RELATIONSHIP BETWEEN SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR, MYELIN BASIC PROTEIN, CALCIUM BINDING PROTEIN AND PANSS SCORE IN CHILDREN WITH SCHIZOPHRENIA

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ABSTRACT

Objective: *To explore the relationship between BDNF, MBP, S100β and PANSS in children with schizophrenia.*

Methods: *For this study, 60 schizophrenic patients admitted to our hospital from February 2014 to April 2019 were selected as the observation group, and 60 healthy volunteers were recruited as the control group. The patients in the observation group were treated with risperidone. The levels of BDNF, MBP and S100β in serum were measured by double-antibody sandwich enzyme-linked immunosorbent assay. According to PANSS score, the mental symptoms of children before and after treatment were analysed. The correlation between serum BDNF, MBP, S100β and PANSS score was analysed by sparson correlation test. The changes of BDNF, MBP, S100β and PANSS were analysed after treatment.*

Results: *Compared with the control group, the BDNF level before treatment in the observation group was significantly lower (P<0.01), and the PANSS level was significantly higher (P<0.01). After treatment, the BDNF level in the observation group was significantly higher (P<0.01), and the PANSS level was significantly lower (P < 0.01). Compared with the control group, the MBP level before treatment in the observation group was significantly lower (P<0.01), while the S100β level was significantly higher (P<0.01). After treatment, the MBP level of the observation group was significantly higher (P < 0.01), S100β level was significantly lower (P<0.01). The noted differences were statistically significant (P<0.01). A negative correlation was seen between the serum BDNF, MBP level and PANSS score in contrast to a positive correlation between S100β level and PANSS score, a statistically significant difference (P<0.05).*

Conclusion: *The serum BDNF and S100β in schizophrenic children were significantly lower than those in normal people. Furthermore, the serum BDNF, MBP and S100 β levels were significantly correlated with PANSS scores.*

Keywords: *Child schizophrenia, serum brain-derived neurotrophic factor, myelin basic protein, calcium-binding protein, PANSS.*

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Introduction

Schizophrenia is a clinical syndrome comprising a group of symptoms. Although the aetiology of schizophrenia is not clear, the common aetiology is related to genetic factors, and the onset is slow. With increasing age, the condition gradually aggravates[(1)]. The incidence of genetic factors can be as high as 16% - 64%, most occurring in children aged 12-14. Organic damage in the perinatal period, strong stimulation of a child's spirit, an impact of psychosocial factors, or imperfections in a child's character can cause the onset of schizophrenia. Early clinical symptoms are not typical, manifesting as inattention, sleep disorders, obsession with aging and symptoms of obsessive-compulsive behaviours that are similar to those of adults[(2)]. It has been found that neurotrophic factors and serum protein factors have important clinical significance in the pathogenesis of schizophrenia. Brain-derived neurotrophic factor (BDNF), the most abundant neurotrophic factor in the body with a receptor that is widely expressed in the nervous system, serves to regulate the growth of neurons, promotes the repair of damaged neurons

and increases synaptic plasticity and neurogenesis[3]. Myelin basic protein (MBP), a kind of strong basic membrane protein, contains a variety of basic amino acids that can reveal the degree of central nervous system damage and plays an important role in determining the severity of schizophrenia[4]. S100 calcium-binding protein β (S100β) refers to the marker protein for injury to the central nervous system, which is produced by astrocytes and plays an important role in cell proliferation, differentiation and gene expression.

The detection of S100β protein concentration is closely related to the severity of schizophrenia[5]. Currently, the clinical application of the Positive and Negative Syndrome Scale (PANSS) and Hamilton Depression Rating Scale (HAM-D) is used in the diagnosis of schizophrenia, but its subjectivity is strong, and certain limitations apply. PANSS can accurately reflect the pathological performance of schizophrenia patients by evaluating the positive and negative symptoms of these patients[6]. Thus, investigation of the related factors and PANSS score in the diagnosis of schizophrenia carries great significance. As a consequence, this study explores the relationship between serum brain-derived neurotrophic factor, myelin basic protein, calcium-binding protein and PANSS score in children with schizophrenia. The results are reported as follows.

General information

Materials and methods

For this study, 60 schizophrenics admitted to our hospital from February 2014 to April 2019 were selected as the control group, and 60 healthy volunteers who were examined in our hospital in the same period were recruited as the control group.

Inclusion criteria were as follows:

• Meet the relevant diagnostic criteria of schizophrenia in children in the third edition of Chinese standards for classification and diagnosis of mental diseases;

• PANSS score ≥60;

• Have complete pathological data and follow-up data;

• Normal liver and kidney function with no other organ damage.

Exclusion criteria comprised the following factors:

• Have liver and kidney function damage and other organs with serious complications;

• History of brain injury or organic brain injury;

• History of drug dependence;

• Or self-medication of antipsychotic and impact assessment drugs.

The age of participants in the observation group fell with the range of 7-15 years old with an average age of (9.36±1.24) years old. In comparison, the age range for the control group was 8-15 years old with an average age of (9.86±1.57) years old. Thus, no significant difference in age existed between the two groups (P>0.05). All the family members of the children in this study received informed consent and signed the informed consent form, which was approved by the ethics committee of our hospital.

Method

The patients in the observation group were given conventional antipsychotics in the form of risperidone (Guangdong Huarun Shunfeng Pharmaceutical Co., Ltd, gzz No.: H20150321, specification: 1mg, 10 tablets/plate, 2 plates/box) starting dose on the first day: twice a day, once 1mg. On the second day, the dose was increased to 2mg twice a day. On the third day, the dose was increased to 3mg twice a day. After that, the dose remained the same, and the treatment lasted for two courses, six weeks for each course.

Observation index

• The mental symptoms of the children before and after treatment were evaluated according to PANSS score.

• The levels of BDNF, MBP and S100β in serum were measured by enzyme-linked immunosorbent assay with double-antibody sandwich using the BIO-TEK automatic enzyme labeling instrument. Before and after treatment, 7 ml of fasting venous blood was taken in the observation group in the early morning. After 20 minutes' high-speed centrifugation, the samples were stored at 20 temperature.

The kit was provided by the Shanghai Beihai Institute of Fine Chemistry, and procedures were carried out in strict accordance with the operating instructions for the kit.

• The correlation between serum BDNF, MBP, S100β and PANSS score was analysed by Sparson correlation test.

Statistical methods

SPSS 20.0 software was used for statistical data analysis. Mean ± standard deviation ($\bar{x}\pm s$) was used for measurement data. A t-test was used to compare the data from the observation group and control group. Rate (%) was used for counting data. χ^2 test

was used to compare the data from the observation group and control group. P<0.05 was used to determine statistical significance.

Results

Comparison of BDNF and PANSS scores between the two groups

Compared with the control group, the BDNF level in the observation group before treatment was significantly lower (P<0.01), and the PANSS level was significantly higher (P<0.01). See Table 1.

Group	Cases	BDNF (ng/mL)	PANSS total score (scores)
Observation group	60	5.86±4.48	98.43±3.64
Control group	60	14.28±3.45	75.27±5.24
t		11.534	28.117
p		<0.001	<0.001

Table 1: Comparison of BDNF and PANSS scores between the two groups ($\bar{x}\pm s$).

Changes of BDNF and PANSS levels in children with schizophrenia after treatment

After treatment, the BDNF level in the observation group was significantly higher than before treatment (P<0.01), and the PANSS level was significantly lower (P<0.01). See Table 2.

Group	Time	BDNF (ng/mL)	PANSS total score (scores)
Observation group	Before treatment	5.86±4.48	98.43±3.64
	After treatment	12.45±4.26	78.62±3.84
t		8.257	<0.001
p		29.001	<0.001

Table 2: Changes of BDNF and PANSS levels in children with schizophrenia before and after treatment ($\bar{x}\pm s$).

Comparison of MBP and S100β scores between the two groups

Compared with the control group, the MBP level in the observation group before treatment was significantly lower (P<0.01), while the S100β level was significantly higher (P<0.01). See Table 3.

Changes of MBP and S100β levels in children with schizophrenia after treatment

After treatment, MBP level of the observation group was significantly higher than before treatment (P<0.01), while the S100 β level was significantly lower (P<0.01). See Table 4.

Group	Cases	MBP (ng/mL)	S100β (ng/mL)
Observation group	60	5268.24±854.05	21.45±0.85
Control group	60	9634.13±967.15	18.02±0.64
t		26.210	24.970
p		<0.001	<0.001

Table 3: Comparison of BDNF and PANSS scores between the two groups ($\bar{x}\pm s$).

Group	Time	MBP (ng/mL)	S100β (ng/mL)
Observation group	Before treatment	5268.24±854.05	21.45±0.85
	After treatment	9421.36±921.27	19.54±0.76
t		25.608	12.975
p		<0.001	<0.001

Table 4: Changes of MBP and S100β levels in children with schizophrenia before and after treatment ($\bar{x}\pm s$).

Correlation analysis between serum BDNF, MBP, S100β and PANSS score in children with schizophrenia

The correlation analysis showed that serum BDNF and MBP levels were negatively correlated with PANSS scores, while S100β levels were positively correlated with PANSS scores (P<0.05). See Table 5.

Index	PANSS score	
	r	P
BDNF	-0.374	<0.05
MBP	-0.623	<0.05
S100β	0.213	<0.05

Table 5: Correlation analysis of serum BDNF, MBP, S100β and PANSS scores.

Discussion

Schizophrenia in children is a multifactorial mental disease caused by damage to central nervous system function. Children's prevalence rate is lower than that of adults, and the main characteristics are thinking association disorder and emotional disorder[6]. According to the related literature, the prevalence of schizophrenia in China is as high as 0.05% ~ 0.08%, of which heredity accounts for 16% ~ 64% of the incidence. The causes of schizophrenia involve genetic factors, organic factors, neural development, social psychological factors, pre-disease personality characteristics and biochemical factors. The onset of schizophrenia is slow and the symp-

toms are not typical. Clinical manifestations include emotional isolation from family members and the alienation of partners, a decline in academic performance and the presence of pathological fantasies, delusions and other symptoms that can bring great distress to the patient's family[7].

Related studies have shown that schizophrenia is related to a lack of neurotrophic factors and damage to central glial cells. The expression of BDNF in neurotrophic factors is abnormal in this syndrome[8]. BDNF is a protein with a neurotrophic effect, which plays an important role in the growth and differentiation of neurons and the release of neurotransmitters. It has the function of repairing damaged cells in the brain and protecting the growth of peripheral neurons and is closely related to neurodevelopment in the pathogenesis of schizophrenia[9].

The level of BDNF in patients exhibiting schizophrenia is lower than that in normal people. The more serious the disease is, the lower the level of BDNF. Thus, BDNF plays an important role in the occurrence and development of schizophrenia and in the plasticity of nerves[10] as this protein can enhance synaptic plasticity, regulate synaptic function and biochemical changes. Meanwhile, the PANSS score is an important indicator of a manic state in children[11]. An increase in PANSS indicates abnormal function of the central nervous system[12]. The results of this study showed that in comparison to the control group, the BDNF level in the observation group was significantly lower, and the PANSS level was significantly higher ($P<0.05$). After treatment, the BDNF level increased and the PANSS level in the observation group decreased significantly ($P<0.05$). These results suggest that the level of brain-derived neurotrophic factor is destroyed and the cognitive function of children decreases during the development of schizophrenia.

MBP is composed of the cell membrane of the myelin sheath cells[13], which is the main protein of the myelin sheath in the central nervous system, having the specificity of nerve tissue. Damage to the myelin sheath of schizophrenic patients destroys the function of the blood-brain barrier. Because MBP enters the circulatory system through the blood-brain barrier, elevation of MBP in serum can result, offering an important index to determine the degree of damage to the central nervous system[14]. S100β refers to the central nervous system specific protein, released by the body's astrocytes, which can form a disulphide bond through cysteine residues. It exists in the central nervous system in the form of dimer activity and has the function of promoting brain development and protecting the blood-brain barrier. Thus, this protein serves as a biochemical marker for judging brain injury[15]. The results of this study showed that in comparison with the control group, the MBP level of the observation group was significantly lower and S100β level was significantly higher ($P<0.05$). After treatment, the MBP level of the observation group was significantly higher than before treatment, and the S100 β level was significantly lower ($P<0.05$). A negative correlation was observed between serum BDNF, MBP and PANSS score, while in contrast, a positive correlation between S100β and PANSS score was seen; in both cases, the difference was statistically significant ($P<0.05$), suggesting that MBP and S100β may participate in the pathogenesis of schizophrenia. These conclusions therefore hold great significance for the diagnosis and evaluation of schizophrenia.

In summary, serum BDNF and S100β in schizophrenic children were significantly lower than the values for those found in normal people, whereas PANSS scores and MBP levels were significantly higher than those in normal people. Furthermore, serum BDNF, MBP and S100β levels were significantly correlated with PANSS scores.

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