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Effects of nutritional intervention on body weight and body composition of obese psychiatric patients taking olanzapine

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Abstract

Objective: Weight gain is an established side effect of atypical antipsychotics in patients with severe mental illness (SMI). Previous studies have shown positive effects of nutritional interventions in weight loss. The purpose of this study was to investigate the effects of a nutritional intervention on the body weight and body composition of patients with SMI taking olanzapine in Greece.

Methods: Eighty-two patients with SMI treated with olanzapine (22 men, 60 women) and 58 healthy controls (12 men, 46 women) were followed for 3 mo. All patients with SMI were obese, with an average body mass index of 33.12 ± 0.74 kg/m^2 and body weight of 94.61 ± 2.50 kg. A nutritional program was designed for each participant based on anthropometric characteristics, health profile, and dietary needs. Pre- and postintervention anthropometric and body composition measurements were performed.

Results: Significant weight loss and fat loss were found in the healthy controls and patients with SMI from baseline to 3 mo ($P < 0.05$). However, the patients with SMI had a less significant decrease in waist circumference ($P < 0.05$) compared with healthy controls. The healthy male controls and male patients with SMI demonstrated greater decreases in body weight and waist circumference compared with female participants ($P < 0.05$).

Conclusion: Patients with SMI appear to respond effectively to a nutritional program demonstrating significant decreases in body weight and body composition despite the use of olanzapine. Because gender differences may exist in weight loss, it is possible that gender should be taken into account for a more appropriate treatment of obesity in this population.

Keywords: Obesity; Severe mental disease; Weight loss; Nutritional intervention

Introduction

Obesity and in particular intra-abdominal obesity is a serious health problem because it is associated with a number of chronic diseases such as type 2 diabetes, coronary artery disease, atherosclerosis, hypertension, stroke, cancer, and respiratory diseases [1–3]. Moreover, the prevalence of obese and overweight people has markedly increased in recent decades such that it currently is a growing concern for other population subgroups such as children, adolescents, and pregnant women who previously had a low prevalence of obesity. Patients with severe mental illness (SMI) such as psychosis, depression, and bipolar disease also have a high prevalence of obesity [4]. This is attributed primarily to the treatment with a number of antipsychotic medications that are associated with weight gain and obesity [4,5–7]. These same medications have also been shown to be related to metabolic disturbances such as glucose intolerance, insulin resistance, and dyslipidemia [4,5–7]. Furthermore, weight gain in this population due to its direct association to depression and low self-esteem can lead to decreased compliance to the treatment of mental illness [4].

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In healthy overweight and obese populations, lifestyle interventions through diet and exercise have been shown to produce significant weight loss and reductions in body fat and primarily abdominal fat [8–10]. These changes are related to marked improvements in the metabolic profile of these individuals and thus to lower risks of morbidity and mortality and improved quality of life [8–10]. In patients with SMI, weight-loss interventions through diet, exercise, and behavioral treatments have been used to counteract the effects of the antipsychotic medication-induced weight gain. Short-term studies of 3–12 mo of primarily dietary and behavioral modification interventions have shown significant decreases in body weight in patients with SMI despite the use of antipsychotic agents [11–22]. Moreover, these studies have found significant improvements in the metabolic profiles of the patients as demonstrated by decreases in blood glucose and insulin resistance and improvements in dyslipidemia [15].

Gender differences have been found in the response to weight-loss interventions in healthy overweight and obese populations [23,24]. In particular, research studies have exhibited differences in the storage of body fat and its lipolysis between men and women. Healthy overweight men tend to store more body fat in the abdominal region compared with women who tend to store more fat in the gluteofemoral region [23,24]. In terms of lipolysis, men appear to lose fat from the abdominal and gluteofemoral regions, whereas women appear to be resistant to fat lipolysis in the gluteofemoral region [23,24]. In patients with SMI there is a paucity of research on possible gender differences. Only one study by Littrell et al. [18] has found that men with SMI tend to gain more weight than women in a 16-wk behavioral treatment program while using antipsychotic medications. No studies to our knowledge have been reported investigating possible gender differences in patients with SMI in response to weight-loss regimens.

Given the small number of weight-loss studies, the lack of randomized control models used, and the lack of more scientific outcome measurements of weight loss such as body fat, the effect of weight loss interventions in these individuals is still under investigation and there is a paucity of research data and clinical applications on weight control in the treatment of patients with SMI. The primary purpose of the present study was to investigate the effects of a 3-mo dietary intervention program on body weight and body composition (body fat and fat-free mass) on individuals with SMI in comparison with healthy individuals with similar anthropometric characteristics. Furthermore, we sought to investigate whether gender differences exist in patients with SMI in their response to a weight-loss intervention.

Materials and methods

Subjects

A total 204 subjects (63 healthy controls and 141 patients with SMI) were recruited for the study. Subjects were recommended to participate in the study by the clinical psychologists in the Iaso Hospital (Athens, Greece), by private psychiatry offices located in Athens, and from advertisements in the local newspapers. Patients enrolled in the study through advertisements in the newspapers were not compensated for their participation in any way. The study was carried out from January 2005 to September 2007.

Patients with SMI. Of the patients with SMI ($n = 141$) who volunteered for the study, 82 subjects (60 women, 22 men) with *Diagnostic and Statistical Manual of Menta Disorders, Fourth Edition*, mood or psychotic disorder diagnoses completed the study. All patients with SMI were found competent by a psychiatrist to participate in the research study and to follow the weight-loss intervention at the enrollment visit. All subjects were taking the antipsychotic medication olanzapine for a minimum of 1 y at a stable mean dosage of 8.96 ± 0.2 mg/d. The patients with SMI participating in the study were required to be 18 to 55 y of age and have a minimum body mass index (BMI) of 30 kg/m^2. Fifty-nine patients with SMI dropped out of the study during the first 3 mo of the intervention. Reasons for dropping out of the study included an inability or unwillingness to continue with the prescribed nutritional intervention, change of antipsychotic medications, family problems, health problems, and difficulties with transportation or scheduling.

Healthy/control subjects. Of the healthy subjects ($n = 63$) who volunteered for the study, 58 participants (46 women, 12 men) with no psychiatric or psychological problems completed the study. All healthy subjects were required to be 18 to 55 y of age and have a minimum BMI of 30 kg/m^2. All healthy participants underwent an interview with a certified clinical psychologist to certify that they did not have any mental health problems in the previous 1 y. Five healthy subjects dropped out from the study during the first 3 mo of the intervention primarily due to an inability or unwillingness to continue with the prescribed nutritional intervention.

Nutritional intervention

The intervention period lasted for 3 mo. It consisted of two phases: 1) an evaluation phase and 2) an intensive 3-mo dietary intervention period with sessions taking place every 15 d. Before the beginning of the intervention, each subject participated in a complete screening session to collect information and assess the subject's health profile, lifestyle and eating habits, physical activity, food preferences, and food likes and dislikes. Based on the screening session, an individualized food plan was designed and was prescribed to the subject by a registered dietitian. The individualized food plan was a reduced-energy diet that followed the Mediterranean diet. In particular, the prescribed food plan was based on the consumption of large amounts of fruits, vegetables, cereals, fish (particularly fish with a high content of ω-3 fatty acids), and nuts and seeds with a high-content of

α-linolenic acid. The intake of meat, cured meat, sausage, etc., was replaced by poultry, fish, or vegetarian dishes. Olive oil was the main source of dietary fat. The prescribed diet was characterized by a moderate consumption of carbohydrates (55% of total energy per day) and a high-fiber content, approximately 15% protein, and the intake of fat was ~28–30% of total energy per day, designed to promote weight loss at a rate of 0.5–1 kg/wk. The Harris-Benedict equation multiplied by an activity factor of 1.3–1.5 according to the activity level of the patient was used to estimate energy requirements. Weekly food diaries were given to all subjects to assess adherence to the diet and were collected at each session by the dietitians.

The intervention program consisted primarily of dietary counseling, exercise counseling, and behavioral interventions with the scope of assisting the patient's adherence to a healthy life plan during the intervention period. Sessions consisted of one-to-one counseling, primarily on nutritional issues, and teaching of basic nutritional principles. Topics that were covered included healthy eating menus and recipes, weight-management techniques, cooking techniques, grocery shopping, etc. Counseling on basic exercise principles was also offered to the subjects with the aim of increasing the subjects' physical activity levels. Subjects were instructed to participate in light- to moderate-intensity endurance exercise such as walking, bicycling, or swimming on a daily basis for a minimum of 30 min and a maximum of 45 min. They were also asked to keep a daily exercise log with the exercise duration, frequency, and intensity. At the end of the study, the logs were collected by the researchers.

Outcome measurements

At the beginning of the study (baseline) and at 3 mo of the intervention period, a number of experimental tests were performed on the participants to assess the efficacy of the nutritional intervention program.

At visit 1, subjects participated in a screening evaluation for eating habits, dietary preferences, etc. Anthropometric measurements of body weight, height, and waist circumferences were performed. Body weight was measured without shoes on a standing scale that was calibrated to 0.1 kg. Body height was measured without shoes on a wall-mounted stadiometer. Waist circumference was measured at the narrowest part of a subject's waist. In addition, measurement of body composition (body fat and fat-free mass) was performed on each patient with the use of the BodPod (Life Measurement Inc., Concord, CA, USA) according to the manufacturer's instructions.

During the 3-mo period, subjects were asked to visit the hospital every 15 d. During these visits, measurements of body weight, height, waist circumferences, body fat, and fat-free mass were performed by the same trained technician. Individual counseling was also performed with the scope of improving the participants' eating behavior, increase diet and exercise compliance, lifestyle modification, etc.

Statistical analysis

An independent t test was used to compare the demographic characteristics of the two subject groups (healthy controls versus patients with SMI) and the two genders. A 2×2 analysis of variance with repeated measures was used to assess the changes in the dependent variables between the two groups (healthy controls versus patients with SMI) over time (baseline to 3 mo). An independent t test was used to compare the mean absolute changes in body weight, fat mass, fat-free mass, and waist circumference between genders among patients with SMI. The threshold for significance in all tests was set at $P = 0.05$. Statistical analysis was performed with SPSS 11 for Windows (SPSS, Inc., Chicago, IL, USA). All values are presented as mean ± standard error of the mean.

Statement of ethics

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research study. Institutional review board approval for the study was obtained by the ethical committee of the Iaso Hospital. Before enrollment in the study, all subjects signed an informed consent form for participation in the study and possible side effects were fully explained to them.

Results

Subject characteristics and baseline status

Patients with SMI. Of the 141 patients who initially volunteered to participate in the study, 59 patients with SMI dropped out of the study during the 3 mo of the intervention period and 82 patients with SMI completed the study. Reasons for dropping out were an inability or unwillingness to continue with the prescribed nutritional intervention, difficulties with transportation or scheduling, change of antipsychotic medications, family problems, and health problems. From this dropout sample, 39 subjects were women and 20 were men; their average age was 43 ± 1.5 y, average body weight was 91.3 ± 3.1 kg, and average BMI was 33.8 ± 0.03 kg/m^2. No significant differences were found in the anthropometric characteristics of the dropouts compared with the rest of the subjects ($P > 0.05$).

Healthy/control subjects. Only five healthy subjects dropped out from the control group during the first 3 mo of the intervention primarily due to an inability or unwillingness to continue with the prescribed nutritional intervention.

Table 1 lists subjects' characteristics at baseline. No significant difference was found between the SMI group and the healthy/control group with respect to age, height, body weight, BMI, fat mass, and waist circumference. At baseline

Table 1
Baseline and demographic characteristics of subjects with SMI and healthy controls

Variable	SMI group (n = 82)	Control group (n = 58)	P
Gender			
Male	22	12	
Female	60	46	
Age (y)	36.13 ± 1.45	37.48 ± 1.85	0.562
Height (cm)	1.69 ± 0.01	1.66 ± 0.01	0.710
Weight (kg)	94.61 ± 2.50	92.26 ± 3.17	0.557
BMI (kg/m^2)	33.12 ± 0.74	33.32 ± 0.94	0.868
Fat mass (kg)	40.06 ± 1.69	42.01 ± 1.98	0.056
Fat-free mass (kg)	54.56 ± 1.53	50.25 ± 1.55	0.043*
Waist circumference (cm)	104.91 ± 1.02	100.96 ± 2.74	0.242

BMI, body mass index; SMI, severe mental illness
* Significant difference between healthy controls and patients with SMI, $P < 0.05$.

all patients with SMI were considered obese (BMI >30 kg/m^2) with an average body weight of 94.61 ± 2.50 kg and a BMI of 33.12 ± 0.74 kg/m^2. The same was the case for the control group that had an average body weight of 92.26 ± 3.17 kg and a BMI of 33.32 ± 0.94 kg/m^2. However, a significant difference was found between the fat-free mass of the patients with SMI and the healthy controls, with the patients with SMI having significantly greater fat-free mass ($P <$ 0.05).

Impact of nutritional intervention on anthropometry and body composition

Table 2 presents the absolute change in anthropometric and body composition variables from baseline to 3 mo of the intervention for the patients with SMI and their healthy control counterparts. The nutritional intervention produced significant decreases in body weight, BMI, fat mass, and waist circumference between baseline and the 3-mo intervention period. No significant differences were found in response to the weight-loss intervention between patients with SMI and their healthy counterparts (Fig. 1) in any anthropometric parameter, with the exception of waist circumference, where the healthy controls exhibited a significantly greater decrease in waist compared with the patients with SMI ($P < 0.05$).

Gender differences in SMI and control groups at baseline and in response to nutritional intervention

At baseline a significant difference was found between genders in anthropometric variables and body composition in the SMI and control groups. In particular, men were found to have significantly greater height, body weight, percent fat-free mass, and waist circumference and significantly less fat mass compared with women ($P < 0.05$).

After correcting for the baseline differences in anthropometry and body composition, we found a significant difference between genders in their response to the nutritional intervention in the SMI group (Table 3). More specifically, men were found to have lost significantly greater body weight ($P < 0.05$) and waist circumference ($P < 0.02$) compared with women. In the control group, gender differences were also found from baseline to 3 mo of the intervention, with men exhibiting greater changes in body weight ($P < 0.01$), fat mass ($P < 0.05$), and waist circumference ($P < 0.001$; Table 3).

Discussion

This is the first study, to our knowledge, that has investigated the effects of a nutritional intervention on the body composition and specifically fat mass and fat-free mass of male and female obese patients with SMI taking olanzapine. Our study demonstrates that a personalized nutritional intervention is effective in decreasing not only the body weight of this population but also fat mass and waist circumference, parameters that are closely associated to a number of chronic diseases. Furthermore, this is the first study that has demonstrated possible gender differences in response to a weight-loss regimen in a population of patients with SMI.

The present study demonstrates for the first time the effectiveness of a nutritional intervention program on changes not just in body weight but also in fat mass in male and female patients with SMI. We found a 6% loss in body weight of our patients in the 3 mo of our study. This finding is similar to the weight loss seen in previous studies but in a longer period such as 6–12 mo [13,20,21]. Possible reasons for the faster weight loss in our nutritional program are the personalized design of our nutritional regimens and the one-to-one counseling of the patients in nutrition, exercise, and motivation topics. In terms of fat loss, a parameter that provides

Table 2
Absolute change in anthropometric variables in patients with SMI and healthy controls between baseline and 3 mo of the weight-loss intervention program

Variable	Patients with SMI (n = 82)	Healthy controls (n = 58)
Weight change (kg)	−5.90 ± 0.07*	−7.42 ± 0.25*
BMI change (kg/m^2)	−2.10 ± 0.01*	−2.67 ± 0.05*
Fat mass change (kg)	−5.24 ± 0.04*	−6.78 ± 0.16*
Fat change (%)	−3.09 ± 0.20*	−4.00 ± 0.21*
Fat-free mass change (kg)	+0.68 ± 0.06	+1.38 ± 0.37
Fat-free mass change (%)	+3.09 ± 0.09	+4.00 ± 0.28
Waist circumference change (cm)	−5.59 ± 0.92†	−7.04 ± 0.23*

BMI, body mass index; SMI, severe mental illness
* Significant change from baseline, $P < 0.05$.
† Significant difference in change from baseline between healthy controls and patients with SMI, $P < 0.05$.

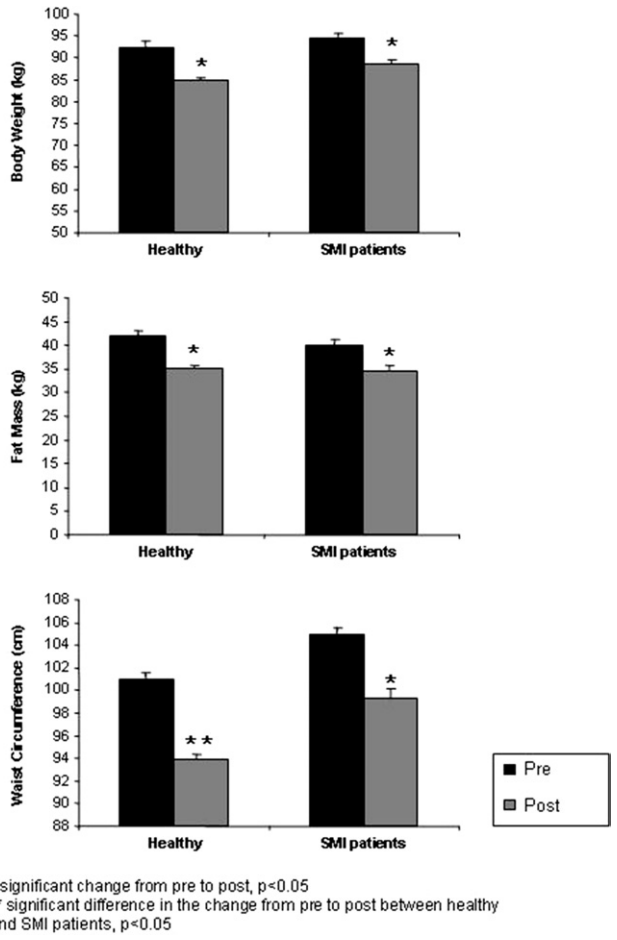

Fig. 1. Change in body weight, fat mass, and waist circumference in patients with SMI versus healthy controls from before (black bars) to 3 mo after (gray bars) the nutritional intervention program. *Significant change from before to after, $P < 0.05$; **significant difference in change from before to after between healthy control subjects and patients with SMI, $P < 0.05$. SMI, severe mental illness.

more scientific and detailed information on the effects of a nutritional intervention, we found significant decreases in fat mass by 13% as a result of the 3-mo nutritional intervention. A decrease of this magnitude in body fat is considered an important improvement in the body composition and overall health of our patients because such improvements in body fat are associated with improvements in metabolic and cardiovascular complications [1]. Associated to the improvements seen in body fat mass, there were significant decreases in the waist circumference of our patients. The measurement of waist circumference is an index of abdominal fat depots, a parameter that is significantly associated to chronic diseases seen in patients with SMI such as insulin resistance, glucose intolerance, and type 2 diabetes, in addition to cardiovascular disease [4,5–7]. Thus, the changes observed in waist circumference in conjunction with the related changes seen in fat mass in our patients with SMI may suggest improvements in the risk factors associated to metabolic and cardiovascular disturbances. We found no significant changes in the fat-free mass (muscle mass) of our patients with SMI after the 3-mo intervention. The lack of changes in fat-free mass is possibly attributed to the lack of structured exercise that can stimulate muscle hypertrophy. In contrast, the maintenance of fat-free mass in our patients with SMI is an advantageous response to the nutritional intervention because most research studies that involve primarily dietary regimens and not structured exercise result in decreases in fat-free mass that in turn can lead to a decrease in the energy expenditure of the patients and to a plateau in weight loss. It is possible that the maintenance of fat-free mass is partly attributed to the regular physical activity, primarily in the form of walking, that our patients were instructed to follow during the intervention.

The changes in anthropometric and body composition variables seen in our patients with SMI were analogous to the changes observed in our healthy controls, despite the use of olanzapine by our patients, a medication that is known to induce weight gain [4,5–7]. However, waist circumference, a key parameter in metabolic and cardiovascular abnormalities due to its close association to abdominal visceral fat deposition, was found to be not as effectively decreased in the patients with SMI compared with the healthy controls. The attenuated change in waist circumference seen in the

Table 3
Absolute change in anthropometric variables in male and female patients with SMI in response to the 3-mo nutritional intervention at 3 mo

Variable	Patients with SMI		Healthy controls	
	Male ($n = 22$)	Female ($n = 60$)	Male ($n = 12$)	Female ($n = 46$)
Weight change (kg)	−8.33 ± 1.48	−4.72 ± 0.79*	−11.41 ± 1.58	−6.49 ± 0.60*
BMI change (kg/m^2)	−2.68 ± 0.47	−1.82 ± 0.29	−3.58 ± 0.45	−2.42 ± 0.23
Fat mass change (kg)	−6.91 ± 1.20	−4.41 ± 0.87	−10.11 ± 1.43	−6.02 ± 0.55*
Fat change (%)	−4.10 ± 0.81	−2.94 ± 0.35	−4.45 ± 0.59	−4.08 ± 0.45
Fat-free mass change (kg)	+1.42 ± 0.43	−0.31 ± 0.38	−1.30 ± 0.36	−0.46 ± 0.30
Fat-free mass change (%)	+4.10 ± 0.76	+2.94 ± 0.28	+4.45 ± 1.43	+4.08 ± 0.55
Waist circumference change (cm)	−7.90 ± 1.37	−4.46 ± 0.71*	−11.41 ± 1.47	−6.23 ± 0.53*

BMI, body mass index; SMI, severe mental illness
* Significant difference between genders, $P < 0.05$.

SMI group could be attributed to a number of factors and primarily the use of olanzapine. Antipsychotic medications have been associated with weight gain since their introduction in the 1950s [4]. However, no studies to our knowledge have investigated the association between these medications and abdominal fat deposition in patients with SMI; hence, it is difficult to speculate on the possible reasons for this adverse phenomenon. More research is needed to investigate such an association because it plays an important role in the metabolic and cardiovascular health of this population.

An important preliminary finding of this study is that gender differences appear to exist in response to a nutritional intervention in patients with SMI. We found greater improvements in body weight and waist circumference in the male subjects with SMI compared with the female subjects. These results are in accordance with the changes seen in our healthy controls, where men also were found to exhibit greater improvements in body weight, body fat, and waist circumference compared with women. The findings of our study are in agreement with only one previous study, where after 10 wk of the Weight Watchers Program, only men were found to lose significant body weight [11]. No other studies, to the best of our knowledge, have investigated possible gender differences in patients with SMI in response to a weight-loss regimen. We hypothesize that these differences in weight loss are due primarily to the greater fat-free mass of the men (by 30%) that could have resulted in a greater energy expenditure and thus greater weight loss compared with the women. In terms of body fat storage and fat lipolysis, in healthy populations men have been shown to have greater abdominal fat depots compared with women who tend to store fat primarily in the gluteofemoral region [23,24]. The greater abdominal fat storage of men could have resulted in a greater fat lipolysis in that region, and that could potentially explain the greater decrease in waist circumference in male compared with female patients with SMI. Future randomized controlled studies are needed to further investigate the possibility of gender differences in this population.

Although the findings of this study are important, it is not without limitations. In our study we had a high dropout rate of 30% in our patients with SMI and healthy subjects. Reasons for dropping out were primarily an inability to attend nutritional sessions and to follow the nutritional intervention. This is, however, similar to previous SMI weight-loss studies, where high dropout rates have also been reported [17,19]. This is certainly a factor that needs to be taken into account in future studies and stresses the importance of compliance techniques to be developed for this population. In the present study, there was no control SMI group. Because this was not a clinical trial, it was unethical for the hospital not to treat patients with SMI and keep them in a control group. For this reason, we used the subjects' baseline data as a control factor.

Conclusion

Weight loss and improvements in fat mass and waist circumference are possible in obese patients with SMI taking olanzapine. When prescribing a nutritional program, it is possible that we need to take into account the patients' gender because our preliminary findings demonstrate possible gender differences in weight loss in this population.

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