

Obesity itself does not influence BDNF serum levels in adults

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Abstract. – OBJECTIVE: In European countries more than 50% of the population are overweight, 30% with obesity. In Poland overweight was present in 41% of men and 28.7% of women (obesity 15.7% and 19.9%). It was examined whether obesity affects serum levels of brain-derived neurotrophic factor (BDNF) and interleukin-6 (IL-6), which may lead to the consequences of obesity, such as type 2 diabetes, hypertension, and finally the metabolic syndrome. We aimed to examine whether obesity affects the serum levels of BDNF and IL-6.

PATIENTS AND METHODS: The study involved 144 people aged 45 to 86 years, 80 subjects with diagnosed obesity and 64 with normal body weight, ≤ 65 years old ($n = 45$) and > 65 years old ($n = 99$). All patients underwent tests of glucose, total cholesterol, HDL, LDL, triglycerides levels, using routine laboratory methods. A test of the concentration of IL-6 and BDNF was carried out. The declared level of physical activity (gymnastics, cycling or walking) was considered.

RESULTS: It was shown that in women ≤ 65 years old, obesity was associated with higher levels of interleukin-6. When the test group, divided into the above categories, was analyzed for the diagnosis of hypertension, heart failure or diabetes mellitus, no statistically significant differences in the investigated parameters were detected. The concentration of brain-derived neurotrophic factor did not differ in the investigated subjects, regardless of sex, age, obesity, or the declared physical activity.

CONCLUSIONS: The concentration of interleukin-6 in younger people, including those with normal body weight, correlated with total cholesterol and triglyceride levels, and it was significantly higher in obese women compared to those with normal body weight.

Introduction

Globally, mean body mass index (BMI) has increased since 1980. Between 1980 and 2008, mean BMI worldwide increased by 0.4 kg/m² per decade for men and 0.5 kg/m² per decade for women.

The USA had the highest BMI of high-income countries. In 2008, an estimated 1.46 billion adults (1.41-1.51 billion) worldwide had BMI of 25 kg/m² or greater, of these 205 million men (193-217 million) and 297 million women (280-315 million) were obese¹. Epidemiological data from the last twenty years in the United States indicate that the prevalence of obesity has doubled. At present, 66% of adults are overweight and 34% are obese. Morbid obesity (BMI > 40 kg/m²) is present in up to 3% of men and 7% of women. It is estimated that in 2015 up to 75% of adults will be overweight and 42% will be obese. In European countries more than 50% of the population suffer from overweight, and 30% have been diagnosed with obesity²⁻⁴. A study conducted in Poland in 2000 showed that overweight was present in 41% of men and 28.7% of women, and obesity in 15.7% of men and 19.9% of women⁵⁻⁷. On the other hand, in a NATPOL study⁸ overweight was diagnosed in 34% of adults (39% of men and 29% of women), and obesity in 19% of men and 19% of women. Many epidemiological studies confirm the impact of decreased physical activity on the development of obesity worldwide⁹.

In view of the reports about the relationship between obesity and brain-derived neurotrophic factor (BDNF) serum levels, a study on this parameter in mature and older people was undertaken, with a simultaneous analysis of the influence of body weight on BDNF. At the same time it was deter-

Key Words:

Obesity, Serum BDNF, Serum IL6.

mined to examine whether obesity affects serum levels of IL-6, given the reports of inflammation induced by fat tissue, which may lead to the consequences of obesity, such as type 2 diabetes, hypertension and, finally, the metabolic syndrome.

The aim of this study was the assessment of the impact of obesity and declared physical activity on the concentration of brain-derived neurotrophic factor and interleukin-6 in serum.

Patients and Methods

The study involved 167 people aged 45 to 86 years, who were under the care of a general practitioner, from outside a large metropolitan area. Ultimately, after rejecting incomplete data, the analysis involved 144 persons, including 80 subjects with diagnosed obesity and 64 with normal body weight. The patients were divided into two age groups: ≤ 65 years old ($n=45$), > 65 years old ($n= 99$). Demographic data are provided in (Table I).

Informed consent was obtained from all of the subjects and the study was approved by the Research Ethics Committee of Poznan University of Medical Sciences and registered under no. 22/10 (07-01-2010). It conformed to all ethical issues included in the Helsinki Declaration.

All patients underwent tests of glucose, total cholesterol, HDL, LDL and triglycerides levels, using routine laboratory methods. A test of the concentration of brain-derived neurotrophic factor and interleukin-6, using the ELISA method with the R&D set (USA) was also performed.

We also examined, by means of a validated questionnaire, the declared level of physical activity, taking into account the performance of such activities as gymnastics, cycling or walking (Table II). In the analysis we also took into account information included in patient medical history reports regarding the following diseases: hypertension, heart failure and diabetes. It should be noted, however, that all of the investigated subjects were un-

der the care of a general practitioner, they regularly took the prescribed medications and during the survey they reported no ailments associated with these diagnoses. In all of the subjects the presence of inflammatory diseases was excluded, and the results of ESR were normal.

Statistical Analysis

The results were statistically analyzed using the Statistica 10.0 software. Parametric statistics for the laboratory tests and non-parametric statistics were used: medians with quartiles for the cytokine assay, the Mann-Whitney U test for the investigation of the differences between the two groups and the Kruskal-Wallis test for the investigation of the differences between many groups, and the Spearman's rho test to investigate the correlations. $p < 0.05$ was considered statistically significant.

Results

We examined the glucose, total cholesterol, HDL, LDL and triglyceride levels by age and body weight (Table II). It was shown that only in women ≤ 65 years old, obesity was associated with higher levels of IL-6, while in the group of elderly women lipid parameters were higher than in younger women.

Next, a study of the correlations was carried out taking into account the division in terms of sex, age and obesity. The following statistically significant correlations were shown: (Spearman's rho coefficient was provided at $p < 0.05$)

Women ≤ 65 with normal body weight: IL-6 with the concentration of triglycerides (0.90)

Obese women ≤ 65 : IL-6 and total cholesterol (-0.63), IL-6 and LDL (-0.62)

Obese men ≤ 65 BDNF and glucose level (-0.60)

Men > 65 with normal body weight IL-6 and HDL (-0.52), IL-6 and triglycerides (0.64) and IL-6 and glucose level (0.44).

Table I. Demographic data and the declared physical activity. The number of people who reported practicing these forms of activity (G - gymnastics, W - walking, B - bicycle) was provided.

Age categories	Women		Men	
	Normal body weight	Obese women	Normal body weight	Obese men
≤ 65 years old	11 (G-3, W- 4 B-3)	15 (G-9, W-8, B-0)	7 (G- 3, W-3, B-1)	12 (G-6, W-6, B-3)
> 65 years old	25 (G-14, W-14, B-3)	39 (G- 16, W- 20, B-10)	21(G- 10, W-10, B-5)	14 (G-11, W-8, B-2)

Table II. Total cholesterol, HDL, LDL, triglyceride, and glucose levels by age and body weight. The mean value and the standard deviation were provided.

Age		Women with normal body weight	Obese women	Men with normal body weight	Obese men
≤ 65 years old	Total cholesterol (mg/dL)	246.6±44.6	205.7±48.8	172.2±32.0	216.1±56.5
	HDL (mg/dL)	45.4±8.6	45.2±8.0	41.2±8.7	34.4±10.0
	LDL (mg/dL)	158.4±43.5	127.8±42.0	103.2±26.0	139.2±46.0
	Triglycerides (mg/dL)	221.6±193.6	162.9±61.7	139.0±61.4	303.0±201.1
	Glucose level (mg/dL)	93.2±6.4	107.5±49.4	97.8±19.2	101.0±22.0
	IL-6 (pg/mL)	2.4±1.7	3.5±1.6*	2.8±1.0	3.4±2.2
	BDNF (pg/mL)	23833.0±4515.2	23895.6±4178.6	22951.9±4642.6	23721.6±3556.1
> 66 years old	Total cholesterol (mg/dL)	232.6±42.9	233.8±47.8	208.0±41.8	220.8±53.9
	HDL (mg/dL)	49.3±12.3	39.2±8.4*	43.8±13.4	35.5±6.3
	LDL (mg/dL)	151.0±38.1	158.0±44.0	132.8±40.3	144.7±31.4
	Triglycerides (mg/dL)	160.0±84.2	183.2±67.0*	153.7±86.0	164.8±70.0
	Glucose level (mg/dL)	99.0±49.3	104.8±34.6	92.4±12.4	96.9±21.0
	IL-6 (pg/mL)	3.1±2.0	3.4±2.2	3.2±2.2	3.2±2.2
	BDNF (pg/mL)	23225.0±3802.4	24107.1±5691.4	23494.8±4498.5	24745.0±6469.5
* $p < 0.05$ the difference between people of the same sex and age group, due to obesity					

There was no correlation between the concentration of IL-6 and the concentration of BDNF.

No statistically significant differences were detected whether a person declared practicing gymnastics or walking. A negative correlation between the declared cycling and the concentration of BDNF in younger obese men was the only one observed.

When the test group, divided into the above categories, was analyzed for the diagnosis of hypertension, heart failure or diabetes, no statistically significant differences in the investigated parameters were detected.

Discussion

No correlation was found between sex, age, body weight or the declared physical activity and serum concentrations of BDNF and there was no simple correlation between the concentrations of BDNF and interleukin-6, although other authors have described such a correlation¹⁰. The BDNF serum levels detected in the subjects do not differ from the values reported in the literature for the investigated age range. It may, thus be concluded that in this age range obesity does not affect the level of BDNF, although it is associated with higher levels of IL-6. The devastating impact of obesity on mental functioning has been studied

rather in younger people^{11,12}. Stabilized midlife and old age obesity probably no longer affects the level of BDNF. There was no correlation between the declared physical activity and the investigated lipid parameters or cytokines. It should, however, be kept in mind that there is often a vast difference between the declared physical activity and the actual physical fitness. Unfortunately, for the purposes of this work the physical fitness of the subjects was not assessed. Thus, it was not possible to analyze the suggested link between BDNF and energy homeostasis¹³.

In people with normal body weight, both in women and men, lipid parameters considered as abnormal correlated with IL-6, which is thought to be a threat of the metabolic syndrome^{14,15}. In obese subjects this correlation is not seen as probably the excessive body weight stabilized for years is, in their case, metabolically compensated. It must be admitted, though, that the literature reports that BDNF plays a role in the regulation of energy¹⁶, but in the subjects excessive weight gain has already taken place, and the literature reports that long acting stimuli cease to cause the increase of BDNF concentrations both in the cerebral spinal fluid and in the peripheral nervous system¹⁷.

The only significant correlation (negative) detected for BDNF refers to glucose level in obese younger men. Probably in the process of

body weight gain at a younger age, which is accompanied by the highest values of TG and the lowest values of HDL, its effect on the body is most devastating. This finding is also supported by the largest differences in the concentrations of IL-6 between individuals with normal or excessive body weight in the younger age group. In people from the older age group obesity does not cause the increase in the concentration of IL-6.

This concentration is not related to lipid parameters, although in the same individuals one could demonstrate a correlation between the concentration of IL-6 and the total cholesterol and triglyceride levels, especially in persons with normal body weight. The concentration of IL-6 is not due to the presence of clinically apparent inflammation in the bodies of the subjects, thus one can only assume that it may be related to the aging process, especially with its production by excessively accumulated fat tissue. Literature clearly shows that abdominal obesity is associated with the production of inflammatory cytokines¹⁸. It should also be emphasized that the problem of obesity has ceased to concern only the inhabitants of large cities, who could be suspected of lack of exercise. The authors¹⁹ have already reported the occurrence of inflammation parameters in children with excessive body weight, also coming from rural areas. The recent report on exercise intervention in obese children showed increase of resting BDNF levels after 12 weeks exercise programme, but no change in inflammatory parameters²⁰.

Conclusions

The concentration of brain-derived neurotrophic factor did not differ in the investigated subjects, regardless of sex, age, obesity, or the declared physical activity.

The concentration of interleukin-6 in younger people, including those with normal body weight, correlated with total cholesterol and triglycerides levels, and it was significantly higher in obese women compared to those with normal body weight.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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