Psychiatr. Pol. 2015; 49(5): 993–1004¶
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: http://dx.doi.org/10.12740/PP/OnlineFirst/32937

Bipolar spectrum features in obese individuals

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Summary

Aim. The relationships between obesity and bipolar spectrum disorders (BSD) are unclear. Thus, the aim of our study was to approximate the prevalence of soft bipolar features in patients seeking treatment for obesity.

Methods. We performed a nested case-control study (cases: 90 patients with the mean BMI=38.1±7.0 [range: 30.1–62.5]; controls: 70 healthy volunteers with the mean BMI=21.6±2.1 [range: 18.5–24.9]). The participants were screened for the BSD symptoms with the Mood Disorder Questionnaire.

Results. Patients with obesity were significantly more likely to score ≥7 pts. on the MDQ 25.6% vs. 8.6%; p=0.01). In comparison to non-obese individuals, the obese patients scored significantly higher in MDQ section I and on the MDQ items referring to the 'irritability–racing thoughts' dimension of hypomania. The multiple logistic regression analysis revealed that obesity had been significantly related to the odds of obtaining ≥7 pts. on the MDQ section 1 (odds ratio [OR] = 2.07; 95% confidence interval [CI]: 1.17–3.63), and marginally significantly related to experiencing periods of 'ups' and 'downs'(OR = 1.67; 95% CI: 1.00–2.81).

Source of funding: The statutory programme no. K/ZDS/003906. Chair of Psychiatry, Jagiellonian University Medical College.

Conclusions. Our study adds to previous suggestions that obesity may be significantly related to the BSD. However, the clinical implications of this finding need to be determined in further studies, performed in accordance with the paradigm of evidence based medicine (EBM).

Key words: obesity, bipolar spectrum disorders, Mood Disorder Questionnaire

Introduction

According to the insights from the Global Burden of Disease Study 2010 (GBD 2010) [1], both obesity and psychiatric disorders are at the forefront of the contemporary health challenges. It had been known that the co-occurrence of obesity and mood disorders might pose significant risks to patients [2-3]. The findings from the GBD 2010 prompt further research on the impact and clinical correlates of the bipolar spectrum disorders (BSD) [4-7].

When compared to general population, most of the available data suggest that obesity is significantly more prevalent in subjects with schizophrenia [5], Bipolar disorder (BD) [8-12], and major depressive disorder (MDD) [11, 13, 14]. Although the risk of developing obesity does not seem to differ between patients with MDD and BD [8], gender is known to be an important moderator of the relation discussed, with obese women being at higher risk of developing either of those disorders [3, 14–16]. It has also been discovered that the connection between body mass index (BMI) and mood disorders (of either unipolar or bipolar course) is particularly strong in patients with severe obesity [11, 17]. Worse still, treatment outcomes tend to be poorer in subjects with obesity and affective disorders (especially BD), as compared to patients with normal weight. Accordingly, the co-occurrence of obesity and BD has been linked to higher rates of impairment (including cognitive decline [18]), recurrence [19], chronicity, psychiatric comorbidities [20], suboptimal lithium response, rapid cycling [21] and suicidality [22].

As opposed to the variety of data on the major psychiatric disorders, the co-occurrence of obesity and BSD has been subjected to very few trials [23, 24]. Given the fact that both BD and obesity are increasingly seen as multi-system inflammatory diseases [25, 26], contributing to excess mortality, medical comorbidity [20, 27–29], and cognitive decline [18, 21, 30, 31], the in-depth studies regarding the "soft-bipolar features [6] in individuals with obesity would become highly beneficial to the patients. Furthermore – following on the hypothesis by Anisman and Hayley, listing obesity among the potential biomarkers of MDD [32] – it would be useful to verify the status of obesity as the clinical indicator for bipolar spectrum disorders BSD [33].

Aim

We have set the following two goals of our study. First: to approximate the prevalence of soft bipolar features in patients seeking treatment for obesity. Second: to check whether the bipolarity traits run in families of obese subjects.

Material and method

Study design

We performed a nested case-control study. The cases were recruited among patients with obesity (BMI ≥ 30kg/m^2) and negative history of psychiatric therapy, seeking either conservative or surgical treatment in the Outpatient Clinic of Obesity and Lipid Disorders in Krakow, and in the 2nd Department of General Surgery, Jagiellonian University Medical College. The control group consisted of volunteers with normal weight (BMI: 18.5-24.99 kg/m^2), and with a negative history of mental disorders. Prior to the launch of the study, the Bioethics Committee of the Jagiellonian University approval was obtained. All the study participants expressed the informed consent and signed the informed consent agreement.

Out of 129 patients invited to join the study, 20 refused participation, and 19 subjects had been diagnosed with a mental disorder (MDD: 11 cases; anxiety disorders: 5 cases, MDD comorbid with anxiety disorders: 3 cases, schizophrenia: 1 case, alcohol use disorder: 1 case, personality disorders: 1 case). Overall, 90 patients were enrolled into the project, making the participation rate of 69.8%.

While 87 healthy volunteers were approached, 74 of them consented to join the control group. As 4 of them were excluded due a positive history of psychiatric disorders (MDD: 3 cases, MDD comorbid with anxiety disorders: 1 case), the participation rate in the control group was 80.5%.

Clinical and demographic characteristics of study's participants are presented in Tables 1 and 2. In the study group, neither women nor men differ in terms of the mean BMI (31.1 ± 10.0 vs. 30.6 ± 9.4; the Mann-Whitney U test; p = 0.89).

Table 1. **Characteristics of the studied population**

Demographic and clinical features						
	Study group (n = 90)		Control group (n = 70)			
	mean ± SD	range	mean ± SD	range	Mann-Whitney U test	
					Z	p
Age	41.8 ± 11.8	21–64	38.5 ± 12.9	21–70	1.74	0.08
BMI	38.1 ± 7.0	30.1–62.5	21.6 ± 2.1	18.5–24.9	10.83	< 0.0001
	N (%)		N (%)		χ^2 test	
					χ^2	p
Gender	Women: 61 (67.78%) Men: 29 (32.22%)		Women: 42 (60%) Men: 28 (40%)		1.04	0.31
Education	Secondary/Primary: 48 (53.3%) Higher: 42 (46.7%)		Secondary/Primary: 42 (60%) Higher: 28 (40%)		0.71	0.40
Employment status[a]	Employees: 64 (71.1%) Students: 5 (5.6%) Non-employees: 21 (23.3%)		Employees: 52 (74.3%) Students: 11 (16.7%) Non-employees: 7 (9%)		8.12	0.02

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Marital status	Married/civil partnership: 64 (71.1%) Single[b]: 26 (28.9%)	Married/civil partnership: 55 (78.6%) Single[b]: 15 (11.4%)	1.15	0.28
Place of abode	Cities: 71 (78.9%) Villages: 19 (21.1%)	Cities: 50 (75.7%) Villages: 10 (24.3%)	0.46	0.50
Somatic disorders in groups				
Diabetes	11 (12.2%)	3 (4.3%)	3.11	0.08
Circulatory disorders	24 (26.7%)	5 (7.1%)	10.11	0.014
Hypothyroidism	5 (5.6%)	4 (5.7%)	0.09	0.8
Arthro-musculo-skeletal disorders	5 (5.6%)	1 (1.4%)	-	0.23[c]
Polycystic ovary syndrome	1 (1.1%)	2 (2.8%)	-	0.58[c]
Gynaecological	8 (8.9%)	4 (5.7%)	0.57	0.45
Others	5 (5.6%)	2 (2.8%)	-	0.47[c]

[a] Indicates higher rate of non-employees and lower rate of students in the obesity sample ($\chi^2 = 8.06$; $p < 0.01$); [b] Including divorced or bereaved; [c] Fisher Exact Test

Table 2. **Family history of obesity, mental disorders or behavioural disturbances in study participants**

	Study group (n = 90)	Control group (n = 70)	χ^2 test	
	N (%)	N (%)	χ^2	p
Aggressive behaviours	2 (2.2%)	1 (1.4%)	–	0.99[c]
Alcoholism	9 (10%)	6 (8.6%)	0.09	0.76
Anxiety disorders	4 (4.4%)	6 (8.6%)	–	0.34[c]
Bipolar disorder	3 (3.3%)	2 (2.9%)	–	0.99[c]
Binge eating	4 (4.4%)	2 (2.9%)	–	0.70
Gambling	0 (0%)	1 (1.4%)	–	0.44[c]
Illicit drugs use	1 (1.1%)	1 (1.4%)	–	0.99[c]
Major depressive disorder	8 (8.9%)	4 (5.7%)	0.57	0.45
Mental disorders NOS	0 (0%)	2 (2.9%)	–	0.19[c]
Obesity	22 (24.4%)	7 (10%)	5.54	0.02
Personality disorders	1 (1.1%)	1 (1.4%)	–	0.99[c]
Psychiatric hospitalizations	5 (5.6%)	5 (7.1%)	–	0.75[c]
Psychotropic drugs use	7 (7.8%)	2 (2.9%)	–	0.30[c]
Schizophrenia	3 (3.3%)	0 (0%)	–	0.26[c]

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Suicidality	3 (3.3%)	1 (1.4%)	–	0.63[c]
Violent behaviours	3 (3.3%)	1 (1.4%)	–	0.63[c]

[c]Fisher Exact Test.

Diagnostic measures

The Mood Disorder Questionnaire (MDQ) [34] was used in order to determine the lifetime presence of bipolarity features. The screening for bipolarity was considered positive in subjects who:

1. scored ≥ 7 pts. on the section 1 (consisting of 13 questions about the manic/hypomanic symptoms);
2. answered positively to the section 2 question (symptom clustering);
3. have been experiencing moderate to severe impairment due to the symptoms (section 3) [35, 36].

Further we took into account the MDQ's section 1 two dimensions of manic/hypomanic symptomatology: "energized–activity" (E/A; items: 3, 5, 8, 9, 10) and "irritability–racing thoughts" (I/R; items: 2, 6, 7, 12, 13) [37]. We also assessed the presence of cyclothymic temperamental traits (as indicated by the participants' responses to question on the repetitive periods of "ups" and "downs", derived from the Hypomania Checklist-32's [HCL-32] section 2) [38, 39].

Additionally, we have attempted to assess the commonness of bipolarity in the study participants' first-grade relatives using the list of manic/hypomanic symptoms included in the MDQ section 1. Accordingly, the participants were asked to respond to the MDQ questions regarding the lifetime history of manic or hypomanic symptoms in their first-grade relatives.

Statistical methods

As the BMI and MDQ scores were not normally distributed, the Mann-Whitney U test was implemented to evaluate the differences between continuous variables. We used the χ^2 test for analysing differences between categorical variables. In order to determine the strength of the relation between obesity (a dichotomous dependent variable) and the outcomes of screening for BSD (independent variable), we performed the logistic regression analysis.

For testing the causal inferences between the dependent and independent variables, we built the multiple logistic regression model.

Results

Eight (8.9%) of the subjects seeking treatment for obesity met the original MDQ criteria for bipolarity, while none of the controls scored positively on the tool (Fisher Exact Test; $p = 0.03$). Having confined the analysis to the MDQ section 1 only, the

cases were also significantly more likely to reach or pass the threshold of 7 pts. (n = 23), as compared to the non-obese individuals (n = 6), (25.6% vs. 8.6%; χ^2 test = 5.59; p = 0.01). We also noticed that the obese individuals tended to score higher in MDQ section I (4.5 ± 3.2 vs. 3.3 ± 2.6, the Mann-Whitney U test, z = 2.19; p = 0.03) and also on the items referring to the irritability–racing thoughts dimension of hypomania (MDQ I/R cluster), (1.5 ± 1.2 vs. 1.0 ± 1.0, the Mann-Whitney U test, z = 2.22; p = 0.03).

Numerically, more obese subjects (n = 21; 23.3%) than non-obese volunteers 8 (13.3%) reported experiencing the periods of "ups" and "downs" but the difference was statistically non-significant (p = 0.13).

BMI was positively correlated both with the MDQ section 1 scores "as a whole" (Spearman's rho: 0.18; p = 0.03), and with the scores on the MDQ I/R cluster (r = 0.18; p = 0.02).

In the logistic univariate regression analysis we found that the subjects with obesity were significantly more likely to obtain ≥ 7 pts. on the MDQ section 1. Having built the logistic multivariate regression model we came to similar conclusions, yet the odds ratio (OR) values for the above-mentioned outcomes were lower when corrected for confounding factors. Also, the multiple logistic regression analysis revealed that obesity had been significantly related to the odds of experiencing periods of "ups" and "downs" (Table 3).

Table 3. **Relationship between obesity and the outcomes of screening for bipolar spectrum disorders (logistic regression)**

Screening criteria	Cases (N=90)	Controls (N=70)	OR (95% CI)
Univariate model			
MDQ ≥ 7 pts.	23	6	**3.66 (1.40–9.58)
Cyclothymic temperamental traits[a]	21	8	2.36 (0.98–5.71)[b]
Multivariate model[c]			
MDQ ≥ 7 pts.	23	6	**2.07 (1.17–3.63)
Cyclothymic temperamental traits[a]	21	8	*1.67 (1.00–2.81)

CI – confidence interval; OR – odds ratio; Bolded text denotes statistically significant results: * $p \leq 0.05$; ** $p \leq 0.01$; [a] as indicated by the participants' responses to question on the repetitive periods of "ups" and "downs"; [b] indicates a marginally significant difference ($0.05 < p < 0.1$); p = 0.06; [c] adjusted by age, gender, marital status, education, employment status, place of abode, somatic diseases, family history of obesity and family history of mental disorders.

Neither the patients nor the healthy controls differed in terms of history of mental disorders or behavioural disturbances in the first-grade relatives (Table 2). Also the mean number of manic/hypomanic symptoms in family members reported in the "family version" of the MDQ was not significantly higher in obese group than in non-obese subjects (2.4 ± 3.2 vs. 1.6 ± 2.2, the Mann-Whitney U test, z = 0.72; p = 0.47). However, significantly more first-degree relatives of obese patients were assessed as having ≥ 7 manic/hypomanic symptoms listed in the MDQ section 1 (n = 14; 15.5%)

when compared to non-obese group (n = 4; 5.7%; χ^2 =3.83; p = 0.05). Moreover, in family members of obese patients, the symptoms discussed tend to happen during the same period of time more frequently (12.2% vs. 2.8%; χ^2 = 4.63; p = 0.03).

Discussion

By providing indirect evidence suggesting that obesity may be significantly related to the BSD, our study likely adds to the results of previous trials on the prevalence of bipolar features in subjects with various medical conditions (i.e. fibromyalgia [40–42], migraine, asthma, allergies [43] and acute coronary syndrome [44].

While the point prevalence of bipolar traits (as indicated by the positive MDQ scores) had been set at 2.5–3.7% in the community-based studies [35, 45–47], we have found that the presumed bipolarity features may be even more widespread among patients seeking treatment for obesity (8.9%). The logistic multivariate regression model revealed that patients with obesity were more likely both to score positively on MDQ section 1, and to confirm the presence of repetitive periods of "ups" and "downs". This seems to support the hypothesis linking BSD to the higher risk of obesity.

In our study, obese individuals were characterised by higher than non-obese ones scoring in MDQ I/R cluster. Moreover MDQ section I scoring and "irritability–racing thoughts scoring was positively correlated with BMI. It suggests that the presumed "dark side" hypomanic symptoms [48] may be added to clinical correlates of obesity. This, along with a tendency to experience "ups" and "downs" in turn supports the link between obesity and cyclothymic temperament, and seems to confirm the results of a similar study by Amann et al. [49].

In general, our conclusions remain in line with data gathered in Italian and German samples, indicating that bipolar traits often go hand-in-hand with obesity [23, 24, 49]. However, there is a staggering discrepancy between the ratio of the MDQ-positive participants of our study (8.9%), and the point prevalence of BSD observed in purely bariatric populations (about 90%) [23, 24, 33]. This variance can be explained either by the wider BMI range in our study sample or by the suboptimal psychometric properties of the tool used in the above-cited studies – the HCL-32. Accordingly, the TRES-DEP study has demonstrated greater prevalence of false positive scores on the HCL-32, in comparison with the MDQ [50–52]. As it was found that by omitting the sections 2 and 3, the MDQ's potential for detecting the DSM-IV-defined BSD markedly improves in some populations of patients with depressive disorders [53–55], it might also be the case in specific medical populations. When confined to the section 1 only, our analysis has suggested that ¼ of obese patients may exhibit bipolar features.

While neither the patients nor the healthy controls differed in terms of family history of mental disorders or behavioural disturbances (as opposed to the results of previous studies, suggesting high prevalence of psychiatric disorders in families of individuals with obesity [17, 49, 56, 57], we found that significantly more first degree relatives of obese patients were reported by them as having ≥ 7 manic/hypomanic symptoms listed in MDQ, including clustering of symptoms. The exact nature of the

relationship between obesity and familial segregation of bipolar features needs to be further determined in large-scale longitudinal studies.

The limitations of our study derive primarily from its case-control design (thus increasing the risk of selection bias) [58], and indirectness of the findings (as the MDQ scores were not verified with a structured diagnostic interview) [59, 60]. The risk of recall bias also needs to be mentioned, as it was recently demonstrated that the MDQ scores provide an accurate reflection of hypomanic or manic episodes in the past year only [61]. We addressed the issue of prognostic imbalance by constructing the multiple logistic regression model [62]. As a result, the width of CIs decreased substantially (thus boosting up the precision of estimation) [63].

Conclusions

In conclusion, our study reveals the association between obesity and bipolarity. Patients with obesity seem to be more likely to exhibit with soft bipolarity (as compared to subjects with normal weight). Irritability and racing thought may be the predominant signs of the bipolar spectrum disorders in this clinical group. The hypothesis of familial co-segregation of bipolarity and obesity is plausible. The results of our project need to be replicated in course of future studies.

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