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Pericardial adipose tissue and the metabolic syndrome is increased in patients with chronic major depressive disorder compared to acute depression and controls

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ABSTRACT

Objective: Major depressive disorder (MDD) is associated with an estimated fourfold risk for premature death, largely attributed to cardiovascular disorders. Pericardial adipose tissue (PAT), a fat compartment surrounding the heart, has been implicated in the development of coronary artery disease. An unanswered question is whether people with chronic MDD are more likely to have elevated PAT volumes versus acute MDD and controls (CTRL).

Methods: The study group consists of sixteen patients with chronic MDD, thirty-four patients with acute MDD, and twenty-five CTRL. PAT and adrenal gland volume were measured by magnetic resonance tomography. Additional measures comprised factors of the metabolic syndrome, cortisol, relative insulin resistance, and pro-inflammatory cytokines (interleukin-6; IL-6 and tumor necrosis factor- α , TNF- α).

Results: PAT volumes were significantly increased in patients with chronic MDD > patients with acute MDD > CTRL. Adrenal gland volume was slightly enlarged in patients with chronic MDD > acute MDD > CTRL, although this difference failed to reach significance. The PAT volume was correlated with adrenal gland volume, and cortisol concentrations were correlated with depression severity, measured by BDI-2 and MADRS. Group differences were found concerning the rate of the metabolic syndrome, being most frequent in chronic MDD > acute MDD > CTRL. Further findings comprised increased fasting cortisol, increased TNF- α concentration, and decreased physical activity level in MDD compared to CTRL.

Conclusion: Our results extend the existing literature in demonstrating that patients with chronic MDD have the highest risk for developing cardiovascular disorders, indicated by the highest PAT volume prevalence of metabolic syndrome. The correlation of PAT with adrenal gland volume underscores the role of the hypothalamus-pituitary-adrenal system as mediator for body-composition changes. Metabolic monitoring, health advices and motivation for the improvement of physical fitness may be recommended in depressed patients, in particular in chronic depression.

Key words: chronic major depressive disorder, cardio-vascular disorder, pericardial adipose tissue, body composition, hypothalamus-pituitary-adrenal system

Introduction

Chronic major depressive disorder (MDD) is defined as a major depressive episode without remission for at least two years. Chronic MDD is common, with a lifetime prevalence of ~5% in the general population; around 20-30% of acutely depressed individuals typically go on to develop a chronic disease course (1, 2). Chronic MDD is distinguished from acute MDD by an earlier onset (1), increased comorbidity with axis 1 disorders (1, 3, 4), higher rates of personality disorders (5), higher rates of childhood trauma (6), greater suicidality (7) and functional impairment (1, 8), higher rates of mood disorders in relatives (9, 10), and worse treatment outcome (11-13). Chronic MDD is associated with significant individual and societal costs, documented by higher unemployment rates and lower rates of marriages across this patient group (14).

The comorbidity of acute MDD with coronary artery disease (CAD) is common, and has also been observed in patients with chronic MDD (14). Depression and coronary artery disease are considered to have a bidirectional relationship. Recent studies examining depression as a risk factor for developing CAD have found increased rates of incident cardiovascular disease (15) and ischemic heart disease mortality (16).

The underlying mechanisms that link MDD with cardio-metabolic disorders are complex. Key factors contributing include the increased rate of the metabolic syndrome in MDD (17), increased rates of type-2 diabetes mellitus (18, 19), increased intra-abdominal adipose tissue (20), dysregulation of the hypothalamus-pituitary-adrenal axis (HPAS) with subsequent alterations in cortisol concentrations (21), dysregulation of pro- and anti-inflammatory cytokines (22), and poor lifestyle habits (e.g. smoking, physical activity, dietary factors) (2, 23, 24).

Recently, increased pericardial adipose tissue (PAT) has been observed in patients with acute MDD (25). PAT is a fat deposit surrounding the heart, with close anatomic proximity to coronary arteries. Research from the general population has shown that similarly to intra-abdominal adipose tissue, PAT secretes pro-inflammatory cytokines that may be implicated in early-stage CAD (26). PAT is strongly associated with myocardial ischemia and coronary heart disease, even after adjusting for body mass index (27) and other cardiovascular risk factors (28, 29). The results of general population-based studies have demonstrated that PAT is positively correlated with coronary artery calcification (30), inflammatory markers, and carotid intima-media thickness (31, 32).

To the best of our knowledge, to date, no study has investigated if PAT volume differs among people with chronic MDD compared to those with acute MDD or controls. Therefore, our primary aim was to examine PAT volumes in patients with chronic MDD by cardiac magnetic resonance imaging (33), and to relate PAT volumes to adrenal gland volumes, a proxy parameter for HPAS activation. Our main hypothesis was that chronic MDD is associated with higher PAT volumes and worse metabolic parameters compared to patients with acute MDD and healthy controls.

Methods

Study procedure and eligibility criteria

The recruitment process, including the eligibility criteria are described in details elsewhere (25). In short, all patients were recruited after written informed consent at the Department of Psychiatry, Social Psychiatry and Psychotherapy of Hannover Medical School, and diagnosed according to the Diagnostic and Statistical Manual of

Mental Disorders, Fourth Edition (DSM-IV-TR) criteria, confirmed by standardized clinical interviews (SCID I/II; German version).

Exclusion criteria included comprised acute or chronic infectious disease, lifetime immune or autoimmune disorders, type-2 diabetes mellitus, lifetime or current cardiovascular disease, pregnancy, schizophrenia, mental retardation, bipolar disorder, current substance abuse age younger than 18 and older than 60 years (25).

PARTICIPANTS

The current study utilizes data from an ongoing study including two groups of people with depression. First, adults with acute MDD (N=34) were defined as those with a major depressive episode, defined as major depression with a duration less than two years, and no comorbidity with dysthymic disorder (N = 34). Second, the chronic MDD group (N=16) was defined as those with MDD with comorbid dysthymic disorder, or MDD with a duration longer than two years, or MDD with partial response but still fulfilling MDD criteria (25). **All patients were treated with psychotherapy, and 40/50 patients received psychopharmacological drugs. In particular, 16 patients were treated with selective serotonin reuptake inhibitors, 11 with agomelatine, nine with dopamine and noradrenaline reuptake inhibitors, eight with selective serotonin and noradrenaline reuptake inhibitors, three with quetiapine, and one patient received lithium. Eight of sixteen patients in the chronic MDD group reported an onset of the disorder before the age of 20y, compared to seven of thirty-four patients in the acute depression group.**

Twenty-five healthy subjects (CTRL) were recruited through announcements on university bulletin boards. Potential control subjects with mental and physical disorders were excluded, determined by using a standardized psychiatric interview and a physical examination.

BEHAVIORAL ASSESSMENTS

Depression severity was assessed using the German versions of the 10-item, clinician-rated Montgomery-Åsberg Depression Rating Scale (MADRS) and the self-reported, 21-item Beck Depression Inventory (34). Physical activity was assessed using a 6-point Likert scale with descriptors ranging from “never” (1) to “very often” (35). Smoking habits were measured in pack-years (the number of cigarettes smoked per day x years of smoking/20), and alcohol consumption was measured in drinks consumed per week.

MAGNETIC RESONANCE IMAGING

Pericardial adipose tissue (PAT) and adrenal gland volume were examined using a 1.5 Tesla MRI scanner (Avanto, Siemens Healthcare) (36). To quantify PAT, ECG-gated T1-weighted dark-blood turbo spin-echo sequences were acquired in short- and long-axis views at the following specifications: TR/TE = 750/37 ms, flip angle = 180°, matrix = 384x187, field of view = 380 mm, and slice thickness = 10 mm. PAT was quantified between the atrioventricular plane and the apex by segmentation using QMass 7.1 software (Medis, Leiden, The Netherlands).

Adrenal gland volumes were determined using a VIBE Dixon sequence with 2 mm slice thickness and QMass 7.1 software (Medis, Leiden, The Netherlands) by manual segmentation. To obtain the intra-observer variability the manual segmentation of the adrenal glands was done twice. Volumes of right and left adrenal gland were added, and expressed as total adrenal gland volume.

All measurements were performed by raters blinded for the status of study participants.

BLOOD SAMPLING

Fasting serum samples were collected between 0700 h and 0800 h and stored at -80°C until the analysis. Concentrations of fasting glucose and fasting cortisol were determined with established immunoassays (Roche Diagnostics, Mannheim, Baden-Württemberg, Germany). Concentrations of tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) were determined using high sensitivity ELISA kits according to the manufacturer's instructions (HS Quantikinine; R&D Systems, Wiesbaden, Germany). Relative insulin resistance was determined using the homeostasis assessment model (37).

STATISTICAL ANALYSIS

Data were analyzed using IBM SPSS Statistics (version 23). Group differences concerning PAT were determined utilizing ANCOVA. Since it was previously demonstrated that gender and age make an essential contribution to the amount of cardiac adipose tissue, we used group and gender as independent variables, PAT as dependent variable, and age, height and weight as potential confounders for the analysis of group differences concerning PAT (25) (38). Group differences concerning adrenal gland volume were analyzed using ANCOVA, with group as independent variable, adrenal gland volume as dependent variable, and age, height and weight as potential confounders. Anthropometric measures, factors of the metabolic syndrome, immune and endocrine measures were analyzed using ANOVA. The chi-squared test was used to compare the incidence of metabolic syndrome between groups, as defined according to ATP III criteria (39), and to compare categorical variables were appropriate. Partial correlations controlling for age, height and weight were calculated when testing for correlations between PAT, adrenal gland volume, endocrine (cortisol) measures, immune (TNF- α) measures and physical

activity. Values are presented as mean $\pm$ SD. All P values <0.05 were considered to be significant.

Results

Full details of the demographics and clinical variables for the control, acute and chronic MDD groups are summarized in table 1. Briefly, anthropometric comparisons of the 3 groups (Table 1) showed group differences concerning age ($F=3.3$; $df=2$; $P=0.042$) and height ($F=4.5$; $df=2$; $P=0.014$) (Table 1). Physical activity was different between the groups ($F=5.9$; $df=2$; $P=0.004$) and highest in CTRL.

Table 1 here

Regarding medication, more patients with acute depression were treated with selective serotonin reuptake inhibitors (acute MDD: 15/34 versus chronic MDD: 1/12; $\chi^2=6.1$; $df=1$; $P=0.016$), and slightly more patients with chronic MDD were treated with dopamine and noradrenaline reuptake inhibitor (acute MDD: 4/34 versus chronic MDD: 5/12; $\chi^2=3.8$; $df=1$; $P=0.094$). Regarding treatment with selective serotonin and noradrenaline reuptake inhibitors (acute MDD: 6/34; chronic MDD: 2/12), agomelatine (acute MDD: 6/34; chronic MDD: 5/12), quetiapine (acute MDD: 2/34; chronic MDD: 1/12), and lithium (acute MDD: 1/34; chronic MDD: 0/12), no group differences were observed. **Of the ten patients with psychotherapy only, 4/16 were chronic depressed, and 6/34 were acute depressed ($\chi^2=0.7$; $df=1$; $P=0.44$).** Employing an ANCOVA with PAT as dependent variable, group and gender as independent variable, and age, height and weight as potentially confounding factors revealed a significant effect of group ($F=7.0$; $df=2$; $P=0.002$) and gender ($F=5.9$; $df=2$; $P=0.018$). Post-hoc analysis revealed significantly increased PAT volume in chronic MDD versus acute MDD ($p=0.021$) and CTRL ($P<0.001$) respectively, and significantly more PAT in acute MDD versus CTRL ($P=0.049$) (Fig. 1).

Insert figure 1 here

When we stratified our results according to gender, a significant group difference for male ($F=3.3$; $df=2$; $P=0.047$) and for female ($F=4.0$; $df=2$; $P=0.031$) was observed. The respective post-hoc analyzes revealed significantly higher PAT volume in male patients with chronic MDD versus CTRL ($P=0.015$), and significantly more PAT volume in females with chronic MDD versus CTRL ($P=0.012$). PAT was also enlarged among males and females with chronic MDD versus acute MDD, and comparing males and females with acute MDD with CTRL, however, these results did not reach significance (Fig. 2).

Insert figure 2 here

When total volume of adrenal glands, expressed as sum of left and right adrenal gland volume, were analyzed, no group differences were observed ($F=1.3$; $df=2$; $P=0.3$). However, adrenal gland volume was slightly enlarged in patients with chronic MDD > acute MDD > CTRL (Table 1).

Correlates of PAT volumes

Full details of the correlates of PAT volumes are displayed in table 2. Briefly, a partial correlation analysis controlling for age, weight and height revealed that PAT was positively associated with total adrenal gland volume ($r=0.37$, $P=0.005$), and with severity of depression ($r=0.41$; $P=0.01$ for BDI-2 sum score; $r=0.26$; $P=0.046$ for MADRS sum score). Fasting cortisol was positively associated with BDI-2 sum score ($r=0.32$; $P=0.013$) and with MADRS sum score ($r=0.36$; $P=0.006$), pointing to elevated cortisol dependent on depression severity. TNF- α was associated with

MADRS sum score ($r=0.31$; $P=0.016$). Physical activity was negatively associated with higher depression scores ($r=-0.39$; $P=-0.001$, and negatively associated with the number metabolic syndrome factors ($r=-0.40$; $P=0.002$) (Table 2).

Insert table 2 here

Further analyses comprised the potential influence of medication status and age at onset of depression on PAT. ANCOVA with PAT as dependent variable, treatment status (antidepressant drugs/ no antidepressant drugs) and gender as independent variables, and age, height and weight as confounding factors, revealed no influence of medication status on the amount of PAT ($F=0.01$; $df=1$; $P=0.90$) (data not shown).

Slightly more patients in the chronic depressed patient group reported an onset of the disorder before the age of 20y (8/16 in chronic MDD versus 7/34 in acute MDD; $\chi^2=4.4$; $df=1$; $P=0.049$). ANCOVA with PAT as dependent variable, age of onset (before age of 20y/ after age of 20y) and gender as independent variables, and age, height and weight as confounding factors, revealed no influence of age of depression onset on the amount of PAT ($F=0.01$; $df=1$; $P=0.90$) (data not shown).

Discussion

The main finding of our study is that PAT volume is particularly increased in patients with chronic depression, compared to patients with acute depression and healthy comparison subjects. Thus, our data suggest that the longer the illness duration of MDD, the greater a person's risk of developing increased PAT volume, a key risk factor for premature mortality from cardiovascular disease. Given the importance of PAT for the development of coronary artery calcification and myocardial ischemia,

our results point to a higher risk for the development of cardiovascular disorders (CVD) in patients with MDD, in particular in patients with a chronic disease course.

A recent meta-analytic study has demonstrated that people with MDD are at an 80% increased risk of developing coronary heart disease (40). The precise underlying reasons for this increased risk have as yet, not been fully explored. The association of cardiometabolic disorders with severe mental illness has received more attention during the last years, leading to a concise monitoring protocol published by the European Psychiatric Association in 2009 (41, 42). Since depression is a heterogeneous disorder with high frequency in the general population, it is clinically important to know whether certain MDD subtypes may carry a higher risk for the development of CVD, and should therefore be monitored more closely. Some studies pointed to the role of depression severity in the development of CVD (43-45). In the study by Windle and colleagues, recurrent depressive disorder was more closely related to CVD incidence compared to a single depressive episode (46), and in the study by Baune and colleagues, dysthymia was found to be stronger associated with CVD compared to unipolar depression (47). Seldenrijk and colleagues reported a dose-dependent increase of CVD in MDD over 6y follow-up, with higher CVD risk in more severely depressed patients at study entry (48). Taken together the previous literature and our results, the role of depression chronicity, recurrence of depression and depression severity seem particularly pertinent factors that may be considered in estimating CVD risk in MDD.

Another important aspect of our study is the observed higher incidence of the MetS in patients with chronic depression compared to acute depression and healthy controls. Several studies found an association of MDD with the MetS (49-53). In a recent

meta-analysis, an estimated increased risk of having the MetS about 60% was found in MDD, compared to healthy controls or data from the general population (17). Our results confirm these results and underscore the particular role of a chronic disease course for the association between MDD and the MetS.

The third important result of our study is the difference in adrenal gland volumes between the groups, showing the highest amount of adrenal gland volume in chronic MDD, followed by acute MDD compared to healthy controls. Furthermore, adrenal gland volume correlated with the amount of PAT. An increase in adrenal gland volume in MDD has also been reported by others (54, 55). Kessing and coworkers reviewed the existing studies on adrenal gland volumes in depression. Three case-control studies were identified with a total of 89 depressed patients and 57 controls, showing enlarged adrenal volume in MDD (54). Adrenal gland volume may serve as a proxy marker for hypercortisolism, and has been found to correlate positively with dexamethasone-suppressed salivary cortisol and total daily salivary cortisol among healthy individuals (56). In a recent study, we found adrenal gland volume enlarged in patients with acute depression, and strongly correlated with the amount of intra-abdominal and pericardial adipose tissue (55). Our data presented here suggest a key role for the hypothalamus-pituitary adrenal axis in the development of heightened PAT volume also in severely depressed patients with a chronic disease course.

Relatively few studies have been conducted concerning biological alterations in chronic depression. A dysregulation of the hypothalamus-pituitary adrenal axis dysregulation in chronic depression has been described in a recent study, depending on the subtype of depression (57). Hypercortisolism was particularly observed in patients with melancholic subtype of chronic depression. In contrast, in the atypical

subtype of chronic depression, metabolic and inflammatory (TNF- α , IL-6) dysregulation was observed. Other groups have found increased salivary cortisol in recovered depressed patients at high risk for recurrence (58), thereby indicating that hypothalamus-pituitary-adrenal dysregulation may be a marker of an unfavorable disease course (59). Taken together, these and our findings support the notion that chronic forms of MDD are associated with a dysregulation of endocrine (HPAS), immune (TNF- α , IL-6) and cardiometabolic (blood pressure regulation, glucose and fat metabolism) systems, and that hypercortisolism may possibly underlie medical problems associated with chronic forms of depression (60).

However, the link between depression and cardiovascular disease is complex. Depression is associated with a number of behavioral cardiovascular risk factors, including physical inactivity (61), cigarette smoking, (62) and depressed patients are less likely to follow health-promoting behaviors, including maintaining healthy diets (63). Nevertheless, the link between depression and cardiovascular morbidity and mortality has been shown to be robust to corrections for behavioral factors, both in our study and in the majority of other studies (64).

Other factors potentially contributing to the link between depression and cardiac disease include increased concentrations of pro-inflammatory cytokines (specifically TNF- α and IL-6), (65) a dysregulation of the hypothalamic-pituitary-adrenal axis, (66) endothelial dysfunction, (67, 68) altered platelet activation and aggregation, (69) autonomic nervous dysfunction, (70, 71) altered intima-media thickness, (72) increased sympathetic and decreased parasympathetic activity, (73) visceral obesity, (74-76) and altered glucose disposal (77). Our study adds to these results in

demonstrating that PAT is another important factor to be considered, and a chronic disease course is more likely to be associated with increased PAT volumes.

Given the potential increased risk of heightened PAT volumes in chronic MDD, our data suggest that earlier interventions in the acute phases of illness, seeking to ameliorate this risk should be employed and prioritized. In particular, exercise interventions, which have been shown to improve cardiorespiratory levels (78), quality of life (79) and depressive symptoms (80). In the general population, exercise is broadly as effective as pharmacological interventions for preventing cardiovascular disease and mortality (81). In addition, interventions seeking to improve diet may also be useful to reduce pericardial adipose tissues (82).

Whilst the study adds to the current literature, some limitations should be noted. We did not assess cardiac function or physical capacity in patients and control subjects. Moreover, the cross sectional nature of the study precludes any conclusions being made regarding the directionality of our results. Therefore, further prospective studies are warranted to explore whether PAT is an independent predictor of CVD or cardiovascular events. The small number of subjects, in particular in the group of chronic depressed patients, limits the **generalizability and the** explanatory power of the study. **Further studies with larger samples of acute and chronic depressed patients are warranted.** We did not differentiate between chronic MDD with melancholic versus chronic MDD with atypical disease course.

In summary, we found that PAT and adrenal gland volume were particularly increased in people with chronic MDD versus those with acute MDD or controls.

Moreover, those with chronic MDD had higher rates of MetS. Given the importance of

PAT and the MetS for the development of CVD, chronic MDD may be considered as particular at risk group and interventions employed in the earlier stages of the disease to ameliorate this risk.

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Author contributions: Kai G. Kahl made the conception and the design of the study, and has the responsibility for the integrity of the work as a whole. Ralf Lichtinghagen and Dagmar Hartung made substantial contributions to acquisition and analysis of data. All authors made substantial contributions to drafting the article, and gave final approval of the version to be published.

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Legend Fig. 1: Pericardial adipose tissue (PAT) was enlarged in patients with chronic MDD compared to acute MDD and CTRL, and in patients with acute MDD compared to CTRL. Bars are presented as mean $\pm$ SD, corrected for age, height and weight. A P-value <0.05 was considered significant.

Legend Fig. 2: Pericardial adipose tissue (PAT) was increased in female patients with chronic MDD $>$ females with acute MDD $>$ CTRL, and in males with chronic MDD $>$ males with acute MDD $>$ CTRL. Bars are presented as mean $\pm$ SD, corrected for age, height and weight. A P-value <0.05 was considered significant.

Fig. 1

Fig. 2

Table 1. Anthropometric, endocrine and cytokine data for patients with acute MDD, chronic MDD, and healthy comparison subjects.

	CTRL (N = 25)	Acute MDD (N = 34)	Chronic MDD (N = 16)	<i>P</i>
Female (N/%)	12 (48%)	16 (47%)	4 (33%)	n.s.
Age (y)	46.8 ± 15.0	41.8 ± 9.6 ^a	37.0 ± 11.7	0.042
Weight (kg)	79.2 ± 21.0	77.5 ± 19.1	82.8 ± 19.3	n.s.
Height (m)	1.80 ± 0.13	1.72 ± 0.08	1.77 ± 0.07	0.014
BMI	24.2 ± 4.8	25.8 ± 4.6	26.2 ± 4.8	n.s.
BDI (sum)	0.7 ± 1.0	29.5 ± 9.4	31.7 ± 10.6	<0.001
MADRS (sum)	1.0 ± 1.6	23.2 ± 8.3	25.8 ± 9.4	<0.001
Physical activity	4.2 ± 1.5	2.7 ± 1.6	2.9 ± 1.9	0.04
Drinks/wk	3.0 ± 1.5	1.6 ± 3.5	4.6 ± 6.1	0.08
Smoking (pack- years)	2.2 ± 5.3	6.5 ± 9.6	5.0 ± 7.9	n.s.
BP _{syst} (mm Hg)	128.4 ± 8.1	129.4 ± 20.8	134.0 ± 13.3	n.s.
BP _{diast} (mmHg)	80.0 ± 6.2	81.0 ± 10.1	84.3 ± 10.3	n.s.
WC (cm)	91.4 ± 15.7	94.3 ± 15.6	94.1 ± 19.6	n.s.
Triglycerides (mmol/L)	1.17 ± 0.86	1.50 ± 0.73	1.35 ± 0.78	n.s.
HDL (mmol/L)	1.47 ± 0.37	1.43 ± 0.26	1.41 ± 0.32	n.s.
Glucose (mmol/L)	5.1 ± 0.5	5.2 ± 0.8	5.4 ± 1.1	n.s.
Nr. MetS criteria	0.9 ± 1.1	1.3 ± 1.0	1.5 ± 1.6	n.s.
MetS (N)	2 (8%)	4 (13.3%)	6 (37.5%)	0.028
Insulin (mU/L)	8.4 ± 4.3	10.4 ± 6.2	11.8 ± 6.4	n.s.

HOMA-IR	1.9 ± 1.2	2.4 ± 1.6	2.9 ± 2.0	n.s.
Cortisol (nmol/L)	423.4±150.1	579.1±162.6	619.9±129.0	<0.001
IL-6 (pg/mL)	1.7 ± 1.4	1.5 ± 0.8	2.1 ± 2.7	n.s.
TNF-α (pg/mL)	0.7 ± 0.5	1.7 ± 1.5	1.9 ± 1.3	0.004

Abbreviations: BDI (sum), sum score of the Beck Depression Inventory; BMI, body mass index; BPsyst, systolic blood pressure; BPdiast, diastolic blood pressure; HDL, high density lipoproteins; HOMA-IR, relative insulin resistance according to homeostasis model assessment; IL-6, interleukin 6; MADRS (sum), sum score of the Montgomery-Åsberg Depression Rating Scale; MetS, metabolic syndrome; TNF-α, tumor necrosis factor-α; WC, waist circumference. Significant results according to ANOVA are given in bold.

Table 2. Results of the partial correlation analysis.

	tAGV	Cort	TNF- α	MetS	Sport	BDI-2	MADRS
PAT	$r=0.37$ $P=0.005$	n.s.	n.s.	n.s.	n.s.	$r=0.41$ $P=0.001$	$r=0.26$ $P=0.046$
tAGV	-	n.s.	n.s.	n.s.	n.s.	$r=0.29$ $P=0.024$	n.s.
Cort	-	-	n.s.	n.s.	n.s.	$r=0.32$ $P=0.013$	$r=0.36$ $P=0.006$
TNF- α	-	-	-	n.s.	n.s.	n.s.	$r=0.31$ $P=0.016$
MetS	-	-	-	-	$r=-0.40$ $P=-0.002$	n.s.	n.s.
Sport	-	-	-	-	-	$r=-0.39$ $P=-0.001$	n.s.
BDI-2	-	-	-	-	-	-	$r=1.0$ $P<0.001$

Partial correlations were performed controlling for age, height and weight. PAT was correlated with the total volume of the adrenal glands, and with depression severity.

Abbreviations: PAT: pericardial adipose tissue; tAGV: total adrenal gland volume; Cort: fasting cortisol; TNF- α : tumor-necrosis factor- α ; MetS: number of metabolic syndrome factors; BDI-2: sum score of the Beck depression Inventory-2; MADRS: sum score of the Montgomery-Åsberg Depression Rating Scale.