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Research report

Does obesity predict bipolarity in major depressive patients?

Giulia Vannucchi [a], Cristina Toni [b], Icro Maremmani [a,b], Giulio Perugi [a,b,*]

[a] Department of Clinical and Experimental Medicine, Unit of Psychiatry, University of Pisa, Pisa, Italy
[b] Institute of Behavioral Sciences, G. De Lisio, Pisa, Italy

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ABSTRACT

Background: Differential association of obesity in bipolar and unipolar Major Depressive Episode (MDE) has not been systematically studied. We explore the relationships between obesity and history of manic and hypomanic symptoms in a large national clinical sample of MDE patients.
Method: The sample comprised 571 consecutive patients with a DSM-IV diagnosis of MDE enrolled in a 7 months period. The study involved 30 psychiatric facilities for outpatients, distributed throughout Italy. Diagnosis was formulated by psychiatrists with extensive clinical experience in the diagnosis and treatment of mood disorders. In all patients height (meters) and weight (kilograms) were systematically measured at the moment of the clinical evaluation. The severity of depressive and anxious symptomatology was self-evaluated by the means of Zung's questionnaires for depression and anxiety. For the evaluation of lifetime manic or hypomanic features, Hypomania Check List-32 was also administered. Obese and Non-Obese subgroups were identified on the basis of a >30 BMI cut off point.
Results: BMI ≤ 30 was observed in 86 (15.1%) of our MDE patients. The Obese and Non-Obese subgroups did not report differences as regards to age and gender distribution. Obese patients reported a lower number of years of education in comparison with Non-Obese patients. As regards to marital status, Obese patients were more frequently married in comparison with the Non-Obese patients. Obese patients were more frequently belonging to the bipolar group than Non-Obese patients. Obese subjects also reported more frequently than Non-Obese an HCL total score >14. The effect of educational level, marital status and bipolar–unipolar distinction on the probability of Obese group membership was analyzed by stepwise logistic regression. Bipolar subtype resulted to be the strongest predictor of Obesity.
Limitations: Pharmacological treatments and co-morbidity with other psychiatric disorders are not explored and accounted for in our analyses.
Conclusions: Obesity in our national sample of patients with MDE is associated with bipolar subtype and (hypo)manic symptoms. These findings suggest the possibility that the presence of obesity in patients with MDE might be related to bipolarity. A common impulsive-addictive diathesis is proposed as mediating mechanism. Further longitudinal studies in clinical and non-clinical populations are necessary to better define the burden and the role of the association between obesity and bipolarity.

1. Introduction

About one third of patients with bipolar disorder (BD) requires more than 10 years from the onset of the first clinical manifestations to the correct diagnosis (Hirschfeld et al., 2003b; Lish et al., 1994; Suppes et al., 2001). The most common incorrect diagnosis is unipolar Major Depressive Disorder (MDD) (Hirschfeld et al., 2003b). According to several epidemiological and clinical studies, almost 40% of BD patients are initially diagnosed with MDD (Ghaemi et al., 1999, 2000) and from 21% to 26% of unipolar depressed patients in primary care settings report some bipolarity aspects after careful screening (Hirschfeld et al., 2005; Manning et al., 1997). These data disclose the age-old diagnostic issue about the implementation of our capacity to immediately give a correct diagnosis. With this purpose during the last decades some clinical features have been identified useful in distinguishing unipolar from bipolar Major Depressive Episode (MDE). Among them earlier age of onset (Lish et al., 1994), positive family history for BD (Bowden, 2005; Hirschfeld et al., 2003a), atypical features (Gold et al., 2002; Perugi et al., 1998), anxiety (Akiskal et al., 2006; Perugi et al., 2003), and substance abuse (Maremmani et al., 2008, 2006) have been observed more commonly in bipolar than unipolar depressive patients.

Obesity is a chronic and relapsing illness which affects from 10% to 35% of the general population (Bray and Bellanger, 2006;

* Correspondence to: Clinica Psichiatrica Università di Pisa, Via Roma 67, 56126 Pisa, Italy. Tel.: +39 050 835414; fax: +39 050 21581.
E-mail addresses: giulio.perugi@med.unipi.it, giulio.perugi@gmail.com (G. Perugi).

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Wilborn et al., 2005). In the last decades obesity has become a public health concern due to the increased prevalence rate and the large percentages of morbidity and mortality associated. A relationship between mood disorders and Obesity has been widely demonstrated. Clinical and epidemiologic studies found a positive association between obesity, MDD and BD (Simon et al., 2006), both for men and women, with some gender-mediated differences in psychiatric comorbidity and clinical features. A one-to-one relationship seems to connect affective illnesses and obesity; depressive symptoms, personal and familial history for depressive episodes and high rates of psychological dysfunction are common among treatment-seeking Obese individuals (Johnston, 2004; Heo et al., 2006; Dong et al., 2004) whereas weight gain, overweight and obesity frequently affect the course and the treatment of mood disorders. Fagiolini and colleagues (Fagiolini et al., 2003) observed that obesity is associated with clinical features such as large number of lifetime depressive and manic episodes, severe and difficult-to-treat index affective episode, large amount of affective recurrence, particularly depressive, and short time to relapse. Conversely depression may play an important role in the success of weight loss. Sherwood et al. (2004) found that improvements in binge eating status, mediated by improvement in depression, predicted significantly weight loss in MDD patients.

Interestingly, the risk of depression seems to increase with growing BMI (Onyike et al., 2003). Furthermore, both childhood and adulthood MDD correlate with obesity in adults in males as in females (Pine et al., 1997, 2001). These results can be explained partly by some clinical overlapping features as overeating, physical inactivity, and high overall carbohydrates intake (Elmslie et al., 2001), partly by comorbid eating disorders as binge-eating disorder (McElroy et al., 2004; Telch and Stice, 1998), and partly by the side-effects of psychotropic medications (Keck and McElroy, 2003). More specifically overweight, obesity and abdominal obesity are associated with atypical depression (Hasler et al., 2004; Kendler et al., 1996) and BD (Elmslie et al., 2001, 2000) both in males and females and with lifetime hypomanic symptoms in males (Hasler et al., 2004).

To our knowledge the differential prevalence rate in bipolar and unipolar MDE of obesity have not been systematically studied so far. The aim of the present study is to explore the relationships between obesity and history of manic and hypomanic symptoms in a large clinical sample of major depressive patients.

2. Method

COME TO ME is a cross-sectional, multi-center, observational study that enrolled 571 consecutive patients with a diagnosis of Major Depressive Episode, according to DSM-IV, in a 7 months period. The study involved 30 psychiatric facilities for outpatients, distributed throughout Italy; 8 centers are located in north Italy, 9 in central regions, 7 in the south and 6 in the Islands (Sicily and Sardinia). In accordance with the observational nature of the protocol, routine medical procedures were not modified. The Ethics Committee of each center approved the study protocol in compliance with the Italian ministerial bulletin issued on September 2, 2002 regarding observational studies. All patients gave their informed consent concerning handling and use of the data collected during the course of study. The study was sponsored by Boehringher Ingelheim, Italy.

2.1. Study population

Subjects who referred to the selected centers between December 2006 and July 2007 were considered for recruitment in the study. Patients were recruited consecutively according to the following inclusion criteria: (i) men and women aged 18–75 years, (ii) diagnosis of Major Depressive Episode according to DSM-IV (major depressive disorder, recurrent major depression, depressive episode types I and II bipolar disorder, and depression NOS), and (iii) ability to complete the self- and hetero-administered questionnaires. The exclusion criteria were (i) comorbidity with schizophrenia and other psychotic disturbances and (ii) current relevant physical illnesses.

The study included 571 depressed outpatients; 383 subjects (67.1%) were female and, regarding age and 255 subjects (44.7%) were from 18 to 50 years old and 316 (55.3%) over 50. The level of education was higher than 11 years for 246 (43.1%) patients; most of them ($n=336$, 58.8%) were married.

Diagnostic procedure, clinical evaluation and symptom assessment have been extensively described in the previous reports (Perugi et al., 2011). Diagnosis of MDE (MDD recurrent and single episode, bipolar disorder types I and II, and MDE NOS) was formulated by psychiatrists with extensive clinical experience in the diagnosis and treatment of mood disorders according to DSM-IV criteria. In all patients height (meters) and weight (kilograms) were systematically measured at the moment of the clinical evaluation. The severity of depressive and anxious symptomatology was self-evaluated by the means of Zung's questionnaires for depression and anxiety (Zung, 1965, 1971). For the evaluation of lifetime manic and hypomanic features, Hypomania Check List-32 (Angst et al., 2005) was also administered.

2.2. Statistics

BMI at the moment of evaluation was calculated. Patients were subdivided into Obese and Non-Obese subgroups on the basis of a ≥ 30 BMI cut off point. Comparisons among the 2 subgroups were conducted by the unpaired Student's t-test for the dimensional variables and χ^2 analysis for the categorical ones. The Mann–Whitney u-test and Fisher exact test were utilized when appropriated. We set significance at 0.05 level, two tailed. Effect of the variables resulted significantly different between the two groups in the univariate analyses on probability of Obese group membership was analyzed using multiple stepwise logistic regression, backward procedure. We used the statistical routines of SPSS.

3. Results

Among the 571 valuable patients with MDE, MDD recurrent ($n=215$, 37.7%) and single episode ($n=197$, 34.5%) were the most common diagnoses. One hundred and nineteen patients (21.1%) presented Bipolar I or II Depression; moreover, 14 or more hypomanic features, as recorded by means of the HCL-32, were reported by 276 (48.3%) patients. Depression NOS was diagnosed only in 39 (7.0%) patients. The mean severity of depression and anxiety as measured by the means of Zung's scales was respectively 53.2 (sd = 9.3) and 47.2 (sd = 10.1).

On the basis of a BMI ≤ 30, 86 (15.1%) were included in the "Obese" and 485 (84.9%) in the "Non-Obese" subgroup. In the Obese subgroup, 24 (27.9%) patients reported a BMI ≥ 35, representing 4.2% of the total sample.

The Obese and Non-Obese subgroups did not report differences as regards to age and gender distribution (Table 1). Obese patients reported a lower number of years of education in comparison with Non-Obese patients (respectively 9.20 ± 4.1 vs. 10.33 ± 4.5, $t=-2.30$, and $p=0.023$). Interestingly, the educational level is lowest in the 24 patients with BMI ≥ 35 in comparison with those with BMI between 30 and 35 ($n=62$) and with Non-Obese subgroup (respectively $7.71+3.3$ vs. $9.77+4.3$ vs. $10.33+4.5$, $F=4.31$, and $p=0.014$; the Scheffe F-test: Non-Obese,