Anger, Hostility, and Visceral Adipose Tissue in Healthy Postmenopausal Women

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Central obesity is an important risk factor for chronic disease. Its etiology remains unclear. We examined whether anger and hostility, ie, psychological attributes that influence cardiovascular morbidity and mortality, prospectively predict central visceral obesity across 13 years. Visceral adipose tissue (VAT) was determined by x-ray computed tomography (CT) at the L4-L5 disc space in a population-based sample of 157 postmenopausal Healthy Women Study participants. Standardized tests were completed to measure separately trait anger (anger frequency and intensity), style of anger expression (holding anger in and expressing it outwardly), and hostile (mistrustful) attitudes. The higher the VAT score, the higher the trait anger and anger-out scores measured 13 years earlier (Ps < .04) and the higher the concurrent hostile attitudes score (P < .02). Moreover, the higher the VAT score, the greater the increase in trait anger over the study period (P < .03). Trait anger and hostility predicted VAT independent of fasting insulin levels, although both predicted an increase in fasting insulin over time. Women were categorized into three groups according to the distribution of the average percent increase in trait anger and in weight across the study period, respectively. The mean VAT scores increased with the likelihood of being in the highest tertile of increasing trait anger (means: 129.1, 131.1, and 155.8, P < .048) and in the highest tertile of increasing weight (means: 122.4, 131.1, and 162.2, P < .003). The association between a high trait anger score and VAT remained significant, controlling for weight gain. We conclude that hostile attributes, fasting insulin, and weight gain in midlife may contribute to the development of VAT in healthy Caucasian women.

CENTRAL, VISCERAL OBESITY carries an increased risk for non–insulin-dependent (type 2) diabetes mellitus, cardiovascular disease, hypertension, certain cancers, and death.[1-4] However, the etiology of central obesity remains unclear, although genetic factors clearly account for 20% to 25% of the population variance.[5]

Smoking,[6-10] low physical activity,[9-11] and alcohol intake[9,12] are associated with increased central obesity as measured by the waist to hip ratio (WHR). Changes in smoking habits[6] and in physical activity patterns[10,13] are related to changes in the WHR. Also, social and emotional distress, such as frequent absent from work, use of psychotropic agents, sleep-related difficulties,[12,14] life dissatisfaction,[14] low social support,[10,13] depression, anxiety, and dysphoric mood,[10,13,14] anger and hostility,[10,15] and mental fatigue,[16] are correlated with an increased WHR. A recent study in women and men with insulin-dependent diabetes mellitus showed that a change in the depression score over 2 years was associated with a change in the WHR.[13]

Whether behavioral and psychosocial factors prospectively predict central obesity in a healthy population is not known. Among the psychosocial candidate variables are hostile attributes, ie, attributes associated with cardiovascular morbidity and mortality and all-cause mortality.[17-19] Moreover, although it is simple and convenient, the WHR is a crude marker of central adiposity.[20-21] Computed tomography (CT) allows a more precise measurement of cross-sectional areas of deep and subcutaneous adipose tissue at any site of the body, particularly the central abdominal area.[22] Accordingly, the first objective of our study was to examine the predictive significance of anger and hostile attitudes for visceral adipose tissue (VAT) as defined by CT in a longitudinal, population-based study of healthy middle-aged women.

Hyperinsulinemia and visceral obesity are closely associated comorbid conditions.[5,23-25] Similarly, weight is correlated closely with the WHR, and changes in weight are associated with changes in the WHR.[26-27] However, it is uncertain whether the behavioral and psychological factors affect central, visceral obesity independently or via an effect on insulin or weight. The second objective of the study was to test whether any potential influences of anger and hostile attitudes on VAT are independent of or mediated by insulin, weight, or an increase in the levels of both over time.

SUBJECTS AND METHODS

Subjects and Procedures

The study subjects were drawn from the Healthy Women Study, a prospective study of the changes in behavioral and biological characteristics of women during the climacteric. In 1983 to 1984, the Healthy Women Study recruited 541 participants from a random sample of licensed drivers in Allegheny County, Pennsylvania, who met the following eligibility criteria at entry: age 42 to 50 years, menstruation within the past 3 months, diastolic blood pressure less than 100 mm Hg, not surgically menopausal, and not taking insulin, thyroid, lipid-lowering, antihypertensive, or psychotropic medications or estrogens.

For the Healthy Women Study, women underwent premenopausal clinic examinations and returned cards monthly to indicate whether they had menstruated. Once classified as menopausal (defined as 12 successive months without menstruation), women returned for follow-up examinations 1, 2, 5, and 8 years postmenopause. This project has approval from the appropriate Institutional Review Board at the University of Pittsburgh. All subjects provided informed consent. Complete details of the Healthy Women Study protocol can be found elsewhere.[10,28-30]

For the current study, women who completed their 8-year postmenopausal clinic examination before August 1997 were invited for an assessment of body fat distribution using single-slice abdominal CT technology. Of 263 eligible women, 173 participated. The women who refused (n = 90, 34% of eligibles) cited disinterest, time constraints, or

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concern over exposure to radiation as reasons for nonparticipation. For the present report, we limited our analyses to 157 women with available concurrent anthropometric data. Those who participated versus those who refused did not differ in hostile attributes, weight, insulin, glucose, or health habits (*Ps* > .23) with one exception: those who refused reported consuming less alcohol daily ($P = .01$).

VAT

Following established methods,[31] subjects underwent a single 10-mm thick, digitally acquired scout view scan, localized cross-sectionally through the center of the L4-L5 disc space using a 9800 CT scanner (General Electric [GE], Milwaukee, WI) at 120 kV (peak) and either 140 mÅ or 170 mÅ for 2 seconds. Commercial CT software (GE Medical Systems, Milwaukee, WI) was used to compute total adipose tissue in the slice by defining the region of interest for attenuation values between −30 and −190 Hounsfield units. The boundary between VAT and subcutaneous adipose tissue was manually circumscribed using a cursor, and the VAT area was computed in the same manner as total adipose tissue. The reproducibility of this technique is very high, with correlations (*r*) of .99 between duplicate measures.[32] The precision error of VAT measurements calculated as the standard error of a single determination and expressed as a percentage of the mean was 3.9%.

Insulin and Glucose

Insulin and glucose levels were measured in the fasting state. Insulin was analyzed by radioimmunoassay using a modification of the method of Herbert et al,[33] and glucose was determined by enzymatic assay (YSI Glucose Analyzer; Yellow Springs Instruments, Yellow Springs, OH). Low, medium, and high control samples were analyzed in each insulin assay with appropriate crossovers. The assay cross-reacted somewhat with pro-insulin. The interassay coefficient of variation for insulin is 17% at 4 μU/mL, 9.4% at 36 μU/mL, and 9.6% at 74 μU/mL; the intraassay coefficient of variation is 5.9% at 7 μU/mL and 8% at 17 μU/mL. Fasting levels of insulin and the glucose to insulin ratio were used as indices of hyperinsulinemia and insulin resistance.

Total Weight and Total Body Fat

Weight (kilograms) was obtained with a balance-beam scale. Total body fat (kilograms) was measured with a model QDR-2000 dual-energy x-ray absorptiometer (Hologic, Waltham, MA). A standardized procedure for patient positioning and utilization of the QDR software (Version 7.10) was used.

Measures of Health Habits

Cigarette smoking was defined as the total number of cigarettes smoked per day, and alcohol intake as the amount of alcoholic beverages per day converted to grams of absolute alcohol (grams per day). The Paffenbarger activity questionnaire[34] was used to obtain the kilocalories per week spent in leisure-time activity.

Anger and Hostile Attitudes

The subjects completed a set of standardized tests of personality and behavior, including the Spielberger Trait Anger Questionnaire,[35] the Anger Expression Scale,[35] and the Cook-Medley Hostility Inventory for hostile attitudes.[36] The Trait Anger Questionnaire measures the frequency and intensity of angry feelings, whereas the Expression Scale yields two scores: anger-out, the tendency to express anger outwardly, and anger-in, the tendency to hold anger in. The Cook-Medley scale measures mistrustful attitudes toward others. These scales have good internal consistency and good test-retest reliability.[35,37] In the present sample, the stability estimates across 3 to 13 years (Pearson *r* values) were .69 to .78 ($P < .001$). Correlations between the measures of anger and hostile attitudes were .48 to .50 (*Ps* < .001).

Due to practical reasons, data on all measures were not available for every measurement point, except data for total weight and life-style measures. Measures were available for VAT and total fat mass from the 8-year postmenopausal examination; insulin and glucose from the premenopausal and 1-, and 2-, and 5-year postmenopausal examination; insulin and glucose from the premenopausal and 1-, and 2-, and 5-year postmenopausal examinations; trait anger from the premenopausal and 1-, 2-, and 8-year postmenopausal examinations; anger-out and anger-in from premenopausal and 1-, and 2-year postmenopausal examinations; and hostile attitudes from 5- and 8-year postmenopausal examiantions.

Statistical Analyses

The principal data analyses used linear regression. First, we conducted analyses with psychological attributes predicting the VAT across 13 years. Separate analyses were conducted to assess the independent effects of total weight, total fat mass, and hormone use and the effects of smoking, alcohol intake, and physical activity on these associations. Also, ANOVA and ANCOVA were used to account for potential nonlinearity in these associations, with the psychological attributes trichotomized based on the sample distributions as grouping variables. Second, we investigated the effect of change in the psychological attributes over 13 years on VAT and entered (1) a trajectory of the attribute (TRND-function in BMDP,[38] p. 67), and (2) the attribute at baseline simultaneously in the regression equation (inclusion of the baseline value in the model is equivalent to an analysis of residualized change scores, ie, scores adjusted for their linear relationship with the baseline values). Following the pairwise associations, regression analyses to test the independence/mediation via insulin (or weight) were performed. In these analyses, the psychological attribute and insulin (or weight) were entered simultaneously in a model predicting VAT. Variables were logarithmically transformed to account for nonnormality where appropriate.

RESULTS

Psychological and biological characteristics of the sample are listed in Table 1. Before proceeding to the question of psychological influences on VAT, we examined the associations between behavioral life-style characteristics and VAT across the 13-year follow-up period. The smoking status (yes/no), number of cigarettes smoked per day, and daily alcohol intake did not

Table 1. Psychological and Biological Characteristics of the Sample

Characteristic	Mean ± SD	Range	No. of Subjects
8 years postmenopause			
VAT (cm^2)	138.7 ± 64.0	36.8-362.4	157
Total weight (kg)	72.7 ± 15.7	42.3-128.2	157
Total fat mass (kg)	30.7 ± 11.7	9.0-75.0	133
Physical activity (kcal/wk)	1,871.9 ± 1,748.8	56-13,051	156
Smokers (%)	16		156
No. of cigarettes per day	15 ± 8.76	1-30	
Alcohol intake (g/d)	6 2 ± 10.2	0-86.1	155
Hormone-replacement therapy (%)	49.4		156
Trait anger	16.3 ± 3.4	10-27	150
Hostile attitudes	13.0 ± 6.6	0-29	152
5 years postmenopause			
Fasting insulin (μU/mL)	15.8 ± 8.1	4.2-40.6	122
Fasting glucose (mg/dL)	97.0 ± 13.0	69-184	140
2 years postmenopause			
Anger-out	13.6 ± 3.2	8-24	128
Anger-in	14.8 ± 4.0	8-24	128

predict VAT significantly across the 13-year follow-up study (*P*s > .08). A change in the smoking status or alcohol intake over the years was not a significant predictor of VAT (*P*s > .07). A low physical activity level measured 2, 5, and 8 years postmenopause predicted VAT significantly (β > −.17, *P*s < .04), but not when measured at baseline or 1 year postmenopause (*P*s > .10). The mean values for VAT by tertiles of physical activity across 2, 5, and 8 years postmenopause were 159.3, 135.2, and 121.4 for those expending less than 1,111, 1,111 to 1,851, and greater than 1,851 kcal/wk, respectively. A decrease in physical activity over 13 years tended to predict VAT (β = −.16, *P* = .06). Differences in VAT between hormone-replacement users versus nonusers at the time of the scan or ever-users versus never-users were not significant (*P*s > .33).

Body weight, fasting insulin, and the fasting glucose to fast insulin ratio (β > .27, *P*s < .03) were all significant predictors of VAT regardless of the point of measurement. Weight gain across 13 years accounted for 14.1% and an increase in fasting insulin over time accounted for 2.3% (*P*s < .04) of the variance in VAT. Models including the trajectory and the baseline of weight or trajectory and baseline of fasting insulin accounted for 50% and 21.8% of the variance in VAT (*P*s < .001), respectively. Mean values for VAT according to average percent change in weight from baseline to each of the assessments are depicted in Fig 1. The trajectory for the to insulin glucose ratio was not significantly associated with VAT (*P* < .12).

Anger, Hostility, and VAT

Associations between the psychological attributes and VAT are presented in Table 2. VAT measured 8 years postmenopause was predicted by trait anger measured premenopausally 13 years earlier and 1, 2, and 8 years postmenopause; by anger-out measured premenopausally and 1 and 2 years postmenopause; and by hostile attitudes measured concurrently. Anger-in did not significantly predict VAT. The mean values for VAT by tertiles of anger and hostile attitudes are presented in Table 3. The pattern of results was substantively similar to the results derived from regression analyses.

Next, we tested whether the change in anger and in hostility over time would significantly predict increased VAT. Results

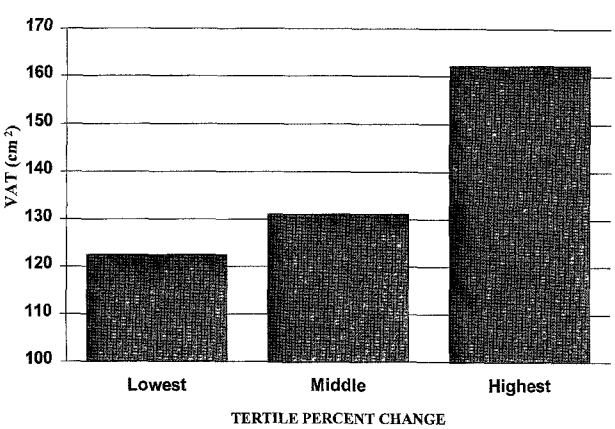

Fig 1. Mean values for VAT by tertiles of average percent change in weight (kg) from baseline to each of the assessments across 13 years. F(2,154) = 5.98, *P* < .003.

Table 2. Psychological Predictors of VAT Across 13 Years

Variable	VAT (cm²) B*	95% Confidence Interval	*P*	*P* Adjusted for Total Weight
Trait anger				
Baseline (n = 157)	.37	0.06-0.68	.02	.12
1 yr postmenopause (n = 142)	.43	0.11-0.75	.01	.02
2 yr postmenopause (n = 144)	.62	0.27-0.97	.001	.03
8 yr postmenopause (n = 150)	.57	0.23-0.91	.001	.01
Anger-out				
Baseline (n = 157)	.30	0.02-0.58	.04	.14
1 yr postmenopause (n = 144)	.33	0.02-0.64	.04	.03
2 yr postmenopause (n = 128)	.40	0.06-0.74	.02	.03
Anger-in				
Baseline (n = 157)	.17	−0.10-0.43	.22	.85
1 yr postmenopause (n = 144)	.15	−0.10-0.41	.25	.23
2 yr postmenopause (n = 128)	.19	−0.11-0.49	.22	.38
Hostile attitudes				
5 yr postmenopause (n = 113)	.15	−0.13-0.43	.31	.12
8 yr postmenopause (n = 152)	.29	0.05-0.54	.02	.15

NOTE. Missing values account for differences in sample size.
*Unstandardized regression coefficient.

relevant to these analyses are shown in Table 4. An increase in trait anger across 13 years predicted VAT significantly, with the model accounting for 6.4% (*P* = .006) of the variance in VAT. Mean values for VAT according to tertiles of the percent change in trait anger from baseline to each of the assessments are depicted in Fig 2. An increase in hostile attitudes from 5 to 8 years postmenopause tended to predict VAT, with the model accounting for 4.4% of the variance in VAT (*P* = .09). Increases in anger-out or anger-in did not contribute significantly to the variation in VAT. Associations between hostile attributes and VAT remained significant after adjusting for hormone use, smoking, alcohol intake, and physical activity (data not shown). When adjustments were made for total weight, total fat mass (data not shown), or weight gain over time, the previously significant associations between hostile attitudes 8 years postmenopause and VAT and the increase in trait anger or in hostile attitudes over time became nonsignificant (Table 4).

Additional analyses were conducted to test associations between the psychological attributes and total weight, total fat mass, and weight gain over time, to test whether weight would act as a mediator between anger, hostility, and VAT. Trait anger was not significantly associated with concurrent measures of weight or total fat mass across 13 years (*P*s > .07). However, trait anger at baseline (β = 0.24, *P* = .01) and an increase in trait anger over 13 years (β = 0.17, *P* = .07) predicted weight gain over time, with the model accounting for 5% (*P* = .05) of the variance in increased weight. This suggests that increased weight does act, at least in part, as a mediator for the effects of increasing trait anger on VAT.

Anger, Hostility, Insulin, and VAT

Cross-sectional correlations between the hostile attributes and insulin were not significant (*P*s > .06). Regression analyses indicated that increases in trait anger, anger-out, or anger-in over time did not significantly predict increases in insulin (*P*s > .10). An increase in hostile attitudes from 5 to 8 years

Table 3. Mean Values for VAT (cm^2) by Tertiles of Hostile Attributes (mean ± SD)

Variable	Tertile 1	Tertile 2	Tertile 3	*P*	*P* Adjusted for Total Weight
Trait anger					
Baseline	124.0 ± 56.1	144.1 ± 70.6	147.9 ± 63.1	.12	.07
1 yr postmenopause	120.0 ± 55.9	143.4 ± 62.6	151.5 ± 67.0	.03	.08
2 yr postmenopause	123.9 ± 54.6	124.0 ± 45.9	170.6 ± 79 0	.001	.26
8 yr postmenopause	122.6 ± 49.9	135 9 ± 59.8	162.1 ± 73.9	.01	.01
Anger-out					
Baseline	132.5 ± 64.4	133.4 ± 54.6	150.5 ± 71.9	.27	.67
1 yr postmenopause	135.2 ± 58.9	121.2 ± 55.7	154.0 ± 68.7	03	.02
2 yr postmenopause	135.6 ± 65.0	127.6 ± 54.3	164.0 ± 77.8	.03	.04
Hostile attitudes					
5 yr postmenopause	134.4 ± 56.8	129.2 ± 62.4	147.8 ± 65 8	41	.51
8 yr postmenopause	132.0 ± 60.0	131.2 ± 59.6	157.0 ± 70.6	.08	.08

postmenopause was significantly associated with an increase in insulin from baseline to 5 years postmenopause ($\beta = .36$, $P < .02$).

The models involving anger or hostility and insulin simultaneously predicting VAT, ie, testing the independence/mediation via insulin, are presented in Table 5. Both trait anger and insulin were independent predictors of VAT, with the model accounting for 25.2% of the variance in VAT ($P = .001$). The association between baseline anger-out and VAT became nonsignificant when tested in the presence of insulin ($P = .17$), while the association between an increase in hostile attitudes from 5 to 8 years postmenopause and VAT became significant in the presence of insulin ($P = .03$). The pattern of results with the glucose to insulin ratio in place of insulin was substantively similar (data not shown).

Table 4. Increases in Anger and in Hostility Over Time Predicting VAT

	VAT (cm^2)			
Variable	β	*P*	R^2	*P*
Trait anger				
Model 1				
Trajectory	21	.03		
Baseline	.30	.001	.06	.006
Model 2				
Trajectory	.06	.37		
Baseline	.14	.04		
Weight trajectory	36	.001		
Baseline weight	.56	.001	.53	.001
Anger-out				
Model 1				
Trajectory	.07	.41		
Baseline	.19	.04	.03	.12
Model 2				
Trajectory	.07	.26		
Baseline	.10	.11		
Weight trajectory	.38	.001		
Baseline weight	55	.001	.53	.001
Hostile attitudes				
Model 1				
5 yr postmenopause	−.12	.42		
8 yr postmenopause	.29	.06	.04	.086
Model 2				
5 yr postmenopause	.01	.94		
8 yr postmenopause	.13	22		
Weight trajectory	.38	.001		
Baseline weight	.55	.001	.55	.001

NOTE. R^2 represents the percent explained by the variables simultaneously in the model.

DISCUSSION

This is the first study to examine the influence of hostile attributes on CT-assessed abdominal, visceral obesity in a longitudinal population-based study of healthy postmenopausal women. We have shown that VAT was predicted by the intensity and frequency of angry feelings, by angry feelings expressed outwardly toward other people and the environment, and by hostile attitudes across the 13-year interval. Moreover, we have shown that an increase in the intensity and frequency of angry feelings over 13 years and an increase in hostile attitudes over 3 years predicted VAT significantly and independently of the baseline levels of hostile attributes. These associations were not attributable to the effects of smoking, alcohol intake, physical activity, or use of hormone-replacement therapy or the changes in them over time. Rather, hostility and anger accounted for 2.9% to 6.4% of the variance in VAT, an amount comparable in magnitude to the effect of associations with smoking, alcohol intake, physical activity, or hormone-replacement therapy observed in previous studies,[6-12] and clearly exceeded the amount of variance accounted for by the life-style measures in the

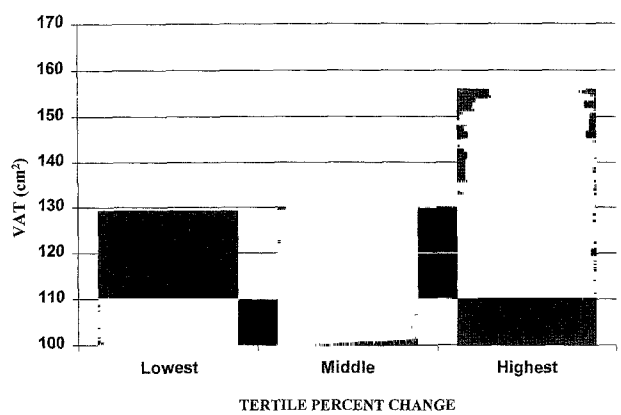

Fig 2. Mean values for VAT by tertiles of average percent change in trait anger from baseline to each of the assessments across 13 years. F(2,154) = 3.09, $P < .048$.

Table 5. Anger, Hostility, and Fasting Insulin Predicting VAT

Variable	VAT (cm^2)			
	β	*P*	R^2	*P*
Trait anger				
Trajectory	.18	.04		
Baseline	.21	.02		
Insulin trajectory	.16	.03		
Baseline insulin	.42	.001	.25	.001
Anger-out				
Trajectory	.03	.68		
Baseline	.11	.17		
Insulin trajectory	.21	.01		
Baseline insulin	.42	.001	.23	.001
Hostile attitudes				
5 yr postmenopause	−.13	.34		
8 yr postmenopause	.29	.03		
Insulin trajectory	.21	.01		
Baseline insulin	.28	.001	.33	.001

NOTE. R^2 represents the percent explained by the variables simultaneously in the model.

current study across the 13-year interval. These results, thus, suggest a role for anger and hostility in the development of abdominal, visceral obesity. The fact that both hostile attributes and visceral obesity are associated with cardiovascular and other morbidity and mortality[17-19] raises the possibility that the pathogenic influences of anger and hostility on increased morbidity and mortality may be due, in part, to the effects of hostile attributes on abdominal, visceral obesity.

This study is also the first to test whether the effects of hostile attributes on VAT are mediated by insulin and weight or are independent of their effects. We have shown that the effects of trait anger and hostile attitudes on visceral obesity were independent of the effects of insulin. Both hostile attributes and insulin contributed significantly and independently of each other to the variation in VAT, with the models accounting for one fourth to one third of the variance in VAT. Regarding weight, the effects of hostile attitudes and an increase in them over time appeared to be secondary to the effects of weight and weight gain over time. However, this was not the case for the associations between angry feelings and VAT. Trait anger and VAT were associated with each other independently of weight, and weight gain across 13 years appeared to mediate, at least in part, the association between increasing anger and VAT. Among the suggested mechanisms accounting for the association between hostile attributes and ill health are health-damaging behaviors, including poor diet and eating behavior. Indeed, hostility is correlated with greater total caloric intake[39] and greater intake of animal fat.[40] A more recent study demonstrated that dramatic positive changes in life-style, including a low-fat vegetarian diet, decreased trait anger.[41] Perhaps this mediation, via weight gain, thus reflects an angry individual's tendency toward increased health-damaging risk behaviors over time.

Other physiological mechanisms potentially affecting the development of abdominal, visceral obesity include cortisol, endogenous sex steroid levels (excess in women), and sympathetic nervous system activity.[5,23-25,42] Interestingly, high cortisol,[43,44] androstenedione, dehydroepiandrosterone, testosterone,[45] and epinephrine and norepinephrine[46] levels and elevated cardiovascular responses to mental stress[47,48] are among the physiological correlates of anger and hostility. It is thus possible, that these neuroendocrine and sympathetic nervous system alterations interact with hostile attributes in the etiology of abdominal, visceral obesity. Clearly, further studies are needed to investigate whether these mechanisms act as pathophysiological links between hostile attributes and VAT.

There are limitations to our study. Most importantly, the good health status of our population-based sample at study entry restricted the variance in health habits, at least to some extent. Consequently, the analyses with life-style measures may have lacked statistical power. Also, the sample consisted of predominantly Caucasians, restricting the generalizability of the findings.

In conclusion, trait anger and hostile attitudes are significant predictors of abdominal, visceral obesity in healthy postmenopausal women across an interval of 13 years. Since both hostile attributes and VAT are identified as risk factors for cardiovascular and other morbidity and mortality, both factors may be used to identify individuals at risk for disease and early death.

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