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ORIGINAL PAPER

Prevalence of the metabolic syndrome in unipolar major depression

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Abstract Previous studies on the association between affective disorders and the metabolic syndrome yielded inconclusive results. Therefore, we examined the prevalence of the metabolic syndrome in 230 men and women with unipolar major depressive disorder during inpatient treatment and compared it to 1,673 subjects from primary care from a similar region in northern Germany. We used the AHA/NHBLI criteria to determine the rate of metabolic syndrome (MetS) and each single criterion of MetS in both groups. The age-standardized prevalence of MetS was 2.4× as high in patients with major depressive disorder (MDD) compared with data from comparison subjects (41.0% vs. 17.0%). With respect to the single criteria, elevations were found in MDD patients for fasting glucose and triglycerides in both genders, and waist circumference in women. Men in the patient and the comparison groups were found to have higher rates of increased fasting glucose and triglycerides than women in the respective groups. Factors associated with the MetS in MDD patients comprise body mass index and the severity of depression. Our results demonstrate an increased prevalence of the MetS in men and women with MDD. Interventions for the frequently untreated metabolic abnormalities and careful screening for physical health conditions among people with MDD are warranted.

Keywords Major depression · Metabolic syndrome · Physical health · Anxiety disorder

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Introduction

The metabolic syndrome (MetS) is a clustering of metabolic risk factors associated with the development of type 2 diabetes mellitus, coronary artery disease and increased cardiovascular mortality, and major depressive disorder (MDD) has been associated with an increased incidence of type 2 diabetes mellitus and cardiovascular disorders [23, 28, 29, 33]. The prevalence of the MetS in psychiatric patients has been studied in association with schizophrenia, bipolar disorders and depression. Among the patients with schizophrenia and bipolar disorders, increased rates of the MetS were observed [6, 10, 19, 39].

Inconclusive results have been obtained concerning an association between MDD and the MetS, gender-specific aspects and the role of anxiety disorders. Some studies reported an association between depression and the MetS [11, 20, 37, 38, 42, 46] and between the MetS and anxiety disorders [37]. However, other studies did not find an association between depression and the MetS [21, 22] or between anxiety disorders and the MetS [21, 42]. In a population-based study, only women with a history of MDD but not men had an increased rate of the MetS [27]. Another population-based study showed an association

between depressive symptoms and the MetS particularly in men [47]. In a study comprising 3,880 healthy employees, an association between depressive symptoms and the MetS was particularly observed in women, [44] and in a cross-sectional community-based study, self-perceived depression was associated with elevated fasting glucose in men and with increased waist circumference in women [34]. The observed discrepancies may be due to the differences in the study design (longitudinal vs. cross-sectional), different study populations (patients with clinical depression versus population-based studies), different assessment instruments for depression (structured clinical interview versus general health questionnaires versus self-report instruments) and whether a comparison group was used.

Therefore, the aim of our study was to compare the prevalence of the MetS in depressed inpatients and data from a comparison group from the same region in northern Germany. Furthermore, factors associated with the MetS were examined among patients with MDD.

Method

The study was approved by the local ethics committee. Over a period of 12 months, 1,194 adult psychiatric inpatients (Department of Psychiatry, University Medical School, Lübeck, Germany) were screened for inclusion and exclusion criteria. The inclusion criteria were an age of 18 or older, the acquisition of written informed consent, while exclusion criteria included compulsory hospitalization, mental retardation or dementia, discharge ahead of time, acute alcohol withdrawal symptoms and pregnancy. Seven hundred and fifteen patients featured at least one of these exclusion criteria. Four hundred and seventy-nine patients were interviewed using the German version of the Structured Clinical Interview for DSM-IV (SCID I and II). For the purpose of this study, we included the 230 patients (102 men and 128 women) that fulfilled the criteria of major depression according to DSM-IV, but did not fulfill the criteria of bipolar disorder, schizophrenia, delusional disorders or borderline personality disorder.

For the purpose of comparison, we selected data from 1,673 study participants (645 men, 1,028 women) from the German Metabolic and Cardiovascular Risk Project (GEMCAS)—a nationwide sample of primary care subjects screened in 2005 for the prevalence of the MetS who lived in a similar region in northern Germany [18]. The characteristics of both study populations are given in Table 1.

One hundred and ninety-nine of two hundred and thirty (86.5%) depressed patients received antidepressant medication (selective serotonine reuptake inhibitors: $N = 83$; selective serotonin and noradrenaline reuptake inhibitors: $N = 64$; tricyclic antidepressants: $N = 36$; mirtazapine: $N = 12$). Twenty-seven patients received atypical neuroleptics (olanzapine: $N = 16$; risperidone: $N = 5$; quetiapine: $N = 5$; aripiprazol: $N = 1$). Fourteen patients received treatment with lithium.

Table 1 Selected characteristic means and standard deviation of the study populations

	Lübeck ($n = 230$)	GEMCAS ($n = 1,673$)
Female (%)	55.6	61.4
Age (year)	47.2 ± 13.2	50.2 ± 15.8
BMI	26.3 ± 5.7	26.8 ± 5.5
Waist (cm)	93.7 ± 14.9	90.9 ± 15.5
Fasting triglycerides (mg/dL)	146.0 ± 91.5	143.2 ± 89.5
Fasting HDL (mg/dL)	63.9 ± 19.4	62.3 ± 17.6
Systole (mmHg)	135.2 ± 17.5	130.8 ± 20.2
Diastole (mmHg)	83.7 ± 11.2	81.0 ± 11.3
Fasting glucose (mg/dL)	103.2 ± 29.0	94.5 ± 22.0*

* $P < 0.05$

Sixteen patients received antihypertensive medication (beta-blockers $N = 10$; sartans $N = 5$; diuretics $N = 3$; alpha-blockers $N = 1$). Treatment with fibrates was not reported by any patient.

Measures

Metabolic syndrome definition

MetS was defined according to AHA/NHBLI 2004 [14]. This includes the presence of any three of the following five criteria: waist circumference (WC) >102 cm in men; >88 cm in women, triglyceride (TG) ≥150 mg/dL (1.7 mmol/L), HDL-C <40 mg/dL (1.08 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women, blood pressure (BP) ≥135/ ≥85 mmHg and fasting blood glucose (GL) ≥100 mg/dL (≥5.6 mmol/L) or known diabetes. According to this definition, the intake of antihypertensive medication was not considered.

Assessment of socioeconomic and lifestyle factors

A structured questionnaire administered by study physicians was used to determine the number of school years, employment status, monthly household income, marital status and number of persons in the household. Physical activity was determined with a 6-point Likert scale, with descriptors ranging from never (1 point) to very often (6 points) [7]. Smoking habits were expressed as pack-years (cigarettes per day × years of smoking/20). Alcohol intake was expressed as drinks per week. Furthermore, psychological examination for the MDD patient group included

the German version of the Beck Depression Inventory (BDI).

Statistical analyses

We performed the analyses using SAS 9.1 (SAS Institute Inc., Cary, NC, USA) and SPSS (version 17.0). The descriptive statistics (mean and standard deviation) for the continuous variables and frequency counts or proportions with their 95% confidence intervals (95% CI) were calculated for categorical variables. We calculated direct age-standardized rates of the MetS and their 95% CIs to compare the prevalence of both samples. The standardization concerning age groups was performed using the German population from 2004 (http://www-ec.destatis.de, 2006).

The sample of men and women with MDD was stratified by sex and the presence of MetS. Group comparisons were made by using t-test for continuous variables and χ^2 or Fischer's exact test as appropriate for categorical variables. Binary logistic regression analysis was calculated using SPSS version 17.0. All tests were two sided, with alpha set at 0.05.

Results

Anthropometric and crude metabolic data are given in Table 1. Patients in the MDD group were similar regarding age (47.2 ± 13.2 vs. 50.2 ± 15.8) and body mass index (26.3 ± 8.3 vs. 26.8 ± 5.5) compared to the GEMCAS sample.

The age-standardized prevalence of the MetS was almost twice as high as that in the GEMCAS comparison group (41.0% vs. 17.0%) (Table 2). The difference was significant for the total MDD group and for the subgroups of men and women. High blood pressure was the most prevalent criterion in both study groups and differed between the MDD and the comparison groups. Fasting glucose and triglycerides were increased in the whole group of MDD patients and in the subgroups of men and women with MDD. Waist circumference was only elevated in the subgroup of female MDD patients (Table 2).

MDD patients were engaged in moderate daily physical activity, regularly smoking (mean pack-years: 14.4 ± 20.0 in men and 12.4 ± 14.8 in women) and had a mean alcohol intake of 12.6 ± 9.3 drinks per week in men and 8.6 ± 9.8 drinks per week in women (Table 3). More women (64.8%) than men (43.1%) had any comorbid axis-1 disorder. Among these, dysthymia (9.8% in men, 22.7% in women), specific phobia (5.9% in men, 20.3% in women) and panic disorder (7.8% in men, 26.6% in women) were more prevalent in women, and alcohol dependency (currently abstinent) was more prevalent in men.

BDI and the number of symptoms of the metabolic syndrome were correlated ($r = 0.24$; $P = 0.003$). Crude

Table 2 Age-standardized prevalence of the metabolic syndrome and single criteria of the metabolic syndrome, stratified by gender (%; 95% CI)

	All (30–65 years)[a]		Men (30–65 years)[b]		Women (30–65 years)[b]	
	%	95% CI	%	95% CI	%	95% CI
Metabolic syndrome						
Lübeck	41.0	33.8–48.2	50.0	38.5–61.5	31.9	23.3–40.5
GEMCAS	17.0	14.7–19.3	19.3	15.4–23.0	14.8	12.2–17.3
Waist circumference (men >102 cm, women >88 cm)						
Lübeck	44.8	37.6–52.0	36.0	24.9–47.0	53.8	44.4–63.1
GEMCAS	35.3	32.5–38.1	32.9	28.5–37.4	37.7	34.3–41.2
Triglycerides (≥150 mg/dL)						
Lübeck	43.1	36.2–50.0	59.3	48.3–70.4	26.5	18.4–34.7
GEMCAS	17.5	14.9–20.2	25.7	20.9–30.5	9.2	7.0–11.4
HDL cholesterol (men <40 mg/dL, women <50 mg/dL)						
Lübeck	14.8	9.4–20.2	16.0	7.4–24.6	13.5	7.1–20.0
GEMCAS	13.5	11.3–15.6	13.8	10.4–17.3	13.1	10.6–15.5
Blood pressure (≥130/85 mmHg)						
Lübeck	70.4	63.8–77.0	79.3	70.0–88.7	61.3	52.1–70.5
GEMCAS	59.2	56.4–62.1	67.9	63.4–72.4	50.3	46.9–53.8
Fasting glucose (≥100 mg/dL)						
Lübeck	49.1	42.0–56.2	60.3	49.1–71.6	37.7	29.0–46.4
GEMCAS	13.7	11.6–15.8	18.2	14.5–21.9	9.1	7.1–11.2

[a] Age- and sex standardized according to the German population 2004

[b] Age standardized according to the German population 2004

Table 3 Psychiatric comorbidity, medication, behavioral risk factors and psychosocial adjustment in 230 men and women with major depressive disorder

Characteristics of study population	Men	Women
n	102	128
Age (year)	46.8 ± 13.6	47.4 ± 12.9
BMI	25.5 ± 4.6	26.9 ± 6.5
Mean physical activity (Likert scale)	3.4 ± 1.5	3.5 ± 1.5
Mean pack-years (tobacco use)	14.4 ± 20.0	12.4 ± 14.8
Mean drinks per week	12.6 ± 9.3	8.6 ± 9.8
Beck depression Inventory (mean sum score)	20.5 ± 10.2	23.8 ± 9.9
Comorbidity, *N* (%)		
Any comorbid axis-1 diagnosis	44 (43.1%)	83 (64.8%)*
Dysthymia	10 (9.8%)	29 (22.7%)*
Specific phobia	6 (5.9%)	26 (20.3%)*
Social anxiety disorder	3 (2.9%)	11 (8.6%)
Panic disorder	8 (7.8%)	34 (26.6%)*
Posttraumatic stress disorder	2 (2.0%)	10 (7.8%)
Obsessive–compulsive disorder	14 (13.7%)	15 (11.7%)
Bulimia nervosa	0 (0.0%)	3 (2.4%)
Alcohol dependency	16 (15.7%)	9 (7.0%)
Benzodiazepine dependency	3 (2.9%)	4 (3.1%)
Cannabis use disorder	2 (2.0%)	0 (0.0%)
School education, *N* (%)		
Elementary school	33 (32.4%)	49 (38.3%)
Secondary school	26 (25.5%)	50 (39.1%)*
High school diploma	43 (42.1%)	29 (22.6%)*
Employment status, *N* (%)		
Unemployed	20 (19.6%)	17 (13.3%)
Apprenticeship	7 (6.8%)	4 (3.1%)
Employee, full-time	37 (36.3%)	27 (21.1%)*
Employee, part-time	12 (11.8%)	20 (15.6%)
Homemaker	2 (2.0%)	28 (21.8%)*
Retired	24 (23.5%)	32 (25.0%)
Number of persons in household, *N* (±SD)	1.9 (±1.1)	2.1 (±1.2)

* $P < 0.05$

rates of the MetS tended to be higher in all depressed patients receiving tricyclic antidepressants or lithium and in females receiving lithium or serotonine and norepinephrine reuptake inhibitors (SNRI); yet, this difference was not significant after correction for age (Table 4). Stepwise logistic regression analysis was performed to determine factors associated with the MetS within the group of depressed patients. We used the factor "MetS" as the dependent variable and BDI, age, medication status, comorbidity status, highest achieved educational level and lifestyle factors as covariates. A significant model emerged. The adjusted R^2 was 0.012. Included factors were BMI (B(SE) −0.82 (0.39) $P = 0.035$), age (B(SE) −0.03 (0.02) $P = 0.056$), and BDI (B(SE) −0.05 (0.02) $P = 0.005$).

Conclusions

Our results demonstrate that men and women with unipolar depressive disorder have a higher age-standardized prevalence of the MetS compared to a population-based sample of subjects attending primary care that live in the same geographic area. The single criteria differentiating between the group with MDD and the comparison groups are blood pressure, fasting triglycerides and fasting glucose. With respect to gender, fasting glucose and triglycerides differentiated between men from MDD and from the comparison groups. In females, waist circumference, triglycerides and glucose were elevated in MDD group compared to that in the comparison group.

Our results are in accordance with others who reported an association of depression with the MetS [11, 20, 37, 38, 42, 46]. Previous studies examining the association between depression and the MetS have demonstrated an association in both young and middle-aged women but not among men [27, 37]. Others have reported an association for both men and women, [42] or no association between depressed men and women and the MetS [21, 22]. Our data extend the above-mentioned findings by performing gender-specific comparisons of a cohort of middle-aged men and women with unipolar MDD with a comparison group from the same region in northern Germany. Indeed, we found an association between the MetS and MDD in both men and women with MDD.

Increased fasting glucose and insulin resistance have been associated with the presence of MDD [1, 43]. Furthermore, individuals with MDD are at particular risk of overweight/obesity and abdominal obesity [32]. In addition to total body weight, the presence of increased intra-abdominal fat stores contributes to the morbidity associated with excess body fat. Body fat distribution has been demonstrated to be a predictor for type 2 diabetes mellitus and incident coronary heart disease [17, 30]. In patients with MDD, increased intra-abdominal fat has been observed and associated with insulin resistance [24].

Studies concerning triglycerides in MDD yielded inconsistent results, either pointing to increased concentrations of triglycerides in women with MDD [27, 38, 45] or no difference between depressed and non-depressed subjects [36]. However, we here demonstrate increased fasting triglycerides in both men and women with MDD. Dyslipidemia, altered glucose homeostasis, hypertension and abdominal obesity have been associated with elevated glucocorticoid concentrations [5], and a dysregulation of the hypothalamus–pituitary–adrenal axis (HPAA) has

Table 4 Prevalence of the MetS in depressed patients according to medication and gender

	All patients ($N = 230$) [F ($N = 128$), M ($N = 102$)]	MetS− ($N = 135$) [F ($N = 80$), M ($N = 55$)]	MetS+ ($N = 95$) [F ($N = 48$), M ($N = 47$)]	Level of significance
Antidepressants				
SSRI, *N* (%)	83 (36.1)	52 (62.7)	31 (37.3)	NS
	F: 40 (48.2)	F: 24 (60)	F: 16 (40)	NS
	M: 43 (51.8)	M: 28 (65.1)	M: (34.9)	NS
SNRI, *N* (%)	64 (27.8)	33 (51.6)	31 (48.4)	NS
	F: 26 (40.6)	F: 10 (38.5)	16 (61.5)	$P = 0.074$
	M: 38 (59.4)	F: 23 (60.5)	15 (39.5)	NS
MAOI, *N* (%)	4 (1.7)	3 (75)	1 (25)	NS
	F: 0 (0)	F: –	F: –	–
	M: 4 (100)	M: 3 (75)	M: 1 (25)	NS
Mirtazapine, *N* (%)	12 (5.2)	7 (58.3)	5 (41.7)	NS
	F: 5 (41.7)	F: 4 (80)	F: 1 (20)	NS
	M: 7 (58.3)	M: 3 (42.9)	M: 4 (57.1)	NS
TCA, *N* (%)	36 (15.7)	16 (44.4)	20 (55.6)	$P = 0.067$
	F: 20 (55.6)	F: 8 (40)	F: 12 (60)	NS
	M: 16 (44.4)	M: 8 (50)	M: 8 (50)	NS
Neuroleptics				
Olanzapine, *N* (%)	16 (7)	12 (75)	4 (25)	NS
	9 (56.2)	6 (66.7)	3 (33.3)	NS
	7 (43.8)	6 (85.7)	1 (14.3)	NS
Risperidone, *N* (%)	5 (2.2)	3 (60)	2 (40)	NS
	F: 1 (20)	1 (100)	0 (0)	NS
	M: 4 (80)	M: 2 (50)	M: 2 (50)	NS
Quetiapine, *N* (%)	5 (2.2)	3 (60)	2 (40)	NS
	F: 2 (40)	F: 1 (50)	F: 1 (50)	NS
	M: 3 (60)	M: 2 (66.7)	M: 1 (33.3)	NS
Aripiprazole, *N* (%)	1 (0.4)	1 (100)	0 (0)	NS
	F: 1 (0.4)	F: 1 (100)	0 (0)	NS
	M: 0 (0)	–	–	–
Lithium, *N* (%)	14 (6.1)	5 (35.7)	9 (64.3)	$P = 0.093$
	F: 8 (57.1)	F: 1 (12.5)	F: 7 (87.5)	$P = 0.023$
	M: 6 (42.9)	M: 4 (66.7)	M: 2 (33.3)	NS
Benzodiazepines, *N* (%)	26 (11.3)	14 (53.8)	12 (46.2)	NS
	F: 10 (38.5)	F: 4 (40)	F: 6 (60)	NS
	M: 16 (61.5)	M: 10 (62.5)	M: 37.5)	NS

F female, *M* male, *SSR* selective serotonine reuptake inhibitor, *SNR* serotonine and norepinephrine reuptake inhibitor, *MAO* monoaminase oxidase inhibitor, *TCA* tricyclic antidepressant

frequently been described in patients with MDD of different age stages [31, 49]. Interestingly, hypercortisolemic depression has been associated with the development of the MetS in late life [48]. Therefore, it seems reasonable to hypothesize that a dysregulation of the HPAA with subsequent relative hypercortisolemia may at least in part play a role in the development of the MetS in patients with MDD.

Other factors that may be relevant to the association between MDD and MetS include alterations in intra-abdominal fat [12], pro-inflammatory cytokines, increased oxidative stress and a dysregulation of the autonomic nervous system. These factors have been shown to interact with glucose homeostasis and insulin resistance (interleukin-6 and tumor necrosis factor-α), oxidation of lipoproteins and an increase in the sympathetic activity in MDD [25, 40]. However, to date, it is unclear to which amount the above-mentioned factors may account for the development of the MetS in patients with MDD.

Within the patient group, disease severity as captured by the BDI was associated with both the symptom number and the presence of the MetS. This association was weak, and there was no evidence of a bimodal or skewed distribution of the parameters. In line with this observation, an

association of severity of MDD with elevated triglycerides was found in a follow-up study of acute depressive inpatients [38].

Yet, in the present study, comorbid psychiatric disorders did not alter the rate of the MetS in MDD patients. In particular, we did not find an association between comorbid anxiety disorders with the MetS in depressed patients. These results are in agreement with former studies that failed to find an association between anxiety disorders and the MetS [21, 42]. Other factors associated with the MetS and MDD comprised the body mass index and the amount of cigarette smoking.

The following limitations of the study need attention: Only inpatients with MDD were included. Inpatients tend to have higher severity of the disorder, higher comorbidity and higher rates of pharmacological treatment and treatment resistance compared to outpatients with MDD. Therefore, our data do not necessarily reflect the prevalence of the MetS in outpatients with MDD. The number of patients is small, particularly in the subgroup of male MDD patients. Given the cross-sectional design, we cannot make any causal inferences regarding the association of MDD with the MetS. We have no or insufficient information about the eating habits and the educational level of either the MDD patients or the primary care subjects. Eating habits have been shown to contribute to the development of the metabolic syndrome, such as overeating, increased intake of processed foods, saturated fatty acids and trans fatty acids and decreased intake of fruits and fish [9, 13, 16, 41]. Furthermore, several studies in different countries found a negative association between the prevalence of the MetS, cardiovascular risk and the socioeconomic status, particularly in females [2, 4, 15, 26]. A detailed discussion of possible selection bias in the recruitment of the comparison group is provided in [35]. Briefly, characteristics of this primary health care sample are comparable with those of other German population-based samples and with the German federal statistical data with regard to anthropometric measures, smoking status, marital status, schooling and unemployment rate (i.e., GEMCAS: 10.2%, Germany October 2005: 10.4%). This high conformance might be explained by the situation that 92% of adults in Germany consult a general practitioner during 1 year. However, the proportion of participants with diabetes and CVD is higher compared with population-based samples, but still lower than in real patient-based samples [35]. We cannot comment on the psychiatric diagnosis in the comparison group, as these data are not available. Given the prevalence of $\sim$5% MDD in the general population, the difference in the rates of the MetS between MDD patients and the control population may be underestimated by our study [3]. Our findings with respect to pharmacological effects on the metabolic syndrome must be viewed with caution because of the heterogeneity of the medication and its duration.

In summary, our data provide evidence that MDD is associated with a higher prevalence of the MetS in men and women compared to a regionally matched primary care sample. Factors associated with the MetS in MDD patients comprise body mass index and the severity of depression. Counselling for healthy lifestyle behaviors and cardiometabolic monitoring is warranted in patients with MDD [8].

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Conflict of interest None of the authors declared conflict of interests.

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