Diabetologia (2005) 48: 215–221
DOI 10.1007/s00125-004-1641-y

ARTICLE

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Prevalence of obesity, glucose homeostasis disorders and metabolic syndrome in psychiatric patients taking typical or atypical antipsychotic drugs: a cross-sectional study

Received: 26 August 2004 / Accepted: 29 October 2004 / Published online: 2 February 2005

Abstract *Aims/hypothesis:* Atypical antipsychotic drugs may be associated with obesity and other components of the metabolic syndrome, but this relationship is controversial. We investigated the hypothesis that atypical antipsychotics are associated with a greater degree of metabolic dysfunction than typical agents. *Methods:* Metabolic parameters were measured in 103 diagnostically heterogeneous psychiatric out-patients. Patients had been taking typical or atypical antipsychotic drugs for a minimum of six months. *Results:* Sixty-nine patients were taking atypical agents, 20 typical agents and 14 a combination. Mean values (±SD) for the whole group were: age 43.8 years (11.4); BMI 29.1 kg/m^2 (5.1); *W*:*H* ratio 0.88 (0.09). Metabolic parameters, including beta cell function and insulin sensitivity, measured by HOMA, did not differ with regard to the prescribed antipsychotic drug. Six patients had undiagnosed diabetes, six patients had impaired fasting glucose, and eight fulfilled criteria for the metabolic syndrome, all of whom were taking atypical agents (p=0.07 vs typical agents). Subgroup analyses of those taking atypical agents revealed differences in BMI (mean, ±SD) between olanzapine (27.3 kg/m^2±5.1) and quetiapine (31.9 kg/m^2±5.1), p=0.01, and HbA_{1c} (olanzapine, 5.1%±0.6 vs quetiapine, 5.6%±0.6; p=0.03). Other atypical agents were intermediate with regard to these parameters. *Conclusions:* Obesity, dyslipidaemia and abnormalities of glucose homeostasis are prevalent in this group. Patients taking atypical agents showed a trend towards abnormalities of glucose homeostasis. Prospective studies are needed to explore the precise relationship between antipsychotic drugs, glucose homeostasis, obesity and the metabolic syndrome.

Keywords Antipsychotic drugs · Atypical antipsychotic drugs · Diabetes · Metabolic syndrome · Obesity · Dyslipidaemia · Glucose homeostasis · Diagnosis

Abbreviations HOMA: homeostatic model assessment

Introduction

The relationship between impaired glucose tolerance and serious mental illness has been recognised for over a century, and the eminent Victorian psychiatrist Henry Maudsley (1835–1918) found occasion to comment, 'Diabetes is a disease which often shows itself in families in which insanity prevails' [1]. The introduction of the phenothiazine antipsychotic agent, chlorpromazine, in 1952 heralded a new era in the treatment of schizophrenia, but reports were soon published which suggested that chlorpromazine had diabetogenic potential [2]. However, the reported increased prevalence of diabetes in patients with schizophrenia [3], together with poor methodology complicated the interpretation of these early studies.

Clozapine, the prototype of the atypical, or second generation antipsychotic agents was introduced in early 1970s but was withdrawn following several reports of fatal agranulocytosis. It was reintroduced, with mandatory haematological monitoring in 1988 after its efficacy was established in treatment-resistant schizophrenia [4]. Subsequently a number of other atypical antipsychotics have been introduced (e.g. olanzapine, quetiapine, risperidone) all of which have a lower propensity to cause extrapyramidal symptoms, a common side effect of the older generation drugs, and a superior profile with regard to the treatment of the 'negative' symptoms of schizophrenia (blunt affect and anhedonia, impaired volition, social withdrawal). Antipsychotics also have proven efficacy in the treatment of mood disorders [5] and the use of these drugs in psychiatry is widespread.

These data were presented at the North American Association for the Study of Obesity Annual Scientific Meeting, Las Vegas, November 2004.

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In recent years the debate concerning the relationship between metabolic disturbance, diabetes mellitus and antipsychotic use has taken on a new momentum. Cases of new onset diabetes and glucose intolerance have been reported with all commonly prescribed atypical agents, including olanzapine [6], quetiapine [7] and risperidone [8]. A recent 14-week prospective study reported glucose dysregulation in patients taking atypical and typical antipsychotics, and also increased cholesterol levels in patients taking atypical agents [9]. Other studies have reported glucose intolerance only in patients taking atypical antipsychotics [10]. The debate is further complicated by reports of increasing rates of obesity and diabetes in the general population [11] as well as the intriguing relationship between severe mental illness and impaired glucose homeostasis [12, 13]. Responding to these areas of uncertainty, a Consensus Statement has been issued by a panel representing the American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity [14]. The limitations of current research in this area were highlighted, and physicians were encouraged to monitor patients prescribed atypical agents for signs of weight gain, and other metabolic disturbance.

This cross-sectional study was designed to investigate the prevalence of metabolic derangement in psychiatric patients taking antipsychotic drugs, and the relationship between metabolic disturbance and antipsychotic use. We hypothesised that patients taking atypical antipsychotic agents would have a higher prevalence of abnormal glucose homeostasis and metabolic disturbance compared with those prescribed typical antipsychotics.

Subjects and methods

We randomly recruited 106 patients from psychiatric outpatient clinics in the North of England between January 2002 and March 2004. Subjects were recruited irrespective of psychiatric diagnosis. The only inclusion criterion was that the individual was taking prescribed typical or atypical antipsychotic medication for a minimum of 6 months. Although changes of drug within the same class (i.e. typical or atypical) during this period of 6 months were permitted, all recruited subjects had been receiving the same antipsychotic drug for a minimum of 6 months. Exclusion criteria were as follows: a known diagnosis of type 1 or type 2 diabetes mellitus, anorexia nervosa, bulimia nervosa, neoplastic disease or alcohol dependence. All patients gave written informed consent to participate in this study which was approved by the Newcastle upon Tyne Regional Ethics Committee.

On the day of assessment patients were invited to attend the University Department of Psychiatry following an overnight fast, having previously been given written instructions to fast from midnight on the evening prior to assessment. Demographic details were obtained, which included age, gender, and racial origin. Current tobacco, alcohol and illicit substance use was recorded as well as family history of cardiovascular disease and diabetes mellitus. Information regarding psychiatric diagnosis, duration of illness, number of admissions to psychiatric in-patient facilities, medication (including non-psychiatric drugs) and dosage was recorded and confirmed, where necessary, by reference to the case notes and prescription charts. In addition, height, weight, and waist and hip circumference were recorded. A single venous blood sample was withdrawn from the antecubital fossa, and was analysed for glucose, HbA_{1c}, insulin and lipid profile (total cholesterol, HDL, LDL and triglycerides). Insulin was measured by ELISA. Intra-assay coefficient of variation (CV) was 7.5%, and inter-assay CV was 4.2%. The homeostatic model assessment (HOMA2; [15]) was used to assess insulin resistance and is expressed as %β (beta cell function) and %S (insulin sensitivity). The updated HOMA model (HOMA2) takes account of variations in hepatic and peripheral glucose resistance, increases in the insulin secretion curve for plasma glucose concentrations above 10 mmol/l and the contribution of circulating proinsulin. The model is calibrated to give %β and %S values of 100% in normal young adults when using currently available assays for insulin. Impaired fasting glucose (IFG) was defined as fasting blood glucose between 6.1 and 7.0 mmol/l, and diabetes mellitus as fasting blood glucose >7.0 mmol/l or HbA_{1c} >9% [16].

Primary outcome measures were: (1) the proportion of patients with undiagnosed diabetes mellitus or impaired fasting glucose, (2) differences in metabolic parameters (fasting blood glucose, insulin and lipid profiles, HbA_{1c}, HOMA, body mass index (BMI) and waist to hip (*W*:*H*) ratio) between those taking typical or atypical antipsychotic drugs.

Statistical analysis Data were analysed using the Statistical Package for Social Sciences (SPSS version 11). Serum triglycerides were not normally distributed and values were $\log_{10}$ transformed. Differences between groups of patients with regard to the prescribed antipsychotic agent were assessed using one-way ANOVA with post-hoc Student's *t*-tests, as appropriate. The chi-square (χ^2) statistic was used to compare the distribution of discrete variables. Values are expressed as mean (±SD) unless otherwise stated, except for non-normally distributed data which is expressed as median (range). Statistical significance is defined as $p<0.05$.

Results

A total of 106 patients were recruited to the study. Three patients were non-compliant with prescribed medication and were excluded from further study. The characteristics of the remaining 103 patients are given in Table 1. Twenty patients (19.4%) were prescribed typical antipsychotic medication, 69 (66.9%) atypical agents, and 14 (13.6%) patients were taking a combination of typical and atypical antipsychotics. Individual drugs and average daily doses are given in Table 2. With regard to diagnosis, 33 (32.0%) patients had a diagnosis of bipolar disorder, 35 (33.9%)

Table 1 Whole group characteristics, and comparisons between the three treatment groups

	Whole group (*n*=103)	Typical antipsychotic (*n*=20)	Atypical antipsychotic (*n*=69)	Combination (*n*=14)
Age (years)	43.9 (11.4)	47.2 (14.1)	42.9 (10.9)	43.7 (8.8)
Gender (% m/f)	52/48	45/55	52/48	64/36
Ethnicity (% cauc)	98	100	97	100
Duration (months)	208 (152)	261.9 (155.6)	182.7 (149.9)[a]	258.9 (134.6)
Admissions	5.4 (5.5)	5.6 (4.8)	4.7 (5.5)	8.4 (5.4)[b]
FH CVD (%)	59.2	65.0	63.8	28.6
FH DM (%)	30.1	40.0	29.0	21.4
Smoke (%)	51.5	35.0	54.4	64.3
Cigarettes per day	12.6 (16.0)	10.5 (18.7)	11.7 (13.5)	22.8 (20.1)[c]
Alcohol (U/week)	6.1 (9.9)	5.4 (7.5)	6.4 (9.9)	5.7 (13.1)
Substance misuse (%)	32.0	15.0	31.9	57.1
BMI (kg/m^2)	29.1 (5.2)	28.8 (4.2)	28.9 (5.2)	30.3 (6.2)
Waist/hip ratio	0.88 (0.09)	0.86 (0.08)	0.88 (0.09)	0.91 (0.09)
FBG (mmol/l)	5.3 (1.0)	5.1 (0.5)	5.4 (1.2)	5.2 (0.9)
HbA_{1c} (%)	5.3 (0.5)	5.2 (0.3)	5.3 (0.6)	5.3 (0.3)
%β	112.2 (42.8)	111.6 (37.2)	110.7 (42.8)	120.1 (52.3)
%S	95.7 (60.7)	102.6 (67.8)	94.4 (59.6)	92.5 (59.8)
Cholesterol (mmol/l)	5.6 (1.2)	5.4 (0.8)	5.7 (1.2)	5.4 (1.1)
Triglycerides (mmol/l)	1.8 (0.6–8.4)	1.5 (0.6–4.8)	1.8 (0.6–8.4)	1.9 (0.6–5.5)
HDL (mmol/l)	1.3 (0.4)	1.4 (0.3)	1.4 (0.4)	1.2 (0.3)
LDL (mmol/l)	3.2 (0.9)	3.2 (0.7)	3.2 (0.9)	3.2 (0.9)
Lipid treatment (%)	2.9	5.0	1.4	7.1
Antihypertensive (%)	5.0	10	4.3	0

m Male, *f* female, *FH* family history, *CVD* cardiovascular disease, *DM* diabetes mellitus, *BMI* body mass index, *FBG* fasting blood glucose; *%β* beta-cell function (assessed by HOMA), *%S* insulin sensitivity (assessed by HOMA), *HDL* high-density lipoprotein, *LDL* low-density lipoprotein

[a] p=0.03 vs typical antipsychotic group

[b] p=0.02 vs atypical antipsychotic group

[c] p<0.05 vs typical antipsychotic and atypical antipsychotic group

schizophrenia, 11 (10.7%) schizoaffective disorder, and the remaining 24 (23.5%) patients were treated with antipsychotic medication for a variety of mood and anxiety disorders. All subjects were outpatients, and none was acutely unwell. There were no differences between the diagnostic categories with regard to any of the parameters measured in this study.

Patients taking only atypical antipsychotics had a significantly shorter duration of psychiatric illness than those taking typical agents either alone or in combination (ANOVA, F=3.5, df=2, p=0.03). Those taking a combination of typical and atypical agents had significantly more hospital admissions (ANOVA, F=2.7, df=2, p=0.02) compared with those taking atypical agents, and smoked more cigarettes per day than those prescribed a single antipsychotic drug (ANOVA, F=2.7, df=2, p<0.05). All other parameters, including measures of obesity, glucose homeostasis and lipid profiles did not differ significantly between the three treatment groups.

Twelve patients (11.6%) were found to have a previously undiagnosed glucose homeostasis disorder; six were classified as having IFG, and a further six fulfilled criteria for diabetes mellitus. All patients with IFG or diabetes mellitus were taking atypical antipsychotic drugs (olanzapine *n*=6, clozapine *n*=3, quetiapine *n*=2, risperidone *n*=1). The association with atypical antipsychotic medication did not reach conventional levels of statistical significance (χ^2=3.24, df=1, p=0.07), but a trend was identified. Twenty-six percent of patients had total fasting cholesterol >6.5 mmol/l, and 55% had fasting serum tri-

Table 2 Typical and atypical drugs, and average doses in patients taking antipsychotic monotherapy

	Number	Percent	Average dose
Typical drugs (*n*=20)			
Chlorpromazine	4	20	112.5 mg/day
Clopixol[a]	5	25	495 mg/2-weekly
Depixol	10	50	82.7 mg/2-weekly
Haloperidol[a]	3	15	200 mg/2 weekly
Fluphenazine	2	10	47.5 mg/day
Atypical drugs (*n*=69)			
Amisulpiride	5	7	480 mg/day
Clozapine	8	12	622.2 mg/day
Olanzapine	32	46	12.3 mg/day
Risperidone	11	19	5.6 mg/day
Quetiapine	13	16	414.2 mg/day

Four patients in the 'typical' group were taking two agents.

[a] Prescribed as a depot preparation

Table 3 Characteristics of 12 patients with evidence of abnormal glucose homeostasis

Patient	Gender	FBG (mmol/l)	HDL (mmol/l)	Triglycerides (mmol/l)	BMI kg/m^2	W:H	Antihyp	Antipsychotic	Metabolic Syndrome[a]
1	Female	9.4	1.5	6.0	33.5	0.87	Yes	Quetiapine	Yes
2	Male	6.3	1.1	5.0	31.4	0.93	No	Clozapine	Yes
3	Male	6.1	1.2	5.0	31.3	0.93	No	Olanzapine	Yes
4	Male	8.9	0.9	6.9	37.6	1.01	No	Clozapine	Yes
5	Male	10.3	1.1	3.3	36.1	1.0	Yes	Quetiapine	Yes
6	Male	6.4	1.1	2.3	33.7	1.09	No	Risperidone	Yes
7	Female	6.1	1.7	1.2	24	0.95	No	Olanzapine	No
8	Female	8.4	1.6	1.9	30.1	0.86	No	Olanzapine	Yes
9	Female	7.4	1.5	1.5	28.7	0.91	No	Olanzapine	No
10	Male	6.9	0.7	2.5	29.7	1.01	No	Olanzapine	Yes
11	Female	6.2	0.9	1.7	24.6	0.85	No	Clozapine	No
12	Female	7.0	1.6	1.8	26.7	0.81	No	Olanzapine	No

FBG Fasting blood glucose, *HDL* high-density lipoprotein, *BMI* body mass index, *W:H* waist-to-hip ratio
[a]As defined by the WHO [17]

glyceride levels >1.7 mmol/l (one of the criteria for metabolic syndrome). Alarmingly, only 2.9% of patients were receiving lipid-lowering therapy. Eight patients (7.8%) fulfilled criteria for the metabolic syndrome as defined by the World Health Organization [17]. Characteristics of these 12 patients are presented in Table 3.

Subgroup analysis of those patients taking only atypical antipsychotics was performed to investigate whether there was an association between individual atypical antipsychotic drugs and measures of obesity, glucose homeostasis and dyslipidaemia. These data are presented in Table 4. The BMI of patients taking olanzapine was significantly lower than that of patients prescribed quetiapine (p=0.01), and similarly HbA_{1c} was significantly lower in olanzapine-treated patients (p=0.03) compared with those prescribed quetiapine. Serum triglycerides were significantly higher in patients taking clozapine compared with amisulpiride- and risperidone-treated patients (p=0.03). Other atypical agents were intermediate with regard to these parameters. No other significant differences between atypical drugs were observed.

Discussion

Antipsychotic drugs have revolutionised the management of serious mental illnesses such as schizophrenia and bipolar disorders, and they have provided countless individuals with an enhanced quality of life and improved psychosocial functioning. Notwithstanding the therapeutic effectiveness of the antipsychotic drugs, increasingly attention has turned to the possible deleterious side effects of these agents, and the metabolic derangements associated with antipsychotics have been the focus of considerable

Table 4 Sub-group analysis of measures of obesity, glucose homeostasis and dyslipidaemia in 69 patients taking atypical antipsychotic medication

	Amisulpiride (n=5)	Clozapine (n=8)	Olanzapine (n=32)	Quetiapine (n=11)	Risperidone (n=13)	p Value
BMI (kg/m^2)	28.2 (5.7)	30.8 (5.3)	27.3 (5.1)	31.9 (5.1)	29.8 (4.5)	0.01 (olanzapine vs quetiapine)
W:H ratio	0.83 (0.08)	0.93 (0.06)	0.88 (0.09)	0.88 (0.02)	0.89 (0.09)	NS (0.46)
FBG (mmol/l)	4.8 (0.5)	6.0 (1.3)	5.3 (0.9)	5.9 (2.0)	5.2 (0.6)	NS (0.17)
HbA_{1c} (%)	5.1 (0.6)	5.4 (0.6)	5.1 (0.6)	5.6 (0.6)	5.3 (0.3)	0.03 (olanzapine vs quetiapine)
%β	107.7 (21.8)	106.1 (35.5)	111.9 (51.1)	100.3 (20.9)	120.5 (46.1)	NS (0.84)
%S	104.9 (33.3)	68.9 (43.4)	101.6 (67.5)	94.9 (65.6)	87.8 (51.1)	NS (0.70)
Total cholesterol (mmol/l)	5.2 (0.8)	5.8 (1.1)	6.0 (1.2)	5.7 (1.6)	5.2 (0.9)	NS (0.36)
Triglycerides (mmol/l)	1.0 (0.7–2.2)	2.4 (0.6–8.4)	1.9 (0.6–6.6)	2.1 (0.9–6.0)	1.4 (0.6–3.9)	0.03 (amisulpiride vs clozapine) 0.04 (risperidone vs clozapine)
HDL (mmol/l)	1.5 (0.3)	1.1 (0.2)	1.4 (0.3)	1.5 (0.6)	1.4 (0.4)	NS (0.42)
LDL (mmol/l)	3.1 (0.9)	2.8 (0.3)	3.4 (1.0)	3.3 (1.6)	3.1 (0.7)	NS (0.71)

BMI Body mass index, *W:H* waist-to-hip ratio, *FBG* fasting blood glucose, *%β* beta-cell function (assessed by HOMA), *%S* insulin sensitivity (assessed by HOMA), *HDL* high-density lipoprotein, *LDL* low-density lipoprotein

interest and debate for many years. We report data from a representative sample of 103 psychiatric outpatients, from across the spectrum of psychiatric illness, who had been taking antipsychotic drugs for a minimum of six months. An outpatient sample overcomes, to some extent, the confounding impact of physical inactivity on glucose homeostasis [18] which is inherent in studies of psychiatric inpatients [19]. In addition, we intentionally recruited subjects from across the diagnostic spectrum as many previous reports have focused specifically on schizophrenia [9, 13]. These data highlight several important points regarding the physical health characteristics of this population, the degree of metabolic disturbance associated with typical and atypical antipsychotic drugs, and the poor detection and treatment rates in this patient group.

This population is overweight and shows a propensity towards obesity. Obesity is a worldwide epidemic estimated to affect 300 million people worldwide [20], but the relationship between obesity and mental illness is controversial. Undoubtedly, some patients gain substantial weight during treatment with antipsychotic drugs [21], but an independent association between schizophrenia and physical illnesses that have a metabolic signature, including obesity, has been proposed [22]. Retrospective data analyses have also reported that the prevalence of obesity is higher in patients with bipolar disorder compared with the general population [23], but the relative contribution of treatment and other factors such as genetic influences, environment and socio-economic status cannot be ascertained from these data.

Dyslipidaemia is also prevalent in this group, but less than 3% of patients are receiving lipid-lowering therapy. A high incidence of family history of cardiovascular disease is also reported. In addition, over 50% of this group smokes cigarettes regularly, which is consistent with previously published data [24]. Patients receiving antipsychotic polypharmacy smoke more than those receiving monotherapy. Those individuals taking more than one antipsychotic drug are likely to have a more refractory illness, as suggested by the increased number of hospital admissions, and possibly a greater prevalence of negative symptoms. As such this group may be less receptive to health education, including smoking cessation campaigns.

Twelve patients (11.6%) had a previously undiagnosed disorder of glucose homeostasis (diabetes mellitus=6; IGT=6). All patients were taking atypical antipsychotic medication, but this association was not statistically significant. The prevalence of undiagnosed glycaemic disorder here is similar to that reported in a recent study in which case notes from hospitalised patients prescribed antipsychotic drugs were examined for evidence of testing for diabetes [25]. The study by Taylor et al. reported a prevalence of glucose homeostasis disorder of 15.6% in those tested, and no association between the prevalence of hyperglycaemia and the type of antipsychotic medication was found. Alarmingly, however, testing for diabetes was undertaken in less than half of the patients studied.

Eight (7.8%) patients from our study also fulfilled WHO criteria for the metabolic syndrome, which has important implications with regard to cardiovascular disease risk [26]. Blood pressure measurements and urinary albumin excretion rate were not assessed in this study and it is therefore possible that an even greater number of those with impaired fasting glucose fulfilled criteria for the metabolic syndrome.

Taken together, these data, drawn from a representative sample of psychiatric outpatients, provide compelling evidence that this population is at significant risk for cardiovascular disease and premature mortality. As such, there is a clear need for regular monitoring of glycaemic control and screening for other components of the metabolic syndrome. It is of concern, however, that only a small proportion of patients with hyperlipideamia are receiving lipid-lowering therapy, suggesting that diagnostic screening and treatment may not be routinely offered to this patient group.

The differences between typical and atypical agents with regard to the risk for weight gain and disorders of carbohydrate and lipid metabolism are unclear. Much of the current data is methodologically poor and is derived from retrospective studies or case series. The recently published consensus statement [14] recognised the methodological limitations of the currently available data, and encouraged more prospective, controlled trials. One such 14-week prospective randomized trial of 101 inpatients with a diagnosis of schizophrenia or schizoaffective disorder reported that both typical (haloperidol) and atypical (clozapine and olanzapine) antipsychotics were associated with an increase of plasma glucose levels albeit within the normal range, and 14 patients developed abnormal glucose levels during the trial [9]. Although these data are valuable in assessing the short-term differential metabolic effects of the various antipsychotic drugs, it is important to understand the evolution and progression of metabolic derangement in the longer term as many patients receiving antipsychotic drugs require long term maintenance treatment. In this study we have shown that the metabolic parameters in a diagnostically heterogeneous group do not differ between patients taking typical and atypical antipsychotics for a minimum of 6 months.

Although weight gain is a commonly reported side effect of antipsychotic medication, it may be more common in those patients taking atypical agents. A meta-analysis of the data suggests that weight gain appears to be commonest and greatest with clozapine and olanzapine, moderate with risperidone, and probably least with amisulpiride [27]. A company sponsored trial found no overall weight increase in patients taking quetiapine [28], but other reports suggest that quetiapine may cause weight gain comparable to olanzapine [29]. In our study patients receiving quetiapine had a BMI significantly higher than that of those treated with olanzapine. Values of BMI for the other atypical agents were intermediate. The design of this study does not allow for the direction of causality to be determined. These data may suggest that quetiapine has a propensity to cause weight gain similar to, or in excess of that of other atypical agents. An alternative explanation is that patients with a BMI in the overweight or obese range may have been commenced, or switched, to an agent (e.g. quetiapine) with

a perceived lower propensity to cause weight gain. The observed increase of HbA_{1c} in the quetiapine-treated group is likely to reflect the increased BMI in this group.

It is difficult to interpret the significance of the higher serum triglycerides observed in clozapine-treated patients compared with patients treated with amisulpiride or risperidone as no large scale trials have quantified the effects of atypical drugs on lipid metabolism. However, studies have suggested that clozapine and olanzapine may be associated with greater adverse changes in serum triglycerides and cholesterol [14, 30].

The major limitation of this study is its cross-sectional design which precludes causal relationships to be identified. There is a wealth of non-prospective studies which report rates of glucose homeostasis disorders (often based on fasting blood glucose values) in patients taking antipsychotic drugs, but our study has reported a range of metabolic parameters, as well as assessing the proportion of patients fulfilling criteria for the metabolic syndrome. Although it is clear that metabolic derangement is prevalent in this population, the risk attributable to antipsychotic drugs, or the differential risks between individual drugs or classes of drugs cannot be quantified in this study. Any study which attempts to determine the direction of causality needs to account for the multifactorial aetiology of the disorder, and it is well recognised that risk factors for diabetes include family history, obesity, race, diet and physical activity. We did not assess dietary intake or physical exercise in this study and future studies should consider measuring these parameters when attempting to establish causality. The increased risk of obesity and glucose homeostasis disorders in patients with severe mental illness is less clear, but emerging data suggests that such an association exists.

In summary, we have shown that a significant proportion of this representative sample of psychiatric out-patients treated with antipsychotic drugs suffer from obesity. Previously undiagnosed disorders of glucose homeostasis are also evident, and a number of these patients also fulfil criteria for the metabolic syndrome. It is imperative that this population, which already has a high burden of physical morbidity and excess mortality, is closely monitored, offered appropriate screening and, where necessary, treatment. To this end, we advocate closer integration of physical and mental health services, and the provision of clear protocols for screening and appropriate intervention which highlight the role of primary care and secondary care physicians. We did not identify any statistically significant excess of metabolic derangement associated with atypical antipsychotic drugs compared with typical agents in this cross-sectional study, but longer-term follow-up data on this cohort of patients may provide valuable data regarding the longer-term evolution of the metabolic consequences of these widely prescribed drugs.

Acknowledgements This study was supported by an unrestricted educational grant from Jannsen-Cilag.

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