Neuron-specific Enclose and Myelin Basic Protein in Cerebrospinal Fluid of Patients with First Episode Schizophrenia

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Summary: In order to study whether patients with schizophrenia have cerebral injury, neuron-specific enolase (NSE) and myelin basic protein (MBP) in cerebrospinal fluid (CSF) of 33 patients with first episode schizophrenia and 9 from the control group were determined by double antibody sandwich enzyme immunoassay method. The results showed that there was significant difference in the NSE contents between the experimental group and control group ($P<0.01$). The NSE contents in CSF in the experimental group were positively correlated with MBP in schizophrenia patients ($P<0.05$). These findings suggested that patients with schizophrenia had cerebral injury.
Key words: schizophrenia; cerebrospinal fluid; neuron specific enolase; myelin basic protein

Schizophrenia, the most common disease of mental illness, was regarded as functional disease without organic change in the past. But recently, more and more evidence indicates that there are organic changes in patients with schizophrenia, with the advance of neuropathology and neuroimaging[1,2]. But it is unknown whether these organic changes are caused by congenital aplasia or acquired brain damage[1]. Since 1980's, many researchers reported that neuron-specific enclose (NSE) and myelin basic protein (MBP) in neurons can be released into cerebrospinal fluid (CSF) and blood in cerebral injury or lesions. NSE and MBP contents in CSF are paralleled with the degree of brain damage[3]. So some researchers suggested that levels of NSE and MBP in CSF could be regarded as a marker of central nervous system (CNS) damage or degeneration[4,5]. In this study, the contents of NSE and MBP in CSF were determined in the patients with the first episode schizophrenia not subjected to antipsychotics in order to investigate the cerebral injury in these patients.

1 MATERIALS AND METHODS

1.1 Subjects

Experimental group: Thirty-three cases with CCMD-3 were diagnosed as first episode schizophrenia based on the Andreasen consistent criteria, who were hospitalized in the Department of Psychiatry from January 2003 to May 2003. The patients with mental retardation (MR), brain trauma, other nervous diseases and drug dependence were excluded from this study at the time of diagnosis. Physiological and other various kinds of examinations were normal, and they didn't receive therapy with any antipsychotics. There were 10 males and 23 females with the age ranging from 17 to 40 years old (mean 24.9±7.1). The course of disease ranged 5-82 days (mean 34±25 days). There were 20 patients with positive symptoms (SAPS≥50, positive group), with their age ranging from 17−40 years old (mean 24.4±7.0), the course of disease from 5−82 days (mean 37.9±29.2). Thirteen patients presented with negative symptom (SANS≥50, negative group), with their age ranging from 17−37 years old (mean 25.2±7.5), the course of disease from 15−78 days (mean 33.7±23.0). There was no significant difference in age and course of disease between the two groups. Control Group: Nine individuals were selected after excluding brain trauma and other diseases of the neural system. There was no significant difference in age and gender between experimental groups and control group.

1.2 Methods

CSF from the patients in experimental group and individuals in control group were collected by lumbar puncture under local anesthesia with 40 mg of lidocaine and cryopreserved at −20 ℃ for measuring. NSE and MBP were determined by double antibody sandwich enzyme immunoassay. The NSE and MBP reagent kits were offered respectively by the Institute of Radio-medicine of Beijing Military Academy of Medical Sciences (China) and Recombinant DNA Department of Western Medical University (China). The NSE and MBP contents in different groups were analyzed by W-test of normality followed by rank sum in experimental group and control group. K independent samples comparison by rank sum test and K independent samples comparison each other rank sum test among negative, positive and control groups were also carried out. The rank correlation analysis of the NSE and MBP in experimental group and control group were

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then done separately.

2 RESULTS

2.1 NSE Contents

The NSE in CSF from experimental group and control group were 3.48±3.59 ng/mL and 1.00±0.74 ng/mL respectively, with the difference being significant (Uc=2.6412, $P<0.01$). The contents of NSE were 5.27±5.11 ng/mL in negative group and 2.36±1.37 ng/mL in positive group respectively. There was significant difference in NSE contents among negative group, positive group and control group (Hc=13.64, $P<0.01$). The results of rank test of NSE content between the two of the three groups were shown in table 1.

Table 1 Rank test of NSE between the two of the three groups

Control group A and B		n	R_A-R_B	CX_α^2, k-1[N(N+1)/12][1/n_A+1/n_B]		P
				0.05	0.01	
Negative vs positive	13	20	4.96	10.440	12.948	>0.05
Positive vs control	20	9	13.46	11.764	11.588	<0.05
Negative vs control	13	9	18.42	12.710	15.760	<0.01

2.2 MBP Contents

The MBP contents in experimental and control groups were 0.39±0.55 ng/mL and 0.15±0.21 ng/mL respectively with the difference being not significant (Uc=1.1299, $P>0.05$). There was no significant difference among the negative group, positive group and control group in MBP of CSF (Hc=1.3429, $P>0.05$).

2.3 Relationship between NSE and MBP

There was a linear correlation between the contents of NSE and MBP in CSF ($r=0.4533$, $P<0.01$) in experimental group. There was significant correlation between NSE and MBP in negative group ($r=0.6177$, $P<0.05$), but no correlation in positive group ($r=0.0466$, $P>0.05$). There was no significant relationship between NSE and MBP in control group ($r=0.1333$, $P>0.05$).

3 DISCUSSION

It has been reported that the patients with schizophrenia had reduced volume and weight of brain, thinner brain cortex and deeper brain channel by autopsy. The reduced brain tissue was not related with electroshock therapy. The expanding of ventricle in type II of schizophrenia was more significant than that in type I of schizophrenia. Using MRI, Jop[6] found that it had significant meanings of the expanding of side ventricle and shrinking of cerebra cortex in patients with first episode of schizophrenia. The expanding of ventricle was correlated with schizophrenia, but not with antipsychotics therapy. These findings were proved by following researchers[7]. Suddath[8] *et al* studied 15 siblings using MRI and found that the expanding of the third ventricle was more significant in patients than that in normal individuals. Therefore, they suggest that the expanding of ventricle in the patients with schizophrenia may not be determined by hereditary factors.

It was reported that there was a difference in NSE of brain after death between 9 patients with schizophrenia and 15 normal individuals, assayed by ELISA. The results indicated that the NSE level in sense cortex from patients with schizophrenia was increased by 70 % as compared with that in normal individuals ($P<0.01$) and the NSE level in thalamencephalon reduced by 70 % in the patients with schizophrenia as compared with normal individuals ($P<0.05$). Burbaeva[9] reported that there was a reduced NSE level and activity in different tissues of brain after the death of these patients with schizophrenia, as assayed by ELISA.

Vermucyten[10] reported that the NSE level in CSF assayed by ELISA was increased in patients with schizophrenia, cerebral hemorrhage, cerebral thrombosis, which was not correlated with patient's gender and age. However, other scientists reported that the NSE level in CSF from patients with schizophrenia was in normal range. The possible reason may be the elevated time point of NSE was missed when collecting CSF samples, because there was a short peak time of NSE in CSF.

In this paper, it was found that there was significant difference in NSE level from CSF in 33 patients with schizophrenia and control groups. Also there was significant difference among positive group, negative group and control groups. Though level of NSE in negative group was higher than that in positive group, there was statistically significant difference. These findings indicate that there is neuron damage in patients with schizophrenia, which is supported by the findings from Burbaeva. As NSE is an enzyme with short half-life, it reaches peak at day 6 to 7 after the onset of disease. The patients from this research aged from 17 to 40 years old, indicating that neuron damage in these patients is caused by acquired factors. The elevated level of NSE in CSF from patients with schizophrenia in this group was not induced by antipsychotics drugs as all patients did not receive any antipsychotics therapy before collecting CSF samples.

There was no significant difference in MBP level between experimental group and control group. Also there was no difference among nega-

tive group, positive group and control group. These findings suggest that there may be no white matter damage in these patients.

There was no significant correlation between NSE and MBP in control group, suggesting that NSE and MBP represented different brain tissue damage. There was a relationship between NSE and MBP in experimental group, which mainly occurred in the patients with negative symptoms by further analysis. These results suggest that the patients with negative symptoms not only had neuron damage, but also had accompanying damage of the whiter matter.

To sum up, this study demonstrated that schizophrenia may be a brain damaged disease caused by acquired factors and suggested that NSE could act as a biological marker in diagnosis of schizophrenia.

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plasmids that can drive the expression of HA and HA_1 antigen in HEK293 cells as confirmed by immunofluorescence microscopy. HA is the major protective antigen of influenza virus, which can induce the production of HA specific-neutralizing antibodies. HA specific-neutralizing antibodies are thought to play a major role in the immunity against secondary infection and to decrease the generation of viral particles upon primary influenza infection[6]. Hence, it is critical to ensure the expression of immunologically active HA or HA_1 in order to design any DNA vaccine for the protection of influenza attack. The successful construction of HA- and HA1-expressing eukaryotic systems in this study has not only paved the way for further investigation of DNA-based influenza vaccine strategy, but also provided a tool for dissecting the targeting site(s) of anti-influenza drugs.

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