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Analysis of Changes in BDNF Levels Before and After Bariatric Surgery in Obese Patients

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Abstract: Objectives: The rate of obesity has been increasing globally, so is the number of obese patients undergoing bariatric surgery. The relationship between brain-derived neurotrophic factor (BDNF) and body weight has been highlighted in recent years, but there are few related studies in China. The purpose of this study was to investigate the changes of BDNF in obese patients before and after bariatric surgery and to provide evidence for obesity-related mechanisms. *Methods:* The BDNF levels in 44 obese patients who underwent bariatric surgery were measured by enzyme-linked immunosorbent assay (ELISA) before and 4.5 months after surgery. SPSS 27.0 was used for statistical analysis. *Results:* Among the 44 patients, 30 were female and 14 were male. The body mass index (BMI) decreased significantly after bariatric surgery ($P < 0.001$); the serum BDNF of the patients significantly increased ($P < 0.001$) after surgery. There was no significant difference in BDNF among patients with different degrees of obesity before and after surgery ($P > 0.05$). There were no significant differences in BMI and BDNF levels between different sexes before and after surgery ($P > 0.05$). *Conclusion:* The BDNF levels of obese patients increased significantly after bariatric surgery, which proved that bariatric surgery has an effect on BDNF levels.

Keywords: Obesity; BDNF; Bariatric surgery

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1. Introduction

Obesity is a chronic metabolic disease caused by excessive accumulation or abnormal distribution of body fat caused by a combination of environmental, genetic, social, and other factors [1]. Obesity rates are rising sharply around the world. This issue has become a challenge for public health systems and the global economy. The main cause of obesity and overweight is an energy imbalance between consumption and calorie expenditure [2].

Obesity has emerged as a worldwide public health crisis, and China, in particular, boasts the largest population of obese individuals globally, with around 46% of adults and 15% of children falling into the obese or overweight category. Chinese society is increasingly contending with a mounting epidemic of obesity and the associated chronic diseases [3]. The prevalence of overweight and obesity among Chinese residents aged 18 and above stands at 34.3% and 16.4%, respectively. Alarmingly, over 50% of the population faces obesity-related health risks, making China the global leader in the total number of obese individuals [4].

The surgical treatment for morbid obesity has been improving, especially since the introduction of laparoscopic techniques. As the most effective method to treat obesity and obesity-related comorbidities, bariatric surgery has gradually increased in both the number of procedures and the types of techniques. The most common laparoscopic procedures are laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB) [5].

Brain-derived neurotrophic factor (BDNF) is a member of the neurotrophic protein family, and it plays an important role in the development, maintenance, and plasticity of the central and peripheral nervous systems [6]. In recent years, BDNF has received a lot of attention because of its distribution and important role in the brain. BDNF plays a role in anorexia and is used as a regulatory element for food intake, and it can also achieve metabolic regulation by affecting peripheral tissue energy consumption [7]. More and more studies have shown that body weight is related to blood BDNF levels.

To our knowledge, although several studies have been performed with different populations, the relationship between BDNF level changes and bariatric surgery in obese Chinese patients has not been studied. Thus, this study aimed to evaluate BDNF levels in obese Chinese patients before and after bariatric surgery and provide new clues to the mechanism of bariatric surgery in patients with obesity.

2. Subjects and methods

2.1. Subjects

This study was approved by the Ethics Committee of Shanghai Ninth People's Hospital (Ethics Approval No. SH9H-2023-T78-2). All study participants also read and signed informed consent forms. A total of 44 obese patients aged 18–60 years who underwent bariatric surgery and post-operative review in the Ninth People's Hospital Affiliated to Shanghai Jiaotong University from March 2019 to April 2022 were selected as the study objects. Patients with a BMI ≥ 30 kg/m^2 were diagnosed with obesity. A body mass index (BMI) of 30–35 kg/m^2 indicates mild obesity, a BMI of 35–40 kg/m^2 indicates moderate obesity, and BMI > 40 kg/m^2 indicates severe obesity. The exclusion criterions were mental anomaly, a history of alcohol or drug abuse, severe liver and renal insufficiency and heart failure, and other serious diseases.

2.2. Research method

2.2.1. Clinical data collection

The gender and ages of the patients were recorded. The height and weight of the patients were also recorded and their BMIs were calculated 2 days before and after surgery. The mean time of data collection after surgery was 18.64 ± 6.76 weeks (4.5 months).

2.2.2. Serum sample collection and BDNF level analysis

Serum samples were collected 2 days before surgery and after surgery. The average postoperative sampling time was 18.64 ± 6.76 weeks (4.5 months). 3 mL of blood was collected between 6:30 am and 7:00 am from the elbow vein before breakfast. The blood samples were left at room temperature for 2 h and centrifuged at 2000 r/min for 20 min. Then, the serum was collected and stored at -80 ℃. Human BDNF ELISA kit of Xiamen Lunchangshuo Biotechnology Co., LTD was used to determine the level of serum BDNF.

2.3. Statistical analysis

Data analysis was conducted using the SPSS 27.0. For continuous variables, data that fit the normal distribution was expressed as mean ± standard deviation, and data that did not fit the normal distribution was expressed as M (P25, P75). A *t*-test was also used for quantitative variables with a normal distribution. Non-parametric test was used to compare data with non-normal distribution. Two-tailed *P* values of < 0.05 were considered statistically significant.

3. Results

3.1. General information

The 44 patients were aged 21–44 years, with an average of 31.27 ± 5.52 years. Among them, there were 30 females, aged 31.90 ± 5.34 years old, and 14 males, aged 30.14 ± 5.92 years old. LSG operation was performed on 39 patients (88.64%). Five patients (11.36%) underwent LRYGB surgery. The patients with mild, moderate and severe obesity were 18, 15 and 11 (40.91%, 34.09%, and 25.00%), respectively.

3.2. Comparison of BMI and BDNF levels before and after operation

BMI before and after surgery was consistent with normal distribution and homogeneity of variance, so paired sample t-test was used. The preoperative BMI of the patients was on average 37.39 ± 6.20 kg/m^2, which was higher than postoperative BMI (28.45 ± 5.14 kg/m^2), and the difference was statistically significant ($P < 0.001$). The serum BDNF levels before and after operation did not conform to normal distribution, so a non-parametric test was used. The BDNF level in obese patients increased significantly after bariatric surgery, and the difference was statistically significant ($P < 0.001$). Further details are shown in **Table 1**.

Table 1. Changes of BMI and BDNF levels before and after surgery

	Pre-operation	Post-operation	Statistical value	*P*
BMI (kg/m^2)	37.39 ± 6.20	28.45 ± 5.14	$t = 20.129$	< 0.001
BDNF (ng/mL)	6.55 (3.26, 11.36)	14.7 (7.40, 40.95)	$Z = 4.330$	< 0.001

3.3. Comparison of BDNF levels between patients with different obesity levels

There was no significant difference in preoperative BDNF levels among patients with different obesity levels ($P > 0.05$), while the postoperative BDNF levels were significantly different than the preoperative BDNF levels ($P < 0.05$). However, there was no significant difference in BDNF changes in patients with different degrees of obesity before and after surgery, ($P > 0.05$), as shown in **Table 2**.

Table 2. BDNF levels in patients with different obesity levels before and after surgery

	Mild obesity	Moderate obesity	Severe obesity	Statistical value	*P*
Preoperative BDNF (ng/mL)	5.25 (2.45, 10.49)	6.09 (4.73, 9.09)	10.23 (2.57, 31.96)	$H = 2.494$	0.287
Postoperative BDNF (ng/mL)	18.88 (6.82, 44.90)	8.42 (4.67, 21.61)	28.13 (11.68, 57.41)	$H = 6.913$	0.032
Changes (ng/mL)	7.18 (0.37, 33.31)	1.84 (-0.43, 15.78)	6.34 (1.45, 33.79)	$H = 2.985$	0.225

3.4. Comparison of BMI and BDNF before and after operation in patients of different sexes

There was no significant difference in BMI between different genders before and after surgery ($P > 0.05$). Independent sample Mann-Whitney U test was used to compare BDNF of different sexes before and after surgery, and the results showed no significant difference $P > 0.05$), as shown in **Table 3**.

Table 3. BMI and BDNF levels of patients of different sexes before and after surgery

	Female	Male	Statistical value	*P*
Preoperative BMI (kg/m^2)	36.74 ± 5.63	38.77 ± 7.31	F =1.716	0.197
Postoperative BMI (kg/m^2)	27.72 ± 4.33	30.01 ± 6.46	F = 2.837	0.100
Preoperative BDNF (ng/mL)	6.88 (4.19, 18.00)	5.41 (2.08, 8.14)	Z = 1.638	0.101
Postoperative BDNF (ng/mL)	11.09(5.41, 36.67)	27.69 (8.26, 41.96)	Z = 1.109	0.268

4. Discussion

Obesity is a global social problem, and obese people are more likely to have health problems compared to normal-weight people, including cardiovascular disease, high blood pressure, diabetes and cancer. Obesity also burdens the health care system. Bariatric surgery is currently the most effective long-term treatment for severe obesity and its related complications [8].

In this study, the serum BDNF levels of 44 obese patients were measured before and after bariatric surgery, and the results showed a significant increase in BDNF levels after surgery. Data from several animal models and human subjects suggest that BDNF can prevent metabolic syndrome and obesity by suppressing appetite and improving insulin sensitivity [9]. BDNF in the dorsal and ventromedial hypothalamus of mice reduces body weight by reducing food intake and increasing energy expenditure due to spontaneous physical activity and resting metabolic rate [10], and its loss leads to increased food intake and obesity [11]. In conclusion, BDNF is a key factor in regulating brain energy homeostasis in adult mice. BDNF levels in obese patients are associated with food cravings. In obese patients, plasma BDNF levels are positively correlated with visual food cue-reactivity in the bilateral insulae [12]. In summary, there have been growing evidence that BDNF plays an important role in the occurrence and development of obesity, and that BDNF level increases after bariatric surgery.

There have been studies comparing BDNF levels of normal-weight patients with those of obese patients, but the results have been inconsistent. Celik Guzel *et al.* [13] and Alomari *et al.* [14] found that BDNF levels in obese patients were significantly lower than those in the of normal-weight patients. Compared with normal weight control group, plasma BDNF levels in preadolescent obese children were lower and increased after lifestyle intervention [15]. A German study reported no difference in serum BDNF concentrations between 24 obese patients and 14 non-obese controls [16]. A study in Poland included 144 middle-aged and elderly obese patients and 64 normal weight people, and the results showed that there was no significant difference in BDNF between the two groups [17]. Therefore, further studies are needed to verify the relevant conclusions.

There have been few studies on the correlation between the degree of obesity and BDNF level. Masataka Suwa *et al.* found a positive correlation between serum BDNF level and BMI in female diabetic patients [18]. A study found that people with different BMI levels have different serum BDNF levels, with underweight being the highest, followed by normal BMI, and the higher the degree of obesity, the lower the level of BDNF [19]. However, the results of this study showed that there was no significant difference in the degree of BDNF level increase in patients with different degrees of obesity after bariatric surgery, which may be related to the small sample size of the study.

In this study, there were no significant differences in BMI and BDNF levels before and after surgery in patients of different genders. There have also been some studies on the differences in BDNF levels in terms of gender distribution. BDNF levels were measured in healthy adults with no difference in BMI levels, and there were significant differences in platelet BDNF levels between males and females, with females significantly lower than males, while plasma BDNF levels were not significantly different [16]. However, in our study, there was no significant difference in serum BDNF levels between females and males before and after bariatric surgery, and gender cannot be considered as an influencing factor, which is similar to the results of Glud M *et al* [20]. Therefore, the correlation between serum BDNF level and gender needs to be further verified.

5. Conclusion

In this study, the BMIs of the patients were significantly lower and serum BDNF levels were significantly higher in our patients 4.5 months after surgery. There was no significant difference in the BDNF level in patients with different degrees of obesity after bariatric surgery. There was also no significant difference in BDNF level between different genders before and after surgery. However, the sample size of this study is small with a short follow-up period, so some of our findings are not completely consistent with previous studies. There are differences in the age, number and race of the subjects in different studies, which may affect the blood BDNF level and lead to differences in research results. Studies on obesity and serum BDNF levels are still relatively limited, so further studies with larger sample sizes, wider geographical coverage and longer follow-up time are needed to provide references for the mechanisms and treatment of obesity.

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Author contributions

Zhang Xiaoxu is responsible for designing experimental schemes, reviewing literature, conducting experiments, extracting and analyzing experimental data, interpreting results and writing papers. Xu Bei and Liu Chaofan participated in experimental scheme design and experimental guidance, as well as data analysis. Gu Fen participated in the design of the experimental scheme, reviewed and revised the paper, and provided financial support. Wang Bing provided experimental sites and samples, reviewed the paper and gave feedback.

Disclosure statement

The authors declare no competing financial interests

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