EXPRESSION OF SERUM BDNF IN PATIENTS WITH SCHIZOPHRENIA AND ITS CORRELATION WITH COGNITIVE FUNCTION AND CLINICAL EFFICACY

Chunpeng Fu*, Liang Zhou, Chunxia Fu
The Third People's Hospital of Shangrao, Shangrao 334000, PR China

ABSTRACT

Objective: *To analyze the expression of brain-derived neurotrophic factor (BDNF) in patients with schizophrenia and its correlation with cognitive function and clinical efficacy.*

Methods: *From March 2018 to February 2020, 68 schizophrenic patients hospitalized in our psychiatric department were selected as the study group, and 68 healthy subjects who had a physical examination in the hospital at the same time were selected as the control group. Patients in the study group were given aripiprazole treatment, all patients were treated for two weeks continuously, and electroconvulsive therapy was prohibited during the treatment. Enzyme-linked immunosorbent assay was used to determine the serum BDNF level. The Wisconsin Card Sorting Test (WCST) results and Personal and Social Performance Scale (PSP) scores of the study group before and after treatment were compared. The Pearson correlation test was used to analyze the correlation between serum BDNF level and cognitive function, using the Positive and Negative Syndrome Scale (PANSS).*

Results: *Compared to the control group, the level of BDNF in the study group was significantly lower before treatment ($P<0.05$); and after treatment, the level of BDNF was significantly increased ($P<0.05$). After treatment, the number of completed classification and PSP scores of the study group significantly increased, and the number of wrong answers, the number of persistent errors, self-care, socially beneficial activities, disturbance and aggressive behavior, and personal and social relations were significantly decreased ($P<0.05$). However, there was no significant difference in the number of non-persistent errors ($P>0.05$). Pearson correlation analysis showed that there was a significant negative correlation between PANSS and PSP total score, BDNF change, and BDNF level after treatment. The PANSS score reduction rate and PSP amplitude were significantly and positively correlated, and the number of completed classification was significantly negatively correlated with the number of wrong answers and persistent errors ($P<0.05$). There was no significant correlation among other indicators ($P>0.05$).*

Conclusion: *The level of serum BDNF in schizophrenic patients was significantly lower than that in the control subjects, and there was significant cognitive impairment. Serum BDNF level was significantly related to the clinical efficacy of patients, which can be used as an important indicator for the diagnosis of patients' conditions.*

Keywords: *BDNF, schizophrenia, cognitive function, clinical efficacy, correlation.*

DOI: 10.19193/0393-6384_2021_6_538

Received *March 15, 2020;* ***Accepted*** *October 20, 2020*

Introduction

Schizophrenia is one of the most common and serious mental diseases in clinical practice. It mainly manifests as the incongruity of mental activities and the environment. According to statistics, globally, the prevalence of schizophrenia is about 3.8‰–8.5‰, and the burden of mental illness accounts for about 8‰ of the total burden of disease in the world[1]. The onset of schizophrenia is slow and the course of the disease is prolonged, and, to some extent, there is a chronic tendency and the possibility of decline, which has a serious impact on the lives of patients and their families. At present, the pathogenesis of schizophrenia is relatively complex, and some scholars believe that it may be the result of early neurodevelopmental abnormalities[2]. Patients in the embryonic period, perinatal period, puberty, and other key periods of brain development face a variety of internal and external factors, so that the

brain's structure and function changes, leading to the occurrence of schizophrenia. With the progress of medical science and technology and the deepening of research on schizophrenia, it has been found that the impairment of cognitive function directly affects the social function of patients, thus affecting the rehabilitation of the disease and seriously affecting their quality of life[3].

Brain-Derived Neurotrophic Factor (BDNF) is a small protein molecule secreted by neurons and astrocytes that plays an important role in the development of the nervous system. Studies have found that BDNF can express molecules required for the normal function of neurons, and the loss of BDNF may cause nerve apoptosis or atrophy[4]. In this study, the expression of serum BDNF in patients with schizophrenia and its correlation with cognitive function and clinical efficacy are explored and analyzed.

Materials and methods

Basic information

All the studies in this group received the approval of the ethics committee of our hospital and the principles of medical ethics. A total of 68 patients with schizophrenia, who were hospitalized in the Department of Psychiatry from March 2018 to February 2020, were selected as the research group. Among these were 29 males and 39 females, with an average age of 38.19±11.84 years.

Inclusion criteria:

• All patients met the criteria for diagnosis and treatment of schizophrenia[5];

• The patients were 20 to 60 years old;

• Patients had not received electroconvulsive therapy 5 months before the study;

• All participants gave and signed informed consent.

Exclusion criteria:

• Patients with other mental diseases;

• Pregnant or lactating patients;

• Patients with severe insufficiency in liver, kidney, and/or heart function;

• Patients with endocrine and metabolic disorders;

• Patients with a history of severe drug allergy.

Sixty-eight healthy subjects, 32 males and 36 females with an average age of 37.96±9.84 years, were selected as the control group. There was no statistically significant difference in the basic data between the two groups (P>.05).

Methods

Patients in the study group were treated with aripiprazole (Chengdu Kanghong Pharmaceutical Group Co., Ltd, batch number: 20171501, specification: 5mg*20 tablets) with an initial dose of 10mg, which was gradually increased to 30mg after two weeks of medication according to the efficacy and tolerance of the body.

All patients were treated continuously for two weeks, and electroconvulsive therapy was prohibited during the treatment process.

Experimental methods

The Wisconsin Card Sorting Test (WCST) is a common sorting method to detect neuropsychological changes, including the number of false responses, persistent errors, non-persistent errors, and sorting completed over time. The Personal and Social Performance Scale (PSP) is used to assess a patient's social functioning, including socially beneficial activities, personal and social relationships, self-care, and disruptive and aggressive behaviors. The total score is 100, with a lower score indicating more severe social dysfunction.

The Positive and Negative Syndrome Scale (PANSS) assesses the severity of symptoms of different types of schizophrenia. It consists of 7 items of positive scale, 7 items of negative scale, and 16 items of general pathology scale. The time range of assessment is usually 30-50min for all information in the week before the assessment.

Observation indicators

4mL of fasting elbow median venous blood was extracted from all the subjects before and after admission and placed in a stationary state. A low-temperature, high-speed centrifuge was used to centrifuge at 3000r/min. The supernatant was taken and stored in an ultra-low temperature refrigerator at -80°C for examination. Serum BDNF levels were determined by enzyme-linked immunosorbent assay.

The changes in WCST and PSP scores were compared before and after treatment. The Pearson correlation test was used to analyze the correlation between serum BDNF level, cognitive function, and PANSS scale.

Statistical methods

In this study, an independent sample t-test was used to compare the measurement data between the two groups, which is expressed as (x±s). Enumeration data are expressed as (n(%)) by χ^2 test.

The Pearson correlation test was used for correlation analysis. In this study, SPSS24.0 software was used for statistical data analysis, and a result of P<.05 was considered statistically significant.

Results

Changes in serum BDNF levels in each group

Compared with the control group, BDNF levels were significantly lower in the study group before treatment (P<.05). After treatment, BDNF levels were significantly higher than before treatment (P<.05). See Table 1.

Group	Time	N	BDNF (ng/mL)
Control group		68	24.73±3.62
Study group		68	
	Before treatment		20.11±5.27[a]
	After treatment		23.52±4.06

Table 1: Changes in serum BDNF levels in each group ($\bar{x}$±s).
Note: Compare with the control group, [a]P<.05.

Changes in WCST results before and after treatment in the study group

Compared with before treatment, after treatment, the WCST number in the study group was significantly increased, and the number of false responses and persistent errors significantly decreased (P>.05).

There was no statistically significant difference in the number of non-persistent errors (P<0.05). The results are shown in Table 2.

Time	Number categories	False responses	Persistent errors	Non-persistent errors
Before	4.83±1.11	68.21±13.63	50.66±13.56	18.56±4.82
After	5.53±1.09	58.98±15.82	41.08±14.47	17.93±5.66
t	3.711	3.645	3.984	0.699
P	<.001	<.001	<.001	.486

Table 2: WCST changes before and after treatment in the study group ($\bar{x}$±s).

Changes in PSP scores before and after treatment in the study group

After treatment, PSP scores in the study group were significantly higher than those before treatment, and self-care, socially beneficial activities, disruptive and aggressive behaviors, and personal and social relationships were significantly lower (P<.05). The results are shown in Table 3.

Time	PSP score	Self-care	Socially beneficial activities	Disruptive and aggressive behaviors	Personal and social relationships
Before	47.06±12.96	2.54±1.28	3.92±0.93	2.60±1.41	3.71±1.03
After	72.96±10.94	1.63±0.91	2.25±0.87	1.29±0.62	2.21±0.91
t	12.593	4.778	10.814	7.014	9.000
P	<.001	<.001	<.001	<.001	<.001

Table 3: Changes of PSP scores before and after treatment in the study group ($\bar{x}$±s).

Relationship between serum BDNF level and cognitive function and PANSS score

The Pearson correlation analysis showed that there was a significant negative correlation between PANSS and the total PSP score, and that there was a significant negative correlation between the number of completed classifications, the number of false responses, and the number of persistent errors in each score (P<.05). There was no significant correlation among the other indexes (P>.05). See Table 4.

Index	BDNF	PANSS	PSP	Number categories	False responses	Persistent errors	Non-persistent errors
BDNF	-	0.215	-0.085	-0.142	0.176	0.179	-0.007
PANSS	0.215	-	-0.467*	-0.071	0.067	0.038	0.114
PSP	-0.085	-0.467*	-	-0.081	0.083	0.102	-0.071
Number categories	-0.142	-0.071	-0.081	-	-0.956*	-0.931*	0.196
False responses	0.176	0.067	0.083	-0.956*	-	0.968*	0.142
Persistent errors	0.179	0.038	0.102	-0.931*	0.968*	-	-0.118
Non-persistent errors	-0.007	0.114	-0.071	0.196	0.142	-0.118	-

Table 4: Relationship between serum BDNF level and cognitive function and PANSS score.

Correlation between cognitive function and BDNF level

The Pearson correlation analysis showed that the change in BDNF was positively correlated with the level of BDNF after treatment and the number of classifications completed, and negatively correlated with the number of false responses and persistent errors (P<.05), and there was no significant correlation among the other indexes (P>.05), as shown in Table 5.

Relationship between BDNF level and cognitive function improvement and score reduction rate

The Pearson correlation analysis showed that the PANSS reduction rate was significantly positively

correlated with PSP amplitude, and the number of completed classifications was significantly negatively correlated with the number of false responses and persistent errors (P<.05). There was no significant correlation among the other indexes (P>.05), as shown in Table 6.

Index	BDNF	BDNF	PSP	Number categories	False responses	Persistent errors	Non-persistent errors
BDNF	-	0.553*	0.137	0.290	-0.260*	-0.278*	0.068
BDNF	0.553*	-	0.080	0.222	-0.133	-0.154	0.077
PSP	0.137	0.080	-	-0.081	0.083	0.102	-0.071
Number categories	0.290*	0.222	-0.081	-	-0.956*	-0.931*	0.196
False responses	-0.260*	-0.133	0.083	-0.956*	-	0.968*	0.142
Persistent errors	-0.278*	-0.154	0.102	-0.931*	0.968*	-	-0.118
Non-persistent errors	0.068	0.077	-0.071	0.196	0.142	-0.118	-

Table 5: Correlation between cognitive function and BDNF level.

Index	BDNF	PANSS reduction rate	PSP amplitude	Number categories	False responses	Persistent errors	Non-persistent errors
BDNF	-	-0.012	-0.008	-0.177	0.128	0.179	-0.172
PANSS reduction rate	-0.012	-	0.492*	0.140	-0.032	0.011	-0.146
PSP amplitude	-0.008	0.492*	-	-0.037	0.121	0.160	-0.138
Number categories	-0.177	0.140	-0.037	-	-0.790*	-0.818*	0.154
False responses	0.128	-0.032	0.121	-0.790*	-	0.961*	0.135
Persistent errors	0.179	0.011	0.160	-0.818*	0.961*	-	-0.151
Non-persistent errors	-0.172	-0.146	-0.138	0.154	0.135	-0.151	-

Table 6: Relationship between BDNF level and cognitive function improvement and score reduction rate.

Discussion

Schizophrenia is a disease of unknown etiology, which mainly manifests as a disharmony in emotion, perception, thinking, behavior, and psychological activities in young people aged 15-45. Schizophrenia has a relatively slow onset, a long course of disease, and is prone to repeated aggravation or deterioration. Most patients need long-term maintenance treatment[6]. According to the relevant statistics, the number of patients with schizophrenia in China exceeds 100 million, accounting for the first place in the total burden of disease in China. This causes a serious impact on the patients' families and wider society. At present, the etiology and pathological mechanism of schizophrenia are still not clear, although some studies have confirmed that the onset of schizophrenia is closely related to abnormal embryonic development[7]. The pathophysiological basis of schizophrenia may be the impairment of neuroplasticity and cell regeneration ability. BDNF is a member of the family of nerve influencing factors, mainly secreted by neurons and astrocytes, and can maintain the survival and differentiation of embryonic neurons, as well as the growth and plasticity of neurons. It can also participate in processes related to the stability of the internal neural environment and brain plasticity in the adult stage, and plays an important role in the development of the nervous system[8-9]. Several studies have found that BDNF level is closely related to the occurrence and development of schizophrenia, and can be used as an important indicator to determine the prognosis of patients[10]. The results of this study show that serum BDNF level is significantly reduced in patients with schizophrenia. This may be because the reduced concentration of BDNF causes, to a certain extent, the loss of protection of central neurons, reducing the volume of the temporal and frontal lobes and the density of gray matter in the dominant middle temporal gyrus, thus aggravating the development of the disease[11].

Research has shown that almost all patients with schizophrenia have cognitive impairment to varying degrees, particularly in attention, memory, and executive function, and cognitive impairment is considered the core, persistent symptom of schizophrenia[12]. It has been reported that the prognosis of schizophrenia mainly depends on the degree of cognitive impairment rather than the severity of psychotic symptoms[13]. Cognitive impairment in schizophrenia is persistent, and most of the impairment continues after the relief of other symptoms, thus affecting the recovery of patients' social function[14]. Therefore, the improvement of cognitive dysfunction is an important indicator for predicting the long-term prognosis of schizophrenia and judging the effectiveness of treatments.

The evaluation of cognitive function is relatively complex. In this study, the methods of RANSS, WCST, and PSP were used to measure the mental symptoms and cognitive function of patients. The results showed that patients with schizophrenia had significant cognitive impairment, and the cognitive function of patients significantly improved after drug treatment. This is similar to the results of Bora et al., who found that the cognitive function of patients exists independently of positive and

negative symptoms, and the relationship between social cognition and clinical symptoms is closer than that between neurocognition[15].

In conclusion, the serum BDNF level of patients with schizophrenia is significantly lower than that of subjects without schizophrenia, and there is significant cognitive impairment. The serum BDNF level is significantly correlated with the clinical efficacy of patients and can be used as an important indicator for patients' diagnosis.

References

1) Altamura AC, Bassetti R, Sassella F, Salvadori D, Mundo E. Duration of untreated psychosis as a predictor of outcome in first-episode schizophrenia: a retrospective study. Schizophr Res 2001; 52(1-2): 29-36.
2) Vinogradov S, Luks TL, Schulman BJ, Simpson GV. Deficit in a neural correlate of reality monitoring in schizophrenia patients. Cereb Cortex 2008; 18(11): 2532-9.
3) Reginsson GW, Ingason A, Euesden J, Bjornsdottir G, Olafsson S, et al. Polygenic risk scores for schizophrenia and bipolar disorder associate with addiction. Addict Biol 2018; 23(1): 485-492.
4) Sun ZL, Liu J, Guo W, Jiang T, Ma C, et al. Serum brain-derived neurotrophic factor levels associate with cognitive improvement in patients with schizophrenia treated with electroacupuncture. Psychiatry Res 2016; 244: 370-5.
5) Winship IR, Dursun SM, Baker GB, Balista PA, Kandratavicius L, et al. An Overview of Animal Models Related to Schizophrenia. Can J Psychiatry 2019; 64(1): 5-17.
6) Acar S, Chen X, Cayirdag N. Schizophrenia and creativity: A meta-analytic review. Schizophr Res 2018; 195: 23-31.
7) Nucifora FC Jr, Woznica E, Lee BJ, Cascella N, Sawa A. Treatment resistant schizophrenia: Clinical, biological, and therapeutic perspectives. Neurobiol Dis 2019; 131: 104257.
8) Chen T, Yu Y, Tang LJ, Kong L, Zhang CH, et al. Neural stem cells over-expressing brain-derived neurotrophic factor promote neuronal survival and cytoskeletal protein expression in traumatic brain injury sites. Neural Regen Res 2017; 12(3): 433-439.
9) Giampà C, Montagna E, Dato C, Melone MA, Bernardi G, et al. Systemic delivery of recombinant brain derived neurotrophic factor (BDNF) in the R6/2 mouse model of Huntington's disease. PLoS One 2013; 8(5): e64037.
10) Sanada K, Zorrilla I, Iwata Y, Bermúdez-Ampudia C, Graff-Guerrero A, et al. The Efficacy of Non-Pharmacological Interventions on Brain-Derived Neurotrophic Factor in Schizophrenia: A Systematic Review and Meta-Analysis. Int J Mol Sci 2016; 17(10): 1766.
11) Mohammadi A, Amooeian VG, Rashidi E. Dysfunction in Brain-Derived Neurotrophic Factor Signaling Pathway and Susceptibility to Schizophrenia, Parkinson's and Alzheimer's Diseases. Curr Gene Ther 2018; 18(1): 45-63.
12) Green MF. Impact of cognitive and social cognitive impairment on functional outcomes in patients with schizophrenia. J Clin Psychiatry 2016; 77 Suppl 2: 8-11.
13) Keefe RS, Haig GM, Marder SR, Harvey PD, Dunayevich E, et al. Report on ISCTM Consensus Meeting on Clinical Assessment of Response to Treatment of Cognitive Impairment in Schizophrenia. Schizophr Bull 2016; 42(1): 19-33.
14) Alfimova MV, Kondratiev NV, Golimbet VE. Rezul'taty i perspektivy geneticheskikh issledovaniĭ kognitivnykh narusheniĭ pri shizofrenii: molekuliarno-geneticheskie podkhody Results and promises of genetics of cognitive impairment in schizophrenia: molecular-genetic approaches. Zh Nevrol Psikhiatr Im S S Korsakova 2016; 116(11): 137-144. Russian.
15) Bora E. Peripheral inflammatory and neurotrophic biomarkers of cognitive impairment in schizophrenia: a meta-analysis. Psychol Med 2019; 49(12): 1971-1979.

Corresponding Author:
Chunpeng Fu
No.1 Taokan Road, Fenghuang East Avenue, Shangrao City, Jiangxi Province, China
Email: xjcz0h@163.com
(China)