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# Serotonin Level and Nutritional Behavior of Patients with Primary Insulin Resistance

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## Abstract

**Background:** One of the most important tasks at the initial stage of treatment of patients with primary insulin resistance is a decrease in body weight, which means a decrease in the amount of food consumed. Patients rarely manage to cope with this task independently, and drug therapy does not always provide sufficient effect.

**Methods:** Patients (42 people) aged 38.4 ± 2.0 years, body mass index (BMI) 32.3 ± 4.2 kg/m$^2$. Two groups of observation were formed: group 1 (20 people) received reflexotherapy using special corporal and auricular points and a hypocaloric diet. Patients of the 2$^{nd}$ group (22 people) were given only a diet was studied: BMI, the ratio of WC/HC, HOMA-IR index, insulin and C-peptide. ELISA (Labor Diagnostica NORT Serotonin RESEARCH ELISA, Germany) determined serotonin in serum. The reflexotherapy procedures included daily corporal and auricular acupuncture.

**Results:** Based on the results of their own research, it has been shown that the use of reflex therapy using special corporal and auricular points with obese patients contributes to serotonin in the blood serum and leads to rapid satiety during eating. This allows patients to observe a low caloric diet at the initial stage of treatment. It is also shown that the increase in serotonin in the serum is statistically significant only when the combination of the therapeutic diet with reflex therapy, but not in the case of exclusively dietary correction.

**Conclusion:** The use of reflexotherapy with the use of special corporal and auricular points promoted the increase of serotonin in the blood serum and led to rapid satiety during eating. This allowed patients to observe a hypocaloric diet at the initial stage of treatment.

**Keywords:** Serotonin; Obesity; Food behavior; Reflex therapy; Medical rehabilitation

## Introduction

Among the most common diseases in the world, a special place is occupied by primary obesity. According to various sources, they suffer from 14 to 18% of the world's population (Figure 1).

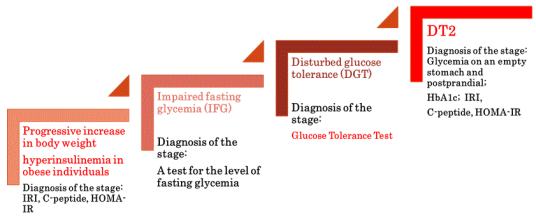


**Figure 1:** Stages of violations of carbohydrate metabolism and methods of primary diagnosis.

The most common obesity is alimentary-constitutional nature (80-85%). As a rule, it is obesity that is the first step on the way to the development of diabetes mellitus.

The treatment of this disease involved specialists of different profiles - endocrinologists, cardiologists, nutritionists, psychologists, etc. However, it is extremely difficult to achieve high results in the treatment of this disease and with a great desire on the part of the patient himself. The change in eating behavior underlies the successful treatment of obese patients, and achieving this change is one of the most difficult tasks for a doctor.

Obesity is a classic example of pathology with a violation of the mechanisms of neuroendocrine regulation. It is quite obvious that the use of complex and systemic therapy is required to treat multifactorial disease with polysystemic lesion. And the diagnostic methods should be such that they allow us to evaluate both the state of the endocrine regulatory mechanisms and the psychological state of the patient.

The body weight of a person is under a complex control of neuro-humoral influences, which ultimately determine the severity of nutritional motivation and the level of basal metabolism. Neuroscience of obesity becomes a rapidly developing field of research, irreplaceable for understanding the pathogenesis of the disease. In the last 15 years, many important discoveries have been made in neurobiology of obesity, including the detection of hormones produced by fatty tissue

(leptin), gastrointestinal hormones (ghrelin, serotonin), and a number of central and peripheral ways of regulating energy balance have been identified [1]. The brain plays a leading role in regulating energy balance, as it affects food intake and energy consumption. It is known that the centers of hunger and saturation, as well as the regulation of basal metabolism, are found in supraoptic nuclei of the hypothalamus [2,3]. The brain systems controlling consumption and energy consumption are divided into anabolic and catabolic. Each system includes different types of neurons, capable of controlling both energy consumption and its consumption. These neurons release various molecules, including neuropeptide Y, agoutine-like protein (AGP), melanostimulating hormone (MSH), endocannabinoids, cocaine-amphetamine-regulated transcript (CART), corticotropin-releasing hormone (CRTH), thyrotropin-releasing hormone (TRH), Serotonin, etc. [4,5]. The activity of these systems is affected by short-term and long-term signals, which report on the state of stocks and energy expenditure. It is known that the central serotonergic system plays importatnt role in regulating the feeling of hunger and satiety [6,7]. An important role in the formation of normal energy homeostasis is played by serotonin. This monamine is synthesized and accumulated in the EC cells of the gastrointestinal tract, stimulates smooth muscles, regulates intestinal motility, peripheral sympathetic thermogenesis, is responsible for the formation of normal energy homeostasis does not penetrate the blood-brain barrier. [8,9]. It is shown that in normal cases, the increase in serotonin under the influence of leptin produced by fat cells causes a feeling of satiety [9]. In contrast, when fasting, diets, there is a lack of serotonin secretion. Reducing its level subjectively causes depression. Published data shows that obese people with low serotonin levels [7,10] due to the development of leptin resistance, which can prevent the formation of a normal structure of eating behavior. Violation of the synthesis of serotonin has an innate and acquired character. At the present time, genes, presumably responsible for food motivation, encoding serotonin receptors [5] have been identified. Increased food intake leads to an increase in the binding of serotonin to the receptors and increases the efficiency of its re-uptake (Figure 2).

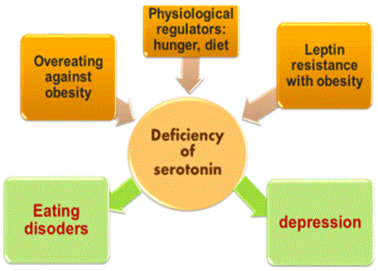


**Figure 2:** Mechanism leading to a decrease in serotonin level.

Increasing the binding of serotonin leads to a decrease in its concentration in the synaptic cleft. Also, the concentration of serotonin in the synaptic cleft decreases due to the activation of its capture [9,11]. Thus, the development of obesity is associated with a decrease in the level of serotonin in the synaptic gap, which leads to the development of a state like the depressive.

In order to "relieve depression" by inducing the synthesis of serotonin, a person is forced to use an increased amount of food, which aggravates the development of obesity.

Serotonin is a monoamine that suppresses appetite and plays an important role in the formation of normal energy homeostasis:

- It forms in the intestine (90% synthesized and accumulates in the EC cells of the stomach and duodenum);
- Regulates peripheral sympathetic thermogenesis regulates energy consumption in obese patients does;
- Not penetrate through the blood-brain barrier;
- A strong stimulator of smooth muscles;
- Regulates intestinal motility;
- Regulates peripheral sympathetic thermogenesis.

A "vicious circle", an imbalance of serotonergic mechanisms leading to the development of obesity is formed [12,13]. Numerous studies have shown that changing lifestyle and switching to a low-calorie diet cannot have an effective effect on obesity: lost kilograms that have been lost with great difficulty are recruited within 0.5-1 year [9,14,15]. Given the importance of the imbalance of serotonergic mechanisms in the development of obesity, it is obvious that the use of an unconventional method of treatment – reflex therapy.

In connection with this, the purpose of this study was to assess the influence of acupuncture on the production of serotonin and the features of the nutritional behavior of patients with primary insulin resistance.

## Methods

### Design

A prospective cohort study was conducted. The distribution of patients in groups was carried out by randomization. The study was conducted from 2015 to 2017.

### Sampling and setting

The present study was conducted on the basis of Clinical Hospital of the Department of Endocrinology of Kazan State Medical Academy (Kazan) and on the Endocrinology Department of City Clinical Hospital name Eramishantsev (Moscow) - clinical basis of the Department of Hospital Therapy with the course of endocrinology of the RUDN University.

The study group consisted of 42 women with primary obesity. The average age of the patients was 38.4 ± 2.0 years, the body mass index (BMI) was 27-43 kg/m$^2$. The main criterion for including patients in the study was a BMI more than 30 kg/m$^2$, which averaged 32.3 ± 4.2 kg/m$^2$. 81% (34 patients) of patients had abdominal obesity, 19% (8 patients) had a gynoid type. The study did not include women who had previously received medication.

The control group consisted of 12 practically healthy women with no signs of obesity with a BMI within normal limits. The subjects and persons of the control group were collected history, body mass index was calculated and anthropometric parameters were measured: weight (kg); BMI - body mass index (kg/m$^2$); WC - waist circumference (cm); HC - hip circumference (cm).

Two groups of observation were formed. The course of treatment group 1 (20 people) consisted in the appointment of 15 sessions of reflex therapy (RT), low caloric diet in combination with physical exertion and the subsequent one-day fasting per week. The course of treatment group 2 (22 people) included only a low caloric diet in

combination with physical activity and the subsequent one-day fasting per week, without RT. The energy value of the therapeutic diet was 3360-4602 kJ (800-1100 kcal). Reflex therapy procedures included corporeal and auricular acupuncture, surface acupuncture according to a certain scheme (11 II, 36III, 7V, 41XI, 60VII, 34, 25, 22, 18, 55). Procedures were conducted daily.

## Ethical Consideration

The study was conducted in compliance with the principles of medical ethics. The compliance of the study with the norms of biomedical ethics is confirmed by the conclusion of the Ethics Committee of the Kazan State Medical Academy (Protocol № 2/09 of September 8, 2016). Participants were fully acquainted with the objectives of the study, its importance, and the method of selecting participants, the right to refuse to participate at any time, the benefits and risks of the study.

### Instruments and data collection procedure

The level of serotonin in the serum was determined by ELISA using the Labor Diagnostica NORT Serotonin RESEARCH ELISA kit, Germany.

Criteria for study of nutritional behavior: Psychological research was conducted on a por computer complex for psycho-physiological testing of NS-PsychoTest (Neurosoft, Russia). The Spielberger test was used for quantitative evaluation in points of the level of reactive and personal anxiety; Bek test was used for quantitative assessment in points of depressive reaction level. The DEBQ test was used to assess the type of eating disorder. Boundary values indicated the presence of eating disorders: emotionally - 2.03 points; Compulsive - 2.60; External - 2, 68; Restrictive - 2.43 [16].

### Data analysis procedures

Statistical processing of the results of the study was carried out using the software package Statistica 6.0 for Windows (StatSoft Inc.). The data are presented in the form M ± SD, where M is the arithmetic mean, SD is the standard deviation. The statistical significance of the differences was determined using the nonparametric U Mann-Whitney criterion. The dynamics of the indices during the treatment was evaluated using the test of the matched Wilcoxon pairs. The Spearman rank correlation coefficient was used to estimate the degree of interrelation of the quantitative characteristics. Differences were considered reliable at a significance level of $p < 0.05$.

## Results and Discussion

The results of the study were evaluated regardless of the type of fat distribution. Anthropometric indices (BMI, OT, OB, OT / OB), serotonin level in serum were studied. In the general group of patients, there were significantly higher indices compared to the control group: BMI 33.8 ± 7.05 and 21.06 ± 1.39 kg/m$^2$, waist circumference (OT) 88.6 ± 5.22 and 72, 5 ± 4.65 cm; The circumference of the hips (OB): 112.4 ± 8.2 and 103.0 ± 8.89 cm. It was noted that the serotonin content in the blood serum of patients was reduced in comparison with the control group (173.3 ± 60.8 and 223.9 ± 90.4 ng/ml). The values of the analytical parameters before treatment between the indices of group 1 and group 2 were not statistically different. Features of dietary behavior in patients of the observation group showed a predominance of a mixed type of disorders (Figure 3).

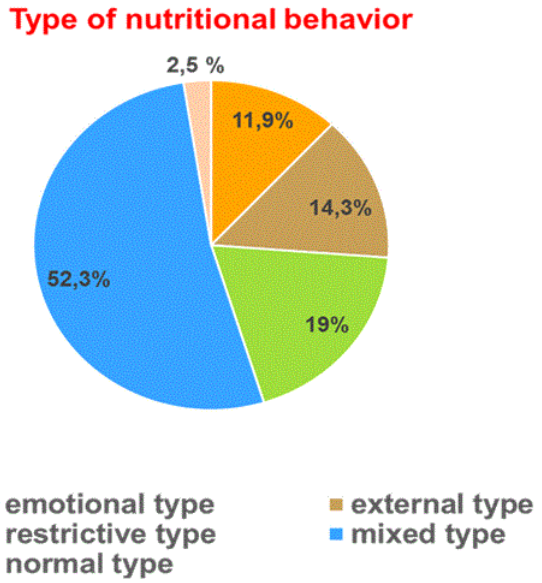


**Figure 3:** Structure of nutrition behavior in the group of examined.

In the first experimental group of patients, after a 2-week course of acupuncture, there was a significant decrease in anthropometric parameters: BMI initially - 33.7 ± 4.5 after treatment - 29.2 ± 4.05 kg/m$^2$ ($p=0.002$); OT initially from 88.7 ± 6.86 to 82.2 ± 6.51 cm ($p=0.004$); OB c 111.8 ± 8.81 cm to 103.5 ± 8.38 cm ($p=0.004$) (Table 1). The body weight of patients decreased by 9.8% (from 88.9 ± 10.6 kg to 80.2 ± 10.5 kg ($p=0.013$). Opt was found that RT correlates with OB $r=0.68$ ($p=0.011$). BMI of $r=0.77$ ($p=0.02$). Such a parallel change in various indicators before and after treatment allowed suggesting the existence of correlation relationships (Figure 4).

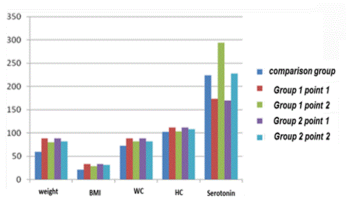


**Figure 4:** Change in BMI end serotonin levels in the group of examined. Weight (kg); BMI - body mass index (kg/m$^2$); WC - waist circumference (cm); HC - hip circumference (cm); Serotonin (ng/ml).

Pearson correlation analysis was performed and statistically significant correlations between BMI and serotonin concentration in serum $r= -0.23$ ($p=0.04$), between OB and serotonin $r= -0.37$ ($p=0.032$) were noted.

A statistically significant increase in the level of serotonin in the blood serum of patients was found 69.5%, up to 294.5 ± 98.7 ng/ml compared to the initial 173.7 ± 71.3 ng/ml in this group of patients ($p=0.0057$).

In the group of patients who received only the hypocaloric diet, a statistically significant difference in the BMI was observed: initially -

33.9 ± 4.2 after treatment - 31.2 ± 4.4 kg/m$^2$ (p=0.043) and RT: initially from 88.4 ± 6.9 to 82.3 ± 6.53 cm (p=0.0044). OB decreased from 112.0 ± 8.86 cm to 108.4 ± 8.62 cm, but the decrease was not statistically significant (p=0.18). The body weight of patients in this study group decreased by 7.4% (from 88.2 ± 10.1 kg to 82.1 ± 10.0 kg (p=0.051). Ot in this group of patients was also correlated with BMI R=0.72 (p=0.04).

The tendency of serotonin level increase in the serum of patients in this group was established by 34.4%, up to 227.9 ± 95.9 ng/ml in comparison with the initial 169.6 ± 72.4 ng/ml (p=0.031).

It should be noted that when comparing the effectiveness of the treatment in two experimental groups, a statistically significant difference was observed in the serotonin content (p=0.032).

The revealed statistical differences were confirmed by the peculiarities of food behavior (Figures 4 and 5).

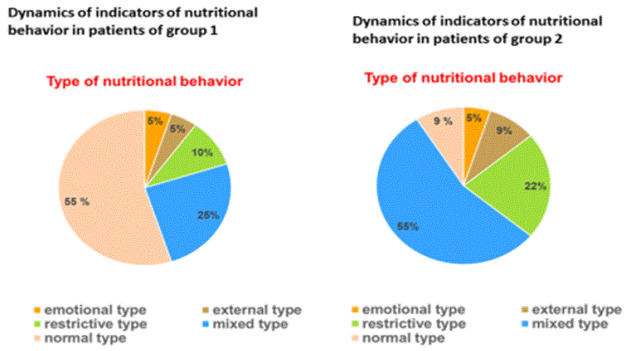


**Figure 5:** Dynamics of indicators of nutritional behavior.

Dynamics of the level of reactive anxiety (in points) and depression in the process of medical rehabilitation presented in Tables 1-3.

| Indicators | Group 1 | | Group 2 | |
|---|---|---|---|---|
| | Point 1 | Point 2 | Point 1 | Point 2 |
| BMI (kg/m$^2$) | 33.7 ± 4.5 | 29.2 ± 4.1 | 33.9 ± 4.2 | 31.2 ± 4.4 |
| | P=0.002 | | P=0.043 | |
| WC (sm) | 88.7 ± 6.8 | 82.2 ± 6.5 | 88.4 ± 6.9 | 82.3 ± 6.6 |
| | P=0.004 | | P=0.004 | |
| HC (sm) | 111.8 ± 8.8 | 103.5 ± 8.4 | 112.0 ± 8.9 | 108.4 ± 8.6 |
| | P=0.004 | | P=0.18 | |
| Serotonin (ng/ml) | 173.7 ± 71.0 | 294.5 ± 98.7 | 169.6 ±7 2.4 | 237.9 ± 95.9 |
| | P=0.005 | | P=0.031 | |

**Table 1:** Criteria for evaluating the effectiveness of reflexotherapy.Notes: Point 1- examination before the start of therapy; Point 2 - examination after completion of the course of reflexotherapy. BMI - body mass index (kg/m$^2$); WC - waist circumference (cm); HC - hip circumference (cm).

| Indicators | Group 1 | | Group 2 | | P1-3 | P2-4 |
|---|---|---|---|---|---|---|
| | Point 1 | Point 2 | Point 1 | Point 2 | | |
| Depression level | 12.8 ± 1.2 | 9.8 ± 1.3 | 12.9 ± 1.1 | 12.6 ± 1.2 | >0.05 | <0.01 |
| | P1-2<0.05 | | P3-4>0.05 | | | |

**Table 2:** Depression in the process of medical rehabilitation in the group of examined. Notes: Point 1- examination before the start of therapy; Point 2 - examination after completion of the course of reflexotherapy. P1-2 – the reliability of the differences between the indicators of group 1 before and after treatment; P3-4 - the reliability of the differences between the indicators of group 2 before and after treatment.

| Indicators | Group 1 | | Group 2 | | P1-3 | P2-4 |
|---|---|---|---|---|---|---|
| | Point 1 | Point 2 | Point 1 | Point 2 | | |
| Level of reactive anxiety | 43.4 ± 1.6 | 39.4 ± 1.7 | 43.2 ± 1.7 | 43.1 ± 1.8 | >0.05 | <0.05 |

| | | | | |
|---|---|---|---|---|
| | P1-2<0.05 | P3-4>0.05 | | |

**Table 3:** Level of reactive anxiety (in points) in the process of medical rehabilitation in the group of examined. Notes: Point 1- examination before the start of therapy; Point 2 - examination after completion of the course of reflexotherapy. P1-2 – the reliability of the differences between the indicators of group 1 before and after treatment; P3-4 - the reliability of the differences between the indicators of group 2 before and after treatment; P1-3 - the reliability of the differences between indicators before treatment in groups 1 and 2; P2-4 - the reliability of the differences between indicators after treatment in groups 1 and 2.

When analyzing data obtained, it was noted that after the course of the therapy in both groups of patients, the body weight, BMI, OT, OB parameters and the serum serotonin level decreased. However, in the group receiving a special reflex therapy along with the diet, the changes in the analytical indices were more pronounced, and the increase in the serum serotonin concentration was statistically significant. Consequently, it is possible to make an assumption about the complex nature of the changes in anthropometric characteristics accompanied by an increase in serotonin levels in the blood serum of patients after treatment.

It should be noted that according to the results of the survey of patients of the first group after the course of treatment, a marked decrease in appetite was noted, which allows to observe the diet and reduce the amount of food, especially at the initial stage of the treatment. In the second group, this effect was extremely low. Thus, the use of complex therapy, including along with the diet regime and reflexology, stimulates the functioning of serotonergic systems of the central nervous system, significantly increasing the serotonin level in the serum, which leads to a decrease in appetite and helps patients to observe a low caloric diet, especially at the initial stage of treatment.

## Conclusion

A low serotonin content in the serum of patients with obesity is established. Diet therapy in conjunction with reflexology of the auricular and corporal acupuncture points leads to a more pronounced increase in serotonin in the blood serum, compared with the exceptionally traditional diet therapy, which leads to a decrease in appetite and allows observing low caloric diet. Against the backdrop of the use of reflex therapy, the positive dynamics of obese patients is much more pronounced, with a clear decrease in appetite, which allows observing the diet and reducing the amount of food, especially at the initial stage of the treatment.

Findings:

Lower serotonin levels in the blood serum of patients in the observation groups - 173.3 ± 60.8 ng/ml (in the comparison group - 223.9 ± 90.4 ng / ml).

The relationship between BMI and serotonin concentration in the serum r= -0.23 (p=0.04).

In group 1 there was an increase in the level of serotonin by 69.5% (p=0.0057), body weight decreased by 9.8%.

In group 2, serotonin levels increased by 34.4% (p=0.031), and body weight decreased by 7.4% (p=0.051).

Patients of Group 1 after the course of treatment noted a decrease in appetite, which allows observing the diet and reducing the amount of food.

The use of reflex therapy with the use of special corporal and auricular points promotes an increase in serotonin in the blood serum and leads to rapid satiety during eating. This allows patients to observe a low caloric diet at the initial stage of treatment.

## Authors' Contributions

Irina Kurnikova was the main author of the manuscript, analyzed and interpreted the patients' data. Tatiana Nikishova participated in the study of patients, the collection of material, analysis and interpretation of these patients. Ramchandra Sargar contributed to the preparation of the manuscript. All authors have read and approved the final manuscript.

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