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ORIGINAL PAPER

Metabolic syndrome: a follow-up study of acute depressive inpatients

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Abstract Previous studies pointed out the high prevalence of the metabolic syndrome among patients with bipolar disorder and major depression. A link between depression and a metabolic syndrome remains in dispute despite these studies. This study was conducted to evaluate the occurrence of the metabolic syndrome in depressive inpatients, to analyze the association between the severity of depression and the metabolic syndrome and to screen specific laboratory values in the course of depressive illness. 60 acute depressive patients were recruited for the study and underwent psychometric testing [21-item Hamilton Depression Rating Scale (HAMD), Beck Depression Inventory (BDI), Clinical Global Impression Scale (CGI) and Global Assessment of Functioning Scale (GAF)] and a metabolic syndrome screening using the modified criteria of the American National Cholesterol Education Program (NCEP) Treatment Panel III (ATP III). Moreover, CRP, cholesterol, HDL-cholesterol, fasting glucose, triglyceride and leptin levels were measured. 42 patients were reexamined in state of (partial) remission. Depression was reassessed using the 21-item HAMD, and laboratory values were analyzed a second time. 25% of the depressive patients fulfilled the criteria of metabolic syndrome (MS+). Only in the MS+ group, a positive correlation between triglyceride blood levels and severity of depression became evident as well in the state of acute depression as in the state of remission. In the group of patients without metabolic syndrome, laboratory values were not associated with severity of depression. An association between metabolic parameters and the course of depression could only be detected in the group of patients with metabolic syndrome. These findings suggest that, in these patients, a beneficial outcome of depressive illness may improve the metabolic situation.

Keywords Depression · Metabolic syndrome · Triglycerides

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Introduction

The metabolic syndrome is a constellation of metabolic risk factors. These risk factors are abdominal obesity, elevated triglycerides, reduced HDL-cholesterol, elevated blood pressure and elevated fasting glucose. The presence of the metabolic syndrome identifies a person who is at increased risk for atherosclerotic cardiovascular disease and type 2 diabetes mellitus [6]. The prevalence of the metabolic syndrome varies across different countries from only 10% in France [7] to 39% in Saudi Arabia [1]. Studies showed a prevalence rate of the metabolic syndrome in the German primary care population of 19.8% [13] and a prevalence rate of 23.8% in the German general population [14]. These figures correspond to the prevalence rate that has been found for the American general population [4]. Recently, several studies have assessed the prevalence of the metabolic syndrome in patients with psychiatric disorders and found a high rate of 30% in patients with bipolar disorder [3]. Heiskanen et al. [8] reported from Finland a prevalence rate of 36% in depressive outpatients. Furthermore, an association between the occurrence of the metabolic syndrome and a current diagnosis of major depression was stated in the study. Another study

pointed out a strong correlation between depression and the prevalence of the metabolic syndrome in women with suspected coronary artery disease [19]. Vice versa, a recent Finnish study reported a twofold higher prevalence rate of depressive symptoms in initially non-depressed men and women with metabolic syndrome at baseline after a 7-year follow-up [12]. Yet, a study by Herva et al. [9], that was part of the Northern Finland 1966 Birth Cohort Study, did not detect any association between the metabolic syndrome and depression and thus left the discussion open. Therefore, the aim of the present study was to evaluate the occurrence of the metabolic syndrome in German depressive inpatients, to analyze a putative association between depression and the metabolic syndrome and to find differences between depressive patients with and without a metabolic syndrome. As previous studies did not take the patients' actual state of depressive illness into account, this study also aimed to focus on acute depressive episodes with a follow-up of metabolic symptoms after partial or complete remission. Furthermore, the present study intended to identify specific laboratory values in the course of depressive illness in order to evaluate the optimal point of time for the diagnostic procedure of the metabolic syndrome in depressive patients.

Methods

Sample

The present study was conducted at the Department of Psychiatry and Psychotherapy, Ruhr University Bochum, Germany. A sample of 60 adult inpatients, who were more than 17 years of age, were recruited between December 2006 and December 2007. All patients were hospitalized because of unipolar or bipolar depression (DSM-IV: 296.xx). Written informed consent of all subjects was obtained before study participation. The study was checked and approved by the local ethics committee of the Ruhr University Bochum, Germany.

Assessment

All patients recruited had a DSM-IV diagnosis of unipolar or bipolar depression (DSM-IV: 296.xx) and were hospitalized due to an acute depressive episode (HAMD $\geq$18) to be included in the study. Exclusion criteria were another DSM-IV axis I diagnosis, depression due to a general medical condition, pregnancy and unwillingness or inability to comply with the study procedures or inability to give informed consent. To assess the severity of depression, the 21-item Hamilton Depression Rating Scale (HAMD), the Beck Depression Inventory (BDI), the Clinical Global Impression Scale (CGI) and the Global Assessment of Functioning Scale (GAF) were used. Personal data (name, gender, age, nationality, ancestry) and socio-demographic data (school education, profession, marital status, number of children) were obtained. Furthermore, data about the medical history (diabetes mellitus, hypertension, myocardial infarction, stroke, allergies, number of pregnancies and births, number of surgeries) and medical history of the family (psychiatric disorder, obesity, diabetes mellitus, hypertension, myocardial infarction, stroke, hypercholesterolemia) were collected. In addition, patients were interviewed about the age of onset of their psychiatric disorder, hospitalization rate, comorbidity, drug abuse, suicide attempts, pharmacological treatment, recent changes of weight or appetite, eating habits (number of meals/day, being on a diet) and history of ECT and psychotherapy.

The diagnosis of a metabolic syndrome was verified according to the criteria of the American National Cholesterol Education Program (NCEP) Treatment Panel III (ATP III). The NCEP ATP III defines the metabolic syndrome as being the presence of three or more of the following criteria: waist circumference >102 cm (40 in.) in men, >88 cm (35 in.) in women, hypertriglyceridemia $\geq$150 mg/dl, HDL-cholesterol <40 mg/dl in men, <50 mg/dl in women, blood pressure $\geq$130/85 mmHg and fasting glucose $\geq$110 mg/dl.

Patients taking cholesterol-lowering, blood-pressure-lowering or glucose-lowering medication were considered to have met the respective criterion.

The waist-to-hip-ratio and body mass index (BMI) were also obtained, the CRP, cholesterol and leptin levels were measured and microalbuminuria was tested.

Patients were reexamined in a state of (partial) remission that was defined as a reduction of the HAMD score of at least 50% or HAMD <8. CRP, cholesterol, HDL-cholesterol, fasting glucose, triglyceride and leptin levels were obtained a second time.

Statistical analyses

Statistical analyses were carried out using SPSS version 16.0 for Windows. For the data analysis, we used means and standard deviations to examine continuous or interval variables and frequency counts to examine categorical variables. Independent sample *t* test and Chi-square tests were applied to analyze significant effects between patients with and without a metabolic syndrome. Paired-sample *t* tests were used for calculating changes between baseline and follow-up. Pearson's correlations were computed to analyze correlations between severity of depression and laboratory values.

Results

A total of 60 acute depressive patients (48 patients suffering from unipolar, 12 from bipolar depression) were recruited for the study. 35 were women (58.3%) and 25 were men (41.7%). The mean age was 49.5 years (SD ±11.5 years) with an age range of between 24 and 72 years. 42 patients were reexamined in (partial) remission.

Baseline demographic data

The majority of the patients were Germans (88.3%) and Caucasians. 53.3% of the patients were married. The number of children was 1.4 on average. 80% of the patients had an elementary or secondary school diploma, 8.3% a high school diploma, whereas 51.6% were unemployed. Socio-demographic data did not differ statistically between patients with a metabolic syndrome (MS+) and without a metabolic syndrome (MS−) (Table 1).

Baseline clinical data

At study entry, the mean CGI score of the subjects was 5.2 (SD ±0.51), the mean GAF score was 47.13 (SD ±4.89), the mean BDI score was 34.54 (SD ±8.50) and the mean HAMD-21 score was 28.59 (SD ±5.35). The mean HAMD-21 score in (partial) remission was 12.9 (SD ±4.38), remission time was 38.7 (SD ±37.62) days on average. The mean number of psychotropic drugs taken by subjects at study entry was 2.53 (SD ±1.19), without any statistical difference between MS+ and MS− patients. The course of psychiatric illness as it is reflected in the number of clinical admissions, weeks of hospitalization, years of outpatient therapy, number of suicide attempts, history of psychotherapy or electroconvulsive therapy did not reveal any statistical difference between MS+ and MS− patients either. However, patients did differ concerning the somatic disorders. MS+ subjects reported significantly more often a history of hypercholesterolemia ($\chi^2 = 6.92$, $df = 1$, $P < 0.01$) and hypertension ($\chi^2 = 8.82$, $df = 1$, $P < 0.01$). Furthermore, they had a significantly higher BMI ($t = -2.42$, $df = 58$, $P = 0.02$) and waist-to-hip-ratio ($t = -4.29$, $df = 58$, $P < 0.01$) and reported a significantly higher current nicotine abuse ($\chi^2 = 9.00$, $df = 2$, $P = 0.01$). The mean number of non-psychotropic drugs taken by MS+ subjects at study entry was 3.07 (SD ±2.67) and, therefore, significantly higher than in MS− subjects ($t = -3.66$, $df = 58$, $P < 0.01$). 33.3% of MS+ patients were on cholesterol-lowering medication, 73.3% on blood-pressure-lowering medication, significantly more than in the MS− group ($\chi^2 = 12.92$, $df = 1$, $P < 0.01$; $\chi^2 = 16.36$, $df = 1$, $P < 0.01$, respectively) (Tables 2, 3).

Metabolic syndrome

25% of our sample met the NCEP ATP III criteria for the metabolic syndrome. 16.7% did not meet any criteria at all, 33.3% met one criterion, 25% met two criteria, 13.3% met three criteria and 11.7% met four criteria (Fig. 1). 86.7% of the MS+ group were suffering from unipolar depression, 13.3% were suffering from bipolar depression. There was no difference between gender or unipolar and bipolar depression and the number of positive criteria. 10% of the sample met the criterion for hyperglycemia, 21.7% met the criterion for low HDL-cholesterol, 33.3% met the criterion for hypertriglyceridemia, 45% met the criterion for abdominal obesity and 60% met the criterion for hypertension. The most fulfilled criterion in the MS− group was the criterion for hypertension (51.1%); the most fulfilled criterion in the MS+ group was the criterion for hypertriglyceridemia (93.3%) (Table 4).

Table 1 Baseline demographic data of unipolar and bipolar depressive patients without metabolic syndrome (MS−) and with metabolic syndrome (MS+)

Characteristics	All patients ($N = 60$)	MS− ($N = 45$)	MS+ ($N = 15$)	Level of significance
Mean age (years, SD)	49.5 ± 11.5	49.3 ± 12.5	49.9 ± 8.3	n.s.
Gender (number) (men/women)	25/35	16/29	9/6	n.s.
Nationality (German/other)	53/7	40/5	13/2	n.s.
School education (elementary school/secondary school/high school diploma)	35/13/5	23/11/4	12/2/1	n.s.
General education (no/apprenticeship/academic)	8/43/9	6/30/9	2/13/0	n.s.
Employment status (no/employed)	31/29	25/20	6/9	n.s.
Marital status (single/married/divorced)	13/32/15	11/23/11	2/9/4	n.s.
Partnership (yes/no)	45/15	33/12	12/3	n.s.
Children (mean ± SD)	1.4 ± 1.4	1.5 ± 1.5	1.2 ± 0.9	n.s.

Table 2 Baseline clinical data of unipolar and bipolar depressive patients without metabolic syndrome (MS−) and with metabolic syndrome (MS+)

Characteristics	All patients ($N = 60$)	MS− ($N = 45$)	MS+ ($N = 15$)	Level of significance
Psychiatric diagnosis (unipolar depression/bipolar depression)	48/12	35/10	13/2	n.s.
Other psychiatric diagnosis (yes/no)	5/55	4/41	1/14	n.s.
Clinical admissions (mean ± SD)	2.42 ± 1.95	2.61 ± 2.14	1.77 ± 0.83	n.s.
Weeks of hospitalization (mean ± SD)	10.10 ± 13.4	9.90 ± 13.64	10.70 ± 13.25	n.s.
Days to remission (mean ± SD)	38.7 ± 37.62	41.52 ± 42.98	31.27 ± 16.21	n.s.
Years of outpatient therapy (mean ± SD)	5.25 ± 5.12	5.28 ± 4.89	5.17 ± 5.93	n.s.
Suicide attempts (mean ± SD)	0.76 ± 0.97	0.68 ± 0.88	1.00 ± 1.20	n.s.
CGI score at study entry (mean ± SD)	5.2 ± 0.51	5.24 ± 0.53	5.07 ± 0.46	n.s.
GAF score at study entry (mean ± SD)	47.13 ± 4.89	46.89 ± 5.10	47.87 ± 4.24	n.s.
BDI score at study entry (mean ± SD)	34.54 ± 8.50	34.31 ± 8.90	35.20 ± 7.50	n.s.
HAMD-21 score at study entry (mean ± SD)	28.59 ± 5.35	28.55 ± 5.50	28.73 ± 5.06	n.s.
HAMD-21 score in remission (mean ± SD)	12.90 ± 4.38	12.7 ± 4.46	13.42 ± 4.34	n.s.
History of psychotherapy (yes/no)	23/37	19/26	4/11	n.s.
History of electroconvulsive therapy (yes/no)	1/59	0/45	1/14	n.s.
History of hypercholesterolemia (yes/no)	8/52	3/42	5/10	$\chi^2 = 6.92$ $df = 1$ $P < 0.01$
History of diabetes mellitus (yes/no)	2/58	2/43	0/15	n.s.
History of hypertension (yes/no)	21/39	11/34	10/5	$\chi^2 = 8.82$ $df = 1$ $P < 0.01$
History of myocardial infarction (yes/no)	2/58	1/44	1/14	n.s.
History of stroke (yes/no)	2/58	1/44	1/14	n.s.
Weight gain in the last 4 weeks (kg) (mean ± SD)	0.68 ± 1.59	0.72 ± 1.75	0.57 ± 1.02	n.s.
Weight loss in the last 4 weeks (kg) (mean ± SD)	1.98 ± 2.54	1.70 ± 2.19	2.83 ± 3.35	n.s.
Appetite at study entry (reduced/increased/unchanged)	36/12/12	26/9/10	10/3/2	n.s.
Body mass index	27.84 ± 7.40	26.56 ± 7.23	31.70 ± 6.73	$t = -2.42$ $df = 58$ $P = 0.02$
Waist-to-hip-ratio	0.86 ± 0.10	0.84 ± 0.08	0.94 ± 0.09	$t = -4.29$ $df = 58$ $P < 0.01$
Smoking (no/$\leq$20 day^{-1}/$\geq$20 day^{-1})	27/21/12	23/17/5	4/4/7	$\chi^2 = 9.00$ $df = 2$ $P = 0.01$
Alcohol abuse (no/sporadic/daily)	50/3/7	40/2/3	10/1/4	n.s.
History of psychiatric disease in family (yes/no)	30/30	25/20	5/10	n.s.
History of unipolar depression in family (yes/no)	21/39	17/28	4/11	n.s.
History of bipolar disorder in family (yes/no)	1/59	1/44	0/15	n.s.
History of obesity in family (no/one parent/both parents/siblings/siblings and one parent/siblings and both parents)	32/12/0/3/10/3	25/9/0/2/7/2	7/3/0/1/3/1	n.s.
History of hypercholesterolemia in family (no/one parent/both parents/siblings/siblings and one parent/siblings and both parents)	38/11/4/4/1/2	32/8/1/2/1/1	6/3/3/2/0/1	n.s.
History of diabetes mellitus in family (no/one parent/both parents/siblings/siblings and one parent/siblings and both parents)	47/9/0/2/2/0	35/7/0/1/2/0	12/2/0/1/0/0	n.s.
History of hypertension in family (no/one parent/both parents/siblings/siblings and one parent/siblings and both parents)	31/13/5/3/3/5	25/11/3/2/3/1	6/2/2/1/0/4	n.s.
History of myocardial infarction in family (no/one parent/both parents/siblings/siblings and one parent/siblings and both parents)	45/12/2/1/0/0	37/6/1/1/0/0	8/6/1/0/0/0	n.s.

Table 3 Patients' medication at study entry

	All patients ($N = 60$)	MS− ($N = 45$)	MS+ ($N = 15$)	Level of significance
Number of psychotropic drugs (mean ± SD)	2.53 ± 1.19	2.67 ± 1.19	2.13 ± 1.13	n.s.
Tricyclic antidepressants (TCAs), *N* (%)	5 (8.3%)	3 (6.7%)	2 (13.3%)	n.s.
Monoamine oxidase inhibitor (MAOI), *N* (%)	1 (1.7%)	0 (0%)	1 (6.7%)	n.s.
Selective serotonin reuptake inhibitor (SSRI), *N* (%)	16 (26.7%)	13 (28.9%)	3 (20%)	n.s.
Norepinephrine reuptake inhibitor (NRI), *N* (%)	0 (0%)	0 (0%)	0 (0%)	n.s.
Serotonin and norepinephrine reuptake inhibitor (SNRI), *N* (%)	22 (36.7%)	16 (35.6%)	6 (40.0%)	n.s.
Noradrenergic and specific serotonergic antidepressants (NASSAs), *N* (%)	17 (28.3%)	15 (33.3%)	2 (13.3%)	n.s.
Neuroleptics, *N* (%)	23 (38.3%)	19 (42.2%)	4 (26.7%)	n.s.
Ziprasidone, *N* (%)	1 (1.7%)	1 (2.2%)	0 (0%)	n.s.
Risperidone, *N* (%)	2 (3.3%)	1 (2.2%)	1 (6.7%)	n.s.
Aripiprazole, *N* (%)	0 (0%)	0 (0%)	0 (0%)	n.s.
Quetiapine, *N* (%)	7 (11.7%)	5 (11.1%)	2 (13.3%)	n.s.
Clozapine, *N* (%)	0 (0%)	0 (0%)	0 (0%)	n.s.
Lithium, *N* (%)	7 (11.7%)	5 (11.1%)	2 (13.3%)	n.s.
Valproat, *N* (%)	3 (5.0%)	3 (6.7%)	0 (0%)	n.s.
Olanzapin, *N* (%)	4 (6.7%)	4 (8.9%)	0 (0%)	n.s.
Mirtazapine, *N* (%)	17 (28.3%)	15 (33.3%)	2 (13.3%)	n.s.
Number of non-psychotropic drugs (mean ± SD)	1.67 ± 1.88	1.20 ± 1.27	3.07 ± 2.67	$t = -3.66$ $df = 58$ $P < 0.01$
Lipid-lowering medication, *N* (%) (statins/fibrates)	5 (8.3%) (4/1)	0 (0%) (0)	5 (33.3%) (4/1)	$\chi^2 = 16.36$ $df = 1$ $P < 0.01$
Blood-pressure-lowering medication, *N* (%)	21 (35.0%)	10 (22.2%)	11 (73.3%)	$\chi^2 = 12.92$ $df = 1$ $P < 0.01$
Glucose-lowering medication, *N* (%)	2 (3.3%)	2 (4.4%)	0 (0%)	n.s.

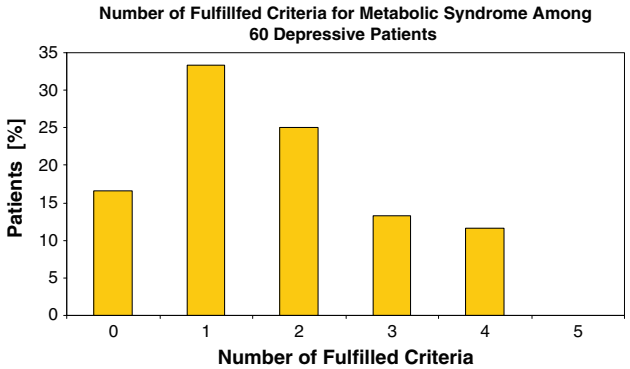

Fig. 1 Criteria of NCEP ATP III in depressive patients

Changes of laboratory values under treatment with antidepressants

Comparing the laboratory values in the course of depressive illness, there was no statistical difference between the state of acute depression and remission regarding the whole sample with the exception of triglyceride levels. Comparing MS+ and MS− patients the MS+ group had significantly higher triglyceride blood levels in acute depression than the MS− group ($t = 4.833$, $df = 56$, $P < 0.01$). A significant increase of triglyceride blood levels in remission ($P = 0.040$) was only found in the MS− group concerning the course of illness, whereas the MS+ group showed a tendency of a decrease of triglyceride blood levels in remission. All the other values did not significantly differ in acute depression and remission (Table 5).

The analysis of Pearson's correlations between laboratory values and depression revealed a positive correlation in the MS+ group between meeting the criterion for hypertriglyceridemia and the CGI score in acute depression ($r = 0.65$, $P < 0.01$) as well as a positive correlation between triglyceride blood levels in remission and the HAMD-21 score in remission ($r = 0.62$, $P = 0.03$).

Table 4 Prevalence of metabolic syndrome criteria in patients with unipolar or bipolar depression having the metabolic syndrome (MS+) and not having the metabolic syndrome (MS−)

Criterion	Description	All patients ($N = 60$) [F ($N = 35$), M ($N = 25$)]	MS− ($N = 45$) [F ($N = 29$), M ($N = 16$)]	MS+ ($N = 15$) [F ($N = 6$), M ($N = 9$)]
MS 1	Waist circumference >102 cm (40 in.) in men, >88 cm (35 in.) in women	27 (45.0%)	14 (31.1%)	13 (86.7%)
		F: 18 (51.4%)	F: 12 (41.1%)	F: 6 (100%)
		M: 9 (36.0%)	M: 2 (12.5%)	M: 7 (77.8%)
MS 2	Hypertriglyceridemia ≥150 mg/dl or being on cholesterol-lowering medication	20 (33.3%)	6 (13.3%)	14 (93.3%)
		F: 10 (28.6%)	F: 5 (17.2%)	F: 5 (83.3%)
		M: 10 (40.0%)	M: 1 (6.2%)	M: 9 (100%)
MS 3	HDL-cholesterol <40 mg/dl in men, <50 mg/dl in women	13 (21.7%)	4 (8.9%)	9 (60.0%)
		F: 6 (17.1%)	F: 1 (3.4%)	F: 5 (83.3%)
		M: 7 (28.0%)	M: 3 (18.8%)	M: 4 (44.4%)
MS 4	Blood pressure ≥130/85 mmHg or being on blood-pressure-lowering medication	36 (60.0%)	23 (51.1%)	13 (86.7%)
		F: 19 (54.3%)	F: 15 (51.7%)	F: 4 (66.7%)
		M: 17 (68.0%)	M: 8 (50.0%)	M: 9 (100%)
MS 5	Fasting glucose ≥110 mg/dl or being on glucose-lowering medication	6 (10.0%)	3 (6.7%)	3 (20.0%)
		F: 4 (11.4%)	F: 2 (6.9%)	F: 2 (33.3%)
		M: 2 (8.0%)	M: 1 (6.2%)	M: 1 (11.1%)

F female, *M* male

In the MS− group, no correlation between laboratory values and depression became evident.

Discussion

Metabolic syndrome and depression

This is the first European study that analyzes the occurrence and the role of the metabolic syndrome in depressive inpatients. Most studies analyzing an association between the metabolic syndrome and depression are epidemiological studies that evaluate the prevalence of the metabolic syndrome and depressive symptoms in mixed samples of depressed and non-depressed men and women [9, 10, 12, 20]. A Brazilian study analyzed the occurrence of the metabolic syndrome in a group of inpatients with diverse psychiatric disorders [18]. The study reported a prevalence of the metabolic syndrome among psychiatric inpatients of 29.4% and for those inpatients with depressive disorder the prevalence was 48.1%. An association between the diagnosis of the metabolic syndrome and the use of lithium was stated. Another study that also focused on depressive patients was the study mentioned by Heiskanen et al. [8]. The study analyzed an association between the metabolic syndrome and depression in depressive outpatients. The reported prevalence of the metabolic syndrome was 36% and for those outpatients who were suffering from a current major depression 56%. Unfortunately, the study of Heiskanen et al. did not mention the patients' medication. In the present study, only 25% of the patients fulfilled the criteria for metabolic syndrome. Possibly, this divergence is due to a different pharmacological regiment. In the present study, only 11.7% of the patients were on treatment with lithium. Apart from that, the results of the Finnish study and the present study are in line. Both studies did not detect an association between gender and the metabolic syndrome. Furthermore, both studies did not find an association between HAMD, BDI or GAF scores, which reflect the severity of depression.

Yet, in both studies, the triglyceride blood levels were significantly higher in patients with a metabolic syndrome. A recent finding of Eich et al. [2] suggested that major depression is a predictor for heart complaints at the age of 40 and that the severity of depressive disorder in younger age has an effect on subsequent heart complaints. Whether elevated triglyceride blood levels may contribute to comorbid cardial complaints is to be questioned.

Moreover, the present study did not reveal any differences between patients with or without metabolic syndrome in correlation to their psychiatric disorder. There were no statistical differences in respect to the psychotropic medication, number of suicide attempts and number or duration of hospitalizations. Patients did only differ when correlated to their somatic comorbidities. Furthermore, leptin blood levels did not change significantly during the course of illness. It was rational to analyze leptin blood levels since obese people are known for having high circulating concentrations of leptin. Another relevant biomarker are CRP levels indicating inflammation. High CRP

Table 5 Laboratory values and HAMD score of MS+ and MS− depressive patients in course of depressive illness

Laboratory value	All patients ($N = 42$)	MS− ($N = 30$)	MS+ ($N = 12$)
Fasting glucose[a] (mg/dl)	89.9 (17.6)	90.6 (7.8)	88.6 (13.4)
Fasting glucose[r] (mg/dl)	93.1 (26.8)	94.2 (30.9)	90.3 (12.7)
Level of significance	n.s.	n.s.	n.s.
HDL-cholesterol[a] (mg/dl)	64.9 (22.4)	68.3 (21.6)	51.0 (15.2)
HDL-cholesterol[r] (mg/dl)	60.6 (22.1)	67.0 (22.3)	45.2 (12.2)
Level of significance	n.s.	n.s.	n.s.
Cholesterol[a] (mg/dl)	221.5 (47.4)	217.0 (46.5)	227.7 (39.2)
Cholesterol[r] (mg/dl)	223.3 (51.9)	226.2 (54.6)	216.0 (46.1)
Level of significance	n.s.	n.s.	n.s.
Triglycerides[a] (mg/dl)	129.7 (61.1)	106.3 (39.1)	192.1 (82.5)
Triglycerides[r] (mg/dl)	131.7 (47.5)	123.3 (43.8)	153.0 (51.5)
Level of significance	n.s.	$t = -2.16$	n.s.
		$df = 29$	($t = 2.13$, $df = 11$, $P = 0.057$)
		$P = 0.040$	
CRP[a] (mg/l)	4.0 (4.9)	3.7 (5.5)	4.4 (3.1)
CRP[r] (mg/l)	4.9 (5.6)	3.9 (3.9)	7.3 (8.3)
Level of significance	n.s.	n.s.	n.s.
Leptin[a] (ng/ml)	18.6 (21.1)	14.5 (15.4)	29.3 (33.9)
Leptin[r] (ng/ml)	18.1 (18.2)	17.7 (18.0)	19.6 (19.9)
Level of significance	n.s.	n.s.	n.s.
HAMD score[a]	29.4 (5.4)	29.2 (5.7)	29.9 (4.8)
HAMD score[r]	12.9 (4.4)	12.7 (4.5)	13.4 (4.3)
Level of significance	$t = 15.07$	$t = 12.21$	$t = 8.68$
	$df = 41$	$df = 29$	$df = 11$
	$P < 0.01$	$P < 0.01$	$P < 0.01$

Values shown as mean (SD)

a acute depression, *r* remission

blood levels are known to increase the risk for developing diabetes type 2. We analyzed CRP blood levels as insulin resistance plays an important role in the onset of the metabolic syndrome. In our study, CRP blood levels did not differ between patients fulfilling the criteria of metabolic syndrome (MS+) and those who did not (MS−).

Triglycerides and depression

A novel finding of the present study was a positive correlation between triglyceride blood levels and severity of depression as a characteristic of the MS+ group of depressive patients. This correlation persisted even in the course of depressive illness. Some studies have already analyzed triglyceride blood levels in depression but with inconsistent results. Kinder et al. [10] found a positive correlation between triglyceride blood levels and depression in women aged between 17 and 39 years. Vaccarino et al. [20] found a positive correlation between triglyceride blood levels and the BDI score in women who had received coronary angiography. Sheikh et al. [17] compared triglyceride blood levels of 80 depressive patients to a control group of 120 non-depressed men and women and found no statistical difference. Similar results were assessed in a retrospective analysis of data on total serum cholesterol and serum triglycerides in 39 seasonal affective disorder (SAD) patients and 40 non-seasonally depressed or schizophrenic control subjects. Total serum triglycerides did not differ significantly between SAD patients and controls [16].

Recently, an association between hypertriglyceridemia and high levels of urinary cortisol levels has been observed in depressive patients. Thus, from a biological point of view, elevated triglycerides and depression may be linked by an assumed activation of the hypothalamic–pituitary–adrenal axis [21]. In addition, depression may activate inflammatory processes that are accompanied by a secretion of interleukin-2 that is also regarded to lead to an increase of triglyceride blood levels [15]. Vice versa, a study published by Glueck et al. [5] in 1993 suggested a reversible causal relationship between high triglycerides and symptoms of depression. 23 patients with familial

hypertriglyceridemia underwent a 54-week single blind treatment with a triglyceride-lowering diet and medication (Gemfibrozil, 1.2 g/day); depressive symptoms were serially tested by BDI. Comparing BDI scores before and after triglyceride-lowering treatment, a major shift toward absence or amelioration of depressive symptoms was observed. Pathophysiologically, Glueck et al. assumed a link between the observed amelioration and an improved cerebral perfusion and oxygenation. As the prevalence of metabolic syndrome is rising [19], the number of MS+ psychiatric patients will probably rise as well. Thus, more research will be needed to meet the requirements of an integrated treatment of depressive patients with metabolic syndrome. One study has already demonstrated the beneficial effect of antidepressant treatment on lipid regulation [11]. The findings of the present study show the need to analyze the effects of triglyceride-lowering therapy on depressive symptoms in depressive patients with a metabolic syndrome.

Diagnosing the metabolic syndrome in depression

This study was designed as a follow-up study in order to find an indication of the best time for diagnosing the metabolic syndrome in depressive illness. Comparing the laboratory values in acute depression and remission, the measured laboratory values remained quite stable despite the triglyceride blood levels that showed a tendency to decrease in MS+ patients and increase in MS− patients. Therefore, it seems to be obvious that all depressive patients should undergo a screening for metabolic syndrome when being hospitalized for depression and it is advisable to re-screen those without metabolic syndrome during remission.

Limitations

The main methodological shortcoming of this study was the small sample size and the lack of a control group. Thus, this study was not designed to contribute to prevalence rates of the metabolic syndrome. Furthermore, the present sample was clinically not subtyped in, e.g., a melancholic, hypercortisolemic or atypical subtype. It is known that the differentiation of a hypercortisolemic and non-hypercortisolemic depression is useful to evaluate the putative association between hypercortisolemia and the metabolic syndrome [21]. Another relevant issue was the effect of medication on the laboratory testing results. Our patients were neither drug-naïve nor untreated. Although our subgroup analyses (exclusion of patients taking lithium, ziprasidone) have not found associations between the intake of medication and the metabolic syndrome, pharmacological treatment definitely remains a relevant intervening variable. Four of the MS+ patients were taking statins and one patient was on treatment with fibrates when enrolled in the present study. During study participation, these patients continued their treatment and there was no dose adjustment regardless of elevated triglyceride levels. It would be of interest in future studies to determine the effects of additive triglyceride-lowering medication on depressive symptomatology.

In view of the statistical analysis, it is also important to consider that the interpretation of these data could be subject to a type-I-error, describing the problem of false positive findings due to multiple testing.

Conclusion

Depression and metabolic syndrome do not seem to be related per se. Depressive subjects with and without a metabolic syndrome did not differ in relation to their psychic disorder. However, they differed in the number of somatic comorbidities and the number of non-psychotropic medication. Metabolic laboratory results remained stable in the course of depressive illness despite elevated triglyceride blood levels in MS− patients and were correlated to severity of depression in MS+ patients. This correlation may potentially be explained by an activated HPA axis, interleukin-2 secretion or the influence of high triglyceride levels on cerebral perfusion. It is probable that antidepressant treatment improves the metabolic situation in depressive patients with a metabolic syndrome. All these findings underline the need and importance of an integrated therapy of depression and metabolic syndrome. In future studies, larger samples will be necessary to further assess the prevalence rates of metabolic syndrome in depression and subtypes of affective disorders and to evaluate the influence of psychotropic and non-psychotropic medication.

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