Depressive Symptoms and Stressful Life Events Predict Metabolic Syndrome Among Middle-Aged Women

A comparison of World Health Organization, Adult Treatment Panel III, and International Diabetes Foundation definitions

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OBJECTIVE — We evaluated whether psychosocial factors that are related to cardiovascular disease and type 2 diabetes predict prospectively the risk for the metabolic syndrome using the different clinical criteria available for defining the syndrome.

RESEARCH DESIGN AND METHODS — Women were enrolled in a population-based prospective cohort study called the Healthy Women Study and were followed for an average of 15 years after baseline. Metabolic syndrome was defined via the World Health Organization, the National Cholesterol Education Program Adult Treatment Panel III, and the International Diabetes Foundation clinical criteria.

RESULTS — Among women who did not have the metabolic syndrome at the baseline, the risk for the metabolic syndrome defined in multiple ways varied from 1.21- to 2.12-fold ([95% CI 1.00–4.25], $P < 0.05$) for more severe depressive symptoms or very stressful life event(s). These associations were largely the same, regardless of the clinical criteria used to define the metabolic syndrome. Those who at the baseline reported feeling frequently and intensely angry, tense, or stressed also had an increased risk for developing the metabolic syndrome at least by one definition (relative risk 1.19–1.66 [1.00–2.39]).

CONCLUSIONS — These are the first data to demonstrate that psychosocial factors predict the risk for developing the metabolic syndrome by multiple definitions. Psychosocial factors may play a causal role in the chain of events leading to the metabolic syndrome.

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Metabolic syndrome refers to a cluster of aberrations of metabolic origin that increase risk for morbidity and mortality from cardiovascular disease (CVD) (1), type 2 diabetes (2), and all-cause mortality (1). There is no one internationally agreed-upon definition of the metabolic syndrome, but its features are generally accepted to include a combination of impaired glucose and lipid metabolism, obesity, and hypertension. Several expert panels assembled by organizations, such as the World Health Organization (WHO) (3), the National Cholesterol Education Program Adult Treatment Panel III (ATP III) (4–6), and the International Diabetes Foundation (IDF) (7), have determined clinical criteria for defining the metabolic syndrome in adults.

No single factor has been elucidated as an underlying causative factor for the metabolic syndrome (6). A large body of literature suggests that psychosocial attributes and stressful events predict incidence of CVD and type 2 diabetes (8,9). Despite the plausible roles of psychosocial factors (10), research devoted to testing whether they also predict the metabolic syndrome is scanty. In older adult men and women not receiving hormone replacement therapy (HRT), psychosocial distress predicted over 15–18 months a factor composed of the components of the metabolic syndrome (11). In middle-aged men and women, greater work stressors predicted over 14 years the metabolic syndrome based on the ATP III definition (12). Both studies lacked a baseline measurement of the metabolic syndrome, which precluded inferences about prospective relationships.

We have previously demonstrated that among middle-aged participants of the Healthy Women Study (HWS), depressive symptoms and intense and frequent feelings of anger predicted increasing risk for the ATP III–defined (4) metabolic syndrome over an average of 7.4 years (13) and that reports of marital dissatisfaction, divorce, and widowhood predicted increasing risk of the ATP III–defined metabolic syndrome over an average of 11.5 years (14). To our knowledge, no other prospective study has examined the risk for developing the metabolic syndrome among individuals without the metabolic syndrome initially in relation to psychosocial factors. In this report, we extended our earlier work in three ways. First, we evaluated the associations across a much longer follow-up period, an average of 15 years. Second, we examined multiple psychosocial factors, i.e., depressive symptoms, stressful events, and intense and frequent feelings of anger, tension, and anxiety. Third, we examined the associations with the meta-

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Abbreviations: ATP III, National Cholesterol Education Program Adult Treatment Panel III; CVD, cardiovascular disease; IDF, International Diabetes Foundation; HRT, hormone replacement therapy; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Clinical criteria for the metabolic syndrome*

Components	WHO: fasting glucose above cutoff or taking medication for diabetes in combination with any two of the listed components	ATP III: any three of the listed components	IDF: waist circumference above cutoff in combination with any two of the listed components
Fasting glucose	*1*) >110 mg/dl*	*1*) ≥100 mg/dl*	*1*) ≥100 mg/dl*
Triglycerides	*2*) ≥150 mg/dl	*2*) ≥150 mg/dl*	*2*) ≥150 mg/dl*
HDL cholesterol	*3*) <35 mg/dl	*3*) <50 mg/dl*	*3*) <50 mg/dl*
Obesity	*4*) BMI >30 kg/m^2 or waist-to-hip ratio >0.85	*4*) Waist circumference >88 cm	*4*) Waist circumference >80 cm
Blood pressure	*5*) SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg	*5*) SBP ≥135 mmHg and/or DBP ≥85 mmHg*	*5*) SBP ≥ 135 mmHg and/or DBP ≥85 mmHg*

*Fulfillment of the cutoff score if alternatively taking medication for diabetes, dyslipidemia, or hypertension; Microalbuminuria was not available when defining the metabolic syndrome via the WHO clinical criteria. DBP, diastolic blood pressure; SBP, systolic blood pressure.

bolic syndrome defined according to the WHO (3), the ATP III (4–6), and the IDF clinical criteria (7).

RESEARCH DESIGN AND METHODS

— Premenopausal healthy women participated in a detailed clinical examination of demographics, psychosocial characteristics, health behaviors, and risk factors at baseline between 1983 and 1985 (n = 541; 90.6% Caucasian, 8.9% African American, and 0.06% other) and ~3 years later (n = 523). Thereafter, women returned for follow-up clinic examinations after 12 successive months without menstruating and/or using hormone therapy, with additional examinations in ~3-year intervals up to 17 years postmenopause. The institutional review board at the University of Pittsburgh approved this project; all subjects gave informed consent.

With few exceptions, the clinic examinations were similar in content. An exception relevant to the present analysis was that waist circumference measures were added late to the baseline protocol, with only 120 women having waist measures. In consequence, metabolic syndrome could only be measured at the 3-year follow-up and later examinations, and the data from the 3-year follow-up were considered the starting point for predicting the prevalence and incidence of the metabolic syndrome in our analysis. To be in the analysis, women had to have metabolic syndrome components at the 3rd year of follow-up and at least one additional later examination (n = 432). Women on average had each of the metabolic syndrome components measured 5.3 (SD 1.5, range 2–9) different times during a follow-up interval of 15.0 (SD 3.7, range 2.6–20.3) years. At the 3-year follow-up, 254 (58.8%), 63 (14.6%), and 115 (26.6%) women were pre-, peri-, and postmenopausal, respectively. To increase the reliability of measurement of the predictors, we averaged the psychosocial and behavioral characteristics measured at both the baseline and 3-year follow-up examinations.

Measures

Metabolic syndrome. Blood samples were collected in the morning after a 12-h fast. Glucose was analyzed by an enzymatic assay (Yellow Springs Glucose Analyzer, YSI, Yellow Springs, OH), triglycerides and total HDL cholesterol were measured in the lipid laboratory of the Graduate School of Public Health, which has been certified by the Centers for Disease Control and Prevention, Atlanta, Georgia, the waist was measured at the smallest circumference and hips at the largest circumference and the waist-to-hip ratio was calculated, weight and height were obtained by a balance beam scale and BMI was calculated (weight in kilograms divided by the square of height in meters), and blood pressure was measured three times on two occasions 2 hours apart with a random zero muddler sphygmomanometer, the final overall reading being the average of the last two readings of these two assessments. Table 1 presents the clinical criteria of metabolic syndrome defined via the WHO (3), the ATP III (4–6), and the IDF clinical criteria (7).

Psychosocial measures. The subjects completed a set of reliable and validated psychosocial tests including the Beck Depression Inventory (15), the Framingham Tension Scale (16), the Spielberger Trait Anxiety Questionnaire (17), the Spielberger Anger Questionnaire (18), and the Perceived Stress Scale (19). These tests were used to evaluate whether life events that had occurred to the subjects during the past 6 months were not at all/moderately (0) to very stressful (1).

Statistical analyses

Logistic regression analyses, odds ratios (ORs), and 95% CI were computed to test whether the psychosocial measures are associated with the cumulative prevalence of the metabolic syndrome during the follow-up. Cox proportional hazards models (assumptions tested and met), relative risks (RRs), and 95% CI were used to test whether in women who did not meet the metabolic syndrome clinical criteria at the starting analytic examination, psychosocial measures (averaged across baseline and starting analytic examination) predicted the risk for developing the metabolic syndrome during the follow-up. In addition to health behaviors (smoking: no versus yes, alcohol consumption in grams per week, and physical activity in kilocalories per week), the analyses took into account the potential confounding of HRT (no versus yes), educational attainment (high school, some college, college graduate, or degree beyond college), and age (all covariates averaged across baseline and starting analytic examination). Scaling corrections were computed for non-normally distributed variables where appropriate, and to allow comparability between the different measurement scales, the psychosocial predictor variables were standardized.

RESULTS

— The WHO, the ATP III, and the IDF clinical criteria for the metabolic syndrome were met, respectively, by 1.2% (n = 5), 9.3% (n = 40), and 9.7% (n = 42) of the sample at the starting an-

Table 2—*Risk factor levels (aggregated across follow-up) of the individual components of the metabolic syndrome, health behaviors, and other sample characteristics according to cumulative prevalence over average 15 years of the metabolic syndrome, defined via the WHO, the ATP III, and the IDF clinical criteria*

	WHO			ATP III			IDF		
	No	Yes	*t*	No	Yes	*t*	No	Yes	*t*
n	391	41		295	137		268	164	
Risk factor levels									
Fasting glucose (mg/dl)	86.4 ± 8.1	115.2 ± 27.2	6.8	84.6 ± 5.8	98.2 ± 20.9	7.3	84.5 ± 5.6	96.6 ± 19.6	7.8
Waist circumference (cm)	79.1 ± 10.0	96.9 ± 13.8	8.1	75.8 ± 7.6	91.6 ± 11.5	14.6	75.5 ± 7.8	89.6 ± 11.6	13.9
Waist-to-hip ratio	0.78 ± 0.05	0.83 ± 0.06	6.9	0.76 ± 0.05	0.82 ± 0.05	13.4	0.75 ± 0.05	0.82 ± 0.05	13.2
BMI (kg/m^2)	25.8 ± 4.2	32.9 ± 6.4	6.9	24.6 ± 3.4	30.4 ± 5.4	11.5	24.5 ± 3.4	29.6 ± 5.4	10.9
Triglycerides (mg/dl)	102.7 ± 49.7	157.08 ± 60.2	6.5	35.3 ± 2.1	62.9 ± 5.4	10.0	86.6 ± 32.1	142.7 ± 61.7	10.8
HDL cholesterol (mg/dl)	61.6 ± 13.9	49.5 ± 11.0	−5.4	65.2 ± 13.1	50.2 ± 10.1	−13.0	65.4 ± 12.9	52.3 ± 12.0	−10.9
SBP (mmHg)	114.6 ± 13.8	122.6 ± 10.03	4.7	112.2 ± 13.3	122.1 ± 12.1	7.4	111.5 ± 13.2	121.5 ± 12.1	10.5
DBP (mmHg)	71.8 ± 7.6	73.6 ± 7.4	1.5	70.8 ± 7.7	74.5 ± 6.8	4.9	70.5 ± 7.4	74.3 ± 7.3	5.2
Health behaviors									
Physical activity (kcal/week)	1,632 ± 1,471	1,154 ± 913	−3.0	1,664 ± 1,435	1,420 ± 1,425	−1.7	1,640 ± 1,365	1,499 ± 1,539	−1.0
Alcohol consumption (g/week)	11.8 ± 10.6	8.2 ± 9.7	−2.0	12.3 ± 10.6	9.6 ± 10.5	−2.5	11.8 ± 10.2	10.8 ± 11.2	−1.0
Smoking status: yes	115 (29.4)	13 (31.7)	0.1 (1)	82 (27.8)	46 (33.6)	1.5 (1)	74 (27.6)	54 (32.9)	1.4 (1)
Other characteristics									
Age (years)	49.1 ± 1.6	48.6 ± 1.6	−1.8	49.0 ± 1.5	49.1 ± 1.7	1.1	48.9 ± 1.5	49.1 ± 1.6	1.3
HRT: yes	45 (11.5)	4 (9.8)	0.1 (1)	32 (10.8)	17 (12.4)	0.2 (1)	25 (9.3)	24 (14.6)	2.9 (1)
Level of education: high school	20 (48.8)	102 (26.1)	11.6 (3)	73 (24.7)	49 (35.8)	9.7 (3)	63 (23.5)	59 (36.0)	10.2 (3)

Data are means ± SD or *n* (%). *t* values represent differences between the groups in independent sample *t* tests: $t > 1.96$, $P < 0.05$; $t > 2.56$, $P < 0.01$; $t > 3.29$, $P < 0.001$; differences between the groups in smoking, hormone replacement therapy and level of education are reported as χ^2statistics (df); none of the differences between the groups in smoking or in hormone replacement therapy are significant, $P > 0.09$, whereas all the differences between the groups in level of education are significant, $P < 0.02$. DBP, diastolic blood pressure; SBP, systolic blood pressure.

alytic examination and by 9.5% ($n = 41$), 31.7% ($n = 137$), and 38% ($n = 164$) over the follow-up (including those at the starting examination). At the starting analytic examination, all the women meeting the WHO criteria met the ATP III and the IDF criteria; of those meeting the ATP III criteria 10% ($n = 4$ of 40) did not meet the IDF criteria, and of those meeting the IDF criteria 14.3% ($n = 6$ of 42) did not meet the ATP III criteria. Over the follow-up, all the women meeting the WHO criteria met the ATP III and the IDF criteria; of those meeting the ATP III criteria 3.6% ($n = 5$ of 137) did not meet the IDF criteria, and of those meeting the IDF criteria 19.5% ($n = 32$ of 164) did not meet the ATP III criteria.

Before proceeding to analyses testing associations between psychosocial characteristics and the metabolic syndrome, we tested differences between the metabolic syndrome risk factor levels, health behaviors, and other sample characteristics for women who did and did not meet the metabolic syndrome clinical criteria over the follow-up. As Table 2 shows, diastolic blood pressure did not differ between groups for the WHO definition but did for the ATP III and the IDF definitions; otherwise, all the metabolic syndrome risk factors differed between groups across definitions. Lower alcohol consumption distinguished groups for the WHO and ATP III groups and lower physical activity for the WHO groups. Educational attainment was lower among the metabolic syndrome groups across all definitions.

Associations between psychosocial characteristics and health behaviors were significant for the following: a low physical activity level was associated with depression ($r = -0.10$, $P = 0.04$); heavier consumption of alcohol was associated with trait anger, trait anxiety, and stress ($r > 0.09$, $P < 0.05$); and smoking status was associated with depression ($r = 0.15$, $P = 0.001$). A lower educational attainment was associated with depression, anger, and anxiety ($r < -0.11$, $P < 0.02$). There were no significant associations with age or HRT ($r < \|0.06\|>$, $P > 0.23$). We also tested whether the psychosocial characteristics were associated with weight at the starting analytic examination or gain in weight over the average 15 years. Although the psychosocial characteristics were associated with greater BMI at the starting analytic examination (depression: $r = 0.14$, $P = 0.002$; trait anger: $r = 0.13$, $P = 0.01$; and severe stressful event(s): $r = 0.16$, $P = 0.001$), these characteristics were not significantly associated with gain in BMI over the follow-up ($r < \|0.07\|$, $P > 0.15$).

Psychosocial predictors of cumulative prevalence of the metabolic syndrome

In the logistic regression models (Table 3), depressive symptoms and severity of

Table 3—*Associations between psychosocial factors with the cumulative prevalence over average 15 years of the metabolic syndrome defined via the WHO, the ATP III, and the IDF clinical criteria*

Psychosocial factors	WHO	ATP III	IDF
Depressive symptoms			
Unadjusted	1.56 (1.11–2.21)	1.44 (1.16–1.78)	1.31 (1.08–1.61)
Full model	1.41 (0.98–2.02)	1.39 (1.11–1.74)	1.28 (1.04–1.59)
Trait anger			
Unadjusted	1.32 (0.96–1.82)	1.43 (1.15–1.76)	1.30 (1.07–1.58)
Full model	1.22 (0.88–1.68)	1.40 (1.13–1.74)	1.27 (1.03–1.55)
Trait anxiety			
Unadjusted	1.23 (0.89–1.70)	1.05 (0.86–1.29)	1.04 (0.86–1.27)
Full model	1.12 (0.80–1.59)	1.03 (0.83–1.28)	1.01 (0.82–1.24)
Framingham tension			
Unadjusted	1.33 (0.97–1.83)	1.30 (1.06–1.59)	1.33 (1.10–1.62)
Full model	1.26 (0.90–1.75)	1.27 (1.03–1.57)	1.30 (1.07–1.60)
Perceived stress			
Unadjusted	1.63 (1.14–2.32)	1.18 (0.96–1.45)	1.12 (0.92–1.36)
Full model	1.59 (1.11–2.30)	1.19 (0.96–1.47)	1.11 (0.90–1.36)
None/mild vs. at least one very severe stressful life event			
Unadjusted	2.55 (1.28–5.09)	1.77 (1.17–2.68)	1.71 (1.15–2.54)
Full model	2.83 (1.38–5.82)	1.84 (1.20–2.81)	1.74 (1.16–2.61)

Data are OR (95% CI), adjusted for age, physical activity, alcohol consumption, current smoking status, use of HRT, and level of education. Psychosocial factors were log-transformed (log + 1 for scales involving 0) where appropriate, and continuous scores were standardized to allow comparability between scales.

stressful life events were associated with the cumulative prevalence of the metabolic syndrome defined by WHO, the ATP III, and the IDF clinical criteria (including those who had metabolic syndrome at the starting examination). In addition, global perceived stress was associated with the WHO clinical criteria, and intense and frequent feelings of anger and tension were associated with the ATP III and the IDF clinical criteria. The association between depressive symptoms and the WHO clinical criteria became somewhat attenuated ($P = 0.06$) after controlling for age, level of education, HRT, and behavioral risk factors; the other associations remained statically significant.

Psychosocial predictors of cumulative incidence of the metabolic syndrome

Cox proportional hazards models (Table 4) demonstrate that each 1 SD increase in depressive symptoms was associated with 1.21- to 1.43-fold increases in risk over the follow-up for developing the metabolic syndrome defined via the WHO, the ATP III, and the IDF clinical criteria (excluding those who had the metabolic syndrome at the starting analytic examination). Women who reported at least one life event during the past 6 months that was rated as very stressful had 2.12 (WHO clinical criteria)- and 1.49 (the ATP III clinical criteria)-fold increases in risk over the follow-up for developing the metabolic syndrome. In addition, global perceived stress predicted the risk over the follow-up for developing the WHO clinical criteria, and intense and frequent feelings of anger and tension predicted the risk over the follow-up for developing the ATP III and the IDF clinical criteria.

After controlling for age, level of education, HRT, and health behaviors, all associations with the ATP III clinical criteria remained significant. Associations between stressful life events and global perceived stress with the WHO clinical criteria also remained significant, whereas depressive symptoms did not ($P = 0.19$). All significant associations with the IDF clinical criteria were nonsignificant in the full model ($P > 0.06$).

CONCLUSIONS — The current study shows that women who reported high levels of depressive symptoms and experienced very stressful life events at the starting point of the study had an increased risk over the average of 15 years of follow-up for developing the metabolic syndrome. Although these associations were largely the same regardless of the clinical criteria used to define the metabolic syndrome, the results showed that psychosocial factors best predicted the WHO, the ATP III, and the IDF criteria,

Table 4—*Associations between psychosocial factors with the risk over 15 years of follow-up of developing the metabolic syndrome via the WHO, the ATP III, and the IDF clinical criteria*

Psychosocial factors	WHO	ATP III	IDF
Depressive symptoms			
Unadjusted	1.43 (1.00–2.03)	1.35 (1.10–1.65)	1.21 (1.01–1.44)
Full model	1.27 (0.89–1.80)	1.29 (1.04–1.60)	1.16 (0.96–1.40)
Trait anger			
Unadjusted	1.20 (0.88–1.64)	1.32 (1.09–1.58)	1.20 (1.02–1.42)
Full model	1.14 (0.84–1.55)	1.30 (1.08–1.57)	1.18 (0.99–1.40)
Trait anxiety			
Unadjusted	1.19 (0.85–1.67)	1.06 (0.87–1.29)	1.05 (0.88–1.26)
Full model	1.08 (0.76–1.54)	1.07 (0.87–1.32)	1.04 (0.87–1.25)
Framingham tension			
Unadjusted	1.25 (0.91–1.71)	1.24 (1.03–1.50)	1.19 (1.00–1.41)
Full model	1.19 (0.86–1.64)	1.22 (1.00–1.48)	1.18 (0.99–1.40)
Perceived stress			
Unadjusted	1.66 (1.15–2.39)	1.19 (0.97–1.46)	1.12 (0.93–1.34)
Full model	1.54 (1.07–2.32)	1.17 (0.95–1.43)	1.09 (0.91–1.30)
None/mild vs. at least one very severe stressful life event			
Unadjusted	2.12 (1.06–4.25)	1.49 (1.00–2.23)	1.40 (0.98–2.01)
Full model	2.19 (1.08–4.45)	1.51 (1.00–2.27)	1.41 (0.98–2.03)

Data are RR (95% CI), adjusted for age, physical activity, alcohol consumption, current smoking status, use of HRT, and level of education. RR indicates relative risk in Cox proportional hazards model. Psychosocial factors were log-transformed (log + 1 for scales involving 0) where appropriate, and continuous scores were standardized to allow comparability between scales.

respectively, in that order. Those who at the baseline reported feeling frequently and intensely angry, tense, or stressed also had an increased risk for developing the metabolic syndrome at least by one definition.

This study is unique in that a population-based cohort of middle-aged women experiencing the menopausal transition was followed for an average 15 years, with the follow-up-time extending up to 20.3 years. Over the follow-up an average woman participated in the study on five separate occasions with some women providing data up to nine separate points in time. The study used standardized psychosocial tests to measure psychosocial factors with relevance to CVD and type 2 diabetes (8,9). Moreover, the study had extensive clinical examinations allowing measurement of the metabolic syndrome according to the different clinical criteria and at multiple time points, including the starting analytic examination. Thus, unlike any other prospective data published thus far (11,12), the HWS dataset (13,14,20) allows comparison of risk when different clinical definitions of the metabolic syndrome were used and testing whether the psychosocial factors predict the risk for developing the metabolic syndrome over time, controlling for the metabolic syndrome status at the baseline. Because the women enrolled were initially healthy and the majority were still premenopausal (58.8% of the sample) at the starting analytic examination, few women met the criteria for metabolic syndrome at the starting analytic examination. The healthy nature of the sample may account for why the cumulative prevalence rates over the follow-up, particularly for the WHO clinical criteria, do not compare to much higher rates found in other samples (21,22). The lower rates may have rather diminished rather than amplified the statistical power and weakened our ability to detect stronger associations with the metabolic syndrome over time. The unique nature of the study sample, while a strength, also limits the generalizability of our findings and the findings cannot be generalized to nonwhite women, men, and individuals of less healthy status initially. However, in line with our findings, high hostility among children and adolescents predicted over 3 years an increasing risk of having at least two of the four components of the metabolic syndrome (BMI, insulin resistance index, triglyceride-to-HDL cholesterol ratio, and mean arterial blood pressure) >75th percentile of age-, sex-, and ethnicity-specific groups (23).

Several mechanisms may explain the pathways underlying the associations between psychosocial characteristics and the metabolic syndrome. First, psychosocial factors related to deleterious health behaviors, such as smoking and nonadherence to medical regimens, are more common among individuals with low socioeconomic backgrounds and may vary according to age (8,9). Although our results show that health behaviors and demographic characteristics may partially explain the associations, particularly when the IDF clinical criteria are being considered, it is unlikely that they fully account for the associations. Second, psychosocial factors are associated with alterations in the autonomic nervous system, such as elevated heart rate and reduced heart rate variability (24), the hypothalamic-pituitary-adrenocortical system, such as elevated cortisol (25), and with hemostatic and inflammatory markers, such as heightened platelet aggregation, fibrinogen, proinflammatory cytokines, and white blood cell count (26–28). All of these physiological changes have been recognized as important in the development of the metabolic syndrome (29). One further possibility involves neurotransmitters: depression and other negative emotions are shown to be related to blunted central serotonin release (30), which, in turn, has been associated with the metabolic syndrome (31). A possibility that both the psychosocial and metabolic syndrome factors share a common factor(s) that can be traced back to the prenatal period also cannot be ruled out (32). Finally, genetic factors might also be involved.

In summary, we found that among middle-aged healthy women, depressive symptoms, very stressful life event(s), frequent and intense feelings of anger and tension, and stress are associated with the cumulative prevalence and risk for developing the metabolic syndrome over 15 years. With regard to the different clinical criteria, the WHO, the ATP III, and the IDF, depressive symptoms and very stressful life event(s) are most consistently associated with the metabolic syndrome across the definitions.

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