

## SHORT REPORT

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# Metabolic syndrome improvement in depression six months after prescribing simple hygienic-dietary recommendations

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## Abstract

**Background:** Changes in diet and exercise have been separately demonstrated to improve Depression, although scientific evidence available is scarce. In a previously published controlled study, just recommending these and other lifestyle measures (sleep restriction and sunlight exposure) in combination once, patients experienced improvements in their depressive symptoms six months later. In this sample, one in three depressive patients had metabolic syndrome (MetS) at baseline. First line treatment of MetS condition is hygienic-dietetic, being Mediterranean diet and exercise especially important. Therefore we analyzed if lifestyle recommendations also improved their metabolic profile.

**Findings:** During the sixth month evaluation, a smaller number of patients from the group receiving hygienic-dietary recommendations met MetS criteria comparing with the control group.

**Conclusions:** This study suggests that costless lifestyle recommendations, such as exercise and Mediterranean diet, have the capacity to promote both mental and physical health in a significant proportion of depressive patients. Further research is needed to confirm or discard these preliminary findings.

**Keywords:** Depression, Metabolic syndrome, Lifestyle recommendations, Diet, Exercise

## Introduction

Depression is a high prevalent disorder, prone to chronicity, and associated with a large burden in terms of suffering, disability, and healthcare costs [1,2]. One of the most common factors associated with depression is the presence of somatic disorders [3]. Metabolic syndrome (MetS) is a combination of risk factors (abdominal obesity, hypertension, dyslipidemia, and glucose intolerance) that are predictive of progression to coronary artery disease, type 2 diabetes, asthma and certain cancers [4,5]. MetS worsens with age and is rapidly growing in adults and adolescents [6,7]. The prevalence of MetS in depression vary from 25 to 41% and depression increases the risk of MetS from 1.7 to 2.8 times [8,9]. A complex bidirectional interrelationship between depression and MetSyn

has been suggested [8-10]. Patients with Depression and other mental disorders may be especially predisposed to MetS since it has been proved it is triggered by psychopharmacologic drug-induced adverse effects, sedentary lifestyle, poor dietary habits, increased substance abuse and possible limited access to health care [11,12]. There are other biological mechanisms underlying the association between metabolic syndrome and depression, but are not clearly established [13]. Biological links that include increased pro-inflammatory cytokines, stress-induced hyperactivity of the hypothalamic pituitary axis (HPA), changes in homeostasis between the sympathetic and parasympathetic nervous systems and cerebral small vessel and circulation disease have been proposed [14,15,8,9]. Pathophysiology overlap of depression and MetS could offers new possibilities for simultaneous prevention and treatment. Modification of risk factors should be considered a primary target [10].

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First line treatment of MetS should be based on lifestyle change, including exercise and nutrition therapy, such as Mediterranean diet [6,7,11,16]. A Mediterranean dietary pattern has been defined as comprising at least two of the following components: high monounsaturated/saturated fat ratio, low to moderate red wine consumption, high consumption of legumes, high consumption of grains and cereals, high consumption of fruits and vegetables, low consumption of meat and meat products and increased consumption of fish, and moderate consumption of milk and dairy products [17]. Diet and exercise have been suggested able to normalize immune and metabolic dysregulation in persons with MetS [18]. Diet and exercise interventions have been also demonstrated to improve depression although the evidence is still scarce [10]. However, to our knowledge, no previous research was specifically aimed to determine the impact of exercise and diet recommendations on patients with Depression and MetS.

We hypothesized that hygienic-dietary recommendations can change the metabolic profile of patients with Depression and MetSyn sixth months later.

## Methods

Eighty outpatients with a depressive episode were recruited for a randomized clinical trial that was designed to test the effectiveness of lifestyle recommendations in Depression [19,20]. The inclusion criteria were male and female patients over 18 years; experiencing a depressive episode according to DSM-IV diagnostic criteria for Major Depressive Disorder, Dysthymic Disorder or Bipolar Disorder; receiving antidepressant treatment; patients who have the ability to communicate in Spanish and give informed written consent and women of childbearing age practicing safe contraceptive methods. Exclusion criteria were: any other severe disease that affects the CNS; uncontrolled or potentially interfering medical condition; delusions or hallucinations at the time of the study; significant risk of suicide and pregnancy or lactation.

Complete analytic parameters (basal and six month's data) were available for fifty-one of those patients who finished the study. Reasons for non-completion included patient decision, protocol violation or appearance of a severe, uncontrolled, or potentially interfering medical condition. The study protocol was approved by the local ethical board (CEIC: Comité Ético y de Investigación Clínica de las Islas Baleares), and was registered (Trial registration: Current Controlled Trials ISRCTN59506583) and published elsewhere [19].

After signed informed consents outpatients were randomly assigned either to the active treatment or the control group. Patients assigned to the active treatment group received an envelope containing a sheet of paper with the four hygienic-dietary recommendations under

consideration. Two of them suggested diet changes, based on Mediterranean diet guidelines, and exercising daily:

1. *Go to bed when sleepy and not before 11 p.m. Use your bed and bedroom only for sleep and sex (do not read, watch TV or lie on the bed during the day). If you do not fall asleep after 15 or 20 minutes, get up and start an activity until you feel sleepy enough to go back to bed. Get up early, never later than 9 a.m., no matter how well you have slept the night before. Do not lie down or take a nap during the day.*
2. *Walk at least 1 hour a day, at a good pace but without becoming short of breath or being unable to talk while walking. If you think you have a medical problem which makes walking difficult or uncomfortable consult your doctor. Use appropriate footwear for walking and have a shower or a bath afterwards.*
3. *Expose yourself to sunlight at least 2 hours per day, taking precautions to avoid sunburn or sunstroke (sunscreen, hat, etc.).*
4. *Try to eat a healthy and balanced diet. Eat at regular hours without snacking between meals. Avoid especially sweet or sugary drinks. Eat fish at least three times per week, plus fruit, cereals, nuts and vegetables daily.*

The control group received an identical envelope, but in this case the recommendation was to perform the pattern of eating and exercise according to what they thought might make them feel better:

1. *Sleep the hours that you feel your body needs.*
2. *Adapt the pace of daily physical activity that meets your needs.*
3. *If exposed to sunlight take precautions to avoid sunburn or sunstroke (sunscreen, hat, etc.).*
4. *Try to eat a healthy and balanced diet.*

The Mini International Neuropsychiatric Interview (MINI), the Hamilton rating scale for depression (HAM-D) 17-item version, the 21-item Beck Depression Inventory, and the Clinical Global Impression scale (CGI) were used. After the sixth month intervention tests were again administered by blind raters. During this time the patients were taking antidepressants, and continued to be treated by their GP or psychiatrist without any interference from the research team. Analytical determinations, blood pressure and weight were measured at baseline and after six months. The "International Diabetes Federation" (IDF) criteria were used to define MetS in the patients [21]: They must have central obesity, defined as excessive waist circumference, with sex and ethnic specific values ( $\geq 94$  cm for European men) or BMI  $> 30$  kg/m<sup>2</sup> plus two or more

of the following four factors; raised triglycerides level:  $\geq 150$  mg/dl or specific treatment for this lipid abnormality; reduced concentration of high density lipoprotein (HDL):  $< 40$  mg/dl in men and  $< 50$  mg/dl in women or specific treatment for this lipid abnormality; raised blood pressure: systolic blood pressure  $\geq 130$  mmHg or diastolic blood pressure  $\geq 85$  mmHg or treatment of previously diagnosed hypertension; raised fasting plasma glucose concentration  $\geq 100$  mg/dl or previously diagnosed type 2 diabetes.

We conducted a statistical analysis using Fisher's exact test for categorical variables and U Man-Whitney test for continuous variables.

### Findings

Main socio-demographic and clinical data are presented in Table 1. The antidepressants prescribed were very similar in both groups; most of the patients used dual and selective serotonin reuptake inhibitors. Scales indicated an improvement of depressive symptoms in the active treatment group, but due to the insufficient sample not all the items reached statistical significance. Adverse effects resulting from these recommendations did not appear. Concerning to the metabolic variables shown in Table 1, most changes were in terms of improving the metabolic profile in the active group versus control recommendations. There was a statistically significant change between pre and post condition in the number of patients in both groups that met MetS criteria ( $X^2 = 4.69$ ,  $p = 0.03$ ).

**Table 1 Demographic and clinical results**

	Active n = 25	Control n = 26	P value
Female sex, N°	20	17	0.24
Age y, Mean (SD)	47.6 (11.6)	50.6 (11.4)	0.36
Major Depression, N°	23	20	0.28
HAM-D increment	- 8.80 (8.9)	- 5.57 (4.9)	0.11
BDI increment	- 8.64 (9.2)	- 4.25 (6.3)	0.05
GCI increment	- 1.72 (1.3)	- 0.69 (1.0)	0.00
BMI increment	- 0.11 (1.5)	0.29 (1.6)	0.46
SBP increment	- 2.33 (15.7)	- 2.04 (16.9)	0.95
DBP increment	1.5 (12.9)	- 1.76 (15.0)	0.47
Serum glucose increment	- 3.9 (20.7)	- 0.6 (21.3)	0.58
Total Cholesterol increment	- 3.92 (21.9)	3.76 (39.2)	0.39
LDL Cholesterol increment	- 7.00 (19.5)	3.00 (33.14)	0.20
HDL Cholesterol increment	1.76 (8.3)	- 0.15 (8.1)	0.40
Triglycerides increment	6.4 (41.9)	9.3(62.8)	0.84
Metabolic Syndrome pre, N°	7	9	
Metabolic Syndrome post, N°	3	10	0.03

Hamilton 17-item scale (HAM-D), Beck Depression Inventory 21-item (BDI), Global Clinical Impression scale (GCI), Body Mass Index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP).

### Discussion

The main finding of this study is that MetS was lower in those patients receiving the active hygienic-dietary recommendations compared to the control group. Perhaps due to lack of statistical power, our study has not found differences among any of the variables included in MetS definition. Nevertheless, it has been suggested that it is more important the association of Depression with the construct of MetS rather than with its components [10].

Seasonality of serum lipids and weight/body mass index may affect MetS prevalence raising their development in the winter [22]. Changes of plasma volume linked to seasonal variations in temperature and/or physical activity could be responsible of this fact [22]. However, these findings cannot explain our results, since patients were assessed throughout the year and assigned randomly to both groups.

Depressed people are more prone to eat highly palatable and caloric food, rich in cholesterol and carbohydrate and low in fish, vegetable and cereals. This diet does not ensure an adequate intake of B vitamins, folic acids, and essential fatty acids for vascular, inflammatory and metabolic balance, and may induce MetS [10]. Depression, when in comorbidity with MetS, shows worse course, more severe clinical picture and a higher tendency to chronicity and suicidality besides lower social functioning [10]. It has been proposed the concept of "metabolic depression" to identify a chronic subtype of depression more frequent in late-life, with metabolic abnormalities and a protracted course [10,21]. Our preliminary data could indicate that this situation can be faced better when combining antidepressant treatment with dietary hygienic measures.

Our study has some weaknesses that need to be acknowledged for proper interpretation. The main limitations of this study are the small sample size and the short follow-up period. However, the small sample size would not explain our positive findings but makes the type I statistical error more probable. Although the vast majority of patients met criteria for Major Depression, we also had patients with Dysthymic and Bipolar Disorder. Due to the limited sample we could not carry out a separate analysis of these patients to determine if they have the same behavior against lifestyle recommendations.

Depression has been associated with poor adherence to diet and exercise regimens [14,18]. There is no measure of adherence in this study. This is a clear limitation because low adherence to the study recommendations cannot be ruled out and this reinforces the fact that these findings may simply be chance. Nevertheless we demonstrated in a pilot study with a small part of these patients using actigraphs, that they did change their lifestyle habits, at least in a short-term period [23]. It would have been interesting to dispose of objective adherence measures from

all the patients during the follow-up. Unfortunately, it could not be put into practice due to logistical limitations.

The benefits of lifestyle changes for patients experiencing a depressive episode and Metabolic Syndrome could be achieved by using a simple combination of hygienic-dietary recommendations on a written piece of paper. These benefits applied to metabolic profile are a key factor for patients' future cardiovascular health which also constitutes a key factor for their Mental Health evolution [1,24-26]. The improvement of the metabolic profile found in this study would be an extra-motivation for patients in order to maintain these lifestyle changes in the long-term [16].

#### Competing interests

The authors declare they have no financial or non-financial competing interests in relation to this manuscript.

#### Authors' contributions

OI, MG, MR, MG and JG were substantially involved in the conception of the study and participate in its design. OI, MG, MR, SM, MV and MS participated in the coordination of the study and the acquisition of data. MG drafted the manuscript with the assistance of RG, SM, OI, MR, MG and JG. The other authors critically revised the text. All have approved the present publication.

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