Glucose abnormalities in newly diagnosed, medication-naïve patients with bipolar disorder, mania, and psychosis

Clemente Garcia-Rizo M.D. Ph.D. [1,2] Brian Kirkpatrick M.D. M.S.P.H[3] Emilio Fernandez-Egea M.D. Ph.D.[4,5] Cristina Oliveira M.D. Ph.D.[1] Ana Meseguer[1,2] R.S. Iria Grande M.D.[2,7] Juan Undurraga M.D.[2,7] Eduard Vieta M.D. Ph.D[2,6,7] Miguel Bernardo M.D. Ph.D [1,2,6]

1 Schizophrenia Program, Department of Psychiatry, Neuroscience Institute, Hospital Clinic, University of Barcelona, Barcelona, Spain
2 CIBERSAM, Madrid, Spain 3 Department of Psychiatry, Texas A&M University College of Medicine and Scott & White Healthcare, Temple, TX, USA 4 Department of Psychiatry, University of Cambridge, Addenbrooke s Hospital, CB2 0QQ Cambridge, UK 5 Cambridgeshire and Peterborough NHS Foundation Trust, Huntingdon PE29 3RJ, UK 6 Institute of Biomedical Research Agusti Pi i Sunyer (IDIBAPS), Barcelona, Spain 7 Bipolar Disorders program, Neuroscience Institute, Hospital Clinic, University of Barcelona, Barcelona, Spain

BACKGROUND

Bipolar disorder is a severe mental illness associated with functional disability (1). Bipolar disorder is also associated with increased medical morbidity and mortality (2). An increased suicide rate, poor healthcare access, poor health habits and medication side-effects contribute to the increased morbidity and mortality. The leading contributor to the excess mortality is cardiovascular disease (3). The prevalence of T2DM in bipolar disorders ranges from 8 to 17% a threefold increase compared to the general population (4). Pharmacological treatment, including both antipsychotic agents and mood stabilizers, may confound this relationship (5). Although the biochemical mechanisms that underlie psychiatric disorders are far from being understood, several lines of evidence suggest that affective disorders (6) and psychotic disorders are highly correlated with glucose abnormalities (7) The aim of the letter is to test the hypothesis that drug-naïve bipolar patients have abnormal glucose tolerance compared to matched control subjects.

MATERIAL AND METHODS

7 Drug-naïve patients with DSM-IV bipolar I disorder and matched controls underwent a two hour glucose tolerance test. All subjects gave informed consent for participation in the study, which was conducted under the supervision of the authors' respective hospital ethics committees, and came from a larger study of metabolic abnormalities and glucose dysregulation in neuropsychiatric disorders (8) in which material and methods were explained.

RESULTS

The two groups were very similar with regard to demographics, socioeconomic status, cortisol, BMI and smoking Table). The bipolar patients had a higher mean two hour glucose (2HG) value compared with matched controls (respective means (mg/dL [SD] of 145.9 [16.9] vs. (84.8 [27.8]; p<0.001;Table). 2HG values were not correlated with severity of psychosis, either Reality Distortion (adding PANSS items 1 and 3) (p=0.902) or Conceptual Disorganization (PANSS item 2) (p=0.361).

	Bipolar Disorder (N=7)	Controls (n=50)	P value
Age (years)	29.4[8.9]	28.9[5.4]	.804
Gender (%Male)	86%	66%	.413
Socioeconomic Status* (N=6/49)	5.5[3.2]	6.7[2.1]	.236
Cortisol (µg/dL)** (N=7/49)	18.8[7.2]	19.1[5.2]	.906
Cigaretes per day*** (N=6/50)	11.2[12.5]	6.1[1.6]	.648
Body Mass Index	23.4[8.0]	23.7[3.1]	.396
Fasting Insulin (mU/L)**** (N=6/48)	10.8[5.9]	8.9[4.0]	.295
Fasting Glucose(mg/dL)	92.6[17.4]	85.5[6.5]	.275
Impaired Fasting Glucose %	29	2	.037
2 Hour Insulin (mU/L)	48.5[24.8]	26.5[39.4]	.157
2 Hour Glucose (mg/dL)	145.9[16.9]	84.8[27.8]	<.001
Impaired Glucose Tolerance %	86	4	<.001

DISCUSSION

We found that newly diagnosed, medication-naïve patients with bipolar disorder, manic, with psychotic features had higher 2HG concentrations than did matched control subjects. These differences could not be attributed to confounding by BMI, gender, age, psychotropic medications, cortisol concentration, socioeconomic status, ethnicity, smoking or drugs that affect glucose tolerance.

This small preliminary study suggests that glucose abnormalities are linked to the diagnosis of bipolar I disorder before the effects of medications and other confounders had taken place. Should an association between bipolar disorder and glucose intolerance be confirmed, this might occur because diabetes and bipolar disorder share some common risk factors and/or genetics.

Birth and gestational problems appear to be risk factors for both bipolar disorder and diabetes, low birth weight being the most notable example (11) suggesting neurobiological adaptative changes that contribute to the risk of both problems. Our results are consistent with the proposals that bipolar disorder is a multi-systemic disease (12) or a syndrome of accelerated aging (13), and with the concept of allostatic load as applied to bipolar illness (14)

BIBLIOGRAPHY

1.Rosa AR, Gonzalez-Ortega I, Gonzalez-Pinto A, Echeburua E, Comes M, Martinez-Aran A, et al. One-year psychosocial functioning in patients in the early vs. late stage of bipolar disorder. Acta Psychiatr Scand. 2012;125:335-41.
2.Bobes J, Saiz J, Montes JM, Mostaza J, Rico-Villademoros F, Vieta E. Consenso Español de Salud Física del Paciente con Trastorno Bipolar. Rev Psiquiatr Salud Ment. 2008;01:26-37.
3.Osby U, Brandt L, Correia N, Ekbom A, Sparen P. Excess mortality in bipolar and unipolar disorder in Sweden. Arch Gen Psychiatry. 2001;58:844-50.
4.McIntyre RS, Konarski JZ, Misener VL, Kennedy SH. Bipolar disorder and diabetes mellitus: epidemiology, etiology, and treatment implications. Ann Clin Psychiatry. 2005;17:83-93.
5.Fiedorowicz JG, Miller DD, Bishop JR, Calarge CA, Ellingrod VL, Haynes WG. Systematic Review and Meta-analysis of Pharmacological Interventions for Weight Gain from Antipsychotics and Mood Stabilizers. Curr Psychiatry Rev. 2012;8:25-36.
6.Garcia-Rizo C, Fernandez-Egea E, Miller B, Justicia A, Heaphy C, Griffith J, et al. Biochemical phenotype in major depression disorders. . Submitted to Brain Behaviour and Immunity.
7.Brietzke E, Kapczinski F, Grassi-Oliveira R, Grande I, Vieta E, McIntyre RS. Insulin dysfunction and allostatic load in bipolar disorder. Expert Rev Neurother. 2011;11:1017-28.
8.Fernandez-Egea E, Bernardo M, Donner T, Conget I, Parellada E, Justicia A, et al. Metabolic profile of antipsychotic-naive individuals with non-affective psychosis. Br J Psychiatry. 2009;194:434-8.
9.Baptista T, Serrano A, Uzcategui E, ElFakih Y, Rangel N, Carrizo E, et al. The metabolic syndrome and its constituting variables in atypical antipsychotic-treated subjects: comparison with other drug treatments, drug-free psychiatric patients, first-degree relatives and the general population in Venezuela. Schizophr Res. 2011;126:93-102.
10.Fernandez-Egea E, Bernardo M, Parellada E, Justicia A, Garcia-Rizo C, Esmatjes E, et al. Glucose abnormalities in the siblings of people with schizophrenia. Schizophr Res. 2008;103:110-3.
11.Laursen TM, Munk-Olsen T, Nordentoft M, Bo Mortensen P. A comparison of selected risk factors for unipolar depressive disorder, bipolar affective disorder, schizoaffective disorder, and schizophrenia from a danish population-based cohort. J Clin Psychiatry. 2007;68:1673-81.
12.Leboyer M, Soreca I, Scott J, Frye M, Henry C, Tamouza R, et al. Can bipolar disorder be viewed as a multi-system inflammatory disease? J Affect Disord. 2012.
13.Sodhi SK, Linder J, Chenard CA, Miller del D, Haynes WG, Fiedorowicz JG. Evidence for accelerated vascular aging in bipolar disorder. J Psychosom Res. 2012;73:175-9.
14.Vieta E, Popovic D, Rosa AR, Sole B, Grande I, Frey BN, et al. The clinical implications of cognitive impairment and allostatic load in bipolar disorder. Eur Psychiatry. 2012.

FUNDING

Funding for this study was provided by grant RO1 DK069265 - National Institute of Diabetes and Digestive and Kidney Diseases (Dr. Kirkpatrick), NARSAD (Dr. Fernandez-Egea) Instituto de Salud Carlos III, FEDER, Centro de Investigación Biomédica en Red de salud Mental, CIBERSAM, Government of Catalonia, Comissionat per Universitats i Recerca del Department d'Innovació, Universitats i Empresa (DIUE) (2009SGR1295) and by Esther Koplowitz Center-Barcelona)(Dr. Bernardo).