Acta Neuropsychiatrica 2010: 22: 63–67

DOI: 10.1111/j.1601-5215.2010.00452.x

ACTA NEUROPSYCHIATRICA

Obesity is associated with previous suicide attempts in bipolar disorder

Gomes FA, Kauer-Sant'Anna M, Magalhães PV, Jacka FN, Dodd S, Gama CS, Cunha Â, Berk M, Kapczinski F. Obesity is associated with previous suicide attempts in bipolar disorder.

Objective: There is a paucity of data about risk factors for suicide attempts in bipolar disorder. The aim of this study is to examine the association between suicide attempts and obesity in people with bipolar disorder.
Methods: Two hundred fifty-five DSM-IV out-patients with bipolar disorder were consecutively recruited from the Bipolar Disorder Program at Hospital das Clínicas de Porto Alegre and the University Hospital at the Universidade Federal de Santa Maria, Brazil. Diagnosis and clinical variables were assessed with Structured Clinical Interview for DSM-IV-axis I (SCID I) and Program structured protocol. History of suicide attempts was obtained from multiple information sources including patients, relatives and review of medical records. Patients with body mass index (BMI) $\geq$30 were classified as obese.
Results: Over 30% of the sample was obese and over 50% had a history of suicide attempt. In the multivariate model, obese patients were nearly twice (OR = 1.97, 95% CI: 1.06–3.69, $p = 0.03$) as likely to have a history of suicide attempt(s).
Conclusion: Our results emphasise the relevance of obesity as an associated factor of suicide attempts in bipolar disorder. Obesity may be seen as correlate of severity and as such, must be considered in the comprehensive management of bipolar patients.

Fabiano A. Gomes[1], Márcia Kauer-Sant'Anna[1], Pedro V. Magalhães[1], Felice N. Jacka[2], Seetal Dodd[2], Clarissa S. Gama[1], Ângelo Cunha[3], Michael Berk[2], Flávio Kapczinski[1]

[1]Bipolar Disorders Program and INCT Translational Medicine, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; [2]Department of Clinical and Biomedical Sciences, University of Melbourne, Geelong, Australia; and [3]University Hospital, Universidade Federal de Santa Maria, Santa Maria, Brazil

Keywords: bipolar disorder; obesity; suicide

Professor Flávio Kapczinski,
INCT Translational Medicine,
Hospital de Clínicas de Porto Alegre,
Ramiro Barcelos,
2350 CEP 90035-003,
Porto Alegre, RS, Brazil.
Tel: +55 51 21018845;
Fax: +55 51 21018846;
E-mail: kapcz@terra.com.br

Introduction

Bipolar disorder is a major public health concern worldwide, and is associated with significant morbidity and mortality (1). In addition to an increased rate of death by suicide, community and clinical studies indicate that bipolar patients usually present a broad range of comorbid general medical conditions, which contribute to overall mortality rates (2,3).

Of significant interest is the co-occurrence of metabolic disturbances in bipolar disorder, particularly obesity. In addition to the burden related to the expanding obesity epidemic in both developed and developing countries such as Brazil, in which prevalence rates have reached up to 11% of the population (4), bipolar disorder and comorbid obesity are associated with increased medical morbidity and worse psychiatric outcome (5). Data from clinical samples have shown that the prevalence of obesity in bipolar disorder patients is exceedingly high, ranging from 20 to 35%, when compared with controls (6–8), even in those not exposed to the weight gaining effects of pharmacological treatments (9,10). Furthermore, obese patients usually have more markers of illness severity, such as more previous affective episodes (11) and suicide attempts (12–14).

Recent studies have addressed the relationship between obesity and psychiatric morbidity (15). Data from community surveys from the United States (16) and Canada (17) have indicated that obesity has been associated with suicidal behaviour, particularly suicidal ideation and previous attempts. This is of particular concern because both obesity and suicidal behaviour are common features of bipolar disorder (18). A recent meta-analysis of 36 suicide

studies in this patient population identified several risk factors for suicide, including early onset of mood episodes, longer duration of depressive symptoms, rapid cycling, family history of suicide, previous suicide attempts and comorbid psychiatric conditions such as substance use disorders (19).

Only a couple of studies have investigated the association of obesity and suicidal behaviour in this group of patients. Fagiolini et al. (12) found a positive association between a higher body mass index (BMI) and previous suicide attempts at baseline, in a sample of 175 patients with bipolar I disorder participating in a clinical trial. Similarly, a second cross-sectional study of 171 patients by the same research group (13) reported an association between both a diagnosis of the metabolic syndrome and the presence of abdominal obesity, and a lifetime history of suicidal behaviour.

There remains a paucity of data regarding this association, with no studies from outside the United States and a relatively low number of patients in previous reports. This study, therefore, aimed to further examine an independent relationship of obesity and suicide attempts in a larger sample of patients with bipolar disorder.

Materials and methods

Subjects

Subjects were recruited from the Bipolar Disorder Program at the Hospital de Clínicas de Porto Alegre and the University Hospital at the Universidade Federal de Santa Maria. Two hundred fifty-five patients, aged 18 years or older, with a diagnosis of bipolar disorder type I or II were consecutively evaluated from January 2004 to December 2007. Written informed consent was obtained from all patients before study entry. This research project received approval from local ethics committees.

Methods

Psychiatric diagnosis of bipolar disorder and psychiatric comorbidities were confirmed with the Structured Clinical Interview for DSM-IV-axis I (SCID I). Sociodemographic and clinical variables were collected as part of a structured standard protocol (20). Depressive and manic symptoms were assessed with validated Portuguese versions of the 17-item Hamilton Rating Scale for Depression (HAM-D) (21) and the Young Mania Rating Scale (22), respectively. A lifetime history of suicide attempt was defined as at least one conscious intent to end his/her life, even if ambivalent, through means that the patient believed could result in death (23). This definition does not include minor self-harm but potentially lethal acts. Data regarding suicide attempts were obtained from best available information including interviews with patients, relatives and review of medical records.

Anthropometrical variables included height, weight and BMI which was calculated as [weight in kilograms/(height in meters)^2]. Patients were classified as normal weight (BMI < 25.0), overweight (BMI ranging 25.0–29.9) or obese (BMI ≥ 30) (24).

Statistical analysis

A multilevel logistic regression analysis to check the association between obesity and suicidality controlling for factors previously associated with suicide or suicide attempts (19). These included age and sex (first level), illness characteristics such as bipolar disorder subtype, rapid cycling, anxiety and substance use disorders (second level) and HAM-D score and obesity (third level). As such, obesity is controlled for all of the above-established risk factors. All tests were two-tailed.

Results

The sample consisted of 255 bipolar patients. A history of suicide attempts was present in 133 subjects (52.2%) and 80 patients (31.4%) were classified as obese. Table 1 shows sociodemographic and clinical variables of the sample. The majority of patients (87.8%) were taking mood stabilisers (lithium, valproate or carbamazepine) alone or in combination, 20.4% were on atypical antipsychotics and 23.5% were receiving antidepressants.

Obese patients were twice as likely to have a history of suicide attempts (OR = 2.00, 95% CI: 1.16–3.44, $p = 0.02$). Furthermore, obesity was not associated with depressive symptoms ($p = 0.77$), rapid cycling ($p = 0.068$) or anxiety ($p = 0.67$), alcohol ($p = 0.87$) and drug use disorders ($p = 0.24$). Data regarding treatment regimens are presented in Table 2.

Obesity remained associated with suicide attempts in the regression model (OR = 1.97, 95% CI: 1.06–3.69, $p = 0.03$). Also associated with suicide attempts in the final model were lifetime anxiety (OR = 2.15, 95% CI: 1.22–3.78, $p = 0.008$) and substance use disorders (OR = 2.36, 95% CI: 1.29–4.30, $p = 0.005$), rapid cycling (OR = 2.09, 95% CI: 1.09–4.00, $p = 0.027$) and current depressive symptoms (OR = 1.06, 95% CI: 1.02–1.10, $p = 0.005$). Age (OR = 0.99, 95% CI: 0.97–1.01, $p = 0.403$) and sex (OR = 1.47, 95% CI: 0.83–2.60, $p = 0.191$) were dropped from the final model.

https://doi.org/10.1111/j.1601-5215.2010.00452.x Published online by Cambridge University Press

Table 1. Clinical and demographic variables in patients with and without suicide attempts

Variable	Total sample ($n = 255$) (%/mean ± SD)
Age	41.51 ± 11.78
Sex	
Female	72.5
Ethnicity	
Caucasian	85.4
Marital status	
Married/living with partner	40.0
Education (years)	9.45 ± 4.08
Age at onset	25.93 ± 11.54
Years of illness length	15.92 ± 11.17
Number of hospitalisations	3.67 ± 5.08
Current mood symptoms	
HAM-D score	10.15 ± 8.01
YMRS score	7.86 ± 9.70
Diagnosis	
Bipolar disorder type I	88.9
Rapid cycling	27.1
Smoking	31.0
Lifetime psychiatric comorbidities	
Anxiety disorders	57.4
Alcohol abuse/dependence	27.9
Drug abuse/dependence	21.7
Eating disorders	7.8
Family history	
Mood disorders	31.4
Completed suicide	18.5
BMI classification	
Normal weight	34.9
Overweight	33.7
Obesity	31.4

Discussion

The main finding of this study is that obesity was associated with a history of suicide attempts in a sample of out-patients with bipolar disorder, even after controlling for well-established risk factors such as lifetime comorbid anxiety and alcohol use disorders and depressive symptoms.

Our finding adds to the notion that obesity is a correlate of severity in patients with bipolar disorder, and replicates earlier findings from Fagiolini et al. (12,13). In recent years, there has been an increasing interest in the relationship of obesity and psychiatric disorders (25), particularly bipolar disorder (5), because weight gain and obesity frequently complicate treatment of mood disorders (15). Furthermore, obese patients with bipolar disorder usually have more markers of adverse outcome, such as greater number of comorbid general medical conditions, increased number of previous mood episodes and more depressive features (7,8,13).

We also found a significant association between suicide attempts and comorbid anxiety and alcohol use disorders and depressive symptoms. This is in line with previous findings from our group (26,27). Bipolar patients with a history of suicide attempts have been shown to have more markers of severity such as greater suicidal ideation, increased number of hospitalisations, aggressive traits, earlier age at onset (28), a family history of suicide (29) and of psychiatric and mood disorders (30), as well as a higher frequency of comorbid anxiety, substance use and cluster B personality disorders (29–32).

One possible link between obesity and suicide in bipolar disorder may be related to depression. Major depression and residual depressive symptoms are the most common phases of bipolar disorder and both are associated with substantial work, social and family functional impairment (33). Depressive episodes are related to changes in appetite, eating behaviour and physical activity that contribute to obesity (5). Bipolar depression differs from unipolar depression in key symptom patterns, with atypical features, particularly hypersomnia and hyperphagia being prominent (34). In addition to the fact that bipolar disorder with predominant depressive polarity is strongly related to suicidal behaviour (27,35), a recent report has shown that depression with atypical features is also associated with suicide in this population (29). We also found a positive association of both depressive symptoms and obesity with suicide attempts.

Recent data have stressed common features in the underlying pathophysiology of obesity and bipolar disorder which may also be another possible explanation for our findings. Leptin, a key hormone in regulation of adiposity has been shown to be positively associated with risk for depression in a prospective study (36). Disturbances in metabolic pathways such as insulin-mediated glucose homeostasis, overactivation of the hypothalamic–pituitary–adrenal axis,

Table 2. Treatment regimens according to patient groups

Medication	Obese ($n = 80$) [N (%)]	Non-obese ($n = 175$) [N (%)]	p-Value	Suicide attempters ($n = 133$) [N (%)]	Non-attempters ($n = 122$) [N (%)]	p-Value
Mood stabilisers	73 [91.2]	151 [86.3]	0.307	120 [90.2]	104 [85.2]	0.253
Typical antipsychotics	30 [37.5]	63 [36.0]	0.889	51 [38.3]	42 [34.4]	0.603
Atypical antipsychotics	20 [25.0]	32 [18.3]	0.242	33 [24.8]	19 [15.6]	0.087
Antidepressants	17 [21.2]	43 [24.6]	0.635	39 [29.3]	21 [17.2]	0.027

https://doi.org/10.1111/j.1601-5215.2010.00452.x Published online by Cambridge University Press

dysregulated immune and inflammatory processes and adipocytokines profiles are present in both conditions (37). Such deleterious alterations in key adaptive mechanisms are a component of allostatic load (38) and may explain some of the complex interactions among bipolar disorder, common general medical conditions and resilience to mood episodes and life events (39). This framework provides another standpoint from which obesity may be seen as a correlate of allostatic load in bipolar disorder and its relationship with suicide attempts a marker of illness severity.

This report described a cross-sectional study in a tertiary treatment setting. Most of our sample consists of difficult-to-treat patients referred to the Bipolar Disorder Program, which may limit the ability to generalise our results to the whole spectrum of bipolar disorder. The retrospective assessment of some variables may be influenced by recall bias; because of the complex nature of obesity and suicidal behaviour, prospective studies are needed to further clarify the causal nature of this association.

In addition to well-established risk factors such as previous suicide attempts, depressive symptoms and comorbid psychiatric conditions, clinicians must be aware that obesity may be a severity feature relevant not only to pharmacological treatment decisions but also to the comprehensive management of bipolar disorder. It is plausible to speculate that therapeutic interventions targeted to obesity may be of potential benefit in the course of bipolar disorder.

Acknowledgements

This research was partially supported by a grant from FIPE-HCPA.

Dr F. A. G. has been an investigator in clinical trials sponsored by Servier.

Dr P. V. M. is supported by a doctoral scholarship from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brazil.

Dr K.-S. A. is supported by a CNPq post-doctoral scholarship and is a NARSAD Young Investigator; she has been an investigator in clinical trials sponsored by the Canadian Institutes of Health Research, and Stanley Foundation and has received salary support from an APA/Astra-Zeneca unrestricted educational grant.

Ms F. N. J has received support from the Australian Rotary Health fund, University of Melbourne, and the National Health and Medical Research Council.

Dr S. D. has received grant/research support from the Stanley Medical Research Foundation, NHMRC, Beyond Blue, Geelong Medical Research Foundation, Bristol Myers Squibb, Eli Lilly, Organon, Novartis, Mayne Pharma, Servier and Astra-Zeneca. He has been a paid speaker for Eli Lilly.

Dr C. S. G. has received grant/research support from CNPq, FIPE-HCPA, Endeavour Award-Australia. She has been a paid speaker for Lundbeck and Astra-Zeneca.

Dr A. C. declares no financial ties.

Dr M. B. has received grant/research support from Stanley Medical Research Foundation, MBF, NHMRC, Beyond Blue, Geelong Medical Research Foundation, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Organon, Novartis, Mayne Pharma, Servier. He has been a paid speaker for Astra-Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen-Cilag, Lundbeck, Pfizer, Sanofi Synthelabo, Servier, Solvay, Wyeth; has been a consultant for Astra-Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen-Cilag, Lundbeck, Servier.

Dr F. K. has received grant/research support from Astra-Zeneca, Eli Lilly, the Janssen-Cilag, Servier, CNPq, CAPES, NARSAD and the Stanley Medical Research Institute; has been a member of the speaker's boards for Astra-Zeneca, Eli Lilly, Janssen and Servier; and has served as a consultant for Servier.

References

1. Kupfer DJ. The increasing medical burden in bipolar disorder. JAMA 2005;**293**:2528–2530.
2. Angst F, Stassen HH, Clayton PJ, Angst J. Mortality of patients with mood disorders: follow-up over 34–38 years. J Affect Disord 2002;**68**:167–181.
3. Roshanaei-Moghaddam B, Katon W. Premature mortality from general medical illnesses among persons with bipolar disorder: a review. Psychiatr Serv 2009;**60**:147–156.
4. IOFT – International Obesity Task Force. Global prevalence of adult obesity. International Obesity Task Force Prevalence Data, 2009 Available from: http://www.iotf.org/database/documents/GlobalPrevalenceofAdultObesityJanuary2009v2.pdf (accessed 23 January 2009).
5. Wildes JE, Marcus MD, Fagiolini A. Obesity in patients with bipolar disorder: a biopsychosocial-behavioral model. J Clin Psychiatry 2006;**67**:904–915.
6. Elmslie JL, Silverstone JT, Mann JI, Williams SM, Romans SE. Prevalence of overweight and obesity in bipolar patients. J Clin Psychiatry 2000;**61**:179–184.
7. McElroy SL, Frye MA, Suppes T et al. Correlates of overweight and obesity in 644 patients with bipolar disorder. J Clin Psychiatry 2002;**63**:207–213.
8. Fagiolini A, Kupfer DJ, Houck PR, Novick DM, Frank E. Obesity as a correlate of outcome in patients with bipolar I disorder. Am J Psychiatry 2003;**160**:112–117.
9. Taylor V, Macdonald K, McKinnon MC, Joffe RT, MacQueen GM. Increased rates of obesity in first-presentation adults with mood disorders over the course of four-year follow-up. J Affect Disord 2008;**109**:127–131.
10. Maina G, Salvi V, Vitalucci A, D'Ambrosio V, Bogetto F. Prevalence and correlates of overweight in drug-naïve patients with bipolar disorder. J Affect Disord 2008;**110**:149–155.
11. Fagiolini A, Frank E, Houck PR et al. Prevalence of obesity and weight change during treatment in patients with bipolar I disorder. J Clin Psychiatry 2002;**63**:528–533.
12. Fagiolini A, Kupfer DJ, Rucci P, Scott JA, Novick DM, Frank E. Suicide attempts and ideation in patients with bipolar I disorder. J Clin Psychiatry 2004;**65**:509–514.
13. Fagiolini A, Frank E, Scott JA, Turkin S, Kupfer DJ. Metabolic syndrome in bipolar disorder: findings from the Bipolar Disorder Center for Pennsylvanians. Bipolar Disord 2005;**7**:424–430.
14. Wang PW, Sachs GS, Zarate CA et al. Overweight and obesity in bipolar disorders. J Psychiatr Res 2006;**40**:762–764.
15. McElroy SL, Kotwal R, Malhotra S, Nelson EB, Keck PE, Nemeroff CB. Are mood disorders and obesity

https://doi.org/10.1111/j.1601-5215.2010.00452.x Published online by Cambridge University Press

related? A review for the mental health professional. J Clin Psychiatry 2004;**65**:634–651.
16. Carpenter KM, Hasin DS, Allison DB, Faith MS. Relationships between obesity and DSM-IV major depressive disorder, suicide ideation, and suicide attempts: results from a general population study. Am J Public Health 2000;**90**:251–257.
17. Mather AA, Cox BJ, Enns MW, Sareen J. Associations of obesity with psychiatric disorders and suicidal behaviors in a nationally representative sample. J Psychosom Res 2009;**66**:277–285.
18. McIntyre RS, Muzina DJ, Kemp DE et al. Bipolar disorder and suicide: research synthesis and clinical translation. Curr Psychiatry Rep 2008;**10**:66–72.
19. Hawton K, Sutton L, Haw C, Sinclair J, Harriss L. Suicide and attempted suicide in bipolar disorder: a systematic review of risk factors. J Clin Psychiatry 2005;**66**:693–704.
20. Gazalle FK, Andreazza AC, Ceresér KM, Hallal PC, Santin A, Kapczinski F. Clinical impact of late diagnose of bipolar disorder. J Affect Disord 2005;**86**:313–316.
21. Fleck MP, Bourdel MC. Method of simulation and choice of factors in the analysis of principal components (Portuguese). Rev Saude Publica 1998;**32**:267–272.
22. Vilela JA, Crippa JA, Del-Ben CM, Loureiro SR. Reliability and validity of a Portuguese version of the Young Mania Rating Scale. Braz J Med Biol Res 2005;**38**:1429–1439.
23. Asberg M, Träskman L, Thorén P. 5-HIAA in the cerebrospinal fluid. A biochemical suicide predictor? Arch Gen Psychiatry 1976;**33**:1193–1197.
24. World Health Organization. Obesity: preventing and managing the global epidemic. Publication WHO/NUT/NCS/98.1. Geneva, Switzerland: World Health Organization; 1997.
25. Berkowitz RI, Fabricatore AN. Obesity, psychiatric status, and psychiatric medications. Psychiatr Clin North Am 2005;**28**:39–54, vii–viii.
26. Cardoso BM, Kauer Sant'Anna M, Dias VV, Andreazza AC, Ceresér KM, Kapczinski F. The impact of co-morbid alcohol use disorder in bipolar patients. Alcohol 2008;**42**:451–457.
27. Rosa AR, Andreazza AC, Kunz M et al. Predominant polarity in bipolar disorder: diagnostic implications. J Affect Disord 2008;**107**:45–51.
28. Grunebaum MF, Ramsay SR, Galfalvy HC et al. Correlates of suicide attempt history in bipolar disorder: a stress-diathesis perspective. Bipolar Disord 2006;**8**:551–557.
29. Sánchez-Gistau V, Colom F, Mané A, Romero S, Sugranyes G, Vieta E. Atypical depression is associated with suicide attempt in bipolar disorder. Acta Psychiatr Scand 2009; **120**:30–36.
30. Rosa AR, Franco C, Martínez-Aran A et al. Functional impairment and previous suicide attempts in bipolar disorder. Acta Neuropsychiatrica 2008;**20**:300–306.
31. Simon GE, Hunkeler E, Fireman B, Lee JY, Savarino J. Risk of suicide attempt and suicide death in patients treated for bipolar disorder. Bipolar Disord 2007;**9**:526–530.
32. Neves FS, Malloy-Diniz LF, Corrêa H. Suicidal behavior in bipolar disorder: what is the influence of psychiatric comorbidities? J Clin Psychiatry 2009;**70**:13–18.
33. Post RM. The impact of bipolar depression. J Clin Psychiatry 2005;**66**(Suppl. 5):5–10.
34. Berk M, Malhi GS, Mitchell PB et al. Scale matters: the need for a bipolar depression rating scale (BDRS). Acta Psychiatr Scand 2004;**110**:1–8.
35. Colom F, Vieta E, Daban C, Pacchiarotti I, Sánchez-Moreno J. Clinical and therapeutic implications of predominant polarity in bipolar disorder. J Affect Disord 2006;**93**:13–17.
36. Pasco J, Jacka F, Williams LJ et al. Leptin in depressed women: cross-sectional and longitudinal data from an epidemiologic study. J Affect Disord 2007;**107**:211–225.
37. McIntyre RS, Soczynska JK, Konarski JZ et al. Should depressive syndromes be reclassified as "metabolic syndrome type II"? Ann Clin Psychiatry 2007;**19**:257–264.
38. McEwen BS. Mood disorders and allostatic load. Biol Psychiatry 2003;**54**:200–207.
39. Kapczinski F, Vieta E, Andreazza AC et al. Allostatic load in bipolar disorder: implications for pathophysiology and treatment. Neurosci Biobehav Rev 2008;**32**:675–692.

https://doi.org/10.1111/j.1601-5215.2010.00452.x Published online by Cambridge University Press