Symptom dimensions of depression and anxiety and the metabolic syndrome

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ABSTRACT

Background
It was our objective to investigate the associations of depression and anxiety symptoms with the metabolic syndrome using a dimensional approach. The association between depression and anxiety on the one hand, and the metabolic syndrome as a cluster or its individual components on the other hand, is equivocal. The categorical nature of the Diagnostic and Statistical Manual of mental disorders might partly explain the inconsistent findings.

Methods
In 2433 Netherlands Study of Depression and Anxiety participants (mean age, 42.3 years; 33.1% male), three symptoms dimensions -lack of positive affect (depression specific); negative affect (aspecific); and somatic arousal (anxiety specific)- were assessed by a shortened adaptation of the Mood and Anxiety Symptom Questionnaire (MASQ). The association between symptom dimensions and metabolic syndrome components (i.e., waist circumference, triglycerides, high-density lipoprotein cholesterol, glucose, and mean blood pressure) was analyzed, using linear regression analysis.

Results
The occurrence rate of the metabolic syndrome was 20.1% (n=490). Somatic arousal, but not positive affect and negative affect, was strongly associated with four out of five metabolic syndrome components, especially waist circumference, triglycerides, and blood pressure ($\beta = 0.046$, $p < .01$; $\beta = 0.077$, $p < .001$; and $\beta = 0.069$, $p < .001$, respectively), and with the total number of metabolic syndrome components ($\beta = 0.098$, $p < .001$).

Conclusions
Our results demonstrate a strong association of most of the metabolic syndrome components with the somatic arousal dimension, but not with the negative affect and positive affect scales.

4.1 INTRODUCTION

Mood and anxiety disorders are related to an increased risk of cardiovascular morbidity and mortality.[147,1] The metabolic syndrome is a cluster of cardiovascular risk factors (i.e., elevated waist circumference, triglycerides, blood pressure, and fasting glucose, and reduced high-density lipoprotein [HDL]) cholesterol)[17] and is thought to partly mediate this relationship.[148] The association between depression and anxiety and the metabolic syndrome has been extensively investigated. Most studies[149] focused on the association between depression and the cluster of the metabolic syndrome and its individual components. Other studies,[23,103] however less numerous, investigated the association between anxiety and both the metabolic syndrome cluster and its individual components. In addition, in a recent publication,[150] we examined whether disorder status and symptom severity were associated with the metabolic syndrome. No significant difference was found between subjects with and without psychopathology (both depression and/or anxiety). Only the subgroups of the most severely depressed or anxious subjects had increased occurrence rates of the metabolic syndrome, an association predominantly driven by abdominal obesity and dyslipidemia. Despite these observations, the question remains whether a complete mood disorder diagnosis or rather only specific symptom dimensions are related to the metabolic syndrome and whether the dichotomous metabolic syndrome diagnosis or only some of its components are related to psychopathology dimensions.

There are three major reasons that could explain why this question has so far remained unanswered. First, the studies have been conducted in widely differing samples, which limits the possibilities to formulate a broadly generalizable model. For instance, there have been differences in the settings (e.g., clinical population or the general population),[151] age of the subjects (an elderly population or young adult patients),[48,152] and the assessment of psychopathology (questionnaires versus clinical diagnoses).[49,153] Second, the categorical diagnostic approach (using the Diagnostic and Statistical Manual of mental disorders, fourth edition [DSM-IV]) for depressive and anxiety disorders, lumping together disparate symptom clusters, may have limited the power to detect subtle associations.[154] Patients with the same diagnosis can be very different in terms of their symptom profiles, whereas other individuals with important mental health problems fail to meet the diagnostic criteria due to symptom heterogeneity. Third, like the DSM-IV diagnosis, the metabolic syndrome concept is also heterogeneous, and is the subject of substantial debate.[116,155] Because at least three of five components are needed to fulfil the criteria of the metabolic syndrome, there are numerous combinations of components possible that all lead to the same metabolic syndrome diagnosis. Studies[156] have shown that sometimes only specific components of the metabolic syndrome are associated with depression, which casts doubt over the usability of the total metabolic syndrome concept in psychopathology research. It is possible that, in the large variety of

depression/anxiety symptoms, some are "specifically" associated with a distinct metabolic syndrome component (e.g., energy loss, often leading to decreased physical activity, might lead to elevated waist circumference [WC]). Based on the criticized definition of the metabolic syndrome and the possible specific associations between diagnostic and metabolic syndrome symptoms, it would thus be informative to investigate the association between specific depression/anxiety symptoms, on the one hand, and the metabolic syndrome, both defined as a cluster of symptoms and as individual components, on the other hand.

So far, research on the association between depression and anxiety and the metabolic syndrome has mainly focused on categorical and heterogeneous assessments of affective disorders symptomatology or anxiety and depression severity scales.[157,158] In addition, diagnoses show overlapping criteria and co morbidity rates are high.[159,160] To overcome these problems, diagnoses should be more homogeneous and not dichotomous. A feasible alternative for categorical diagnoses is the use of a dimensional approach. Within a dimensional approach, a patient is described in terms of coexisting different symptom domains or dimensions, and not in terms of presence or absence of psychopathology. Each dimension provides specific information on the level of a specific symptom domain, running from absent or healthy to severe. Importantly, dimensions are continuous by principle. Along a continuous scale, changes from one level to another are subtle, whereas in a dichotomous scale, changes are rough and restricted (e.g., depressed versus non-depressed). This makes continuous variables more sensible for detection of (small) differentiating factors, thus increasing statistical power.[162]

A well-known dimensional model is the tripartite model for depression and anxiety, which distinguishes three symptom dimensions.[14] The broad "negative affect" dimension describes general symptoms of psychological distress (e.g., lack of concentration or pessimism) that are seen both in depression and anxiety and could account for their high co-morbidity. The (lack of) "positive affect" dimension (also called anhedonic depression), covers anhedonic symptoms, which are mainly specific to depression. The "somatic arousal" dimension covers symptoms of hyperarousal (e.g., palpitations, shortness of breath, and dizziness), which are specific for anxiety, especially panic disorder. The dimensional model was not developed for detection of DSM-IV diagnoses, but rather to provide a descriptive alternative for the presence or absence of psychopathological symptoms in a subject. The tripartite model was developed to circumvent the lack of diagnostic specificity due to the high levels of co morbidity observed in depression and anxiety, one of the major problems of the DSM-IV "golden standard." Typifying patients in terms of their negative affect, positive affect, and somatic arousal scores has two advantages: first, co morbidity is circumvented; and second, based on the profile of the scores, patients can be described in more specific terms of symptomatology. Several studies[163,164] have shown these specific

dimensions to be specifically increased in depression (positive affect) and anxiety (mainly panic disorder, somatic arousal) and that negative affect was more indicative for overall severity across patients.

The aim of the present study was to investigate the relationship between the symptom dimensions of depression and anxiety of the tripartite model, and the metabolic syndrome and its individual components within the Netherlands Study of Depression and Anxiety (NESDA), as a dimensional approach makes it possible to look more specifically into these associations.

4.2 METHODS

Subjects

Subjects selected for these analyses were baseline participants of NESDA, a cohort study among 2981 individuals aged 18 years through 65 years. Respondents were recruited in the community, in primary care, and in specialized mental healthcare settings from September 2004 through February 2007, throughout The Netherlands. All subjects completed a medical examination, a face-to-face interview, and self-report questionnaires. A detailed description of NESDA is reported elsewhere.[95] The study protocol was approved by the Ethical Review Board of each participating centre and all subjects signed an informed consent.

In the same study sample, tricyclic antidepressant (TCA) users were found to have a significantly increased prevalence of the metabolic syndrome.[150] This association was not found for users of other types of antidepressants, such as selective serotonin re-uptake inhibitors.[150] Therefore, the relatively small group of TCA users (n=80) was excluded from our analyses, so that the results would not be affected by the potential confounding influence of TCAs. Subjects with missing metabolic syndrome or Mood and Anxiety Symptom Questionnaire (MASQ) values (n=468) were excluded as well, resulting in a sample of 2433 (81.6%) subjects. An important number of the included subjects comprised healthy controls or remitted patients (n=1449), whereas other subjects had a current diagnosis of pure depression (n=222), pure anxiety (n=226), or co morbid disorder (n=536). No inpatients were included. The included subjects did not differ from the excluded group in sex distribution, presence of cardiovascular disease (CVD), and physical activity. Included subjects were older (42.3 years versus 40.0 years, p <.001), were more educated (12.3 versus 11.3 years, p <.001), were less often smokers (35.8% current smokers versus 50.9%, p <.001), and consumed more alcohol (16.4% consumed >2 glasses/day versus 15.3%, p <.001) compared with the excluded subjects.

MASQ dimensions

The three dimensions of the tripartite model were measured with the 30-item adaptation (MASQ-D30) of the MASQ.[164, 165] The MASQ-D30 was previously validated and showed reliability and validity within the NESDA study.[15, 163, 166] The MASQ-D30 consists of three ten-item scales, representing negative affect, positive affect and somatic arousal (see Table 1). On each item, participants were asked to rate how much in the past week they have experienced "feelings, sensations, problems and experiences that people sometimes have" on a 5 point scale, 1 being "not at all" and 5 being "extremely." Higher scores indicate more severe symptom levels for that specific dimension.

Table 1. Individual symptoms incorporated in the three dimensions of the MASQ-D30

Negative Affect	Positive Affect	Somatic Arousal
Felt confused	Felt successful	Startled easily
Felt worthless	Felt really happy	Felt nauseous
Felt irritable	Felt optimistic	Felt dizzy or light-headed
Felt hopeless	Felt like I was having a lot of fun	Was trembling or shaking
Blamed myself for a lot of things	Felt like I accomplished a lot	Had pain in my chest
Felt dissatisfied with everything	Felt like I had a lot to look forward to	Had hot or cold spells
Felt pessimistic about the future	Felt really talkative	Was short of breath
Felt inferior to others	Felt really 'up' or lively	Muscles were tense or sore
Had trouble making decisions	Felt like I had a lot of energy	Heart was racing or pounding
Worried a lot about things	Felt really good about myself	Had trouble swallowing

The metabolic syndrome

The metabolic syndrome and its components, when expressed as dichotomous variables (i.e., elevated WC, triglycerides, blood pressure, and fasting glucose, and reduced HDL cholesterol), were exactly defined according to the revised criteria of the National Cholesterol Education Program-Adult Treatment Panel III.[17] WC was measured with a measuring tape at the central point between the lowest rib and the highest point of the iliac crest, on light clothing. Triglycerides, HDL cholesterol, and glucose levels were determined by standardized routine laboratory assays, and diastolic and systolic blood pressures were measured during supine rest (OMRON M4 IntelliSense Digital Blood Pressure Monitor, HEM-752A, Omron Healthcare, Inc., Bannockburn, Illinois). Use of triglyceride or HDL cholesterol-influencing medication and use of antihypertensive or glucose reducing drug were registered. In addition, we used continuous variables for the metabolic syndrome components (which is preferable when aiming for more statistical power).[162] In these analyses, we "adjusted" the values for those subjects, using a metabolic syndrome component influencing

medication. This was done following the methods described in several previous publications.[167,168] For the use of fibrates, 0.10 mmol/L (3.8 mg/dL) was subtracted from HDL cholesterol, and 0.67 mmol/L (60 mg/dL) was added to the triglycerides. For the use of nicotinic acid, 0.15 mmol/L (5.8 mg/dL) was subtracted from HDL cholesterol, and 0.19 mmol/L (17 mg/dL) was added to the triglycerides. For the use of antidiabetic medication and a glucose level of < 7 mmol/L (126 mg/dL), a value of 7 mmol/L (126 mg/dL) was given to glucose, as was done previously.[25] Mean blood pressure (MBP) was expressed as the arithmetic mean of systolic and diastolic blood pressures, which were both measured twice during supine rest on the right arm (OMRON M4 IntelliSense Digital Blood Pressure Monitor, HEM-752A, Omron Healthcare, Inc.) and averaged over the two measurements. For persons using antihypertensive medication, 10 mm Hg was added to systolic blood pressure, and 5 mm Hg was added to diastolic blood pressure, in line with earlier studies.[25] These values represent the average decline in blood pressure in antihypertensive medication trials.[169,170]

Severity scales

Information on depression and anxiety severity was collected during the baseline measurement of the NESDA study,[95] using the Beck Anxiety Inventory (BAI)[171] and the Inventory of Depressive Symptoms self-report (IDS-SR),[110] in which the most severe groups were defined as "severe anxiety symptoms" with a score of ≥ 29 on the BAI and "very severe depressive symptoms" with a score of ≥ 49 on the IDS-SR. Previous NESDA research[150] indicated that the prevalence rates of the metabolic syndrome were increased in those with severe anxiety symptoms (n=185) in crude models and independently increased in those with very severe depressive symptoms (n=102) after fully adjusted models. Because information on the BAI and IDS-SR scores was available for our sample, we decided to investigate whether the previous found associations in the same cohort between the highest scores of the BAI and IDS-SR severity scales and metabolic derangements would be driven by symptom dimensions.

Covariates

Covariates were grouped into two types of variables: sociodemographic and lifestyle variables. Sociodemographic variables included age, sex, and years of education. Lifestyle characteristics included smoking status (never/former/current), alcohol use (<1/1–2/>2 drinks per day), both assessed by standardized questionnaires, and physical activity, which was assessed by the International Physical Activity Questionnaire[112] and expressed in 1000 metabolic equivalent of task (MET)-minutes in the past week. MET reflects the ratio of the associated metabolic rate for specific activities divided by the resting metabolic rate multiplied by the minutes performed activity. CVD was considered to be present when participants self-reported a diagnosis of coronary heart disease, cardiac arrhythmia,

angina, heart failure, or myocardial infarction, confirmed with the use of cardiovascular medication. Medication use of any kind within the past month was registered by observation of drug containers brought in and coded according to the Anatomical Therapeutic Chemical Classification System.[111]

Statistical analyses

Sample characteristics were summarized, using means and standard deviations (SD) for quantitative variables and by percentages for categorical variables. Multivariate linear regression analyses were conducted to assess the association between each MASQ-D30 dimensions (i.e., positive affect, negative affect and somatic arousal) and the individual continuous metabolic syndrome components and the total number of metabolic syndrome components. Analyses for each dimension were performed separately. To normalize residuals, non-normally distributed dependent variables were naturally log-transformed. After running crude models, we adjusted for basic covariates (i.e., age, sex, and years of education) in model 1, and for additional lifestyle-related covariates (i.e., smoking status, alcohol use, and physical activity) in model 2. Because sex differences in the association between anxiety, depression, and the metabolic syndrome have previously been observed,[21, 156] appropriate interaction terms with sex were explored. To evaluate the influence of prevalent CVD, participants diagnosed with CVD were excluded in a sensitivity analysis.

To evaluate whether the earlier described association between severity of depressive and anxious symptoms and metabolic syndrome abnormalities were driven by symptom dimensions, additional regression analyses were performed. We analyzed the association of BAI and IDS-SR severity categories with the individual metabolic syndrome components and the total number of components by performing linear regression analyses, adjusting for models 1 and 2 covariates, and additionally adjusting for those symptom dimensions that demonstrated to be associated significantly with the metabolic syndrome components in the main analyses.

Multivariate logistic regression analyses were performed to assess the association between the SDs of continuous scores of the three symptom dimensions and the metabolic syndrome diagnosis. All assumptions for linearity were tested and fulfilled. All tests were two-tailed with p <.05 denoting statistically significance. Statistical analyses were done with SPSS 16.0 (IBM Company, Chicago, Illinois, USA).

4.3 RESULTS

Sample characteristics are shown in Table 2. The mean age was 42.3 years (SD 13.1), 33.1% were men, and mean number of years of education was 12.3 years (SD 3.3). The criteria for the metabolic syndrome were fulfilled by 20.1% (n=490). The reported means and SDs for each dimension are calculated from the continuous values of all subjects included (n=2433) for that dimension.

Table 2. Sample characteristics in 2433 subjects

General characteristics		
Age	42.3	(13.1)
Sex (% men)	33.1	
Years of education	12.3	(3.3)
Cardiovascular disease	5.8	
Smoking status (%)		
Never	29.3	
Former	34.9	
Current	35.8	
Alcohol use (%)		
< 1 glasses/day	61.0	
1-2 glasses/day	22.4	
> 2 glasses/day	16.4	
Physical activity (1000 MET minutes)	3.7	(3.06)
Metabolic syndrome components		
Waist circumference (cm)	88.7	(13.8)
HDL cholesterol (mmol/L)	1.6	(0.4)
Triglycerides (mmol/L)	1.3	(0.8)
Glucose (mmol/L)	5.2	(0.9)
Systolic blood pressure (mmHg)	136.2	(19.7)
Diastolic blood pressure (mmHg)	81.5	(11.1)
Mean blood pressure (mmHg)	108.9	(14.7)
Number of metabolic syndrome components	1.45	(1.3)
Metabolic syndrome (%)	20.1	
MASQ symptom dimensions		
Positive affect	33.4	(9.7)
Negative affect	20.0	(8.6)
Somatic arousal	15.7	(6.1)

Means and standard deviations are given for age, years of education, physical activity, number of metabolic syndrome components and the three symptom dimensions. Percentages are given for sex, smoking status, alcohol use, and presence of metabolic syndrome. Abbreviations: HDL, high-density lipoprotein; MASQ, Mood and Anxiety Symptom Questionnaire; MET, metabolic equivalent of task.

Outcomes of the linear regression analyses between MASQ-D30 dimensions and metabolic syndrome components are shown in Table 3. Positive affect showed a significant association with every metabolic syndrome component in the crude model. Adjustments in model 1 led to a decrease of the β with >10% and to non-significant associations with WC, fasting glucose levels, and MBP. Analyses with the separate covariates of model 1 showed age to be the most important confounder. Associations of positive affect with triglycerides and HDL cholesterol became statistically non-significant after adjustment for lifestyle factors (model 2). No significant associations were found for negative affect with any of the metabolic syndrome components, in the unadjusted and fully adjusted models. On the contrary, in the crude unadjusted model, somatic arousal showed a significant association with all metabolic syndrome components except for fasting glucose. The associations for somatic arousal remained significant in both adjusted models with regard to WC (WC_{crude}: β = 0.061, p = .003; $WC_{model\ 2}$: β = 0.046, p = .01), triglycerides ($Trig_{crude}$: β = 0.077, p <.001; $Trig_{model\ 2}$: β = 0.046, p = .02) and MBP (MBP_{crude}: β = 0.069, p <.001; $MBP_{model\ 2}$: β = 0.068, p <.001). The significant crude association of somatic arousal with HDL cholesterol weakened after adjustment in model 1, and further in model 2 to a non-significant level. Also, the association of somatic arousal with the number of metabolic syndrome components (Nr.) remained highly statistically significant throughout all models ($Nr._{crude}$: β = 0.098, p <.001; $Nr._{model\ 2}$: β = 0.062, p <.001).

The graded, positive association between somatic arousal and the number of metabolic syndrome components, and between somatic arousal and quartiles of the individual fully adjusted metabolic syndrome components are shown in Figure 1. In sensitivity analyses in which 141 subjects with CVD were excluded, results did not change (data not shown). None of the interaction terms between dimensions with sex were statistically significant, which suggests that associations were largely similar for men and women.

To evaluate whether another measure for somatic symptoms would give comparable results, we repeated the linear regression model analyses with the validated BAI somatic subscale.[171] These analyses confirmed an association for the somatic BAI subscale and a much less consistent association for the nonsomatic BAI subscale. The associations with the BAI somatic scale score remained significant in the fully adjusted models for the number of metabolic syndrome components (Nr. metabolic syndrome: β = 0.072, p <.001), and all metabolic syndrome components, except for HDL cholesterol, which showed a trend toward significance with a β = -0.033, p = .08 (WC: β = 0.056, p <.001; Trig: β = 0.083, p <.001; Gluc: β = 0.038, p = .04; MBP: β = 0.046, p = .01). There was a strong intercorrelation between the somatic symptom dimension of the MASQ and the subscale of the BAI (r_{sBAI} = 0.73, p <.001). We did not analyze associations with subscales of the IDS-SR because earlier work by Wardenaar et al.[172] did identify three subscales but none of these was a

Table 3. Linear regression for associations between MASQ dimensions and metabolic syndrome components in 2433 subjects

	Waist circumference		Triglycerides		HDL cholesterol		Glucose		Blood pressure		Number of metabolic syndrome components	
	β	*p*	β	*p*	β	*p*	β	*p*	β	*p*	β	*p*
Negative affect												
Crude	.070	.001	.097	<.001	-.063	.002	.079	<.001	.076	<.001	.107	<.001
Model 1	-.001	.94	.044	.02	-.039	.04	.027	.15	.008	.64	.036	.05
Model 2	-.009	.60	.021	.29	-.012	.52	.026	.17	.009	.63	.019	.29
Positive affect												
Crude	-.002	.93	.031	.12	-.036	.08	.008	.68	-.028	.17	.018	.37
Model 1	.016	.34	.042	.03	-.017	.36	.036	.05	-.001	.94	.033	.07
Model 2	.011	.51	.022	.25	.001	.08	.037	.05	-.002	.90	.020	.27
Somatic arousal												
Crude	.061	.003	.077	<.001	-.056	.01	.025	.22	.069	<.001	.098	<.001
Model 1	.050	.01	.064	.001	-.045	.02	.023	.21	.062	<.001	.074	<.001
Model 2	.046	.01	.046	.02	-.018	.32	.023	.22	.068	<.001	.062	.001

β, standardized beta by linear regression analyses.

Abbreviations: HDL, high-density lipoprotein; MASQ, Mood and Anxiety Symptom Questionnaire.

Model 1: adjusted for age, sex and years of education.

Model 2: additionally adjusted for smoking status, alcohol use and physical activity.

clear somatic subscale (in factor analyses, the rather restricted somatic items were attributed to all three subscales). So, no valid somatic IDS-SR subscale exists. Therefore, it is not appropriate to use a subscale in a comparative analysis. To explore whether results would also be consistent for the nonsomatic symptom subscale, we also conducted linear regression analyses with the nonsomatic BAI subscale (BAI subjective scale score). We expected that associations for the subjective BAI subscale would be similar to those for the positive affect and negative affect dimensions of the MASQ-30, which was confirmed. None of the associations with the BAI subjective scale score were statistically significant in the fully adjusted models, with exception of the number of metabolic syndrome components ($\beta = 0.041$, $p = .02$).

Regression analyses performed to investigate whether previously found positive associations between metabolic syndrome abnormalities and symptom severity were driven by symptom dimensions, in particular the somatic arousal dimension, showed the following: Initial significant outcomes (in which the number of metabolic syndrome components was the dependent variable and BAI and IDS-SR severity categories were the independent variables) lost statistical significance after adjustment with the somatic arousal dimension. This means that the earlier described associations between the high severe groups according to the BAI and IDS-SR with the metabolic syndrome were largely attributable to a high somatic arousal score.

Logistic regression analyses of the symptom dimensions with the metabolic syndrome showed a small but significant crude relationship between positive affect and the metabolic syndrome. Negative affect was not significantly associated with the metabolic syndrome. The initial significant crude relationship between somatic arousal and the metabolic syndrome remained statistically significant throughout multivariable adjustment (odds ratio per SD increase, 1.15; 95% confidence interval, 1.04 –1.28; $p = .008$, see Table 4). Analyses in which the associations of BAI or IDS severity categories with the metabolic syndrome were adjusted for somatic arousal, showed that the severity category indicator lost statistical significance after adjustment.

Table 4. Logistic regression for the association between standard deviations (SDs) of continuous scores on MASQ dimensions and the odds of metabolic syndrome in 2433 subjects

	OR	95% CI	*p*
Positive Affect			
Crude	1.16	1.05-1.28	.004
Model 1	1.02	0.92-1.14	.67
Model 2	0.99	0.88-1.10	.99
Negative Affect			
Crude	1.01	0.92-1.12	.78
Model 1	1.01	0.99-1.02	.28
Model 2	1.04	0.93-1.16	.51
Somatic Arousal			
Crude	1.19	1.08-1.31	<.001
Model 1	1.18	1.06-1.30	.002
Model 2	1.15	1.04-1.28	.008

Abbreviations: OR, odds ratio per SD increase by logistic regression analysis; CI, confidence interval; MASQ, Mood and Anxiety Symptom Questionnaire.
Model 1: adjusted for age, sex, years of education.
Model 2: additionally adjusted for lifestyle factors: smoking status, alcohol use and physical activity.

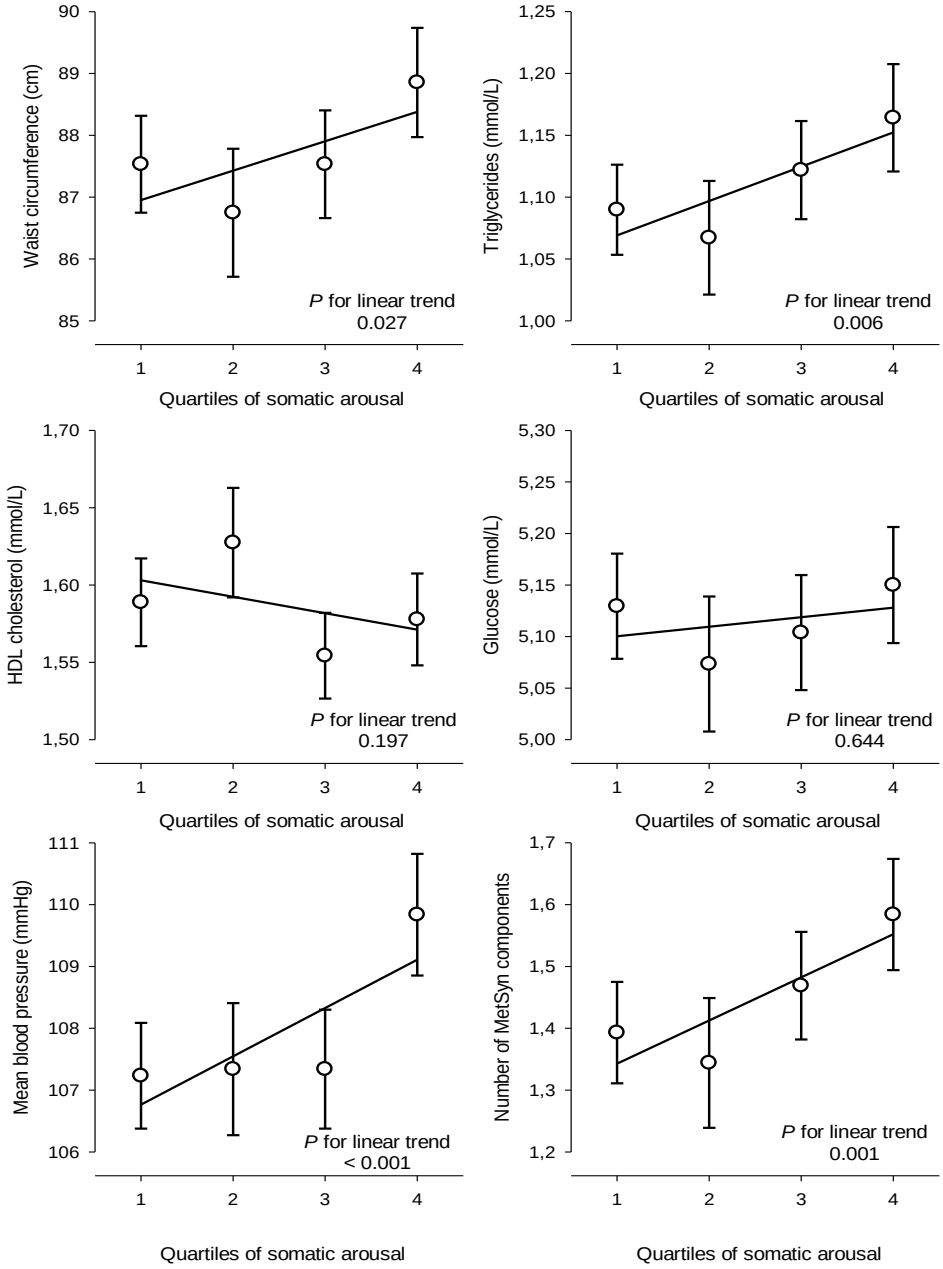

Figure 1. Adjusted (geometric) means across quartiles of somatic arousal on the MASQ-D30, for the individual metabolic syndrome components and the total number of metabolic syndrome components. Data are adjusted for age, sex, educational level, alcohol use, smoking status and physical activity. Error bars indicate 95% confidence intervals of the mean, and regression lines are shown. $n_{quartile\ 1}$=744; $n_{quartile\ 2}$=436; $n_{quartile\ 3}$=652; $n_{quartile\ 4}$=601.

4.4 DISCUSSION

The main finding of this study is that only the somatic arousal symptom dimension is strongly and independently associated with most of the metabolic syndrome components (especially waist circumference [WC], triglycerides, and mean blood pressure [MBP]) and shows a graded association with the number of metabolic syndrome components. Using a dimensional approach, somatic arousal was thus associated with an increased metabolic risk. No independent associations of the metabolic syndrome with negative affect and positive affect were observed. These results are supported by our finding that the somatic scale of the BAI is associated with the metabolic syndrome components, whereas the non-somatic scales are not.

Approaching depression and anxiety dimensionally, the aspecific negative affect dimension and the depression specific positive affect dimension did not show any association with the metabolic syndrome. We only found a strong and consistent relationship between the somatic arousal dimension and multiple metabolic syndrome components. This is in line with previous research on symptom dimensions of especially depression in relation to somatic outcomes, in which the somatic/affective sub-dimension, rather than other important dimensions (e.g., cognitive/affective and appetitive), was most strongly associated with cardiovascular risk and outcome.[173,174] It seems we are looking at a specific sub-dimension: the "somatic depression/anxiety" sub-dimension. On the one hand, this subtype could be reflective of underlying dysregulated homeostasis mechanisms due to anxious or depressed mood states, such as inflammation,[72] impaired hypothalamus-pituitary-adrenal axis function,[68,175] or a higher sympathetic and lower parasympathetic autonomic tone.[176] Elevated levels of inflammatory markers could induce a depressive episode;[177] altered lipid patterns caused by high levels of cortisol[141,148] could lead to other lipid-related symptoms (overweight, abdominal obesity, and hypertriglyceridemia);[161,178] and activation of the sympathetic nervous system leads to increased blood pressure[179] and thus to hypertension.[148,180] This network of pathways can thus result in an increased metabolic or cardiovascular risk and cardiovascular disease. On the other hand, the reverse mechanism could be active: Ongoing metabolic dysregulations could be causing (especially somatic arousal) symptoms of depression and anxiety.[22,181-184] Regardless of the underlying mechanisms and the direction of causality, the dose-response gradient between the number of metabolic syndrome components and levels of somatic arousal indicates that when more somatic arousal symptoms are present, more metabolic syndrome abnormalities are present. Apart from biological mechanisms, other processes may be involved during a depressive episode as a consequence of anhedonia, such as altered lifestyle patterns (poor diet and decreased physical activity),[185,186] which might induce metabolic changes and cardiovascular risk factors.

Previous research based on NESDA data[150] showed that the prevalence rates of the metabolic syndrome were increased in those with the highest levels of anxiety or depressive symptoms based on the BAI and the IDS-SR. After adjustment for the MASQ somatic arousal dimension, the earlier described associations lost statistical significance. These results indicate that the earlier described association between the metabolic syndrome and the most severe depression and anxiety symptom scales can be explained by the fact that these persons had high scores on the somatic arousal dimension.

In terms of metabolic risk evaluation and detection, a dimensional approach has more differentiating capacities compared with the widely used diagnostic DSM-IV categories. The somatic symptom dimension could therefore be the key feature in the association between depression/anxiety and somatic outcomes.

Using a dimensional approach, the level of a symptom dimension varies differentially between diagnostic groups (e.g., singular depression, singular anxiety, or co-morbid state). At the same time, all symptom dimensions can be present at a significant level within every diagnostic group. This means that the clinical presentation of a subject is dependent on the symptom dimension(s) with the highest scores. Our results demonstrate that the somatic arousal dimension is associated with several metabolic syndrome components. The fact that somatic arousal levels are not equally high for every depressed and/or anxious subject might explain the inconsistent findings in literature on the association with the metabolic syndrome.

Our study has several strengths. This is, to our knowledge, the first study describing the relationship of depression and anxiety dimensions in relation to the metabolic syndrome. We not only approached the metabolic syndrome and its components as continua, in line with the idea that metabolic syndrome components have a natural continuous distribution,[187] but also distinguished depression and anxiety symptom dimensions.[187] Because we chose this approach, we were able to show a dose-response gradient with somatic arousal levels. Furthermore, the results are based on a large sample, making results reliable. Finally, in the analyses, we adjusted for a substantial number of covariates, minimizing the chance that the findings can be explained by confounding.

This study presents some limitations. First, the tripartite model is a rather simple dimensional model. Probably, there are more relevant subdimensions present.[188] Second, the sample includes both healthy controls and subjects with (remitted) psychopathology, who were recruited from the community as well as mental healthcare settings. As inpatients were excluded, our results cannot be generalized to this group. Third, the concept of the metabolic syndrome has been criticized,[116,155] and our findings support the idea that it may be worthwhile to study (the number of) individual metabolic components in addition to a dichotomous metabolic syndrome variable. Finally, due to the cross-sectional design,

our results cannot be used to make any causal inferences. Prospective studies, especially across more heterogeneous populations, would help to understand the direction of the potential causal relationship.

In this sample, in which previously the association between a categorical diagnosis on the one hand and the metabolic syndrome components on the other hand, was found only for the most severe depressive symptoms,[150] we demonstrate a strong association between the somatic arousal symptom dimension and the metabolic syndrome and its individual components, especially WC, triglycerides, and blood pressure, and the number of metabolic syndrome components. Not every depressed subject is at increased metabolic risk. But our findings suggest that those with an elevated somatic arousal level are. Those with elevated non-somatic dimensions scores (i.e., positive affect and negative affect) did not show an increased metabolic risk. This indicates the additional value of a dimensional approach in terms of metabolic risk evaluation. In addition, we found that the association between depression severity (BAI severity categories) and the metabolic syndrome is, in part, driven by the somatic arousal dimension. Although our results need to be replicated, the discriminating ability of a dimensional approach could facilitate the identification of those with a higher metabolic risk within a clinical population with apparently the same diagnoses.