

Effects of Different Doses of BDNF on Postoperative Cognitive Function in Aged Rats Undergoing Abdominal Surgery

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Abstract: *Objective:* To investigate the effects of different doses of BDNF on postoperative cognitive function in aged rats undergoing abdominal surgery. *Methods:* 72 aged healthy male SD rats of SPF grade were selected. According to the random number table method, the rats were randomly divided into the control group, model group, low dose BDNF injection group, and high dose BDNF injection group, with 18 rats in each group. The model group, low dose group, and high dose group underwent abdominal surgery after anesthesia, and 5 μ L/time of BDNF was intranasally administered to the rats in the low dose and high dose groups 6 hours after abdominal surgery, of which the dose of the low dose group was 0.1 g/L, while that of the high dose group was 0.2 g/L. The drug was administered alternately through both nostrils, with an interval of 2 minutes each time, for 5 times. The control group did not undergo surgery after anesthesia. The escape latency and swimming distance of the four groups of rats were compared before surgery, the first day, the third day, and the seventh day after surgery; similarly, the BDNF protein expression level in the hippocampus of the four groups of rats was compared on the first day, the third day, and the seventh day after surgery. *Results:* The escape latency and swimming distance of the control group were not statistically significant on the first day, the third day, and the seventh day after surgery, $p > 0.05$; the escape latency and swimming distance of the model group, low dose group, and high dose group on the first day, the third day, and the seventh day after surgery were statistically significant, $p < 0.05$. Before surgery, the escape latency and swimming distance of the four groups were not statistically significant, $p > 0.05$; on the first day, the third day, and the seventh day after surgery, the escape latency and swimming distance of the model group $>$ low dose group $>$ high dose group $>$ control group, $p < 0.05$. The BDNF protein expression level in the hippocampus of the control group on the first day, the third day, and the seventh day after surgery showed no statistical significance $p > 0.05$; the expression level of BDNF protein in the hippocampus of the model group, low dose group, and high dose group on the first day, the third day, and the seventh day after surgery was statistically significant, $p < 0.05$. On the first day, the third day, and the seventh day after surgery, the expression level of BDNF protein in the hippocampus of the model group $<$ low dose group $<$ high dose group $<$ control group, $p < 0.05$. *Conclusion:* Compared with 0.1 g/L of BDNF, 0.2 g/L of BDNF can improve the postoperative cognitive function of aged rats undergoing abdominal surgery.

Keywords: BDNF; Abdominal surgery; Aged rats; Postoperative cognitive function

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1. Introduction

Studies have found that surgical stimulation can lead to vasoconstriction and cause a rise in blood pressure

[1]. Anesthetics can reduce negative cardiovascular effects and blood pressure, as well as result in an imbalance of oxygen supply to the brain under the dual effects of anesthesia and surgery, thus affecting brain oxygen saturation and increasing the tendency for postoperative cognitive dysfunction. At the same time, age is a major risk factor for postoperative cognitive dysfunction [2]. Studies have found that the incidence of cognitive dysfunction in patients aged 60-69 years is about 23% one week after surgery, while the incidence of cognitive dysfunction in patients over 70 years old is about 29% [3]. The incidence of cognitive dysfunction in the elderly over 70 years old three months after surgery is about 14%, indicating that the incidence of cognitive dysfunction increases with age, which may be attributed to the decrease of brain oxygen saturation with age, resulting in cognitive dysfunction [4]. In recent years, the aging population in China has been increasing, along with the proportion of surgery among the elderly, which in turn increases the incidence of postoperative cognitive dysfunction [5]. Brain-derived neurotrophic factor (BDNF) is a small molecular protein isolated from pig brain. The amino acid coding sequence of BDNF in humans, rats, and pigs is identical. Additionally, its sequence of nerve growth factor is similar, and it is also a member of the nerve growth factor family [6-8]. Laboratory studies have found that BDNF is negatively correlated with the severity of postoperative cognitive function in aged rats. Therefore, this time, aged rats undergoing abdominal surgery were given different doses of BDNF to analyze its effects on postoperative cognitive function, so as to provide a basis for improving the severity of postoperative cognitive dysfunction in elderly patients.

2. Materials and methods

2.1. Study population

A total of 72 SPF-grade healthy aged male SD rats, with age ranging from 18-20 months and weight ranging from 480-600 g, were purchased from the Animal Center of School of Medicine, Xi'an Jiaotong University. After a week of adaptive feeding, the rats were randomly divided into a control group, model group, low dose BDNF injection group, and high dose BDNF injection group, with 18 rats in each group, based on the random number table method.

2.2. Reagents and instruments

BDNF antibody was purchased from Biosharp Company, China, Western blot kit was purchased from Wuhan Seville Biotechnology Co., Ltd., Morris water maze equipment was purchased from Nanjing Calvin Biotechnology Co., Ltd., and BDNF protein was purchased from American Sigma Corporation.

2.3. Study design

All 72 rats were anesthetized, in which the rats in the model group, low dose group, and high dose group were anesthetized via intraperitoneal injection with 10% chloral hydrate at a dose of 0.3 ml/100 g. After the loss of righting reflex, the rats were fixed in a supine position, and their abdominal skin was disinfected. In each rat, a longitudinal incision of about 3 cm was made 0.5 cm below the ribs along the abdominal midline, and then abdominal exploration of the stomach, liver, large intestine, and small intestine was performed every 5 minutes. The operation time was set to 20 minutes, and thereafter, the abdominal cavity was closed. The control group did not undergo surgery after anesthesia.

For the low dose and high dose groups, the rats were anesthetized and placed in a supine position, their heads and necks were raised, and 5 μ L/time of BDNF was administered intranasally using a micro-syringe six hours after abdominal surgery. The low dose group received 0.1 g/L, while the high dose group received 0.2 g/L. The drug was administered alternately through both nostrils, with an interval of 2 minutes each time, for 5 times.

2.4. Observation indicators

- (1) Water maze test [6] was performed before surgery on the first day, the third day, and the seventh day after surgery, and the escape latency and swimming distance of the four groups were recorded.
- (2) After completing the water maze test on the seventh day, the rats in the two groups were killed, and the BDNF protein expression level in the hippocampus of the four groups was detected by Western blot.

2.5. Statistical analysis

SPSS 23.0 was used for analysis; counting data were expressed in frequency and analyzed by Chi-square test; measurement data were expressed as $\bar{x} \pm s$ and tested by one-way ANOVA. $p < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of escape latency and swimming distance of rats in the four groups before surgery, the first day, the third day, and the seventh day after surgery

The escape latency and swimming distance of the control group were not statistically significant on the first day, the third day, and the seventh day after surgery, $p > 0.05$; the escape latency and swimming distance of the model group, low dose group, and high dose group on the first day, the third day, and the seventh day after surgery were statistically significant, $p < 0.05$. Before surgery, the escape latency and swimming distance of the four groups were not statistically significant, $p > 0.05$; on the first day, the third day, and the seventh day after surgery, the escape latency and swimming distance of the model group $>$ low dose group $>$ high dose group $>$ control group, with $p < 0.05$.

Table 1. Comparison of escape latency and swimming distance of rats in the four groups before surgery, the first day, the third day, and the seventh day after surgery (n = 18, $\bar{x} \pm s$)

Group	Escape latency (s)				F/p	Swimming distance (cm)				F/p
	Pre-operation	Post-operation				Pre-operation	Post-operation			
		1d	3d	7d			1d	3d	7d	
Control	24.71 ± 3.67	24.91 ± 4.67	24.81 ± 3.02	24.82 ± 3.09	0.009/0.999	353.10 ± 78.09	356.02 ± 82.34	360.99 ± 82.36	358.99 ± 77.67	0.033/0.992
Model	24.92 ± 4.02	46.31 ± 5.21	43.31 ± 7.61	34.67 ± 6.03	48.406/ < 0.001	352.89 ± 81.02	729.89 ± 106.56	658.02 ± 105.77	526.56 ± 87.62	52.936/ < 0.001
Low dose	24.78 ± 3.89	36.34 ± 5.23	34.10 ± 4.23	30.78 ± 5.12	21.195/ < 0.001	352.99 ± 84.23	687.92 ± 89.78	624.10 ± 92.13	476.89 ± 76.54	58.372/ < 0.001
High dose	24.78 ± 4.12	28.76 ± 4.99	26.56 ± 3.90	25.34 ± 4.12	3.139/ 0.031	352.89 ± 85.10	644.10 ± 85.23	591.32 ± 87.34	423.13 ± 65.43	51.444/ < 0.001
F	0.009	63.333	34.400	17.818		0.000	61,681	38.228	15.635	
p	9.999	< 0.001	< 0.001	< 0.001		1.000	< 0.001	< 0.001	< 0.001	

3.2. Comparison of BDNF protein expression level in the hippocampus of rats in the four groups on the first day, the third day, and the seventh day after surgery

The comparison of BDNF protein expression level in the hippocampus of the control group on the first day, the third day, and the seventh day after surgery showed no statistical significance, $p > 0.05$; the expression level of BDNF protein in the hippocampus of the model group, low dose group, and high dose group on the first day, the third day, and the seventh day after surgery was statistically significant, $p < 0.05$. On the first day, the third day, and the seventh day after surgery, the expression level of BDNF protein in the

hippocampus of the model group < low dose group < high dose group < control group, with $p < 0.05$.

Table 2. Comparison of BDNF protein expression level in the hippocampus of rats in the four groups on the first day, the third day, and the seventh day after surgery (n = 18, $\bar{x} \pm s$)

Group	Post-operation 1d	Post-operation 3d	Post-operation 7d	F/p
Control	148.02±15.81	149.02±14.88	148.99±15.45	0.025//0.975
Model	89.16±8.25	99.03±10.23	105.76±9.23	14.596/<0.001
Low dose	100.34±11.34	105.45±13.12	120.78±12.13	13.643/<0.001
High dose	123.67±12.45	124.10±15.34	134.13±14.23	3.191//0.049
F	81.690	49.372	36.472	
p	<0.001	<0.001	<0.001	

4. Discussion

Memory and learning are both major cognitive functions. Elderly patients often have cognitive dysfunction after surgery. These patients will show changes in personality, mental activities, cognitive ability, social activities, and other functions. In addition to reduced social ability, their attention, memory, and language ability are also affected. These are caused by the joint action of many factors, which seriously affect the quality of life of elderly patients undergoing surgery [9-11]. BDNF is a neurotrophic factor synthesized by the central nervous system and widely found in various brain tissues. It can improve brain injury. The stress effect of surgery on elderly patients causes certain damage to their brain tissues [12-14]. This paper analyzed the effect of exogenous BDNF on brain injury, a topic that has garnered increasing attention in recent years [15].

The results showed that the escape latency, swimming distance, and BDNF protein expression level in the hippocampus of the control group on the first day, the third day, and the seventh day after surgery were not statistically significant, whereas the escape latency, swimming distance, and BDNF protein expression level in the hippocampus of the model group, low dose group, and high dose group on the first day, the third day, and the seventh day after surgery were statistically significant. The escape latency, swimming distance, and BDNF protein expression level in the hippocampus of the four groups on the first day, the third day, and the seventh day after surgery were statistically significant. The escape latency and swimming distance of the model group > low dose group > high dose group > control group, while the expression level of BDNF protein in the hippocampus of the model group < low dose group < high dose group < control group, with $p < 0.05$. This shows that BDNF can improve the postoperative cognitive function of aged rats undergoing abdominal surgery. The effect of high-dose BDNF was found better than that of low-dose BDNF. BDNF is composed of 120 proteins, which are mainly mediated by two transmembrane proteins: low-affinity neurotrophin receptor and high-affinity receptor TrkB [16]. When BDNF binds to TrkB extracellular ligand binding region, autophosphorylation and substrate phosphorylation occur, thus information is transmitted from cell membrane to nucleus, resulting in cellular response effect, which improves brain injury and reduces postoperative cognitive dysfunction in aged rats [17,18].

In conclusion, compared with 0.1 g/L of BDNF, 0.2 g/L of BDNF can improve the postoperative cognitive function of aged rats undergoing abdominal surgery.

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Disclosure statement

The authors declare no conflict of interest.

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