Trait Antagonism and the Progression of Arterial Thickening

Women With Antagonistic Traits Have Similar Carotid Arterial Thickness as Men

Angelina R. Sutin, Angelo Scuteri, Edward G. Lakatta, Kirill V. Tarasov, Luigi Ferrucci, Paul T. Costa, Jr, David Schlessinger, Manuela Uda, Antonio Terracciano

Abstract—A large body of evidence links antagonism-related traits with cardiovascular outcomes, but less is known about how psychological traits are associated with intermediate markers of cardiovascular disease. Using a large, community-based sample from Sardinia, Italy, this study examined how trait antagonism (low agreeableness) and its facets are associated with carotid artery intima-media thickness, a measure of arterial thickening. Controlling for demographic and cardiovascular risk factors, low agreeableness and, in particular, low straightforwardness and low compliance, were associated with greater carotid thickening, measured concurrently and prospectively, and with increases in intima-media thickness over 3 years. Indeed, those in the bottom 10% of agreeableness had a 40% increase in risk for elevated intima-media thickness. Although men have thicker arterial walls, women with antagonistic traits had similar carotid thickening as antagonistic men. Antagonistic individuals, especially those who are manipulative and aggressive, have greater increases in arterial thickening, independent of traditional cardiovascular risk factors. (Hypertension. 2010;56;617-622.)

Key Words: intima-media thickness ■ antagonism ■ anger ■ atherosclerosis ■ personality

When the Type A behavioral pattern was dissected into its constituent parts, hostility emerged as the dominant predictor of coronary heart disease.1–3 Subsequent work demonstrated that the interpersonal aspects of hostility, such as the expression of anger in interpersonal contexts, were particularly predictive of coronary heart disease.4,5 Within the framework of the Five-Factor Model of personality, trait agreeableness captures individual differences in this interpersonal orientation toward others. In contrast to agreeable individuals, who tend to be trusting, straightforward, and show concern for others, individuals who score high on antagonism (low agreeableness) tend to be cynical, manipulative, self-centered, arrogant, and quick to express their anger.6 A substantial literature now shows how individual differences in these antagonism-related traits predict a variety of cardiovascular outcomes, including stroke, fatal and nonfatal coronary events, silent myocardial infarctions, and cardiac revascularization procedures.7–9

Much of this work has necessarily focused on the clinical manifestations of coronary heart disease. However, advances in noninvasive technology have made it possible to assess potential markers of atherosclerosis, a preclinical state of coronary heart disease. Specifically, carotid artery intima-media thickness (IMT) is a measure of arterial wall thickness, measured via ultrasound, which can be used to assess healthy people who do not yet clinically manifest the disease. Arterial thickness increases with age but is sensitive to elevated blood pressure and chronic hypertension10 and tends to be accelerated in the presence of cardiovascular disease; it also is an independent predictor of stroke and future myocardial infarction.11,12

Evidence for the role of antagonism in arterial thickening primarily comes from cross-sectional studies on specific populations. For example, measures of anger and hostility have been associated with concurrent measures of IMT among untreated hypertensive men,13 elderly women,14 women transitioning to menopause,15 and young adults who grew up in low socioeconomic environments.16 Among postmenopausal women, these traits are also associated with IMT measured prospectively17 and with increases in IMT over time.18 With few exceptions,19 the antagonism–IMT associations have been examined using specific populations; large, population-based samples are needed to test whether these associations hold across different demographic groups (ie, men, women; younger, older). Further, ≥2 assessments of IMT are needed to test whether antagonism predicts the progression of arterial thickening.
In the present study, we examine the concurrent and prospective associations between 6 facets of trait antagonism (agreeableness) and IMT in a large, population-based sample. In addition, with 2 measures of IMT taken 3 years apart, we test whether these traits predict increases in arterial thickening. Finally, several studies have looked at these relations separately for men and women; few have the power to directly test sex as a moderator. The large sample size in the present study provides sufficient power to test demographic moderators of the antagonism–IMT relations.

**Method**

**Participants**

Participants were drawn from the SardiNIA project, a large, ongoing multidisciplinary study of the genetic and environmental basis of complex traits and age-related processes. Approximately 62% of the population (n=6148 individuals; 57% female), 14 to 102 years of age, from a cluster of 4 towns in the Lanusei Valley enrolled in the study. The current study includes 5614 participants (58% female; mean age 42.51 years; SD=16.86, range 14 to 94) who had valid personality and IMT measurements at wave 1. A total of 4634 participants (59% female; mean age 45.77; SD=16.22, range 18 to 98) had a second valid assessment of IMT 3 years later. The project was approved by institutional review boards in Italy and the United States, and all subjects gave informed consent.

**Personality Assessment**

Agreeableness was assessed using the Italian version of the Revised NEO Personality Inventory. The 48-item Agreeableness scale assesses 6 facets of this trait: A1, Trust; A2, Straightforwardness; A3, Altruism; A4, Cooperation; A5, Modesty; and A6 Tender-mindedness. All items are answered on a 5-point Likert scale, from strongly disagree to strongly agree; scales are roughly balanced to control for the effects of acquiescence. Participants filled out the self-report questionnaire (89%) or chose to have the questionnaire read by a trained Sardinian psychologist (11%). A variable (test of IMT taken 15 minutes from the onset of testing was used for subsequent analyses. In this sample, the Revised NEO Personality Inventory was used as a covariate in the analyses. In this sample, the Revised NEO Personality Inventory showed good psychometric properties, and the factor structure replicated the American normative structure.

Raw scores were converted to T scores (mean=5; SD=1) using American combined-sex norms. Thus, every T-score increase corresponds to an r=1-SD increase in agreeableness.

**Intima-Media Thickness**

As described previously, high-resolution B-mode carotid ultrasoundography was performed by use of a linear-array 5- to 7.5-MHz transducer (HDI 3500; ATL Ultrasound Inc.). The subject lay in the supine position in a dark, quiet room. The stabilized blood pressure after 15 minutes from the onset of testing was used for subsequent analyses. A region 1.5 cm proximal to the carotid bifurcation was identified, and the IMT of the far wall was evaluated as the distance between the luminal–intimal and the medial–adventitial interfaces.

**Covariates**

In addition to age, sex, education, and test administration, we controlled for several major cardiovascular risk factors: waist-circumference, systolic and diastolic blood pressure, LDL and HDL cholesterol, triglycerides, fasting glucose and insulin, smoking, and antihypertensive, statin, and diabetes medication use (Table 1). Waist circumference was measured in centimeters. Blood pressure was measured 3 times after a 5-minute resting period; we used the average of the second and third measurements of systolic and diastolic blood pressure. Blood was drawn from the anteceubital vein between 7 and 8 AM after an overnight fast. Participants were asked not to smoke, engage in significant physical activity, or take medications before the blood collection. Standard enzymatic methods were used on fasting lipid measurements to determine serum HDL cholesterol and triglycerides. LDL cholesterol was derived using the Friedewald equation. LDL cholesterol=total cholesterol–HDL cholesterol−triglycerides/5. The glucose oxidase method (Beckman Instruments Inc.) was used to determine fasting plasma glucose concentration. Solid-phase, 2-site chemiluminescent immunometric assay (Immulite 1000; SR1 Insulin - Biochem Immuno-Systems) was used to determine insulin concentration. Smoking was a binary variable, as were antihypertensive, statin, and diabetes medication use.

**Statistical Overview**

To determine the associations between agreeableness and IMT, we ran a series of linear regressions predicting concurrent and prospective IMT from agreeableness and its facets. We ran these analyses first with the basic demographic covariates and then added the cardiovascular risk factors as covariates. To examine change in IMT, we predicted prospective IMT controlling for concurrent IMT in addition to all of the other covariates. Using Aiken and West’s methodology for testing interactions, we tested whether sex or age (entered as a continuous variable) moderated the personality–IMT associations. We focus on moderators that replicated across both the concurrent and prospective analyses. Finally, we used logistic regression to test whether agreeableness increased risk for having IMT in the top quartile of the distribution. Because of missing values on some of the cardiovascular risk factor covariates, the sample size varied for the analyses that included these variables (n=5460 for concurrent IMT; n=4516 for prospective IMT; and n=4478 for follow-up).
Agreeableness and Its Facets

Table 2. Linear Regressions Predicting IMT From Agreeableness and Its Facets

<table>
<thead>
<tr>
<th>Personality</th>
<th>Concurrent</th>
<th>Prospective</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreeableness</td>
<td>-0.03†</td>
<td>-0.04†</td>
<td>-0.03*</td>
</tr>
<tr>
<td>A1: Trust</td>
<td>-0.01</td>
<td>-0.02</td>
<td>-0.01</td>
</tr>
<tr>
<td>A2: Straightforwardness</td>
<td>-0.04†</td>
<td>-0.04†</td>
<td>-0.02‡</td>
</tr>
<tr>
<td>A3: Altruism</td>
<td>-0.01</td>
<td>-0.01</td>
<td>0.00</td>
</tr>
<tr>
<td>A4: Compliance</td>
<td>-0.02</td>
<td>-0.04†</td>
<td>-0.03†</td>
</tr>
<tr>
<td>A5: Modesty</td>
<td>-0.02*</td>
<td>-0.02</td>
<td>-0.01</td>
</tr>
<tr>
<td>A6: Tender-mindedness</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Full model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreeableness</td>
<td>-0.03*</td>
<td>-0.04†</td>
<td>-0.03*</td>
</tr>
<tr>
<td>A1: Trust</td>
<td>-0.01</td>
<td>-0.02</td>
<td>-0.01</td>
</tr>
<tr>
<td>A2: Straightforwardness</td>
<td>-0.03†</td>
<td>-0.03†</td>
<td>-0.02*</td>
</tr>
<tr>
<td>A3: Altruism</td>
<td>-0.01</td>
<td>-0.02</td>
<td>-0.01</td>
</tr>
<tr>
<td>A4: Compliance</td>
<td>-0.01</td>
<td>-0.03†</td>
<td>-0.03†</td>
</tr>
<tr>
<td>A5: Modesty</td>
<td>-0.02</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
<tr>
<td>A6: Tender-mindedness</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Standardized betas controlling for covariates. The basic model includes age, sex, education, and test administration as covariates. The full model includes these demographic variables and cardiovascular risk factors as covariates (waist circumference, systolic and diastolic blood pressure, LDL and HDL cholesterol, triglycerides, fasting glucose and insulin, smoking, and antihypertensive, statin, and diabetes medication use). For the basic model, n = 5614 for concurrent IMT, n = 4634 for prospective IMT, and n = 4593 for change in IMT. For the full model, n = 5460 for concurrent IMT, n = 4516 for prospective, and n = 4478 for change in IMT.

*P < 0.05; †P < 0.01; ‡P < 0.05.

Results

Table 2 shows the results of the linear regressions for concurrent IMT, prospective IMT, and change in IMT. Controlling for the basic demographic covariates, domain-level agreeableness, A2 (Straightforwardness) and A5 (Modesty) were negatively associated with IMT, indicating that those who were antagonistic, manipulative, and arrogant had greater carotid thickening. The negative associations between IMT and agreeableness and A2 (Straightforwardness) were unchanged when we added the full list of cardiovascular risk factors as covariates; however, A5 (Modesty) was reduced to nonsignificance. Although modest, the effect size of agreeableness on IMT, by comparison, was similar in magnitude to that of other major risk factors for carotid thickening, including smoking (β = 0.04; P < 0.01), use of antihypertensive medication (β = 0.03; P < 0.01), and HDL Cholesterol (β = -0.04; P < 0.01).

Replicating the concurrent analyses, domain-level agreeableness and A2 (Straightforwardness) were both negative predictors of IMT measured 3 years later. In addition, A1 (Trust) and A4 (Compliance) also prospectively predicted carotid thickening. Although the effect size did not change, A1 (Trust) was reduced to nonsignificance when all of the cardiovascular covariates were included in the analyses; the other 3 predictors remained significant. Age-adjusted mean-level differences in concurrent and prospective IMT for high and low agreeableness are shown in Table 3. It is of note that the difference in IMT between high and low agreeableness is roughly similar to the difference between individuals with metabolic syndrome and controls.

Trait antagonism was associated with the progression of carotid artery thickening: agreeableness, A2 (Straightforwardness), and A4 (Compliance) predicted change in IMT between time 1 and time 2. Specifically, participants who scored higher on antagonism (low agreeableness), especially those who were manipulative (low A2 [Straightforwardness]) and quick to express their anger (low A4 [Compliance]), had greater thickening, controlling for their previous IMT levels, than participants who scored lower on these traits. The same associations were found when either the basic covariates or all of the cardiovascular covariates were included in the analyses. In addition, all of the findings above held after accounting for the presence or absence of plaque, when controlling for carotid artery diastolic diameter, and when we excluded participants who had had a stroke.

Although age was not a consistent moderator both concurrently and prospectively, it did moderate the association between agreeableness and change in IMT. Older participants who were disagreeable had greater progression of IMT over 3 years than older participants who were more agreeable; this association did not hold for younger participants (βA×age = -0.04; P < 0.01). The same moderating effect of age was found for 4 of the facets: A1 (Trust; βA1×age = -0.03; P < 0.01), A2 (Straightforwardness; βA2×age = -0.04; P < 0.01), A4 (Compliance; βA4×age = -0.02; P < 0.05), and A6 (Tender-mindedness; βA6×age = -0.02; P < 0.05). That is, among older adults, the IMT of those who tended to be cynical, be deceitful, express anger, and be less concerned for others increased over time.

Both concurrently and prospectively, sex moderated the association between IMT and agreeableness and 3 of its facets. Women who scored low on agreeableness (βA×sex = -0.04; P < 0.01, and βA×sex = 0.04; P < 0.05, respectively), A2 (Straightforwardness;
antagonism-related traits tended to close that gap among the most antagonistic participants in the sample (Figure). That is, antagonistic women tended to have IMT values more similar to antagonistic men. Finally, sex only moderated one of the sex interactions are

Table 4. Logistic Regressions Predicting the 75th Percentile of IMT From Agreeableness and Its Facets

<table>
<thead>
<tr>
<th>Personality</th>
<th>Concurrent</th>
<th>Prospective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreeableness</td>
<td>0.84 (0.77–0.93)†</td>
<td>0.86 (0.78–0.95)†</td>
</tr>
<tr>
<td>A1: Trust</td>
<td>0.91 (0.84–0.99)*</td>
<td>0.92 (0.85–1.00)‡</td>
</tr>
<tr>
<td>A2: Straightforwardness</td>
<td>0.88 (0.81–0.96)†</td>
<td>0.90 (0.82–0.99)*</td>
</tr>
<tr>
<td>A3: Altruism</td>
<td>0.89 (0.82–0.96)†</td>
<td>0.95 (0.87–1.04)</td>
</tr>
<tr>
<td>A4: Compliance</td>
<td>0.95 (0.88–1.03)</td>
<td>0.91 (0.84–0.98)*</td>
</tr>
<tr>
<td>A5: Modesty</td>
<td>0.94 (0.86–1.03)</td>
<td>0.95 (0.87–1.05)</td>
</tr>
<tr>
<td>A6: Tender-mindedness</td>
<td>0.92 (0.85–0.99)*</td>
<td>0.94 (0.86–1.02)</td>
</tr>
</tbody>
</table>

Odds ratios (95% CI) controlling for age, sex, education, test administration, waist circumference, systolic and diastolic blood pressure, LDL and HDL cholesterol, triglycerides, fasting glucose and insulin, smoking, and antihypertensive, statin, and diabetes medication use.

n=5460 for concurrent IMT; n=4516 for prospective IMT.

*P<0.05; †P<0.01; ‡P=0.06.

Discussion

IMT, a measure of arterial wall thickness, is an independent predictor of stroke and future myocardial infarction that is sensitive to elevated blood pressure and chronic hypertension.10 In the present study, participants who scored high on trait antagonism, and in particular, those who were manipulative (low A2 [Straightforwardness]) and aggressive (low A4 [Compliance]), had greater carotid thickening, measured both concurrently and prospectively. Indeed, those who scored in the bottom 10% of agreeableness (ie, those who were the most antagonistic) had an approximately 40% increase in risk for elevated IMT. Perhaps most notable, these traits also predicted greater progression of arterial thickening across the 3 years of the study.

Several hypotheses have been advanced that speculate on the mechanisms linking antagonistic-related traits with atherosclerosis. Key candidates include metabolic, behavioral, and social risk factors. For example, individuals scoring high in antagonism-related traits are more likely to have metabolic syndrome, a constellation of metabolic risk factors.18 Among postmenopausal women, metabolic syndrome has been found to partially mediate the association between interpersonal anger and arterial thickening.18 However, in the present research, even after controlling for the components of metabolic syndrome, such as blood pressure and triglycerides, the association between antagonism and arterial thickening persisted. This result suggests that other mediators need to be considered.

Lifestyle factors, such as smoking and exercise, have also been hypothesized to mediate this relations.26 However, as with the metabolic risk factors, the association between antagonism and IMT persisted after controlling for smoking. Although we were unable to control for physical activity, antagonism is typically not associated with exercise behav-
ior, and thus, physical activity is unlikely to be a mediator. However, antagonism is associated with increases in adiposity over time, which may contribute to IMT. Although controlling for waist circumference did not reduce the antagonism–IMT relation to nonsignificance, antagonistic individuals may be at greater risk for the progression of atherosclerosis because they tend to gain weight at a more rapid pace over time.

Finally, other social and psychological factors associated with antagonism may link this trait with the progression of atherosclerosis. Antagonistic individuals tend to have a more competitive and conflictual style of social interaction that undermines interpersonal relations. Even when social support systems are in place, they do not benefit physiologically from such support. Over time, deficits in social support may culminate in greater cardiovascular risk. In addition to social isolation, their attitudes may also increase risk. Antagonistic individuals tend to hold negative beliefs about groups other than their own and are thus more prone to stereotyping. Interestingly, such stereotyping is associated with cardiovascular outcomes: younger adults who hold negative stereotypes about aging are more likely to experience a cardiovascular event themselves over the next 4 decades. Antagonistic individuals may be at greater cardiovascular risk, in part, because they tend to hold negative stereotypes.

In the present study, both sex and age moderated some of the associations between the antagonistic traits and IMT. Men tend to have thicker arterial walls than women, making sex a strong risk factor for coronary heart disease. Antagonism-related traits among women appear to close this gap: antagonistic women have similar carotid thickening to that of antagonistic men. Antagonism, particularly anger, has been related to greater cortisol reactivity and such reactivity in women has been linked to a faster progression of atherosclerosis. In addition, hormonal exposure (especially during critical phases) or other physiological differences may have effects that lead women to express more masculine traits, both physiologically (arterial thickness) and psychologically (antagonism); that is, the same influences that lead to the expression of more masculine physiological traits may also lead to greater arterial thickness. Finally, although the association between antagonism and IMT was similar across all age groups at any given time (ie, age did not moderate the concurrent or prospective associations between antagonism and IMT), antagonism predicted greater progression of arterial thickening only among the older participants in our sample.

The present study used a large sample size, 2 assessments of IMT approximately 3 years apart, and a comprehensive measure of trait antagonism to show that antagonism predicts the progression of carotid artery thickening. Further, our effects were independent of traditional demographic and cardiovascular risk factors. However, these strengths need to be qualified. For example, there may be confounding variables that we did not assess. Further, our sample was from a rural population in Sardinia, Italy. Despite demographic differences, our findings were consistent with research on more cosmopolitan populations. Although they may appear small, the effect sizes found in the present study need to be considered within a broader context. As noted above, our associations were of similar magnitude to those of other major risk factors, including smoking, HDL cholesterol, and antihypertensive medication use, both in the current study and in others. In comparison, antagonism ranks alongside many of the other major behavioral and physiological risk factors for cardiovascular disease. In addition, the associations were consistent across the concurrent, prospective, and progression analyses, indicating that these effects are unlikely to be random fluctuations. The findings were also consistent with the literature on antagonism-related traits and IMT and other cardiovascular outcomes, which, with our community-based sample, nicely complements the findings from more circumscribed samples. Finally, we did not test for any genetic mediators or moderators of the agreeableness–IMT relations. Genome-wide association analyses are currently under way in the SardiNIA and other cohorts to individuate replicable genetic variants associated with IMT. Once such variants are identified, it would be worthwhile to add a genetic component to this line of research.

Perspectives
The present research showed that interpersonal antagonism, particularly the disposition to be manipulative and aggressive toward others, was associated with carotid arterial thickening cross-sectionally and prospectively, and predicted increases in arterial thickening over time. These associations persisted even after accounting for traditional cardiovascular risk factors, such as hypertension and weight. Of note, the difference in IMT between those who score low and high in antagonism was roughly similar to the difference between individuals with metabolic syndrome and controls. Further, women with antagonistic traits had similar arterial thickening as men with antagonistic traits, indicating that the effect of sex on IMT was diminished among those high in antagonism.

Clinicians have long noted that those who experience cardiovascular events tend to manifest anger and hostility-related traits. Research has supported this observation: individual differences in antagonism-related traits predict a variety of cardiovascular outcomes, including stroke, fatal and nonfatal coronary events, silent myocardial infarctions, and cardiac revascularization procedures. We extend these associations to an intermediate phenotype: carotid artery IMT. In particular, trait antagonism predicts the progression of arterial thickening and may be one potential mechanism through which antagonism leads to the development of cardiovascular disease. Whereas personality traits, such as antagonism, are basic tendencies that are resistant to change, the expression of these traits, or their characteristic adaptations, is modifiable. Determining which personality traits contribute to arterial thickening will help to identify who is most at risk and who would benefit most from targeted interventions. Interventions aimed at modifying coping mechanisms, improving anger management as well as other behavioral, emotional, and cognitive expressions of trait antagonism (including unhealthy lifestyles), can play an important role in clinical practice.
Source of Funding
This research was supported entirely by the Intramural Research Program of the NIH, National Institute on Aging.

Disclosures
P.C. receives royalties from the Revised NEO Personality Inventory.

References
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Hypertension. 2010;56:617-622; originally published online August 16, 2010; doi: 10.1161/HYPERTENSIONAHA.110.155317

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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