the results. Data were collected using the following instruments:

Wisconsin Card Sorting Test (WCST)

WCST was developed by Grant and Berg in 1948 (30). It is the most commonly used test of executive

function in studies on schizophrenia (31). In their neurographical studies, Berman et al. (cited in Remillard et al.) showed that the performance on WCST is correlated with the brain's activity in the dorsolateral prefrontal cortex (32). According to Remillard et al., the local blood flow was less in the dorsolateral prefrontal cortex of schizophrenic patients while taking the WCST than healthy controls (33). In this test, the test-taker is given 64 cards showing 1-4 symbols (triangle, star, cross, and circle) in red, green, yellow, and blue. Four cards showing a red triangle, two green stars, three yellow crosses, and four blue circles are given to the test-taker as stimulus cards. They are then asked to place the remaining cards under the stimulus cards based on the experimenter's feedback.

Several studies, e.g. Purdon and Waldie (2001) (34) have confirmed the reliability and validity of this test. Lezak (1995) has reported the reliability of this test to be 0.86 for measuring cognitive deficits following brain damage (9). According to Spreen and Strauss (as cited in Del Azar), the inter-rater reliability coefficient of this test is 0.83 (8). The computerized version of WCST is designed in Persian and validated by Shahgholian, Azad, Fallah, Fathi, Ashtiani, and Khodadai (as cited in Zare & AbdollahZadeh, 2015) (30).

Continuous Performance Test (CPT)

This test was designed by Rosvold et al. (1956) and was initially used for measuring brain lesions. The major aim of this test is evaluating sustained attention and impulse control. Different formats of this test have been developed for treatment and research purposes. In all formats, the test-takers must focus their attention on a set of relatively simple visual or auditory stimuli and respond to the appearance of the target stimulus by pressing a button. We utilized the Persian format of CPT developed by Sina Cognitive-Behavioral Sciences Research Center. Omission and commission errors are scored in this test. The number of correct responses and the response time are also measured. Hadianfar et al. reported acceptable reliability and validity for the Persian format of the test. In their study, the reliability coefficient was 52%-93% for different sections of the test. The criterion validity of the test was determined by comparing a normal group and a group with attention-deficit hyperactivity disorder. The statistical comparison of means between the two groups revealed a significant difference between their performances, in line with the result of previous studies in other countries (30).

Raven's Progressive Matrices (RPM)

RPM is a non-verbal test, designed by J. C. Raven in 1938 and revised in 1956 (35). This test demands the discovery of relationships between abstract items. It is regarded as the best indicator of general intelligence by British psychologists (36). In one study, the reliability and factorial validity of RPM were examined in 6529 Kuwaiti children aged 8-15 years old. The test-retest reliability ranged from 69% to 85%, while Cronbach's alpha ranged from 88% to 93%, indicating the acceptable-to-good consistency of the test over time as well as its good internal consistency. Baraheni (1998) examined and validated RPM in 3010 students aged 9-18 years in Tehran. In the present study, we employed the format validated by Baraheni, and the results were evaluated using one-way ANOVA.

Results

All the subjects in the 5 groups were male. The mean age of patients was 37.58 years for chronic schizophrenia, 31.25 years for acute schizophrenia, 37.58 years for chronic type disorder, 30.75 years for acute type disorder, and 28.67 years for healthy individuals, showing no significant difference based on one-way ANOVA (F=2.305, p>0.070). The groups matched in terms of intelligence level (F=2.325, p>0.068), showing no significant difference based on one-way ANOVA. They were also homogeneous in terms of education level (x^2=19.58, p>0.07). Research hypotheses were examined using MANOVA.

A significant difference was observed between the acute/chronic schizophrenia, acute/chronic type I disorder (manic episode), and healthy group on the two tests (Table 1).

Furthermore, a significant difference was observed among the five groups of subjects on all the subscales of CPT and WCST (Table 2).

Table 1. Multivariate tests for testing the hypotheses

Effect		Degree	F	Hypothesis Df	Error Df	P value
Comparison of groups on CPT	Pillai's Trace	0.758	4.874	12	165	0.001
	Wilks's lambda	0.314	6.442	12	140	0.001
	Hotelling's Trace	1.881	8.098	12	155	0.001
	Roy's largest root	1.706	23.463	12	55	0.001
Comparison of groups on WSCT	Pillai's Trace	1.021	4.713	16	220	0.001
	Wilks's lambda	0.183	7.402	16	159.50	0.001
	Hotelling's Trace	3.386	10.688	16	202	0.001
	Roy's largest root	3.057	42.031	4	55	0.001

Table 2. Univariate tests for examining the difference among groups on each dependent variable

Source	Dependent Variable	Sum of Squares	Df	Mean of Squares	F	P value
Comparison of groups on the subscales of CPT	Response error	212.267	4	53.067	7.078	0.001
	Omission response	210.433	4	52.608	9.471	0.001
	Correct response	1540.767	4	385.192	21.815	0.001
Comparison of groups on the subscales of WSCT	Correct response	1571.000	4	392.750	19.468	0.001
	Incorrect response	3656.433	4	914.108	12.135	0.001
	Number of categories	128.167	4	32.042	28.348	0.001
	Preservation error	1077.567	4	269.392	18.879	0.001

Table 3. Results of Tukey post-hoc test for comparing the subscales of WCST among acute/chronic schizophrenia, acute/chronic type I disorder, and healthy group

CPT	Comparison of groups		Mean difference	Standard Deviation	Pvalue
Correct response	Acute schizophrenia	Chronic schizophrenia	8.750	1.833	0.001*
		Acute type	0.33	1.833	1
		Chronic type	3.33	1.833	0.374
		Healthy	-7	1.833	0.003*
	Chronic schizophrenia	Acute type	-8.416	1.833	0.001*
		Chronic type	-5.416	1.833	0.036*
		Healthy	-15.75	1.833	0.001*
	Acute type	Chronic type	3	1.833	0.481
		Healthy	-7.33	1.833	0.002*
	Chronic type	Healthy	-10.33	1.833	0.001*
Incorrect response	Acute schizophrenia	Chronic schizophrenia	-12.416	3.543	0.008*
		Acute type	0.166	3.543	1
		Chronic type	-2.916	3.543	0.922
		Healthy	12	3.543	0.011*
	Chronic schizophrenia	Acute type	12.583	3.543	0.007*
		Chronic type	9.500	3.543	0.070
		Healthy	24.416	3.543	0.001*
	Acute type	Chronic bipolar	-3.083	3.543	0.907
		Healthy	11.833	3.543	0.013*
	Chronic type	Healthy	14.916	3.543	0.001*
number of categories	Acute schizophrenia	Chronic schizophrenia	2.500	0.434	0.001*
		Acute type	-1.250	0.434	0.043*
		Chronic type	1	0.434	0.159
		Healthy	-1.416	0.434	0.016*
	Chronic schizophrenia	Acute type	-3.750	0.434	0.001*
		Chronic type	-1.500	0.434	0.009*
		Healthy	-3.916	0.434	0.001*
	Acute type	Chronic type	2.250	0.434	0.001*
		Healthy	-0.166	0.434	0.995
	Chronic type	Healthy	-2.416	0.434	0.001*
Preservation error	Acute schizophrenia	Chronic schizophrenia	-5.250	1.542	0.010*
		Acute type	2.750	1.542	0.394
		Chronic type	-0.50	1.542	0.998
		Healthy	7.666	1.542	0.001*
	Chronic schizophrenia	Acute type	8	1.542	0.001*
		Chronic type	4.750	1.542	0.026*
		Healthy	12.916	1.542	0.001*
	Acute type	Chronic type	-3.250	1.542	0.232
		Healthy	4.916	1.542	0.019*
	Chronic type	Healthy	8.166	1.542	0.001*

Table 4. Results of Tukey post-hoc test for comparing the acute/chronic schizophrenia, acute/chronic type I disorder, and healthy group in terms of performance on CPT

CPT	Comparison of groups		Mean difference	Standard Deviation	P value
Response error	Healthy	Acute type	-3.17	1.118	0.048*
		Chronic type	-3.83	1.118	0.010*
		Acute schizophrenia	-3.58	1.118	0.018*
		Chronic schizophrenia	-5.83	1.118	0.001*
	Acute type	Chronic type	-6.7	1.118	0.975
		Acute schizophrenia	-0.42	1.118	0.996
		Chronic schizophrenia	-2.67	1.118	0.135
	Chronic type	Acute schizophrenia	0.25	1.118	0.999
		Chronic schizophrenia	-2	1.118	0.390
	Acute schizophrenia	Chronic schizophrenia	-2.25	1.118	0.274
Omission response	Healthy	Acute type	-2.75	0.962	0.046*
		Chronic type	-2.83	0.962	0.037*
		Acute schizophrenia	-2.92	0.962	0.029*
		Chronic schizophrenia	-5.92	0.962	0.001*
	Acute type	Chronic type	-0.08	0.962	1
		Acute schizophrenia	-0.17	0.962	1
		Chronic schizophrenia	-3.17	0.962	0.014*
	Chronic type	Acute schizophrenia	-0.08	0.962	1
		Chronic schizophrenia	-3.08	0.962	0.018*
	Acute schizophrenia	Chronic schizophrenia	-3	0.962	0.023*
Correct response	Healthy	Acute type	2.67	1.715	0.532
		Chronic type	9.08	1.715	0.001*
		Acute schizophrenia	8.17	1.715	0.001*
		Chronic schizophrenia	14.42	1.715	0.001*
	Acute type	Chronic type	6.42	1.715	0.004*
		Acute schizophrenia	5.50	1.715	0.018*
		Chronic schizophrenia	11.75	1.715	0.001*
	Chronic type	Acute schizophrenia	-0.92	1.715	0.983
		Chronic schizophrenia	5.33	1.715	0.024*
	Acute schizophrenia	Chronic schizophrenia	6.25	1.715	0.005*

Discussion

The present study aimed to compare the executive function of patients with acute/chronic schizophrenia, acute/chronic type I disorder (manic episode), and healthy controls. Results demonstrated that cognitive and attention deficits are more extensive and deeper in patients with chronic schizophrenia than in patients with acute/chronic type I disorder and healthy individuals. Results also revealed that patients with acute/chronic schizophrenia and chronic type I disorder (manic episode) have fewer correct categories than the healthy group in WCST. This result may indicate a damage to concept formation in these patients, leading to poorer performance in both groups compared with the healthy population. The performance of patients with chronic schizophrenia was significantly poorer than that of the other groups, i.e. acute schizophrenia, acute/chronic type I disorder, and healthy controls. Weakness in this type of cognitive performance may explain the poor performance of patients with chronic schizophrenia in the face of new situations. Results also indicated that the preservation error in "cognitive flexibility" performance was poorer in patients with acute/chronic schizophrenia than in other groups. In other words, these patients cannot change their minds from one cognitive set to another. Therefore, they may act stereotypically and repetitiously and have problems in reaching planned goals. The WCST also showed that the performance of patients with chronic schizophrenia was significantly worse than that of the other groups in terms of the number of correct and incorrect responses in these two subscales. Moreover, patients with acute/chronic type

disorder performed worse than the healthy group on these two subscales. However, there was no significant difference between patients with acute and chronic type disorder. In addition, no significant difference was observed between patients with acute schizophrenia and those with acute/chronic type disorder. Overall, the performance of the groups on WCST reveals the poor executive function of patients with chronic schizophrenia compared with acute/chronic type disorder. This finding is consistent with the result of studies such as Siedman et al. (37), Park and Holzman (38), and Rossi et al. (31), showing a more severe damage in schizophrenic patients compared with type ones. In their study entitled "Neurocognitive performance, psychopathology and social functioning in individuals at high risk for schizophrenia or psychotic type disorder", Gkintoni et al. (2017) concluded that poor verbal fluency and processing speed were observed only in the first-degree relatives of schizophrenic patients (39).

In the present study, the patients with chronic schizophrenia significantly differed from all groups (except for patients with chronic type disorder) on the subscales of correct responses. This finding is in line with the results of other studies. For instance, Morice showed that, like patients with chronic schizophrenia, type (manic) patients have a poor performance on WCST (40). Furthermore, Green et al. (41) reported that patients with schizophrenia and mania show considerable deficits in visual backward masking, compared with the healthy group. Finally, Hoff et al. (42) could not differentiate patients with type disorder from those with schizophrenia. In the present study, patients with acute and chronic type disorder showed a significant difference in all the subscales of WCST except for preservation error. There is evidence for the presence of neuropsychological (e.g. attention), executive function, and memory deficits in patients with mood disorder (40, 43, 44, 45, 46, 47). Research has reported damaged neurological functioning during the acute phase of type disorder. Ferrier and Thompson (2002) found a correlation between the number of phases and cognitive damages in type disorder (48). In addition, Tohen et al. (49) and Dixon et al. (50) examined the effect of symptoms on the executive function of various type patients. Results showed that the deficits in executive function are especially accompanied with mania. In the present study, we evaluated patients with type I disorder in the manic phase. Results indicated that deficits in executive function in patients with type I disorder are much more evident in the manic phase. These results are consistent with the general findings of Ryan et al. (2012) based on which HM/M-BD patients were significantly poorer than patients with type disorder and healthy controls in terms of inhibitory control (24).

In the present study, results of CPT indicated no significant difference between patients with acute type I disorder and the healthy group on the subscale of correct responses. Nevertheless, a significant difference was observed between the subscales of response error and omission response This finding is in line with the result of Liu et al (51) and Qureshi and Frangou (5) who showed no significant difference between stable type outpatients and the controls in terms of performance on CP. On sustained attention in type disorder, scales such as CPT and the Span of Apprehension Task have revealed processing disorder over acute emotional episodes. This deficit may be affected by the time and incidence of psychosis (51). However, it has been proven that it is improved following the alleviation of emotional symptoms (52, 53).

The present study showed no significant difference between acute and chronic type I disorder patients in the subscales of response error and omission response. However, a significant difference was found in the subscale of correct response. According to Liu et al., attention disorder is less severe in type outpatients than type inpatients. The latter improves from the time of admission until discharge, but remains significantly impaired compared with the healthy population (51). This pattern means that certain aspects of attention in type patients may be state-related, while some others are trait-related and may have distinct pathological mechanisms (53). The presence of attention disorder as a function of acute mania or depression is not surprising. Recent studies have found neuropsychological deficits in stable type patients (54). These patients have damages in attentional performance, executive functions, and working memory (55). In addition, the attention deficit measured by CPT occurs in stable type patients after controlling the remaining emotional symptoms, compared with the controls (4). Stable type patients have deficits in CPT (56) and their performance is not related to the remaining mood symptoms or pharmacotherapy. These findings suggest that attention function deficits may be a trait of type disorder.

Results of CRT in the present study revealed a significant difference between patients with chronic schizophrenia and the other 4 groups in the subscales of omission response and correct response, in line with the findings of Seidman et al. (37), Wang et al. (22), and Bozikas et al. (23). On the other hand, a comparison of the performance of stable type and schizophrenic patients on CPT leads to contradictory findings. The former usually performs better than the latter, but this difference does not always reach a significant level (51, 57, 58).

Conclusion

It is obvious that executive dysfunction can affect the activities of daily living. It appears that the severity of these deficits has a determining role in predicting the occupational-social performance, as clearly shown by Semkovska et al. They evaluated the executive dysfunction of patients with schizophrenia during the activities of daily living. Results demonstrated that the executive dysfunction and negative symptoms have a clear, negative effect on the activities of daily living in schizophrenic patients (58). Of course, it appears that the psychosis process, regardless of disease type, disrupts executive function and attention. Executive function and attention deficits may disrupt the mental, personal, and family rehabilitation process. However, since this deficit is less common among type patients, rehabilitation is more persistent and effective for them.

It must be noted that the data in this study were collected from patients who were on antipsychotic medications, which may be a limitation. The other limitation was the fact that all the subjects were men. We recommend a comparison between the sexes on cognitive measures, as well as the use of instruments other than WCST and CPT, in future studies.

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