Anger-Related Personality Traits and Carotid Artery Atherosclerosis in Untreated Hypertensive Men

Maria E. Bleil, MS, Jeanne M. McCaffery, PhD, Matthew F. Muldoon, MD, Kim Sutton-Tyrrell, PhD, and Stephen B. Manuck, PhD

Objective: To determine whether anger-related personality traits are associated with carotid artery atherosclerosis in untreated hypertensive patients. **Methods:** Study participants were 237 men with elevated blood pressure (systolic 140–180 mm Hg and/or diastolic 90–110 mm Hg) but untreated for hypertension. Average age was 56 years; 80% of subjects were white. Eighty-six percent had no history of antihypertensive treatment, and the remainder reported median lifetime treatment exposure of 4 months. Subjects were administered the Spielberger State-Trait Anger Expression Inventory, which measures tendencies to experience anger (Trait Anger) and modes of anger expression (Anger-In, Anger-Out, Anger-Control). Mean and maximum intima-medial thickness (IMT) and plaque occurrence in the extracranial carotid arteries were measured by B-mode ultrasonography. **Results:** Trait Anger was marginally ($p = .065$) related to mean and significantly ($p < .05$) related to maximum IMT, independent of standard risk factors (age, race, body mass index, education, smoking, fasting glucose, total:high-density lipoprotein cholesterol ratio). A component of Trait Anger, Angry Temperament, similarly predicted mean ($p = .062$) and maximum IMT ($p < .05$) and plaque occurrence ($p < .05$). Anger-Out predicted both mean and maximum IMT (p values $<.01$). **Conclusions:** An antagonistic disposition (Trait Anger), particularly a tendency to experience anger on minimal provocation (Angry Temperament) and a propensity to express anger outwardly (Anger-Out), are associated with heightened carotid atherosclerosis. These findings suggest that recently reported prospective associations between these anger dimensions and incident cerebrovascular disease may be mediated, in part, by increased atherosclerotic disease. **Key words:** hypertension, carotid artery atherosclerosis, stroke, anger.

ARIC = Atherosclerosis Risk in Communities; **HDL** = high-density lipoprotein; **IMT** = intima-medial thickening; **REACT** = University of Pittsburgh Reactivity and Cardiovascular Risk Trial; **BP** = blood pressure; **SBP** = systolic blood pressure; **DBP** = diastolic blood pressure; **BMI** = body mass index.

INTRODUCTION

A propensity to experience anger and differences in people's characteristic expression of angry feelings have been shown to increase risk for coronary heart disease, independent of traditional sociodemographic and biological risk factors (1–9). Although occasional clinical studies before 1975 suggest that difficulties in dealing with anger are common among patients who have experienced stroke and may precede clinical events (10–12), it is only recently that anger-related traits have been examined as potential predictors of cerebrovascular events in prospective epidemiologic investigation. Three such studies have now been reported, all of which assessed aspects of anger using components of a common set of psychometric instruments (termed the Spielberger Trait Anger and State-Trait Anger Expression Inventories; 13). The Spielberger scales measure several features of anger: a) anger as a personality trait (reflecting a person's habitual tendency to experience anger, either on minimal provocation or when demeaned, criticized, or treated unfairly); b) anger-out, or the frequency with which anger, when experienced, is expressed as aggression toward people or objects, either verbally or by physical assault; c) anger-in, the tendency to inhibit angry feelings; and d) anger-control, defined as the active management of angry feelings in an effort to avoid the expression of irritation or aggression. Using only the latter three scales, Everson et al. (14) reported that middle-aged men participating in the Kuopio Ischemic Heart Disease Study who obtained high scores on the Spielberger anger-out scale had a 2-fold increased risk of stroke over an average follow-up of 8 years, compared with subjects less prone to express their anger outwardly. This association was significant after multivariate adjustment for common cardiovascular risk factors but was limited to men having a history of ischemic heart disease. The remaining anger expression scales (anger-in and anger-control) did not predict risk for stroke in this sample.

In contrast, Eng et al. (15) reported recently that in a large cohort of male health professionals (50–85 years old) without history of clinically manifest coronary heart disease, subjects attaining high scores on the Spielberger anger-out scale were only half as likely to experience stroke over a 2-year period (adjusted for other risk factors) relative to men with low anger-out scores. Other dimensions of anger and anger expression were not examined here, and the authors note that their cohort was somewhat atypical because of subjects' advanced age, high socioeconomic status, and low average anger-out scores in comparison with other samples of older males. Finally, Williams et al. (16) reported that among men and women younger than 60 years in the Atherosclerosis Risk in Communities (ARIC) study, people who reported high levels of trait anger had nearly 3 times the risk of stroke (ischemic and hemorrhagic combined) on 6-year follow-up as people with lower scores on the Spielberger trait anger scale. Risk for ischemic stroke was also elevated among high trait-anger subjects, with favorable high-density lipoprotein (HDL)

From the Behavioral Physiology Laboratory, Department of Psychology, University of Pittsburgh, Pittsburgh, PA (M.E.B., S.B.M.); the Center for Clinical Pharmacology, Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA (M.F.M.); the Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA (K.S.-T.); and the Centers for Behavioral and Preventive Medicine, Brown Medical School and the Miriam Hospital, Providence, RI (J.M.M.).

Address correspondence to Maria E. Bleil, MS, Behavioral Physiology Laboratory, 506 Old Engineering Hall, University of Pittsburgh, 4015 O'Hara St., Pittsburgh, PA 15260. E-mail: bleil@pitt.edu

Address reprint requests to Stephen B. Manuck, PhD, Behavioral Physiology Laboratory, 506 Old Engineering Hall, University of Pittsburgh, 4015 O'Hara St., Pittsburgh, PA 15260. E-mail: manuck@pitt.edu

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cholesterol concentrations (>47 mg/dl). These findings persisted after adjustment for standard risk factors. Unlike the previously cited studies, components of anger expression were not assessed.

Whatever anger components might be related to risk for cerebrovascular disease, any such association may conceivably reflect effects of anger and its expressive components on the precipitation of clinical events (triggering), predisposing vascular disease (atherosclerosis), or both (16). With respect to atherosclerosis, there is some evidence that anger promotes atherogenesis, as assessed by ultrasound evaluation of carotid artery intima-medial thickening (IMT) and focal plaque in nonpatient samples. For instance, Julkunen et al. (17) reported that high scores on the Spielberger anger-control dimension predicted a greater 2-year progression of carotid artery disease among middle-aged men. A more general anger measure compiled from the Cornell Medical Index was associated with atherosclerotic plaque in the carotid arteries of a relatively small sample of men and women ($N = 34$), of whom eight had a history of ischemia and the remainder at least one of four risk factors for coronary disease (hypertension, hypercholesterolemia, diabetes, smoking; 18). Finally, in a sample of 200 postmenopausal women, Matthews et al. (19) found trait anger and anger-in on the Spielberger scale to predict carotid artery IMT (and in the case of anger-in, plaque occurrence) in measurements obtained 10 years after behavioral assessment, although trait anger did not remain a significant predictor of IMT after multivariate adjustment for covariates. It may also be noted that, unlike in the report by Matthews et al. (19), anger-in was not associated with carotid atherosclerosis in the study by Julkunen et al. (17).

Altogether, these findings present a somewhat confusing picture. In one study, anger-control, but not anger-in, predicted the progression of carotid artery disease among men (17), and in a second, anger-in was associated with carotid IMT in women, but trait anger was not (19). Moreover, neither anger-in nor anger-control has been found to predict the occurrence of stroke in prospective investigation, and anger-out, which was associated with risk of stroke (albeit differently) in the studies of Everson et al. (14) and Eng et al. (15), has not been evaluated in relation to carotid artery atherosclerosis. In the present study, we further examine associations between the dispositional components of anger and measures of both IMT and plaque occurrence, as documented by carotid ultrasonography in a sample of 237 untreated hypertensive men. In contrast with previous studies, all dimensions of trait anger and anger expression assessed by the Spielberger Trait Anger and State-Trait Anger Expression Inventories were evaluated here as potential correlates of carotid artery atherosclerosis.

METHODS

Participants

Subjects were participants enrolled in the University of Pittsburgh Reactivity and Cardiovascular Risk Trial (REACT), a study of behaviorally-evoked cardiovascular reactivity as a potential correlate of preclinical atherosclerotic disease in untreated hypertensive men. Participants were recruited from the communities of southwestern Pennsylvania (principally Allegheny County) via mass-mail solicitation. Subjects were 40 to 70 years of age, and their hypertensive status was confirmed on two screening sessions, at each of which the average of two resting blood pressure measurements, assessed manually by mercury sphygmomanometer, were between 140 and 180 mm Hg systolic BP (SBP) and/or 90 and 110 mm Hg diastolic BP (DBP). Of 251 REACT hypertensives, 237 subjects with complete psychometric and carotid ultrasound data were included in the present analyses. No participant had taken antihypertensive medication within the previous 2 months; also, none had received antihypertensive therapy for >1 year in the 5 years preceding enrollment and for >2 years ever. Two hundred four participants (87%) had no history of antihypertensive treatment, and of the remainder, median lifetime exposure to treatment was 4 months. Other exclusion criteria included secondary hypertension; cerebrovascular accident or stroke; insulin treatment for diabetes or diabetic neuropathy; fasting serum glucose >200 mg/dl; obesity; cancer; serum creatinine >2 mg/dl; hepatitis or cirrhosis; known coronary artery disease; myocardial infarction or angioplasty in the past 12 months; angina pectoris; congestive heart failure; valvular heart disease; atrial fibrillation; pulmonary disease; alcoholism; psychiatric disorder or current use of psychotropic medication; and coronary bypass, carotid, or peripheral vascular surgery. The study protocol was approved by the University of Pittsburgh Biomedical Institutional Review Board, and informed, written consent was obtained from all study participants.

Carotid Atherosclerosis

Participants underwent B-mode ultrasonography at the Department of Epidemiology ultrasound research laboratory at the University of Pittsburgh to assess mean and maximum carotid intima-medial thickness (IMT) and carotid plaque occurrence. A Toshiba SSA-270 scanner (Tobisha, Nasu, Japan) equipped with a 5-MHz linear array imaging probe was used by trained sonographers to image the right and left common carotid artery, carotid bifurcation, and the first centimeter of the internal carotid artery. Mean and maximum IMT were derived from digitized images of the lumen-intima and media-adventitia interface across each carotid segment and were averaged across the near and far walls of the right and left distal common carotid artery (1 cm proximal to the carotid bulb), the far wall of the carotid bulb (starting at the point at which the near and far walls of the common carotid artery are no longer parallel and ending at the flow divider), and the far wall of the internal carotid artery (from the flow divider to the first centimeter distal to this point). Because distributions of average and maximum IMT values were positively skewed, reciprocal transformations were performed to normalize these data before statistical analysis.

Plaque was defined as a delimited or focal area with IMT exceeding adjacent areas by more than 50% and scored for occurrence at artery location according to the following criteria: 0 = no plaque, 1 = one plaque less than 30% of vessel diameter (small plaque), 2 = one plaque 30% to 50% of the vessel diameter (medium plaque) or multiple small plaques, and 3 = one plaque greater than 50% of the vessel diameter (large plaque) or multiple plaques with at least one medium plaque. These values were summed across the right and left carotid arteries to produce an overall plaque score. The resulting values ranged from 0 to 12, with a marked positive skew; because 51.5% of the participants had plaque scores <2, values were dichotomized (0–1 vs. ≥2 plaques) for statistical analysis.

Cardiovascular Risk Factors

Standard cardiovascular risk factors were assessed, including age (in years), body mass index (BMI), education (years of schooling), race (1 = white; 2 = African American), smoking status (1 = never smoked; 2 = past or current smoker), fasting glucose, and the ratio of total cholesterol to HDL cholesterol. BMI was calculated as weight (kg)/height (m^2), and smoking status was determined by self-report (dichotomized as having ever smoked vs. never smoked). Fasting serum glucose was assayed by standard colorimetry, and determinations of serum total cholesterol and HDL were performed by the Heinz Nutrition Laboratory, Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, which has met the criteria of the

Centers for Disease Control—National Heart, Lung, and Blood Institute Lipid Standardization Program since 1982.

Trait Anger and Anger Expression

The 34-item State-Trait Anger Expression Inventory (13) was administered to assess dispositional (trait) anger and habitual modes of anger expression (Anger-Out, Anger-In, and Anger-Control). Trait anger scores may also be decomposed into two component subscales, termed Angry Temperament and Angry Reaction. Angry Temperament reflects quick-temperedness, or the tendency to experience anger on minimal provocation, whereas Angry Reaction denotes the tendency to become angered in response to criticism or mistreatment by others. On a 4-point scale, participants rated the intensity or frequency with which they experience and express anger (1 = never; 2 = sometimes; 3 = often; and 4 = almost always). Responses were summed to yield a score for each anger dimension. Reliabilities of the several trait anger and anger expression scales were all satisfactory, with α coefficients of 0.70 to 0.89 across multiple samples (13). As reported in Table 1, bivariate correlations between anger dimensions were all significant (r = 0.28–0.81), with the exception of Anger-In found unrelated to Anger-Out (p = .819), as has been observed previously (13), and Angry Temperament and Anger Control.

Data Analysis

Multiple regression analyses were performed to assess the relationship of each anger variable (Trait Anger [Angry Temperament and Angry Reaction subscales], Anger-Out, Anger-In, Anger-Control) to carotid atherosclerosis. Dependent variables included mean and maximum IMT (reciprocally transformed) and the dichotomized plaque score. Linear multiple regression was used for analyses involving mean and maximum IMT, logistic multiple regression when predicting plaque occurrence. The following demographic and cardiovascular risk factors were entered simultaneously on the first step of each regression equation: age (in years), race (1 = white; 2 = African American), education (years in school), smoking status (1 = never; 2 = past/current), BMI, SBP, and DBP (mean of the two screening assessments), fasting glucose, and the ratio of total cholesterol to HDL cholesterol. Each anger variable was entered individually on the second step of separate regression equations. In linear regression, the proportion of variance in carotid IMT accounted for by the covariates (R^2) was reported on step one, and on step two, the incremental variance accounted for by each anger variable (ΔR^2). In logistic regression, odds ratios were calculated to determine the likelihood of having a plaque score of 2 or greater based on each of the several dimensions of anger examined here. β Values reflecting the strength of association between each anger variable and dependent measure were considered significant at $p < .05$. In analyses including the reciprocally transformed mean and maximum IMT values, the direction of association was reversed for presentation of results in the text and in Tables 2 and 3.

RESULTS

Sample Characteristics

Table 3 lists descriptive information and bivariate correlations between cardiovascular risk factors and carotid artery IMT and plaque score. The average age of the sample was 56 ± 8.9 years, and 20% were African American. The sample mean for BMI (28.2 ± 3.2) fell within the range for the overweight classification (25.0–29.9) according to clinical guidelines for obesity; cholesterol (total:HDL ratio) and glucose values were within the normal range. The majority of the sample reported current or past smoking (63.3%), and participants attended school an average of 14.8 ± 2.7 years. As expected, participants showed elevated SBP (148 ± 10.9 mm Hg) and DBP (93 ± 7.1 mm Hg). Compared with carotid IMT values in healthy adults (20,21), average mean (0.91 ± 0.16 mm) and maximum (1.19 ± 0.24 mm) carotid IMT were moderately elevated in this hypertensive sample, with 48.5% of the present sample having focal carotid plaques scored 2 or greater.

Bivariate Associations Between Cardiovascular Risk Factors and Carotid Atherosclerosis

As summarized in Table 3, bivariate correlation analyses showed that increased age, lower educational attainment, higher glucose levels, higher screening SBP, and lower screening DBP were associated with greater mean carotid IMT (all p values $<.01$). The same cardiovascular risk factors were also associated with greater maximum IMT (all p values $<.01$), with the addition of current or past smoking status (p = .042). With respect to plaque score, bivariate correlations showed increased age, higher screening SBP, and lower screening DBP significantly (all p values $<.01$), and glucose levels marginally (p = .052), related to plaque occurrence (plaque graded ≥ 2).

Unique Associations Between Anger and Carotid Artery Atherosclerosis

In step 1 of all linear multivariate regression analyses, the covariates (age, race, education, smoking, BMI, total:HDL ratio, glucose, SBP, DBP), entered on step 1 of each regression equation accounted for 36.0% and 34.1% of the variance in mean and maximum IMT, respectively. Among covariates in the final models of each regression equation, greater age, higher screening SBP, and lower screening DBP were significant independent predictors of mean and maximum IMT (all p values $<.05$). Lower educational attainment tended also to be related to greater mean IMT (p value range, .042-.082) and maximum IMT (p value range, .016-.040). In contrast with

TABLE 1. Bivariate Correlations Between Anger Dimensions (N = 237)

	Trait Anger *r*	Angry Temperament *r*	Angry Reaction *r*	Anger-Out *r*	Anger-In *r*	Anger Control *r*
Trait Anger	—	0.76***	0.81***	0.66***	0.29***	−0.53***
Angry Temperament		—	0.28***	0.60***	0.07	−0.48***
Angry Reaction			—	0.40***	0.39***	−0.33***
Anger-Out				—	0.02	−0.55***
Anger-In					—	−0.05
Anger Control						—

* $p < .05$; ** $p < .01$; *** $p < .001$.

TABLE 2. Sample Characteristics and Bivariate Correlations Between Cardiovascular Risk Factors and Carotid Ultrasound Measures ($N = 237$)[a]

Characteristic	Value	Mean IMT[b] *r*	Maximum IMT[b] *r*	Plaque[c] *r*[b]
Age, y	55.7 (8.9)	0.49***	0.45***	0.23***
Race, % white[c]	79.7%	−0.04	−0.07	−0.01
Education, y	14.8 (2.7)	−0.21**	−0.20**	−0.07
Smoking status, % ever smoke[c]	63.3%	0.10	0.13*	0.06
BMI, kg/m^2	28.2 (3.2)	0.04	0.03	−0.09
Total:HDL	4.6 (1.4)	0.08	0.08	−0.02
Glucose, mg/dL	94.5 (14.5)	0.18**	0.18**	0.13
Screening SBP, mm Hg	148.3 (10.9)	0.33***	0.31***	0.22**
Screening DBP, mm Hg	93.1 (7.1)	−0.36***	−0.35***	−0.20**
Mean IMT, mm	0.91 (.16)	—	0.96***	0.49***
Max IMT, mm	1.19 (.24)	—	—	0.56***
Plaque, % ≥2	48.5%	—	—	—

[a] Plaque coded 0 = 0–1 plaques, 1 = ≥2 plaques; race coded 1 = white, 2 = African American; smoking status coded 0 = never smoked, 1 = ever smoked. Values in parentheses indicate SDs.
[b] Because reciprocal transformations were used to normalize IMT values, signs denoting direction of association were reversed.
[c] Denotes point by serial correlation coefficients. *r* denotes Pearson correlation coefficients.
* $p < .05$; ** $p < .01$; *** $p < .001$.

TABLE 3. Multiple Regression Analyses Assessing the Relationship Between Self-Reported Anger and Ultrasound Measures of Carotid Artery Atherosclerosis ($N = 237$)[a]

Linear Regression	β	*p*	R^{2b}	ΔR^{2b}
DV: Mean IMT[c]				
Trait Anger	.099	.065	.370	.010
Angry Temperament	.101	.062	.370	.010
Angry Reaction	.063	.241	.364	.004
Anger-Out	.142	.009	.379	.019
Anger-In	−.022	.687	.361	.000
Anger Control	−.083	.130	.367	.006
DV: Maximum IMT[c]				
Trait Anger	.136	.012	.360	.018
Angry Temperament	.133	.015	.358	.017
Angry Reaction	.080	.141	.348	.006
Anger-Out	.187	.001	.375	.033
Anger-In	−.031	.583	.342	.001
Anger Control	−.092	.099	.349	.008
Logistic Regression	β	*p*	**Odds Ratio**	**95% Confidence Interval**
DV: Plaque Index				
Trait Anger	.054	.166	1.055	.978–1.138
Angry Temperament	.224	.008	1.251	1.060–1.476
Angry Reaction	−.025	.701	.975	.859–1.108
Anger-Out	.053	.217	1.054	.969–1.147
Anger-In	−.034	.366	.967	.898–1.041
Anger Control	−.023	.424	.978	.925–1.034

[a] Covariates were entered on the first step of each regression equation: age, race, education, smoking, BMI, SBP, DBP, glucose, cholesterol.
[b] R^2 and R^2 change values are reported for the final model of each regression equation.
[c] Because reciprocal transformations were used to normalize IMT values, signs denoting direction of association were reversed.

bivariate associations, smoking was unrelated to maximum IMT, and glucose was no longer associated with either mean or maximum IMT.

As summarized in Table 2, linear multiple regression analyses showed that, after covariate adjustment, higher Trait Anger scores predicted greater mean ($\beta = 0.099$; $p = .065$) and maximum IMT ($\beta = 0.136$; $p = .012$), accounting for an additional 1.0% and 1.8% of the variance, respectively. Examination of Trait Anger subscales showed Angry Temperament, but not Angry Reaction (all *p* values ≥.05), to also predict mean ($\beta = 0.101$; $p = .062$; $\Delta R^2 = 0.010$) and maximum IMT ($\beta = 0.133$; $p = .015$; $\Delta R^2 = 0.017$). Among the anger expression variables, only Anger-Out predicted mean ($\beta = 0.142$; $p = .009$; $\Delta R^2 = 0.019$) and maximum IMT ($\beta = 0.187$; $p = .001$; $\Delta R^2 = 0.033$). Based on the untransformed IMT variables, the unstandardized regression

coefficient (b) shows a 1 SD change (either increase or decrease) in Trait Anger score to yield a corresponding change of 0.017 mm in mean IMT and 0.032 mm in maximum IMT, after controlling for covariates; similarly, a 1 SD change in Angry Temperament yields a change of 0.015 mm and 0.028 mm, and in Anger-Out, a change of 0.024 mm and 0.044 mm in mean and maximum IMT, respectively.

In contrast with bivariate correlations showing age and screening SBP and DBP related to plaque score, multiple logistic regression analyses showed only SBP significantly ($p < .05$) and DBP marginally ($p < .065$) independently associated with plaque occurrence. Logistic multiple regression analyses showed Trait Anger to be unrelated to plaque occurrence ($p = .166$). Examination of Trait Anger subscales, however, showed Angry Temperament, but not Angry Reaction, to predict carotid plaque ($\beta = 0.224$; $p = .008$; OR = 1.25; 95% CI = 1.06–1.48). The odds ratio indicates that for every 1-unit increase in Angry Temperament, the likelihood of exhibiting higher plaque scores (values 2 or greater) increased by 25%; alternatively, a 1 SD increase in Angry Temperament was associated with a 50% increased risk of having plaque scored 2 or greater. No anger expression variables (Anger-Out, Anger-In, Anger-Control) were associated significantly with carotid plaque (all p values $\geq .05$).

DISCUSSION

In this study, we found that extracranial carotid artery IMT, as measured by duplex ultrasonography among untreated hypertensive men, was greatest in people who reported a heightened propensity to experience anger (high Trait Anger) or, when angered, to display such feelings outwardly, as aggression directed against other persons or objects in the environment (high Anger-Out). Moreover, the first of these associations was attributable to just one of the two components of Trait Anger, namely Angry Temperament, or the tendency to become angered in the absence of significant provocation. Focal plaque in the carotid arteries of people who scored high on the Angry Temperament subscale was also more extensive than among low-scoring hypertensives. Further, these anger-related characteristics predicted carotid atherosclerosis after multivariate adjustment for standard risk factors, including age, race, education, smoking, BMI, blood pressure, and fasting serum lipids and glucose.

These results parallel findings of two recent prospective studies of incident cerebrovascular disease. In one, elevated Trait Anger scores were found to predict the occurrence of stroke over a period of 6 years in men and women younger than 60 years (16). In the second study, dimensions of anger expression (but not Trait Anger) were evaluated (14); there, men who attained high Anger-Out scores experienced a similarly increased risk of stroke over follow-up intervals averaging 8 years. The consistency of association between our observations and these two large, population-based epidemiologic investigations suggests that anger-related personality traits may heighten vulnerability to stroke, at least in part, by an exacerbation of carotid artery atherosclerosis. In this regard, it is noteworthy that extracranial carotid IMT has been found associated with the occurrence of atherothrombotic stroke in both case-control (22–25) and prospective investigations (26–28). Although the relation of IMT to other, less common categories of stroke (eg, hemorrhagic, cardioembolic) remains uncertain (24,25), carotid ultrasonography also predicts coronary disease events (29) and mortality (30) and covaries significantly with coronary artery atherosclerosis as assessed by cineangiography (31,32). Interestingly, in the same cohort in which Trait Anger was found to predict incident stroke (ARIC) (16), Trait Anger likewise predicted clinical manifestations of coronary heart disease (e.g., fatal and nonfatal coronary events, silent myocardial infarction, and cardiac revascularization procedures) on average follow-up of 53 months (8). Subsequent analyses showed this association to be caused specifically, as in our data, by Angry Temperament, a component of the Trait Anger construct (9). These findings are also consistent with numerous other studies in social epidemiology showing dispositional attributes of anger and hostility to confer increased risk for coronary heart disease (1–9). Thus, our results may bear on the mediation of behavioral influences on coronary, and cerebrovascular, disease.

Among other studies using carotid ultrasonography, Julkunen et al. (17) showed variation in Anger-Control to predict change in IMT over a period of 2 years in middle-aged men; however, these investigators did not report on the Anger-Out dimension, which was associated with greater carotid IMT in our analyses. As in the present study, Matthews et al. (19) reported that Trait Anger correlated positively with IMT (albeit not significantly so after multivariate adjustment for other risk factors). In contrast with our findings, IMT also covaried significantly with subjects' tendency to inhibit the expression of angry feelings (Anger-In). Because the participant sample studied by Matthews et al. (19) was composed entirely of women and we evaluated only men, it is possible that individual differences in anger proneness (Trait Anger) are associated similarly with atherosclerosis in both males and females, whereas modes of anger expression may differ in their atherogenicity as a function of sex. Of course, an adequate test of this hypothesis would require further evaluation among samples of otherwise comparably selected men and women.

It is worth reiterating that the anger-related traits associated with carotid atherosclerosis in this study remained significant predictors after adjustment for standard cardiovascular disease risk factors (i.e., age, race, education, smoking, BMI, blood pressure, and fasting serum lipids and glucose). The mechanisms by which such traits promote arterial changes, therefore, remain unclear. In this regard, it might be hypothesized that variation in acute hemodynamic responsivity to stress, which has been found to covary with anger (e.g., 33,34) and to predict carotid thickening in previous investigations (e.g., 35,36), contributed to the anger and atherosclerosis associations seen here. In a previous REACT publication, we reported that the magnitude of blood pressure response to common laboratory stressors (e.g., Stroop Color-Word

interference task) accounted for significant variance in carotid IMT (35). Although not examined in analyses presented here, adding indices of blood pressure and heart rate reactivity to our multivariate models does not alter the predictive significance of these anger-related traits for preclinical carotid disease or provide evidence that they mediate this association. Nonetheless, dispositional features of anger must promote atherosclerotic changes in the carotid artery through some associated biologic process. Other candidate mechanisms might include alterations in cardiac autonomic control, concomitant activation of neuroendocrine responses thought to potentiate atherogenesis (e.g., in the hypothalamic-pituitary-adrenal, sympatho-adrenal, or renin-angiotensin systems), or the neuroimmune modulation of inflammatory processes and associated endothelial dysfunction (e.g., 37–40).

It should be noted too that anger-related traits may enhance risk of stroke for reasons other than, or in addition to, a worsening of atherosclerosis. For instance, hostile people tend to have other cardiovascular risk factors and may be more likely to engage in health-impairing behaviors (41,42). Relatedly, even if the anger-IMT relationships we observed have pathophysiologic significance, these associations might not contribute similarly to cerebrovascular risk in all population groups. Our findings did not vary by race, for example, yet the strength of extracranial carotid atherosclerosis as a predictor of stroke among white people may differ from that in African American people, in whom intracranial lesions figure more prominently (43–47). Finally, a potential limitation of the present study stems from the fact that our participants were a high-risk sample; all subjects were hypertensive and untreated, and hypertension itself is a primary risk factor for stroke. It is interesting that in the population sample reported by Everson et al. (14), high Anger-Out scores predicted stroke incidence similarly in high-risk people (ie, only in men having a history of ischemic heart disease). In the ARIC study, on the other hand, high Trait Anger scores predicted stroke primarily in people with favorable risk profiles (men and women younger than 60 years and men with high HDL concentrations; 16), and in the same sample, predicted incident coronary disease only among normotensives (8). These apparent inconsistencies suggest that the pathogenicity of anger-related personality traits warrants further investigation, particularly in relation to the presence or absence of other risk factors for heart disease and stroke.

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