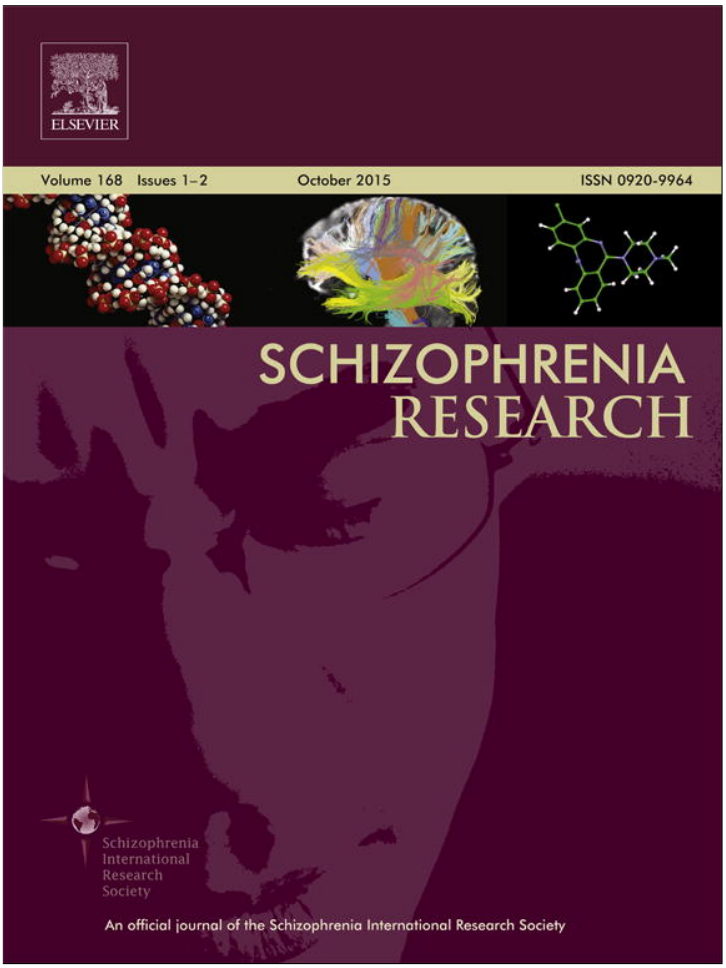

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Metabolic syndrome, abdominal obesity and hyperuricemia in schizophrenia: Results from the FACE-SZ cohort

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ABSTRACT

Objective: Abdominal obesity was suggested to be a better predictor than Metabolic Syndrome (MetS) for cardiovascular mortality, however this is has not been extensively studied in schizophrenia. Hyperuricemia (HU) was also suggested to be both an independent risk factor for greater somatic comorbidity and a global metabolic stress marker in patients with schizophrenia.
The aim of this study was to estimate the prevalence of MetS, abdominal obesity and HU, to examine the association between metabolic parameters with HU in a cohort of French patients with schizophrenia or schizo-affective disorder (SZ), and to estimate the prevalence rates of treatment of cardio-vascular risk factors.
Method: 240 SZ patients (age = 31.4 years, male gender 74.3%) were systematically included. Metabolic syndrome was defined according to the International Diabetes Federation and HU if serum uric acid level was above 360 μmol/L.
Results: MetS, abdominal obesity and HU were found respectively in 24.2%, 21.3% and 19.6% of patients. In terms of risk factors, multiple logistic regression showed that after taking into account the potential confounders, the risk for HU was higher in males (OR = 5.9, IC95 [1.7–21.4]) and in subjects with high waist circumference (OR = 3.1, IC95 [1.1–8.3]) or hypertriglyceridemia (OR = 4.9, IC95 [1.9–13]). No association with hypertension, low HDL cholesterol or high fasting glucose was observed. Only 10% of patients with hypertension received a specific treatment, 18% for high fasting glucose and 8% for dyslipidemia.
Conclusions: The prevalence of MetS, abdominal obesity and hyperuricemia is elevated in French patients with schizophrenia, all of which are considerably under-diagnosed and undertreated. HU is strongly associated with abdominal obesity but not with psychiatric symptomatology.

1. Introduction

MetS is defined by the presence of three or more of the following five criteria: increased waist circumference, hypertriglyceridemia, low HDL cholesterol level, high blood pressure, and high fasting glucose concentration (Alberti et al., 2006). High prevalence of metabolic syndrome (MetS) has been reported repeatedly in patients with schizophrenia (Mitchell et al., 2013b; Vancampfort et al., 2013), partly because of a sedentary lifestyle and lack of exercise, and partly because of the administration of second-generation antipsychotics (Mitchell et al., 2013a), especially olanzapine and clozapine, known to induce more metabolic disturbances than other antipsychotics (Ma et al., 2014; Mitchell et al., 2012).

In the general population, proposed criteria for identifying subjects with MetS have contributed greatly to preventive medicine, but the value of metabolic syndrome as a scientific concept remains controversial (Despres and Lemieux, 2006). The presence of metabolic syndrome alone cannot predict global cardiovascular disease risk. But abdominal obesity — the most prevalent manifestation of metabolic syndrome — is a marker of 'dysfunctional adipose tissue', and is of central importance in clinical diagnosis (Despres and Lemieux, 2006).

Epidemiological and clinical studies have confirmed a positive correlation between body weight and serum uric acid level in different non-psychiatric populations (Han et al., 2014; Lin et al., 2008; Shiraishi and Une, 2009). HU in obesity is mainly attributed to an impaired renal clearance of uric acid (Yamashita et al., 1986). Beyond the well-known risk of gout, hyperuricemia has been suggested to be an independent risk factor of MetS and other somatic comorbidities (including kidney disease, type II diabetes, sexual dysfunction, coronary heart disease, vascular disease, and ischemic stroke) (Aribas et al., 2014; Chen et al., 2009; Huang et al., 2012; Kim et al., 2009, 2010; Li et al., 2014; Reininghaus et al., 2014; Viazzi et al., 2011; Xu et al., 2013). HU was also identified as an independent risk factor for all-cause mortality (Liu et al., 2012; Niskanen et al., 2004; Park et al., 2011; Xu et al., 2013). Only one study assessed uric acid levels in patients with schizophrenia to date (Chiu et al., 2012). In this sample of 637 patients, high acid uric levels were associated with hypertriglyceridemia, low HLD cholesterol levels, hypertension and MetS (with an odds ratio of 9.28) in males, but not in females.

HU may not be only a marker of cardiovascular risk in schizophrenia, but also a marker of general oxidative stress. Circulating uric acid was described as one of the major antioxidants of the plasma that protects cells from oxidative damage (Ishizaka et al., 2014; Pingmuangkaew et al., 2015). Based on other oxidative markers than HU, a considerable body of research has identified a disturbed antioxidant defense in patients with first episode schizophrenia as well as in later stages of the disease (for review see (Yao et al., 2013)). A chronic sub-inflammation of the central nervous system may underline pathophysiological mechanisms in schizophrenia and activate anti-oxidative pathways. It is therefore unclear if higher uric acid level in schizophrenia may be considered as a biomarker of an anti-oxidative protective mechanism occurring in psychiatric illness or of the cardiometabolic disturbances via impaired renal clearance.

The primary objective of this study is to estimate the prevalence of MetS, abdominal obesity and hyperuricemia in a cohort of French patients with schizophrenia, to determine their correlations with socio-demographic, clinical, and treatment-related characteristics and to investigate the gap between optimal care and effective care in treated patients. The secondary objective is to examine the association between MetS, abdominal obesity, HU, and psychiatric clinical characteristics, including psychiatric treatments.

2. Methods

2.1. Study population

The FondaMental Advanced Centers of Expertise in Schizophrenia (FACE-SZ) cohort is issued from an ongoing French national network of schizophrenia expert centers, set up by a scientific cooperation foundation in France, the FondaMental Foundation and funded by the French Ministry of Research in order to create a network strongly connected to primary and specialized care, providing support for routine care and aiming to spread good clinical practice to improve the outcome of the disease (Schürhoff et al., 2015). The cohort was created in 10 Centers (Bordeaux, Clermont-Ferrand, Colombes, Créteil, Grenoble, Lyon, Marseille, Montpellier, Strasbourg and Versailles) allowing observational follow up of patients referred by their general practitioner or psychiatrist, who subsequently receive a detailed evaluation report with suggestions for therapeutic interventions. All outpatients aged 16 years and over evaluated in an Expert Center and diagnosed with schizophrenia or schizoaffective disorders according to DSM-IV-TR criteria, were enrolled in the FACE-SZ cohort. Patients were evaluated when being apart from an acute episode, using dedicated electronic medical records including thorough psychiatric, somatic, and neuropsychological assessments.

The assessment protocol was approved by the relevant Ethical Review Board (CPP-Ile de France IX) on January 18th, 2010.

2.2. Data collected

At baseline, information on education, marital status, economic status, onset and course of illness, family history, tobacco smoking status, somatic disease and comorbidities was recorded. Psychopathology was assessed using Positive and Negative Syndrome Scale (PANSS). Current depressive symptoms were evaluated using the Calgary scale (Addington et al., 1993). Antipsychotic use is systematically recorded as well as all other psychiatric and somatic treatments. The types of antipsychotic drug prescribed were categorized into "clozapine/olanzapine" group and "other antipsychotics" group considering that clozapine and olanzapine may have a higher potential in generating metabolic abnormalities (Newcomer, 2007) and weight gain (Allison et al., 1999).

2.3. Measurements

Sitting blood pressure (BP) and anthropometrical measurements were recorded. Two BP measurements were made 30 s apart in the right arm after the participant had sat and rested for at least 5 min. A third BP measurement was made only when the first two BP readings differed by more than 10 mm Hg. The average of the 2 closest readings was used in the analysis. Waist circumference was measured midway between the lowest rib and the iliac crest while the subjects were standing. This was performed with a tape equipped with a spring-loaded mechanism to standardize tape tension during measurement. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Overnight fasting blood was collected for metabolic profile analysis. Fasting levels of serum triglyceride (TG) and fasting plasma glucose were measured by an automated system, and serum high-density lipoprotein cholesterol (HDL-C) level was measured by electrophoresis. Serum uric concentrations were determined by spectrophotometry.

2.4. MetS definition

Measures of systolic and diastolic blood pressure were performed after the patient had rested for at least 5 min. Weight, height and waist circumference were also measured in Expert Centers. A blood draw for routine blood exam was performed and triglycerides, LDL, HDL and total cholesterol as well as glucose (if patients were confirmed fasting for at least 10 h) were collected. All measures of MetS components were based on laboratory blood exam performed in Expert Centers.

The diagnosis of metabolic syndrome was defined according to the modified criteria of the International Diabetes Federation (IDF) (Alberti et al., 2006), which requires the presence of three or more of the following five criteria: high waist circumference (>94 cm for men and >80 cm for women), hypertriglyceridemia (≥1.7 mM or on lipid lowering medication), low HDL cholesterol level (<1.03 mM in men and <1.29 mM in women), high blood pressure (≥130/85 mm Hg or on antihypertensive medication), and high fasting glucose concentration (≥5.6 mM or on glucose-lowering medication). All patients treated by metformin received a previous diagnosis of diabetes.

2.5. Abdominal obesity definition

Abdominal obesity was defined by the presence of both hypertriglyceridemia (≥1.7 mM or on lipid lowering medication) and high waist circumference (>94 cm for males and >80 cm for females) (Despres and Lemieux, 2006; Girerd et al., 2009).

2.6. Hyperuricemia definition

We defined a patient as having HU if serum uric acid was above 360 μmol/L (Khanna et al., 2012a, 2012b).

2.6.1. Definition of adequate treatment of metabolic components

As promoted by the American College of Preventive Medicine (The American College of Preventive Medicine, 2009), we considered that an adequate treatment was composed of first-line life-style recommendations, mainly based on dietary and physical activity recommendations. Relevant medications targeting each metabolic disturbance were also qualifiers for adequate treatment, irrespective of the adherence to the first-line lifestyle recommendations.

2.7. Statistical analysis

Socio-demographics, clinical characteristics and co-morbidities were described using measures of means and dispersion (standard deviation) for continuous data and frequency distribution for categorical variables. Associations between demographic and clinical characteristics of patients as well as metabolic components with HU were performed using chi-square test for categorical variables and Wilcoxon test for continuous variables.

Multivariate logistic regression analysis was used to determine the risk of having HU according to MetS components after adjusting for age, gender and education level were carried out. Additional adjustment on tobacco consumption, PANSS score, age at onset, and type of antipsychotic treatment (clozapine or olanzapine versus other antipsychotics). The same model was performed to evaluate the association between abdominal obesity and the risk of HU. Statistical analyses were performed with SAS (release 9.3; SAS Statistical Institute, Cary, NC). All statistical tests were two-tailed, with α level set at 0.05.

3. Results

This study was based on a total of 240 patients with schizophrenia or schizoaffective disorder (SZ) who were the first patients enrolled in FACE-SZ. Table 1 shows demographical and clinical characteristics of the sample as well as associations with MetS and hyperuricemia respectively. Abdominal obesity was found to be significantly associated with the same characteristics as metabolic syndrome (data not shown).

The majority of the subjects in the sample (74.3%) were men and the mean age of the patients was 31.4 +/− 10.7 years old. The mean age at schizophrenia/schizoaffective onset was 21.4 +/− 6.7 years, the mean duration of illness was 9.5 +/− 9.1 years and the mean PANSS total score was 71.6 +/− 18.5. 125 patients in the cohort (52.5%) were current tobacco smokers.

Metabolic syndrome was found in 24.2% of the patients (34.8% with hypertension, 39.8% with high waist circumference, 28.3% with hypertriglyceridemia, 42.3% with low HDL cholesterol, 19.9% with high fasting glucose) (Table 2). Overall, only 10% received adequate treatment (as defined by life-style, including dietary and physical activity, recommendation or medication adapted for each metabolic disturbance) for hypertension, 18% for high fasting glucose and 8% for dyslipidemia. Abdominal obesity (defined by high waist circumference and hypertriglyceridemia) was found in 21.3% and hyperuricemia in 19.6% of patients.

Metabolic syndrome and hyperuricemia were both found to be associated with higher BMI (respectively $p < 0.0001$ and $p = 0.0004$) while metabolic syndrome only was found to be associated with higher duration of illness ($p < 0.0001$) and hyperuricemia only with olanzapine or clozapine current treatment ($p = 0.0486$). SZ patients with hyperuricemia (HU+) were more likely to be men ($p = 0.002$) and had significantly higher education level ($p = 0.0172$) compared to patients without hyperuricemia (HU−). There was no association with other psychiatric clinical or sociodemographical characteristics.

Table 1
Demographical and clinical characteristics of the 240 patients with schizophrenia and association with metabolic syndrome (MetS) and hyperuricemia.

	n (%)	Metabolic syndrome		p[a]	Hyperuricemia		p[a]
		No (n = 182)	Yes (n = 58)		No (n = 193)	Yes (n = 47)	
Demographic characteristics							
Male gender	178 (74.2)	138 (75.8)	40 (69.0)	0.2987	135 (69.9)	43 (91.5)	**0.002**
Age, mean (SD)	31.4 (10.7)	30.1 (9.6)	35.2 (12.8)	**0.005**	30.9 (10.8)	33.1 (9.5)	0.1
Education, mean (SD)	11.8 (3.2)	11.7 (3.2)	12.3 (3.1)	0.2603	11.6 (3.1)	12.8 (3.2)	**0.0172**
Clinical characteristics and comorbidities							
Age of onset, mean (SD)	21.4 (6.7)	21.5 (6.9)	21.0 (6.1)	0.8111	21.1 (6.8)	22.5 (6.8)	0.2066
Duration of illness, mean (SD)	9.9 (9.1)	8.5 (8.0)	14.5 (11.0)	<**0.0001**	9.6 (9.5)	10.7 (7.6)	0.1157
PANSS total score, mean (SD)	71.6 (18.5)	71.0 (19.0)	73.4 (17.0)	0.2663	71.8 (19.3)	70.3 (16.1)	0.4812
PANSS negative score, mean (SD)	21.3 (7.4)	21.4 (7.5)	21.1 (6.9)	0.7989	21.5 (7.6)	20.6 (6.9)	0.4792
Score positive score, mean (SD)	14.9 (5.4)	14.7 (5.3)	15.6 (5.6)	0.2847	14.9 (5.4)	15.0 (5.1)	0.9
Depressive symptoms (Calgary), mean (SD)	4.1 (4.2)	3.8 (4.2)	4.8 (4.3)	0.0882	4.0 (4.3)	4.2 (4.2)	0.6242
BMI, mean (SD)	27.0 (5.4)	25.4 (4.5)	31.6 (5.2)	<**0.0001**	26.4 (5.3)	29.1 (4.9)	**0.0004**
Current daily tobacco smoking	125 (52.5)	91 (50.6)	34 (58.6)	0.2848	103 (53.9)	22 (46.8)	0.3813
Treatment							
Current clozapine/olanzapine treatment	60 (33.5)	47 (33.3)	**13 (34.2)**	**0.919**	**43 (30.1)**	**17 (47.2)**	**0.0486**
Current antidepressant treatment	51 (28.5)	41 (29.1)	10 (26.3)	0.7378	41 (28.7)	10 (27.8)	0.9155

Significant associations are in bold.
[a] Chi-square for categorical variables and Wilcoxon Mann–Whitney tests for continuous variables.

Associations between hyperuricemia, metabolic syndrome and each of its components are shown in Table 2. Compared to HU− patients, HU+ SZ patients were more likely to have high waist circumference and hypertriglyceridemia, but not other MetS risk factors (hypertension, high fasting glucose or low HDL cholesterol).

In terms of risk factors, multiple logistic regression showed that, after taking into account potential confounders (age, gender, education level), the risk of hyperuricemia was higher in males (OR = 5.9, IC95 [1.7–21.4]) and in subjects with high waist circumference (OR = 3.1, IC95 [1.1–8.3]) or hypertriglyceridemia (OR = 4.9, IC95 [1.9–13]) (Table 3). No associations with hypertension, low HDL cholesterol or high fasting glucose were observed. Additional adjustment on tobacco consumption, PANSS score, age at onset, and type of antipsychotic treatment (clozapine or olanzapine versus other antipsychotics or clozapine alone versus other antipsychotics) did not change our results (data not shown). All the above-mentioned associations remained significant when only males were analyzed, but not females (data not shown).

The presence of abdominal obesity was associated with an increased risk of hyperuricemia (OR = 15.4, IC95 [4.6–52]), much higher than each isolated risk factor (OR = 4.7 for high waist circumference and 7.8 for hypertriglyceridemia) (Fig. 1).

4. Discussion

This study was assessed in a French observational cohort of patients with schizophrenia and schizoaffective disorder, the prevalence of metabolic syndrome, abdominal obesity and hyperuricemia. In this sample of patients, a prevalence of 24.2% of metabolic syndrome, a prevalence of 21.3% of abdominal obesity and a prevalence of 19.6% of hyperuricemia were observed. Hyperuricemia was found to be significantly associated with metabolic syndrome and abdominal obesity respectively (defined by the presence of hypertriglyceridemia with high waist circumference), but not with other components of metabolic syndrome (hypertension, high fasting glucose and low HDL cholesterol). Hyperuricemia was also associated with olanzapine or clozapine intake, contrary to metabolic syndrome and abdominal obesity, but was not associated with psychiatric clinical characteristics (illness duration, psychotic or depressive symptomatology or level of functioning). Clozapine alone was not significantly associated with hyperuricemia in our results, probably due to the lack of power (only 29 patients were administered clozapine in our sample).

This study is the first to assess the prevalence of MetS, abdominal obesity and HU in patients with schizophrenia or schizoaffective disorders in France. Consistently with the results of the FACE-BD cohort in French patients with bipolar disorders (Godin et al., 2014), we found a lower rate of metabolic syndrome in the FACE-SZ cohort compared to other European countries (with a mean of 33.9% in the Meteor study (De Hert et al., 2010)), probably due to better dietary lifestyle and medical care factors. The variation in prevalence may also reflect differences in methods or in sample characteristics (notably age, education level and diagnostic subgroup), place of recruitment, and sample size. The prevalence of metabolic syndrome in schizophrenia is twice higher than in the general French population (around 10%) (Balkau et al., 2003; Pannier et al., 2006), despite the fact that our sample was younger (mean age of 31 years in our sample vs 40 years for French general population) (Institut National de la Statistique et des Etudes Economiques (INSEE), 2015). Moreover because our patients were recruited in 10 Expert Centers that cover the whole French continental territory, we assumed that our population was representative of the French population with schizophrenia regarding lifestyle, dietary and medical care factors.

Table 2
Association between hyperuricemia, metabolic syndrome and each of its components in a sample of 240 patients with schizophrenia or schizo-affective disorder.

Cardiovascular risk (number of blood tests available)	n (%)	Hyperuricemia		p
		No (n = 193)	Yes (n = 47)	
Hypertension (N = 227)	79 (34.8)	61 (33.5)	18 (40.0)	0.4136
High abdominal circumference (N = 221)[a]	**88 (39.8)**	**7 (16.3)**	**81 (45.5)**	**0.0004**
Hypertriglyceridemia (N = 230)	**65 (28.3)**	**39 (21.3)**	**26 (55.3)**	<**0.0001**
Low HDL cholesterol (N = 227)	96 (42.3)	75 (41.0)	21 (47.7)	0.4162
High fasting glucose (N = 221)	44 (19.9)	33 (18.9)	11 (23.9)	0.4448
Metabolic syndrome	**58 (24.2)**	**38 (19.7)**	**20 (42.6)**	**0.001**

Significant associations are in bold. N number of measures available for each parameter.
[a] >94 cm for male and >80 cm for female.

Table 3
Multivariate association between metabolic component and the risk of having Hyperuricemia in a sample of 240 patients with schizophrenia or schizo-affective disorder.

	Risk of hyperuricemia		p value
	Odds ratio	95% CI	
Sex (male)	**5.9**	**1.7 – 21.4**	**0.0126**
Age	1	0.9 – 1.0	0.6925
Abdominal circumference (94/80)	**3.1**	**1.1 – 8.3**	**0.0270**
Hypertriglyceridemia	**4.9**	**1.9 – 13.0**	**0.001**
Low HDL cholesterol	0.8	0.3 – 2.1	0.6588
High fasting glucose	0.8	0.3 – 2.3	0.7199
Hypertension	0.9	0.4 – 2.1	0.8536
Education level	1.1	0.9 – 1.0	0.1855

Multivariate logistic regression analysis, C index = 0.80. Significant associations are in bold.

It should be underlined that 74% of our sample were males contrary to the 1:1 sex ratio of schizophrenia in the general population (McGrath et al., 2004). This could be due to the fact that male SZ patients are more at risk of a relapse due to lower insight, substance abuses, and lower treatment adherence (Abel et al., 2010). Therefore, these patients were more often referred by psychiatrists to the Expert Centers for a clinical assessment and therapeutic advice. Consistent with previous findings, 52.5% of our sample are regular tobacco smoker, which is comparable to the rates described in the literature(Bobes et al., 2010; McClave et al., 2010), and higher than the French general population (about 30% according to the World Health Association in 2012) (WHO, 2014).

Secondly, we found that more than 80% of patients with SZ were not treated for each metabolic abnormality composing the metabolic syndrome. The management of each components of the metabolic syndrome have also been reported as suboptimal in the general population, due to both clinical inertia and poor adherence (Jonsdottir et al., 2013; Martínez-St John et al., 2015; Whitford et al., 2014).

This aspect unveils and urges for the need to improve medical care in French patients with schizophrenia to decrease morbidity and cardiovascular mortality in this population.

Thirdly, HU appeared as the consequence of the metabolic features of metabolic syndrome, especially abdominal obesity (OR = 15.4) (Fig. 1), which was previously described in a population of obese patients (Matsuura et al., 1998). The very strong link between metabolic features and HU is convincingly demonstrated by the very good predictive capacities of the metabolic model to predict HU (C index 0.8) (Table 3). As previously mentioned, recent studies suggested that HU was an independent risk factor of MetS, others suggested that HU was a general metabolic stress marker that may be seen as a risk factor of multiple other metabolic disturbances (Chen et al., 2009; Huang et al., 2012; Kim et al., 2009, 2010; Li et al., 2014; Reininghaus et al., 2014; Viazzi et al., 2011; Xu et al., 2013).

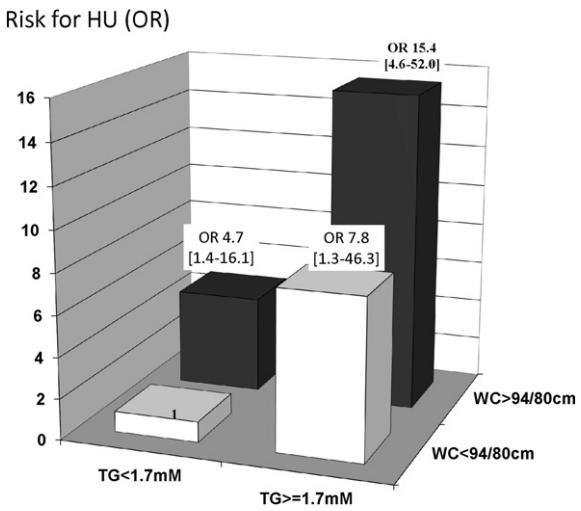

Fig. 1. Interaction between high waist circumference (WC) (>94 cm for male and 80 cm for female), hypertriglyciridemia (TG) (> = 1.7 mM) and risk of hyperuricemia (HU) (odd ratios ordinate with 95% confidence intervals).

Fourthly, no association was found between HU and psychiatric characteristics of schizophrenia (i.e. psychotic symptomatology, age at onset, illness duration) except for olanzapine and clozapine treatments in univariate analyses. These results did not confirm our hypothesis that HU may be considered as a potential biomarker for clinical staging or treatment response. As clozapine and olanzapine were found to be classified among the most effective second-generation antipsychotics (Leucht et al., 2009), it may however be suggested that one of the mechanisms of their effectiveness in schizophrenia may be due to the antioxidant potency of increased circulating uric acid. Yet, if HU is under the dependence of metabolic factors in patients with schizophrenia, the impact of HU on the outcome of schizophrenia, considering its intrinsic inflammatory properties, is unknown, and should be specifically explored in further studies.

This study has several limitations. Due to the cross-sectional nature of the study, we were unable to draw any firm conclusions concerning the causal nature of the associations observed. Longitudinal studies are required for this purpose. Furthermore, our sample is probably not representative of all patients with schizophrenia, particularly because institutionalized, hospitalized or very handicapped patients (making thorough assessment difficult) were not referred to the Expert Centers. However, it can be assumed that this bias has led to an underestimation, rather than an overestimation, of the prevalence of MetS, abdominal obesity and HU.

The present study endorses clear strengths: use of homogenous and exhaustive standardized diagnostic protocols across the centers and the inclusion of a large number of potential confounding factors in the multivariate analysis.

5. Conclusion

We demonstrate that metabolic syndrome, abdominal obesity and hyperuricemia are common in patients with schizophrenia. We specifically show that patients with both increased waist circumference and hypertriglyceridemia, who are very likely to have a large amount of intra-abdominal visceral fat, are at very high risk for hyperuricemia. Importantly, both uric acid and visceral obesity are involved in the onset and regulation of inflammatory processes. As inflammation is suggested as an important underlying mechanism of schizophrenia, the impact of uric acid and visceral obesity on the outcome of patients with schizophrenia needs to be studied in future follow-up studies. The prevention and treatment of cardiovascular diseases in patients with schizophrenia should help to reduce mortality in this population and to improve quality of life and the overall prognosis of schizophrenia. In everyday practice, the various components of MetS have to be systematically assessed, and attempts to improve the patient's lifestyle should be made, through diet, physical exercise, and decreased tobacco consumption. In addition, the psychotropic drug used to treat a given patient with schizophrenia should be chosen with care, taking into account the impact of each drug on weight gain. These findings also highlight the need for integrated care, with enhanced interactions and improved coordination between psychiatrists, primary care providers and specialist teams.

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None.

Conflicts of interest

None declared.

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