Effect of lifestyle modification on schizophrenia patients on antipsychotics

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Background
Schizophrenia affects physical health, represented in the form of change in behavior, such as decrease in physical activity, tendency to isolation, and changes in eating behavior, including increase intake of food (junk food and fat) and increase in consumption of sugar. Patients with schizophrenia tent to increase consumption of cigarettes and caffeine. All of these contribute toward having a bad effect on physical health, as they increased the risk of occurrence of comorbid diseases, such as hypertension, diabetes mellitus, and metabolic syndrome (MetS). Although there is treatment for schizophrenia, it has serious adverse effects, including sleepiness and slowness, weight gain, interference with sex life, and increased chance of developing diabetes and hypertension.

Patients and methods
A total of 36 patients underwent programmed lifestyle modification, which include pharmacological intervention and lifestyle interventions, including psychoeducational, dietary, and exercise programs. The psychoeducational program focused on the roles of eating and activity in weight management. Dietary program included individualized well-balanced diet plan for each patient by a clinical nutritionist in the hospital according to patient's measurements, physical health, and acceptance. Exercise program included aerobic exercise intervention and stretching-toning control program, which was planned by the physical trainer of the hospital in the playground. Assessment is done at the beginning of the study and monthly through 3-month duration. We used Positive and Negative Syndrome Scale to assess and follow-up symptoms of schizophrenia, GASS for follow-up of adverse effects of antipsychotics, and Health Promoting Lifestyle Profile Scale II to detect the effect of lifestyle modification.

Results
The mean age of the studied group of patients was 34.5±5.87 years, with 56.41% of them being male. Overall, 25% of patients were found to have MetS at the beginning of the study, and after 3 months of commitment to the program of lifestyle modification, they decreased to 16.67%. There was a significant difference between the studied participants regarding metabolic parameters throughout the 3 months. There was significant improvement in all other dimensions of Positive and Negative Syndrome Scale and significant improvement in total GASS scale after the second months of commitment of lifestyle modification, with significant improvement in all dimension except for cardiovascular and screening for diabetes.

Conclusion
Schizophrenia and antipsychotics have an effect on lifestyle of the patients, leading to more exposure of them to medical comorbidities such as hypertension, diabetes mellitus, and MetS, and it also effects the sedentary life, diet, and smoking. This can be avoided by applying a lifestyle modification program that targets to improve quality of life, symptoms of schizophrenia, and decreased number of relapses by increasing adherence to treatment.

Keywords:
lifestyle modification, metabolic syndrome, schizophrenia

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Introduction

Schizophrenia is a serious disorder that affects how a person thinks, feels, and acts. Patient with schizophrenia may have difficulty distinguishing between what is real and what is imaginary; may be unresponsive or withdrawn; and may have difficulty expressing normal emotions in social situations. Schizophrenia affects men and women equally but has an earlier onset in males (Tandon *et al.*, 2013).

Antipsychotic medications are prescribed to treat schizophrenia and to reduce the symptoms associated with psychotic conditions such as bipolar, psychotic depression, senile psychosis, various organic psychosis, and drug-induced psychosis (Wu *et al.*, 2015).

For the past 10 years or so, doctors have talked about two different groups of antipsychotics: typical (the older drugs) and atypical (the newer drugs). Those groups showed a wide range of different adverse effects, including sleepiness, slowness, weight gain, interference with sex life, and increased chance of developing diabetes and hypertension (Hynes *et al.*, 2015).

People with schizophrenia have a reduced life expectancy compared with the general population, primarily because of premature cardiovascular disease (Laursen *et al.*, 2007; Bobes *et al.*, 2010). This condition may be explained in terms of a high rate of metabolic syndrome (MetS) in these patients (Arango *et al.*, 2008), which carries with it a series of risk factors for cardiovascular disease, such as central obesity, atherogenic dyslipidemia, hypertension, and impaired insulin and glucose metabolism.

Two studies (Brown *et al.*, 1999; McCreadie, 2003) have compared the lifestyle of people with schizophrenia living in the community with that of low social class cohorts from existing general population studies of lifestyle habits. In both studies, people with schizophrenia made significantly poorer dietary choices, took less exercise, and smoked more heavily than the comparator groups in the general population. McCreadie (2003) also found that women with schizophrenia were significantly more likely to be overweight or obese than women in the general population (a result not found by Brown *et al.*, 1999).

The study by Heald *et al.* (2017), stated that the high prevalence of poor diet, inadequate exercise, and obesity among patients with schizophrenia may contribute to core psychiatric symptoms, including avolition and tiredness.

Lifestyle modification is a long and variable process. Many studies have recently started to redirect their resources to see the effect of different types of modification on chronic mental illness.

Patients and methods

This was an interventional study, with a 3-month follow-up from February 2019 till July 2019. It had been carried out at Al-Abbassia Hospital for Mental Health in Cairo. Informed consent was obtained from all participants and their care giver. The procedureswere approved by the local ethical committee. The estimated sample was 36 patients. The sample was selected randomly from the patients admitted at Al-Abbassia Hospital for Mental Health, Egypt, and continued their follow-up after discharge. All participants were screened to determine eligibility for participation in the study according to the specified inclusion and exclusion criteria. Inclusion criteria included the following: (a) age 18–60 years, (b) both sexes, (c) all patients should meet diagnostic statistical manual of mental disorder version 5 (DSM-5) criteria for schizophrenia, and (d) all participants must be under the care of adult caregiver (nurses–family members) who monitored and recorded food intake, exercise activity, and medication intake each day of the trial to monitor compliance. Exclusion criteria were as follows: (a) patients who have received a psychiatric diagnosis other than schizophrenia; (b) if during the screening they have evidence of liver or renal dysfunction, severe cardio vascular disease (CVD) causing dysfunction, or diabetes mellitus complications, as well as patients who are pregnant or lactating or had conditions that limited their ability to perform the lifestyle modifications, such as arthritis, pulmonary disease, or neurological or dietary restrictions; and (c) patients who have previous history of substance abuse in 1-year duration. Participants were subjected to history taking through a semistructured questionnaire. Laboratory and clinical screening of MetS (waist circumference, blood pressure, triglyceride, high-density lipoprotein, and fasting blood glucose) was done. Different assessment scales, including Positive and Negative Syndrome Scale (PANSS), Glasgow Antipsychotic Side-effect Scale, Health Promoting Lifestyle Profile Scale II, eating scale, and Morisky scale, were used. History of present illness and patient's experience of symptoms were also noted. All patients were thoroughly screened and diagnosed for schizophrenia using DSM-5 diagnostic criteria. Participants were subjected to a semistructured questionnaire which was specially designed to collect the following: sociodemographic data, including name, age, sex, education, occupation, residence, and marital state, as well as clinical data, including age of onset of the disease, duration of illness, family history, number of hospitalizations, number of episodes, duration of episode, impairment, compliance, and smoking (duration and severity). History of medical or surgical diseases, and history of psychiatric or neurological disorders were collected. Obstetric/gynecological

history, last menstrual period, and exclusion of pregnancy was done. Measurements of the weight, height, waist circumference, and BMI [weight (kg)/ height (m^2)] were done and were compared with patients' usual weight, and vital signs (pulse, blood pressure, and temperature) were assessed. Weight was recorded on the same scale without shoes, with the individuals wearing light clothes. Waist was considered at the level of the navel. Blood pressure was measured twice, and the mean of both measures was considered. Measures were collected by the same investigator in all assessments. ECG was done to exclude any cardiac disease. Thyroid function test was done for exclusion of thyroid diseases. Liver function test (alanine aminotransferase, aspartate aminotransferase, serum albumin, total bilirubin) was done to exclude any liver diseases that could be affected by antipsychotic medication. Kidney function tests (urea and creatinine) were performed. Complete blood count was done for detection of any adverse effects such as agranulocytosis owing to clozapine. Screening for MetS was done according to the new International Diabetes Federation (IDF) definition; for a person to be defined as having the MetS, they must have the following: central obesity (defined as waist circumference with ethnicity-specific values), and any two of the following four factors.

Pharmacological intervention

Appropriate antipsychotics were prescribed according to each patient's condition regarding attitudes, behaviors, comorbidities, severity of signs and symptoms, demographic and environmental factors, and the cognitive functioning of patients (García *et al.*, 2016). Used doses were calculated to be haloperidol equivalent dose, as we used olanzapine 10 mg, aripiprazole 20 mg, haloperidol 10 mg, risperidone 4 mg, and quetiapine 400 mg (Leucht *et al.*, 2014). Doses of antipsychotics were fixed during the period of 3 months (risperidone 4 mg/day, olanzapine 10–15 mg/day, aripiprazole 5–15 mg/day, haloperidol 5–10 mg/day, quetiapine 100–200 mg/day, benztropine 2–3 mg/day, and haloperidol depot twice/month). The medication adherence was assessed by Morisky scale (Castellucci *et al.*, 2015).

Lifestyle intervention

The lifestyle interventions included psychoeducational, dietary, and exercise programs (Table 1). The psychoeducational program included information offered to patients regarding their medication and illness in a manner that can enhance medication adherence and promote relapse prevention and focused on the roles of eating and activity in weight management. Topics included healthful weight management techniques, such as benefits of nutrition, physical fitness, and available behavioral techniques. It was administered to patients in lifestyle groups at baseline and at weeks 4, 8, and 12.

Table 1 The psychoeducational program includes

List of topics	Speaker	Duration (min)
Schizophrenia (causes and symptoms)	Psychiatrist	30–40
Medication (importance to adherence)	Psychiatrist	30–40
Adverse effects of medication	Psychiatrist	30–40
Lifestyle modification	Psychiatrist and physician	30–40
Dietary program	Nutritionist	30–40
Exercise program	Physical trainer	30–40
Comorbid disease	Physician	30–40
Smoking sessions	Physician	30–40
Follow up sessions	Nurses	30–40 min every 4 weeks

Dietary program

Individualized well-balanced diet plan for each patient was done by the clinical nutritionist in the hospital according to patient's measurements, physical health, and acceptance. Each diet plan was suitable to each patient according to their conditions, and daily follow-up of the diet was done by nurses and care givers.

Exercise program

Aerobic exercise intervention and stretching-toning control program was planned by the physical trainer of the hospital in the playground. The intensity of aerobic exercise intervention was based on each individual's age-adjusted maximum heart rate (maximum heart rate: 220-age). Moderate exercise for 2.5 h/week should help heart stay healthy. The patient was doing moderate exercise if his/her heart rate was 50–70% of your maximum heart rate. This means that a 20-year-old individual with a maximum heart rate of 200 beat/min should have a target heart rate of 100–140 beat/min during moderate exercise. Doing vigorous exercise for 75 min/week or more will improve heart's health. On doing vigorous exercise, heart rate is 70–85% of your maximum heart rate. For a 20-year-old individual, this would be 140–170 beat/min during vigorous exercise. Each aerobic exercise session included 5 min of walking for a warm-up, followed by 30 min of aerobic exercise, then finally a 5-min cool-down period, that is, 40 min in total. To ensure that participants were exercising safely at their target intensity, hear rate monitors were used to monitor exercise intensity throughout the 12-week training program under one-to-one supervision (Wang *et al.*, 2018). The stretching and toning

control program consisted of a 30-min recorded program of 14 exercise routines, including a 3-min warm-up, 25-min flexibility, toning, and balance exercises designed to use all major muscle groups of the upper and lower extremities, and a 2-min cool-down exercise performed to music. The supervisor gave every participant one-to-one monitoring through every session to maintain fidelity. The attendance goal for both programs was five times per week. Participants of both groups were scheduled to contact the trainer three times per week for 3 months to ensure that their rate of attendance exceeded 60%. Thus, all participants completed at least 36 sessions (Wang *et al.*, 2018). Patients were interviewed by the psychiatrist at baseline and every 4 weeks thereafter (at beginning, after 1 month, after 2 months, and after 3 months). The interviewer asked questions pertaining to all included scales and encouraged participants to discuss their history, circumstances surrounding their hospitalization, their current life situation, and their symptoms. The objective of this process is to establish rapport and allow participants to express areas of concern. During each clinical interview, patient's affective, motor, behavioral, and cognitive functions were observed. Their ability to participate by empowering them through their creative expressions and their integrative and interactive functions were also directly observed by the interviewers. The duration of each clinical interview was 45–60 min. Each rating was assigned by first referring to the item definition to determine presence of a symptom. The severity of an item is then determined by deciding which anchoring point best described the participant's functioning, whether or not all components of the description are observed. Each patient was followed with a monthly card on which PANSS, Glasgow Antipsychotic Side-effect Scale (Health Promoting Lifestyle Profile Scale II) and Eating Scale were recorded. This card was used in each follow-up to record any change in previous data throughout the study.

Statistical analysis

All data were analyzed using SPSS 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA) and MedCalc 13 for Windows (MedCalc Software bvba, Ostend, Belgium). Continuous variables were expressed as the mean±SD and median (range), and the categorical variables were expressed as a number (percentage).

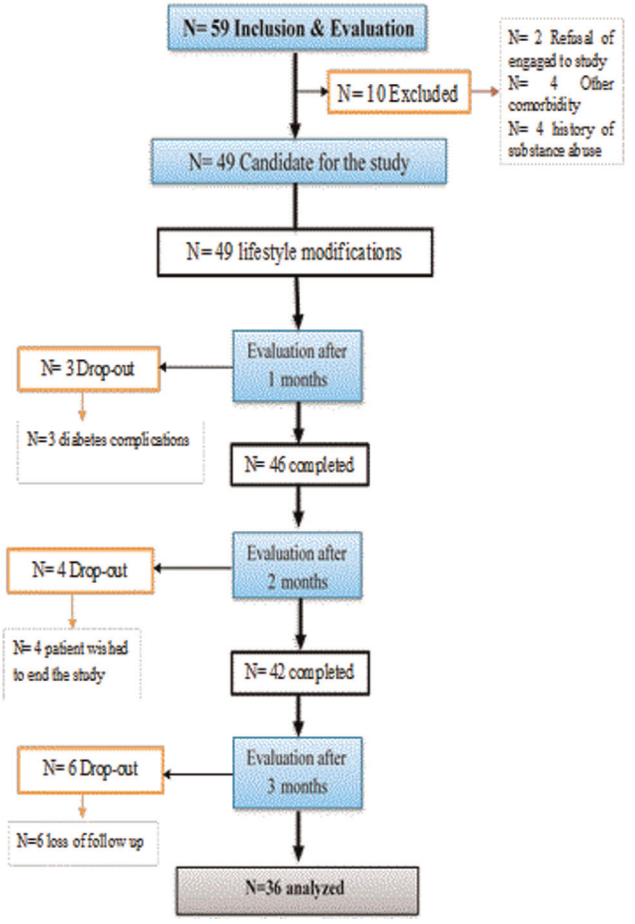
Continuous variables were checked for normality by using Shapiro–Wilk test. Independent sample Student's *t* test was used to compare two groups of normally distributed data, whereas Mann–Whitney *U* test was used for non-normally distributed data. One-way analysis of variance test was used to compare more than two measurements of non-normally distributed data.

All tests were two sided. *P* value less than 0.05 was considered statistically significant (S), *P* value less than 0.01 was considered highly statistically significant (HS), and *P* value more than or equal to 0.05 was considered non-statistically significant (NS).

Results

The study showed after 3 months of follow up a number of dropouts, as shown in Fig. 1.

Figure 1



Drop-out was inevitable during the study as from 56 patients included and evaluated throughout the study about 10 patients were excluded before the start of intervention. Two of them refused to engage to the study, four had comorbid orthopedic and rheumatic complications that interfere with our program, and four had previous history of substance abuse in the year prior to the study. When patients were reevaluated after one month from the beginning of the study, we discovered that three patients had diabetic complications in the form of autonomic neuropathy which posed a potential risk arrhythmia development. At the end of the second month, 46 patients were reevaluated however 4 patients wished to end the study and wanted to be discharged from hospital. After 3 months, we lost contact with 6 patients after being discharged and didn't come for reevaluation. Thirty-six patients completed the study for three months without any dropping out and the results of those patients only were entered the statistical analysis.

There were changes in anthropometric measures and blood pressure throughout the study (Tables 1 and 2 and Fig. 2).

Discussion

People with schizophrenia experience increased morbidity and mortality compared with the general population, having a life expectancy that is ~20% shorter. The excess mortality is largely owing to CVD. Furthermore, people with schizophrenia and other severe and enduring mental illnesses are twice as likely to die owing to CVD compared with those in the general population, and the excess mortality is higher in younger individuals (Reininghaus *et al.*, 2014). The known risk factors for CVD include smoking, being overweight, insufficient physical activity, and low intake of fruits and vegetables. These risk factors are more common in people with schizophrenia than in the general population (Holt *et al.*, 2010).

We hypothesized that if we modify lifestyle of patients with schizophrenia, it will affect their physical health, reduce adverse effects of medication, and improve their compliance on treatment.

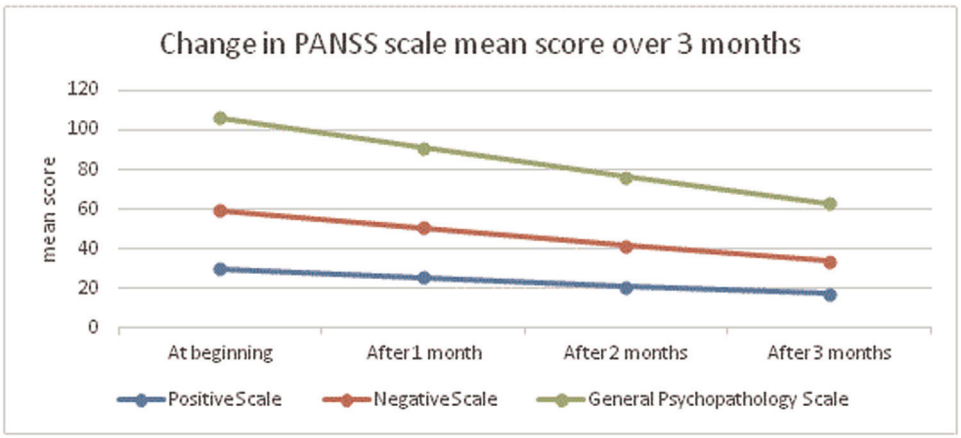
Drop-out was not evitable as shown in Table 1 during the study, as from 56 patients included and evaluated throughout the study, ~10 patients were excluded before the start of intervention. Two of them refused to engage to the study, four had comorbid orthopedic and rheumatic that interfere with our

Table 2 Significant change in the lipid profile and blood glucose levels among our patients throughout the 3 months

At beginning (*N*=36)	After 1 month (*N*=36)	After 2 months (*N*=36)	After 3 months (*N*=36)	Test*	*P* value (significance)
Mean±SD Median (range)	Mean±SD Median (range)	Mean±SD Median (range)	Mean±SD Median (range)		
Triglyceride (normal <150 mg/ dl)					
161.8±40.1	158.46±31.69	141.85±30.88	130.62±27.16	0.75	0.04 (significance)
158 (120–210)	122 (115–185)	130 (109–176)	140 (89–160)		
Cholesterol (normal <200 mg/dl)					
234.1±53.9	215.2±45.2	186.4±43	163.8±39	0.81	0.035 (significance)
189 (120–290)	166 (120–260)	155 (98–245)	164 (100–210)		
LDL (normal <130 mg/dl)					
135.77±23.1	129.54±21.4	118±19.01	113.23±15.64	0.89	0.025 (significance)
121 (110–160)	112 (79–146)	113 (82–140)	109 (80–130)		
HDL (normal >40 mg/dl)					
23.15±15.74	28.23±15.67	32.54±13.58	43.08±13.9	0.75	0.04 (significance)
290 (20–40)	32 (22–48)	33 (29–53)	45 (30–69)		
Fasting blood glucose (normal <100 mg/dl)					
130.08±25.68	124.45±19.02	122.92±27.15	117.25±13.41	0.94	0.012 (significance)
123 (98–180)	128 (113–145)	119 (97–156)	115 (109–138)		

HDL, high-density lipoprotein; LDL, low-density lipoprotein. *$P<0.05$ was considered statistically significant (S), $P<0.01$ was considered highly statistically significant (HS), and $P\geq0.05$ was considered non-statistically significant (NS).

Figure 2



Positive and Negative Syndrome Scale (PANSS) of all patients throughout the 3-month study period.

program, and another four had previous history of substance abuse in the last year. When patients were reevaluated after 1 month of study, we found out that 3 patients with diabetic complications (autonomic neuropathy) had potential risk for them to have arrhythmia. At the end of the second month, 46 patients were reevaluated; however, four patients wished to end the study and wanted to be discharged from the hospital. After 3 months, we lost contact with six patients after being discharged, and they did not come for reevaluation. A total of 36 patients completed the study for 3 months without any dropping out, and the results of those patients only were entered in the statistical analysis.

Our study focused only on patients who had been diagnosed as having schizophrenia without any comorbid mental illness. Regarding age distribution in our patients, the age ranged between 36 and 45 years old, and the number of males was 22 and females was 14. The level of education of majority was middle studies in 41.66%, ~55.55% were married, 38.8% were employee, and 83.3% lived in urban area. The history of present illness was less than 5 years in 36.1% of patients, whereas 33.3% of them experienced schizophrenia for 5–10 years of duration. Approximately 77.7% of our patients were smokers, 91.6% had high caloric diet, and 86.1% showed low physical activity.

Our findings were based on the study by Heald *et al.* (2017), which stated that the high prevalence of poor diet, inadequate exercise, and obesity among patients with schizophrenia may contribute to core psychiatric symptoms including avolition and tiredness

Deenik *et al.* (2019), found that an integrated multi-component and multidisciplinary lifestyle enhancing treatment can improve PA and metabolic health substantially compared with treatment as usual. No changes in positive psychotic symptoms were observed, but there was a decrease in negative symptoms in patients receiving MULTI, indicated by blunted affect passive/apathetic social withdrawal and lack of spontaneity and flow of conversation. This may have happened because of the different approaches we used, focused on psychoeducation.

Our results showed no significant changes in weight over 3 months, but there was significant decrease in mean BMI after 3 months, with P=0.049. Mean waist circumference showed significant reduction after 3 months, with P=0.039. Blood pressure also significantly improved over the study, as mean systolic blood pressure decreased, with P=0.047, as well as mean diastolic pressure, with P=0.019.

There was a positive effect on weight, BMI, and blood glucose measurements, thus indicating the effectiveness of combining diet and exercise. After 12 months, in participants with type II diabetes and severe mental illness in Lindenmayer *et al.* (2009) trial, BMI was reduced. Furthermore, blood glucose also decreased significantly (P<0.001). This reduction was significantly related to the nutrition module that was completed during the beginning of the intervention. Similarly, all of Teachout *et al.* (2011) participants reduced their weight and 40% of fasting glucose levels.

Moreover, the results of Yarborough *et al.* (2013), and Gurusamy *et al.* (2018), showed that lifestyle interventions including psychoeducation, dietary modification, and physical activity were safe and effective for improving lipid profile.

The greater improvement in PANSS mean symptoms score, including positive, negative and general psychopathology scales, observed in this study, is in accordance with results of some previous studies.

Andrade *et al.* (2015), declared improvement of PANSS total score for disease symptoms and quality of life, especially in group that depended on resistance and concurrent exercise group.

The study by Sicras-Mainar *et al.* (2015), agreed with our results, as it stated that prevalence of MetS was increased in patients with schizophrenia who had negative symptoms, as sedentary lifestyle and lack of physical exercise due to decreased spontaneity and drive, as well as other negative symptoms, may contribute to a higher prevalence of MetS. The presence of negative symptoms may also reduce help-seeking and physical health controls and has recently been negatively correlated with BMI and positively correlated with high-density lipoprotein and cholesterol (Sicras-Mainar *et al.*, 2015).

The study by Wu *et al.* (2015), also agreed with us, as it stated that after applying physical exercise on patients of schizophrenia with MetS, there was improvement in negative and general psychopathology scales. They also reported decreased BMI. The study by Arango *et al.* (2008), explained that improvement in positive symptoms and negative symptoms, as physical exercise kept them away from stressful stimuli by distracting their attention away from stressful stimuli and therefore helps to lessen their anxiety symptoms.

However, there were other studies that did not agree with us. Scheewe *et al.* (2013), found after applying 10 weeks of aerobic exercise, lifestyle modification, psychosocial treatment, and behavior therapy on 33 obese schizophrenia patients in their thirties ages that only improvement was on metabolic parameters but no effects on psychotic symptoms. Moreover, Methapatara and Srisurapanont (2011) showed in their study after applying a 12-week program in mildly ill patients with schizophrenia divided into two groups (control and interventional); both groups underwent individual motivational interviewing, group education, and goal setting. Practicing of pedometer walking was applied only to interventional group. Increased physical activity by pedometer walking plus individual motivational interviewing may be an effective program for the reduction of body weight and BMI in patients with schizophrenia who are obese or overweight, showing no improvement on psychotic symptoms.

From our observation during the study, despite the difficulties in implementation of close lifestyle intervention for our patients, it was promising that small decreases of body weight and BMI in this population were possible. It appeared that health promotion interventions targeting physical exercise and eating habits in patients with schizophrenia might be useful for prevention of weight gain. Furthermore, patients with schizophrenia usually want to learn more about healthy lifestyles and background theories of lifestyle interventions

This was compatible with the study by McDevitt *et al.* (2006), of perceptions of barriers to and benefits of physical activity among patients with severe mental disease; participants saw exercise as positive and desirable, with benefits for both physical and mental health. This suggested that patients with severe mental disease are prepared to participate in health promotion interventions.

However, Holt *et al.* (2010), obtained different findings. After applying structured lifestyle education for 414 patients with schizophrenia, who were divided into two groups, over 12 months. The results were not promising, as weight changes did not differ between both groups, either physical activity nor nutrition. Glycated hemoglobin, fasting glucose, and lipid profile remained unchanged by the intervention. Quality of life, psychiatric symptoms, and illness perception did not change during the trial. However, this intervention did not meet each patient's needs, despite the presence of enough interest among patients to improve quality of life.

Such findings support the integration of health promotion interventions targeting physical activity and eating habits into mental health care, whereby patients should be motivated to follow this type of intervention. When health promotion becomes a part of daily care, mental health professionals could play an important role in motivating their patients to participate. According to patients' perceptions, mental health professionals can provide support, motivation, and structure, and feel comfortable with this support.

Conclusion

The results of the 12-week preliminary study period showed statistically significant improvement in total score as well as in positive, negative, and general psychopathology scales.

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Conflicts of interest

There are no conflicts of interest.

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