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Title: Metabolic syndrome and Obsessive-Compulsive Disorder: a naturalistic Italian study

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Abstract

Objective: The increased risk for Metabolic Syndrome (MetS) in individuals with schizophrenia and bipolar disorder has been documented. No study examined MetS in patients with OCD, despite the fact that a great proportion of them are treated with antipsychotic addition. The aim of our study was to investigate the prevalence and the socio-demographic and clinical correlates of MetS in an Italian sample of patients with OCD.

Method: Subjects with DSM-IV-TR OCD and a YBOCS \geq 16 were included. Socio-demographic and clinical characteristics, current and lifetime pharmacological treatments, lifestyle information and comorbidity for cardiovascular diseases and diabetes were collected. MetS was diagnosed according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III-modified criteria.

Results: We enrolled 104 patients with OCD. MetS was present in 21.2% (95% CI: 13.7-30.3%) of the sample. Abdominal obesity was present in 36.5%, hypertension in 42.3%, high triglycerides in 23.1%, low HDL-C levels in 22.1% and fasting hyperglycemia in 4.8% of the sample. MetS was associated with cigarette smoking (duration of cigarette smoking), absence of physical activity, a higher BMI and a greater proportion of obesity. Among pharmacological treatments, MetS was associated with the duration of the exposure (lifetime) to antipsychotics.

Conclusions: This is the first study that examined the prevalence and correlates of MetS in a sample of patients with OCD. Our cross-sectional evaluation found a prevalence of MetS higher than those reported in the Italian general population, although the confidence interval encompasses the general population estimate reported. Patients with OCD on antipsychotic treatment are particularly at risk for MetS and should be carefully monitored for metabolic abnormalities and cardiovascular complications.

Introduction

The metabolic syndrome (MetS) is a collection of clinical and biochemical risk factors that predispose affected individuals to cardiovascular disease (CVD), type 2 diabetes mellitus, stroke, and premature mortality [1-10]. Metabolic syndrome includes abnormal glucose metabolism (type 2 diabetes, impaired glucose tolerance or altered fasting glycemia), central obesity, atherogenic dyslipidemia, reduced HDL cholesterol and hypertension. The age-adjusted prevalence of MetS in the US general population is 27.0% [11], while European studies have found lower rates, between 8% and 17% [12-15].

The increased risk for MetS in individuals with schizophrenia has been well documented [16]. In recent years, particularly studied has been the association between Bipolar Disorder (BD) and MetS [17]; the rate of MetS in subjects with BD is increased relative to the general population, although rates are higher in USA (30-54%) [18-21] and Canada (32.6%) [22] than in Europe (16.7-27.5%) [23-25]. In Italy, the rate of MetS in subjects with BD is estimated to be 25.3% according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP-III) [26].

There is a strong association between overweight or obesity and psychopharmacological treatments, particularly antipsychotic drugs. Together with illness-related factors such as the adoption of unhealthy and chaotic lifestyles (such as increased caloric intake, cigarette smoking, alcohol abuse and low physical activity) and probably inherited biological factors (such as HPA axis dysregulation), psychopharmacological treatments play an important role in inducing weight gain and metabolic abnormalities, eventually leading to the MetS [20, 27-30].

Few studies investigated the prevalence of MetS in patients with Anxiety Disorders. A study found a positive cross-sectional association of generalized anxiety disorder (GAD) with MetS in a large sample of male US veterans, although the prevalence of MetS among subjects with GAD was not reported [31]. In patients with PTSD, MetS prevalence rates were reported to be higher than those in the general population, ranging from 25% to 47.8% [32-34]. In addition, an association has been demonstrated between a diagnosis of PTSD and the presence of metabolic syndrome in psychiatric outpatients receiving antipsychotic medications: the prevalence of MetS was 72% among antipsychotic-treated subjects with PTSD [35].

No study, to our knowledge, investigated the prevalence of MetS among subjects with OCD, despite the fact that antipsychotic augmentation of SRI is one of the most effective and studied strategies in resistant OCD [36-38]. In subjects with OCD, the long-term (1-year) use of antipsychotics added to SRIs has been associated with an increase in BMI and fasting blood sugar [39]. Moreover, the use of antidepressants (SSRIs and clomipramine) over the long-term is also associated, independently from the association of antipsychotics, with a significant weight gain [40].

The aim of our study was to investigate the prevalence and the socio-demographic and clinical correlates of MetS (according to the NCEP ATP III criteria) in a naturalistic Italian sample of in- and outpatients with OCD.

Methods

The study had a naturalistic design and involved all patients with a principal diagnosis of Obsessive-Compulsive Disorder consecutively admitted to the Psychiatric Inpatient Unit and to the Mood and Anxiety Disorders Outpatient Unit of the University of Turin (Italy) from January 2005 to December 2011.

Subjects

All patients with a DSM-IV-TR principal diagnosis of Obsessive-Compulsive Disorder and a minimum total score of 16 on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) [41-42] were included. The aims of the study as well as study procedures were thoroughly explained to potential participants who gave written consent before participation. The study design was reviewed by the local ethics committee. Exclusion criteria included age ≤ 18 years, pregnancy or having just given birth and refusal to give consent prior to participating in the study. All subjects were of Caucasian Italian origin. Of the potential participants (N=115), 11 subjects refused to participate (9.6%). The sample included comprised 104 subjects.

Assessments and procedures

All diagnoses were confirmed by means of the Structured Clinical Interview for DSM Axis I Disorders (SCID-I). At study entry, general socio-demographic information (age, gender, occupational and marital status) was collected for each subject. Clinical data (age at OCD onset, duration of illness, Axis I and II comorbidities) were obtained through the administration of a semi-structured interview that we developed and used in previous studies [43-46] and included the SCID-I and II. In addition, the following rating scales were included in the assessment: Yale-Brown Obsessive Compulsive Scale (Y-BOCS) [41-42], Hamilton Anxiety Rating Scale (HAM-A), and 17-item Hamilton Depression Rating Scale (HAM-D) [47-48]. The Y-BOCS, HAM-A and 17-item HAM-D have good levels of internal consistency and test-retest reliability [41-42, 47-48]. The inter-rater reliability of DSM-IV diagnoses using the SCID-I was tested before the beginning of the study (>0.80 for the presence of any lifetime Axis I disorders). Inter-rater reliabilities of the Y-BOCS, HAM-A and HAM-D total scores were also good ($>.80$).

Use of medications at the time of interview was assessed; moreover, lifetime exposure to antidepressants, antipsychotics or mood stabilizers was recorded by means of direct interview, family members' interview (when available) and medical records review. We also calculated months of lifetime exposure to drugs with the same procedure.

Lifestyles were also investigated: information about exposure to cigarette smoking, use and duration of alcohol beverages, and physical exercise were obtained by directly interviewing the patients. Information about substance consumption (other than cigarette and alcohol consumption) was obtained from the patient without laboratory screening. A score was assigned to the frequency of physical exercise: absent, mild (<4 h/week), moderate (4 h/week with a tolerance of ± 30 min) and intense (>4 h/week, regular). Comorbidity and family history for diabetes or cardiovascular diseases, and current treatments for hypertension, diabetes, or dyslipidemia were assessed by looking at medical reports, and by direct interview of the patients. Family history for diabetes and cardiovascular diseases was evaluated in first-degree relatives relying on information given by patients.

At index visit weight, height, waist circumference, and blood pressure were measured. Weight was measured undressed and fasting, height was measured barefoot. Body Mass Index (BMI), defined as the ratio of body weight (in kilograms) and height (in meters squared), was calculated. Based on the score of BMI, patients were divided into classes according to the criteria of the World Health Organization [49-50] in:

obese (BMI ≥ 30 kg/m²), overweight (BMI between 25.0 and 29.9 kg/m²) and normal weight (BMI between 18.5 and 24.9 kg/m²). Waist circumference, measuring central adiposity, was taken at midway between the inferior margin of the ribs and the superior border of the iliac crest, at minimal respiration. Two blood pressure measurements were obtained by using a mercury sphygmomanometer: the first with the subject in a lying position, the second with the subject in a seated position at least two minutes after the first measurement. The mean blood pressure of the two measurements was used. The attending physician in hospital setting performed all procedures.

A blood draw for routine blood exam was performed at hospital admission for inpatients, as a part of the clinical management routine. For outpatients, results of previous blood examinations were considered valid if the last blood sample was drawn within two months before entry in the study, otherwise patients were scheduled for a blood test within a week from the study visit. At the time when blood was drawn, patients were fasting for the previous 10 hours; patients who were not fasting were rescheduled. Blood exams included glucose, total cholesterol, triglycerides, LDL and HDL-C. Blood samples were drawn in our clinic and examined in the “Baldi e Riberi” laboratory of analysis, San Giovanni Battista Hospital, Turin, Italy.

MetS was diagnosed according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III-modified criteria (NCEP ATP III 2002) [51-52]:

- Abdominal obesity: waist circumference ≥ 102 cm in men and ≥ 88 cm in women
- Hypertriglyceridemia: ≥ 150 mg/dl or on lipid-lowering medication
- Low HDL-C: < 40 mg/dl in men and < 50 mg/dl in women
- High blood pressure: systolic pressure ≥ 130 mmHg and/or diastolic pressure ≥ 85 mmHg or on antihypertensive medication
- High fasting glucose: ≥ 100 mg/dl or on glucose-lowering medication

Statistical analysis

Subjects' characteristics were summarized as mean and SD for continuous variables and frequency and percentage for categorical variables. We divided the sample according to the presence or not of MetS and then we examined demographic and clinical factors potentially associated with MetS by way of chi-

square test in the case of categorical variables and independent samples t-tests in the case of continuous variables. All data were analyzed using SPSS version 18.0 (SPSS Inc., Chigaco, IL).

Results

One hundred four patients with a principal diagnosis of OCD were recruited in our study. The mean (\pm SD) age of the sample was 35.95 (\pm 14.00) years; 62 patients (59.6%) were males and the mean (\pm SD) duration of illness was 16.18 (\pm 11.99) years. All socio-demographic and clinical characteristics are displayed in Table 1. Patients were on a mean (\pm SD) of 1.69 (\pm 1.12) medications at assessment; 20.2% were not on psychotropic medication at assessment, 75.0% were treated with at least an antidepressant, 14.4% were receiving at least one mood stabilizer and 41.3% were receiving at least one antipsychotic. The mean (\pm SD) BMI was 25.42 (\pm 5.26) kg/m². The prevalence of obese, overweight and normal weight subjects were 14.4%, 29.8% and 55.8%, respectively.

All patients had complete laboratory and clinical data: 22 patients (21.2%; 95% CI: 13.7-30.3%) met criteria for metabolic syndrome, according to NCEP ATP III. Blood high pressure was the most frequently criteria (42.3%), followed by abdominal obesity (36.5%). High triglycerides, low HDL-C levels and fasting hyperglycemia were observed in 23.1%, 22.1% and 4.8% of the sample, respectively (Table 2).

Socio-demographic and clinical features associated with MetS are shown in Table 3. Subjects with MetS had a longer duration of illness (20.50 \pm 11.54 years) than those without the syndrome (15.02 \pm 11.90 years), although the difference only approached significance ($p=.057$). Other clinical variables were not significantly associated to the presence of MetS.

The presence of MetS was significantly associated with cardiovascular and diabetes comorbidity: 59.1% of patients with MetS had a diagnosis of either cardiovascular disease or diabetes, versus 34.1% of those without MetS ($p=.034$). Patients with MetS, moreover, had a longer duration (years) of cigarette smoking, did not perform physical activity, and had a higher BMI.

Table 4 shows current and lifetime treatments of subjects with or without MetS; subjects with MetS had been exposed to antipsychotics for a significantly longer period (19.68 \pm 29.13 months) than those without MetS (6.38 \pm 11.35 months). No other significant differences were found between the two groups.

4. Discussion

This is the first study, to our knowledge, that examined the prevalence and correlates of MetS in a sample of patients with OCD. Our cross-sectional evaluation found a prevalence of MetS of 21.2%, higher than those reported in the Italian general population; studies conducted in Italy using the same NCEP ATP III criteria found prevalence rates in the general population ranging from 16 to 17.8% [14, 53-55]. However, the 95% confidence interval around our estimate (13.7-30.3%) encompasses the general population estimate reported. Given that our study lacks a control group from the general population, we can only conclude that our study failed to demonstrate that subjects with OCD are, as a group, more at risk for developing MetS than the Italian general population.

When analyzing the prevalence of the single components of MetS in our population, we found that hypertension is the most common metabolic abnormality, followed by abdominal obesity, hypertriglyceridemia and low HDL-C levels. Very few patients with OCD displayed high fasting glucose.

We could not find other studies investigating MetS in patients with OCD. Although the sample size of our study is rather low, then, this is the first report on MetS in a group of patients with OCD as their principal diagnosis. There is also little research examining the physical health of patients with OCD; a recent study found that severe patients with OCD were more likely than the general psychiatric patients to have raised blood lipids and raised creatinine; this result is not likely to be attributable to comorbid diagnoses other than OCD, as only 1.9% of the sample had also BD, 4.8% Schizophrenia, 15.4% other Anxiety Disorders [56]. Several studies, moreover, found that patients with OCD experience more physical symptoms and ill health than individuals from the general population [57-60], and that specific symptom dimensions (contamination/cleaning) are associated with poorer health-related quality of life [58-59]. All these studies, together with results of the present one, strongly point to the need for integrated care between psychiatry and primary care providers.

When examining socio-demographic and clinical factors potentially associated with MetS in OCD, we did not find any significant association. Given that MetS is highly prevalent among subjects with Bipolar Disorders (BD), with an estimated rate in Italy of 25.3% [26], we also evaluated whether a BD diagnosis was

associated with MetS; although patients with OCD with comorbid BD had a higher rate of MetS (33.3%) than those without (18.6%), we could not find a significant association between MetS and BD. Our lifetime comorbidity rates are comparable to those found in other clinical samples of patients with OCD [74].

MetS was associated in our sample with cigarette smoking (duration of cigarette smoking), absence of physical activity, a higher BMI and a greater proportion of obesity. Cigarette smoking is an important cardiovascular and metabolic risk factor: it has been shown that it may alter body lipids, predispose to central obesity, lead to hypertension, hyperinsulinemia and insulin resistance. Also, it seems to be an independent risk factor for MetS [61-67]. Physical activity promotes fat oxidation, which is believed to reduce weight and improve insulin sensitivity [68-70]. Obesity is an important cardiovascular risk factor, and it is a core component of MetS. All of these factors associated with MetS (cigarette smoking, absence of physical activity, obesity) are susceptible to modifications; psychoeducational programs aimed at reducing these risk factors should be tested in patients with OCD, to see whether MetS could be prevented.

Once established, MetS is a strong risk factor for cardiovascular disease and/or diabetes. The association found in our study between MetS and cardiovascular-diabetes comorbidity is then a confirmation of literature reports [7-8, 71]. It is however necessary to prospectively follow-up patients with OCD (particularly those on antipsychotic augmentation strategies) to determine whether they are at higher risk for cardiovascular mortality.

When examining pharmacological treatments with respect to the presence of MetS, we found that the duration of the exposure (lifetime) rather than the mere cross-sectional exposure to antipsychotics correlated with the presence of MetS. No other pharmacological treatments were associated with MetS. In subjects with OCD, the long-term (1-year) use of antipsychotics added to SRIs has been associated with an increase in BMI and fasting blood sugar [39]. Our results are then in agreement with those of Matsunaga and colleagues and point to the need of carefully monitoring patients with OCD on antipsychotic augmentation. Since discontinuation of antipsychotics once response is achieved with augmentation strategies in resistant patients is associated with a relapse [72], the choice of the antipsychotic to be added should be guided by efficacy but also metabolic adverse event profile. The small sample of subjects included in the present study prevented us to examine separately the influence of specific antipsychotics on MetS; future studies should address this issue. Concerning lifetime exposure (and months of exposure) to drugs, a limitation of our study is the fact

that not all patients had medical records available and so we estimated months of lifetime exposure in some patients on the basis of self-report only.

Our study had several limitations; the first one is the cross-sectional design. This design does not allow inferences on the temporal relationship between the variables, and only shows measures of association. Moreover, the only significant association between MetS and an independent variable found in our study was that with exposure to antipsychotics (months); this prevented us from performing a logistic regression analysis. Future studies should investigate the potential determinants of MetS in subjects with OCD using greater sample sizes and better statistical methodologies. Nevertheless, our study is the first to highlight the importance of routinely assess weight, waist circumference and perform blood examinations even in patients with OCD, and particularly in patients on antipsychotic treatment. A second limitation is the lack of a control group from the general Italian population. A third limitation is that family history of cardiovascular diseases was not operationally defined and we relied on information from the patients; this could have resulted in an underestimation of the true prevalence of cardiovascular diseases and diabetes among family members. Another limitation is the use of outside blood samples in a proportion of outpatients, so we could not confirm duration of fasting; however, given that the majority of patients enrolled in our study were continuously followed in our Department, the proportion of patients whose blood examinations were performed in another laboratory was small (13 patients - 12.5%). Self-reported exposures to treatments and a limited assessment of health behaviors are other potential limitations of our study.

It has to be acknowledged also that our sample of patients with OCD had high rates of Axis I lifetime comorbid disorders (67.3% had at least another Axis I disorder), which might have contributed to our result of a 21% rate of MetS. Our comorbidity rates, however, although high, are in line with epidemiological data that report, for example in the NCS-R [75] a 90% rate of lifetime comorbid Axis I disorders in those patients from the general population with lifetime OCD.

In conclusion, we suggest that clinicians should carefully screen all subjects with OCD for risk factors related to MetS as well as comprehensively review medical and family history. Moreover, all patients should receive evaluation and surveillance of metabolic and laboratory measures. This should be particularly done when the patient with OCD is treated with the addition of antipsychotics. It is worth reminding that screening recommendations for antipsychotics (see for example the International Society for Bipolar

Disorders - ISBD - consensus guidelines for the safety monitoring of bipolar disorder treatments [73]) are not just for individuals with Bipolar Disorder or Schizophrenia on antipsychotics.

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Table 1. Socio-demographic and clinical characteristics of the sample (n = 104).

BMI: Body Mass Index

Characteristics	Value
Males, n (%)	62 (59.6)
Age (years), mean \pm <i>sd</i>	35.9 \pm 14.0
Education (years), mean \pm <i>sd</i>	12.5 \pm 3.6
Occupational status, n (%)	
<i>White collar</i>	28 (26.9)
<i>Blue collar</i>	15 (14.4)
<i>Homeworker</i>	4 (3.8)
<i>Student</i>	19 (18.3)
<i>Retired</i>	8 (7.7)
<i>Unemployed</i>	30 (28.8)
BMI, mean \pm <i>sd</i>	25.4 \pm 5.3
<i>Obese, n (%)</i>	15 (14.4)
<i>Overweight, n (%)</i>	31 (29.8)
<i>Normal weight, n (%)</i>	58 (55.8)
Age of onset (years), mean \pm <i>sd</i>	19.7 \pm 7.3
Duration of illness (years), mean \pm <i>sd</i>	16.2 \pm 12.0
Y-BOCS, mean \pm <i>sd</i>	
<i>Total score</i>	25.2 \pm 6.2
<i>Obsession score</i>	12.7 \pm 3.2
<i>Compulsion score</i>	12.5 \pm 3.6
HAM-D, mean \pm <i>sd</i>	12.0 \pm 6.2
HAM-A, mean \pm <i>sd</i>	11.6 \pm 5.7
CGI-S, mean \pm <i>sd</i>	3.8 \pm 0.9

HAM-D: Hamilton Depression Rating Scale; HAM-A: Hamilton Anxiety Rating Scale

CGI-S: Clinical Global Impression scale-Severity of Illness;

Y-BOCS: Yale-Brown Obsessive Compulsive Scale

Table 2. Prevalence of MetS (NCEP ATP III) and its components.

Criteria	OCD (N=104) N (%)
Abdominal obesity: > 102 cm (men) and > 88 cm (women)	38 (36.5)
Hypertriglyceridemia: ≥150 mg/dl or being lipid-lowering medication	24 (23.1)
Low HDL-c: < 40 mg/dl (men) or < 50 mg/dl (women)	23 (22.1)
High blood pressure: ≥ 130/85 mmg/Hg or being on antihypertensive medication	44 (42.3)
High fasting glucose: ≥ 110 mg/dl or being on glucose-lowering medication	5 (4.8)
MetS (three or more criteria)	22 (21.2)

Table 3. Characteristics of patients with OCD with and without metabolic syndrome

	No MetS (n = 82)	MetS (n = 22)	t/ χ^2	df	p
Male gender, n (%)	49 (59.8)	13 (59.1)	.003	1	.955
Age (years), mean \pm sd	34.8 \pm 13.8	40.2 \pm 14.4	-1.625	102	.107
Education (years), mean \pm sd	12.8 \pm 3.5	11.6 \pm 3.7	1.374	102	.172
Age of onset (years), mean \pm sd	19.7 \pm 7.4	19.7 \pm 7.1	-.032	102	.975
Duration of illness (years), mean \pm sd	15.0 \pm 11.9	20.5 \pm 11.5	-1.929	102	.057
Y-BOCS, mean \pm sd					
<i>Total score</i>	24.6 \pm 6.2	27.2 \pm 6.0	-1.742	102	.085
<i>Obsession score</i>	12.4 \pm 3.2	13.6 \pm 3.1	-1.458	102	.148
<i>Compulsion score</i>	12.2 \pm 3.6	13.6 \pm 3.4	-1.723	102	.086
Lifetime Axis I comorbidity, n (%)	54 (65.9)	16 (72.7)	.372	1	.542
<i>Lifetime Mood Disorders</i>	43 (52.4)	13 (59.1)	.309	1	.578
<i>Lifetime Anxiety Disorders</i>	12 (14.6)	5 (22.7)	.831	1	.362
<i>Bipolar Disorder</i>	12 (14.6)	6 (27.3)	1.936	1	.164
Psychiatric family history, n (%)	56 (68.3)	13 (59.1)	.658	1	.417
<i>Mood Disorders</i>	38 (46.3)	9 (40.9)	.207	1	.649
<i>Anxiety Disorders</i>	24 (29.3)	10 (45.5)	2.065	1	.151
Cardiovascular/diabetes family history, n (%)	35 (42.7)	10 (45.5)	.054	1	.816
Cardiovascular/diabetes comorbidity, n (%)	28 (34.1)	13 (59.1)	4.520	1	.034
Tobacco smoke, n (%)	21 (25.6)	4 (18.2)	.524	1	.469
<i>Number of cigarettes/day, mean \pm sd</i>	12.5 \pm 6.5	16.3 \pm 9.5	-.995	23	.330
<i>Years of cigarette smoking, mean \pm sd</i>	13.1 \pm 10.2	33.0 \pm 12.8	-3.447	23	.002
Alcohol consumption, n (%)	20 (24.4)	7 (31.8)	.498	1	.480
<i>Years of alcohol consumption, mean \pm sd</i>	17.7 \pm 13.9	21.0 \pm 9.6	-.588	25	.562
Substance consumption, n (%)	5 (6.1)	0 (0.0)	1.409	1	.235
Physical activity, n (%)					
<i>Absent</i>	25 (30.5)	12 (54.5)	4.380	1	.036
<i>Present</i>	57 (69.5)	10 (45.5)			
BMI, mean \pm sd	24.2 \pm 4.6	29.9 \pm 5.2	-4.924	102	<.001
<i>Obese</i>	9 (11.0)	6 (27.3)	20.103	1	<.001
<i>Overweight</i>	18 (22.0)	13 (59.1)			
<i>Normal weight</i>	55 (67.0)	3 (13.6)			

BMI: Body Mass Index

Y-BOCS: Yale-Brown Obsessive Compulsive Scale

Table 4. Treatments (current and lifetime) of patients with OCD with and without metabolic syndrome

	All sample (N=104)	No MetS (N=82)	MetS (N=22)	t/ χ^2	df	p
Not on psychotropic medication at assessment, n (%)	21 (20.2)	17 (20.7)	4 (18.2)	.070	1	.791
Number of drugs, mean \pm sd	1.7 \pm 1.1	1.7 \pm 1.1	1.6 \pm 1.1	.264	102	.793
Number of drugs for OCD, mean \pm sd	1.4 \pm 1.0	1.4 \pm 1.0	1.4 \pm 1.1	.009	102	.993
On antidepressants at assessment, n (%)	78 (75.0)	61 (74.4)	17 (77.3)	.077	1	.782
Lifetime exposed to antidepressants, n (%)	93 (89.4)	74 (90.2)	19 (86.4)	.276	1	.599
Months on antidepressants (lifetime), mean \pm sd	34.1 \pm 45.5	34.4 \pm 48.1	33.1 \pm 34.8	.127	102	.899
On antipsychotics at assessment, n (%)	43 (41.3)	34 (41.5)	9 (40.9)	.002	1	.963
Lifetime exposed to antipsychotics, n (%)	62 (59.6)	47 (57.3)	15 (68.2)	.850	1	.356
Months on antipsychotic (lifetime), mean \pm sd	9.8 \pm 18.5	6.4 \pm 11.4	19.7 \pm 29.1	-3.315	102	.001
On lithium or valproate at assessment, n (%)	15 (14.4)	12 (14.6)	3 (13.6)	.014	1	.906
Months on lithium or valproate (lifetime), mean \pm sd	10.1 \pm 27.9	14.1 \pm 29.8	9.0 \pm 27.4	-.755	102	.452