Childhood Hyperactivity as a Predictor of Carotid Artery Intima Media Thickness Over a Period of 21 Years: The Cardiovascular Risk in Young Finns Study

LIISA KELTIKANGAS-JÄRVINEN, PHD, LAURA PULKKI-RÅBACK, PHD, SAMPSA PUTTONEN, PHD, JORMA VIIKARI, MD, PHD, AND OLLI T. RAITAKARI, MD, PHD

Objective: We investigated whether childhood temperament was able to predict carotid artery intima media thickness (IMT) and/or its risk factors in adulthood 21 years later. **Methods:** The subjects were the three youngest age cohorts of the population-based sample of the Cardiovascular Risk in Young Finns study, i.e., those who were aged 3 to 9 years ($n = 708$) at the baseline. IMT was assessed by ultrasound, and temperament in terms of negative emotionality, hyperactivity, and sociability (following Buss and Plomin). In addition, the levels of traditional risk factors for atherosclerosis were measured in both childhood and adulthood. **Results:** Childhood temperament was found to predict adulthood risk factors such as smoking in both genders and body mass index (BMI), systolic blood pressure (SBP), and educational level in women. In women, childhood hyperactivity predicted adulthood IMT after adjustment for childhood and adulthood risk factors for atherosclerosis. **Conclusion:** These findings suggest that temperament may contribute to the development of IMT in two ways: indirectly through risk factors in both genders and in women directly through a mechanism that is not considered in the present study. There were no significant gender-related differences in temperament, but it seemed to play different roles in different genders. Hyperactivity was a greater risk for girls than for boys. **Key words:** intima media thickness, body mass index, hyperactivity, negative emotionality, sociability, childhood temperament.

BMI = body mass index; **LDL** = low-density lipoprotein; **IMT** = intima media thickness; **CHD** = coronary heart disease; **SBP** = systolic blood pressure.

INTRODUCTION

There is evidence that the atherosclerotic process begins in childhood and develops for decades before cardiovascular complications appear. Autopsy studies on children and adolescents have discovered the presence of preclinical atherosclerotic lesions at a very young age (1), and studies using ultrasound imaging have demonstrated atherosclerotic wall thickening in the arteries of children with risk factors of cardiovascular disease (2,3). Moreover, longitudinal studies have shown that childhood risk-factor levels are predictive of adulthood atherosclerosis (4–6).

Less is known about the early tracking and predictive value of the behavioral risk factors for cardiovascular disease. The problems in examining the life-course development of behavioral risk factors include age-specificity. Such behavioral risk factors as anger, hostility, depression, and type A behavior may have different manifestations and varying roles during different developmental phases, and the most important childhood behavioral risk factors for coronary heart disease (CHD) have not yet been identified.

The present study was undertaken with a view to contributing to this discussion. We examined whether temperament in childhood was able to predict carotid artery IMT in adulthood. It is not customary to address temperament in the context of behavioral risk factors of CHD, and no previous study has focused on an association between childhood temperament and adulthood CHD risk.

Thickness of the common carotid intima media thickness (IMT) measured by ultrasound represents a marker of preclinical atherosclerosis. Increased carotid IMT correlates with vascular risk factors (7,8), relates to the severity and extent of coronary artery disease (9), and predicts the likelihood of cardiovascular events in population groups (10–14).

Temperament refers to constitutionally based individual differences in reactivity and self-regulation. It arises from genetic endowment and is strongly related to individual differences in brain function. Owing to its neurological basis, it is very stable. It is seen as the biological core of the personality, i.e., the personality is an outcome of the interaction between innate temperament dispositions and environmental effects such as parental child-rearing practices (15).

Temperament plays a crucial role in stress. It explains individual variance in stress experiences, i.e., why different stimuli are experienced as stress by different people. In particular, individual differences in temperament (differences in brain function underlying temperament) explain the great variety of somatic consequences that stress has for different people. Stress, in turn, is known to contribute to the development of CHD (16–18).

The empirical basis for examining temperament in this particular context was the following. Previous literature convincingly demonstrates that difficult childhood temperament consisting of three dimensions, i.e., hyperactivity, negative emotionality, and low sociability (19), is an appropriate predictor of many harmful adulthood consequences, including social and mental problems and high stress vulnerability (19) that are relevant in this context. Previous findings derived from data from the Cardiovascular Risk in Young Finns Study suggest that childhood temperament contributes to the early development of CHD risk, i.e., it is correlated with childhood and adulthood risk factors. We have found that hyperactivity, negative emotionality, and low sociability in childhood correlate with apolipoproteins A-I and B (with high B and low

From the Department of Psychology, University of Helsinki, Helsinki, Finland (L.K.-J., L.P.-R., S.P.); Department of Medicine, University of Turku, Turku, Finland (J.V.); Department of Clinical Physiology and PET Centre, University of Turku, Turku, Finland (O.T.R.).

Address correspondence and reprint requests to Liisa Keltikangas-Järvinen, Department of Psychology, University of Helsinki, P.O. Box 9, FIN-00014 Helsinki, Finland. E-mail: liisa.keltikangas-jarvinen@helsinki.fi

This study was supported by the Academy of Finland (Grants 111056, 209514 and 209518, LKJ; 53392, J.V. and O.R.).

Received for publication June 30, 2005; revision received March 7, 2006.

DOI: 10.1097/01.psy.0000227752.24292.3e

0033-3174/06/6804-0509

A-1) (20) and precursors of insulin resistance syndrome and that they predict an increase in the parameters of this syndrome over a period of 3 years (21). Further, hyperactivity was found to increase significantly in childhood and adolescence with the apoE phenotypes in the order of E2/2, E3/2, E4/2, E3/3, E4/3, and E4/4 (22). Finally, in a study using the same sample as this report, childhood hyperactivity has been shown to predict young adulthood obesity (23). The idea that hyperactivity could predict obesity may seem paradoxical. But hyperactivity has been shown to sharply increase the probability of environmental conflicts and the resulting increased likelihood of childhood stress (19) is related to abdominal obesity.

We have also shown that childhood temperament correlates with and predicts the development of behavioral risk factors. Negative emotionality in childhood predicted depression in adolescence and young adulthood (24) and hostility in young adulthood (25), and childhood hyperactivity predicted risk-prone type A behavior in adolescence (26). Depression, hostility, and type A behavior are among the traditional behavioral risk factors for CHD (27).

In a population-based sample, we examined whether negative emotionality, hyperactivity, and low sociability as assessed in early childhood predicted adulthood carotid artery IMT over a follow-up period of 21 years. We wanted to establish whether there was a direct association between childhood temperament and adulthood IMT or whether the association was explained by the well-documented risk factors for atherosclerosis. Based on previous findings (19–23), we hypothesized that among the characteristics of difficult temperament, hyperactivity would be most strongly associated with adulthood IMT. Given the fact that the role of temperament is gender related (28,29), we examined men and women separately.

METHODS

Participants

This study is part of the Cardiovascular Risk in Young Finns study that was launched in Finland in 1978 as a collaborative effort between all university departments of pediatrics and several other institutions in Finland to study the risk factors for cardiovascular diseases and their determinants in children and adolescents (30). In order to select participants who were broadly representative of Finnish children and adolescents in terms of living conditions and socioeconomic and demographic background, Finland was divided into five areas according to the location of the university cities with a medical school (Helsinki, Kuopio, Oulu, Tampere, and Turku). In each area, urban and rural boys and girls were randomly selected on the basis of their personal social security number from the Social Insurance Institution's population register, which covers the whole population of Finland. The study plan was approved by the ethical committees of all participating universities. The first cross-sectional study in 1980 included 3596 children and adolescents (83.2% of the invited subjects) aged 3, 6, 9, 12, 15, and 18 years. Follow-up studies were conducted in 1983, 1986, and 2001. The participation rates for the follow-up studies were 83%, 78%, and 64% (31).

The present study included 310 men and 398 women from the three youngest age cohorts. The participants were 3 to 9 years of age at the baseline in 1980, when temperament and childhood risk factors for IMT (low-density lipoprotein [LDL] cholesterol, systolic blood pressure [SBP], body mass index [BMI], parental socioeconomic status) were measured. Temperament and childhood risk factors for IMT were measured again at the 3-year follow-up examination at ages 6 to 12. Carotid artery IMT was measured in 2001, when the participants had reached the age of 24 to 30 years. Only those for whom we had complete information for all the study variables were included. It has been shown previously that those who dropped out during the 21-year follow-up period were more often male, had a lower socioeconomic status, and had a more sedentary lifestyle than those who remained (23,32). With respect to serum lipoprotein levels, blood pressure, smoking, and BMI, no systematic selection dropouts were observed (32).

Measures

Temperament

The temperament of the children was rated by their mothers on a temperament scale derived from the Health Examination Survey (33). The temperament dimensions were negative emotionality, hyperactivity, and sociability, which correspond to the temperament theory developed by Buss and Plomin (15,34). Three values of each dimension were used: the baseline value in 1980, the follow-up value in 1983, and the average of the baseline and the 3-year follow-up value. *Negative emotionality*, which included aggression and angry outbursts, was evaluated on six items ranked on a 5-point Likert-type scale at the baseline (1 = totally disagree, 5 = totally agree) and on a 2-point scale at the 3-year follow-up (1 = disagree, 2 = agree). Because the scales were different at the two follow-up examinations, they were standardized before calculating the average score of the two measurements. The sample items were "Other children's parents often complain about the child's behavior," "The child often hits, pushes, or provokes other children," "The child often gets into fights" (Cronbach α = 0.62 in 1980 and 0.81 in 1983). *Hyperactivity* referred to motor activity and restlessness and was assessed by asking, "Which of the following describes your child most accurately?" The alternative responses were "Always controlled, stays calm even in situations were most children would become restless," "Normal activity level, overactive or restless only occasionally; for instance, when tired," "Slightly more active and restless than the average child or young person," and "Always extremely active and restless, talks and moves incessantly." *Sociability* was assessed according to the child's social responsivity and cooperation. The mothers were asked to choose which of the following described their child most accurately: "Well-adjusted and always very cooperative and responsive to others," "Sometimes has problems with peers, but mostly cooperative," and "Has continuous problems with peers; sometimes I am afraid that he/she is socially maladjusted." These temperament dimensions had previously shown significant stability over the 3-year period (35). In the present sample, the test-retest correlation between the baseline and follow-up was 0.40 for hyperactivity, 0.27 for negative emotionality, and 0.32 for sociability. The scales used in the present study have been shown to have predictive validity with respect to such health-relevant constructs as hostility, type A behavior, and BMI (21,23,26,35,36).

Carotid Artery Studies

Ultrasound tests were carried out during the 21-year follow-up examination between September 2001 and January 2002, using Sequoia 512 ultrasound mainframes (Acuson, CA) with 13.0-MHz linear-array transducers. The left carotid artery was scanned by ultrasound technicians following a standardized protocol (32). In brief, a magnified image was recorded from the angle showing the greatest distance between the lumen-intima interface and the media-adventitia interface. A moving scan with a duration of 5 seconds, which included the beginning of the carotid bifurcation and the common carotid artery, was recorded and stored in digital format on optical discs for subsequent off-line analysis. They were manually analyzed by a single reader who was blind to the subjects' details. The analyses were carried out using ultrasonic calipers. The best-quality end-diastolic frame was selected from the 5-second clip image (incident with the R-wave on a continuously recorded electrocardiogram), and at least four measurements of the common carotid far wall were taken approximately 10 mm proximal to the bifurcation in order to derive the mean carotid IMT. To reduce observer bias, the sonographers were instructed to scan the common carotid in the angle showing the greatest IMT. We have previously reported a 6.4% between-visit coefficient and a 5.2% between-observer coefficient of variation in the IMT measurements (32).

Childhood Risk Factors for IMT

The medical risk variables measured at the baseline and the 3-year follow-up were LDL cholesterol, BMI, SBP, and parental socioeconomic status. These variables were chosen because they have previously been shown to be major risk factors for carotid IMT in Finnish samples (32,37). Measurements of lipid levels were taken in duplicate in the same laboratory using standardized enzymatic methods. LDL-cholesterol concentration was calculated according to the Friedewald formula (38). BMI was calculated as weight (kg)/height (m^2). Blood pressure was measured in 3-year-old children with an ultrasound device and from the older children with a standard mercury sphygmomanometer in 1980 and in1983 and a random zero sphygmomanometer in 2001. An average of three blood-pressure measurements was used in the statistical analysis (39). Parental socioeconomic status was indexed in terms of educational level and occupational status based on information provided by the parent with the higher educational/occupational level. Occupation was categorized as 1 = manual, 2 = lower nonmanual, and 3 = upper nonmanual. Educational level was classified as 1 = low (elementary school), 2 = intermediate (high school or vocational school), and 3 = high (college/university).

Adulthood Risk Factors for IMT

The risk factors used at the 21-year follow-up in adulthood were LDL-cholesterol, BMI, SBP, smoking, and educational level. Smoking status was self-reported: those smoking daily were classified as smokers; others were classified as nonsmokers. Because the youngest participants were 24 years old and did not have an established occupational position, educational level was used as the indicator of socioeconomic status in adulthood. Educational level and other risk factors were measured following similar procedures as in childhood.

Data Analysis

In order to in determine whether childhood temperament was associated with adulthood risk factors, we used the General Linear Model Multivariate procedure with adulthood risk factors (in 2001) as the dependent variables and age, childhood risk factors (in 1980 and 1983), and temperament dimension (in 1980 and 1983) as continuous independent variables. Only the significant temperament dimensions were included in the next analyses, where each risk variable (LDL cholesterol, SBP, BMI, smoking, educational level) was separately regressed on each significant temperament dimension in order to examine the associations of childhood temperament with risk factors for IMT in adulthood. For each risk factor except smoking, age and the childhood value of that risk variable were used as covariates (e.g., the association between baseline hyperactivity and adult BMI was adjusted for age and baseline childhood BMI, the association between follow-up hyperactivity and adult BMI was adjusted for age and follow-up BMI, and the mean childhood BMI and age were used when the effect of average hyperactivity on adult BMI was tested).

To study whether temperament dimensions in childhood predicted IMT in adulthood, regression analyses were conducted with IMT as the dependent variable and each temperament dimension separately as the predictor variable. Participant age was used as a covariate. Possible gender differences were checked by running Gender × Temperament interactions as predictors of IMT.

The final phase included only the temperament dimensions that were significant predictors of IMT in previous analyses. We were interested in seeing whether childhood temperament was associated with adult IMT after adjustment for childhood and adulthood risk factors. We therefore conducted regression analyses in three hierarchical steps: first, temperament and age as predictors of IMT; second, temperament, age, and childhood risk factors as predictors of IMT; and third, all of the previous variables and adulthood risk factors as predictors of IMT.

RESULTS

The correlations between the temperament dimensions were all significant (p values $<.001$). Sociability was negatively associated with negative emotionality (r values = −0.12 and −0.21 at baseline and follow-up) and hyperactivity (r values = −0.15 and −0.24 at baseline and follow-up), whereas negative emotionality and hyperactivity were positively correlated (r values = 0.14 and 0.21 at baseline and follow-up). The following Gender × Temperament interactions predicted IMT: Gender × Negative emotionality (p values = .010 and .018 at baseline and follow-up), Gender × Hyperactivity (p values = .022 and .027 at baseline and follow-up), and Gender × Sociability (p values = .024 and .021 at baseline and follow-up). Consequently, we ran all the analyses separately by gender. Table 1 shows the descriptive statistics of the study sample. Of the childhood variables, the boys had higher levels of negative emotionality and lower levels of LDL cholesterol than the girls, whereas in adulthood, the men had higher mean IMT, higher LDL cholesterol, higher SBP, higher BMI, and a higher rate of smoking than the women.

Table 2 gives a summary of the significant associations between the temperament dimensions and the IMT risk factors. Generally, the factors most strongly associated with temperament were smoking and educational level, whereas temperament had no associations with LDL cholesterol. In men, smoking was associated with hyperactivity and a low level of sociability. In women, high levels of negative emotionality and hyperactivity were associated with a higher prevalence of smoking, higher BMI, and a lower educational level. A high level of sociability, in turn, was associated with a lower BMI, SBP, and a higher educational level. In sum, negative emotionality and hyperactivity were associated with more adverse risk profiles in adulthood, whereas sociability was associated with benign levels of several risk factors.

Table 3 shows that there were no significant associations between the temperament dimensions and IMT in men, whereas hyperactivity had a significant or almost significant association with IMT in women (p values = .031, .036, and .010 for the baseline, the follow-up, and the average score, respectively). The multivariate regression analyses reported in Table 4 show that the average hyperactivity score remained a significant predictor of IMT after adjustment for childhood (step 2) and adulthood risk factors (step 3). As seen from step 3, adult BMI and hyperactivity were significant predictors of IMT in the model in which all of the risk variables were simultaneously taken into account. These three-step regression analyses were also run with the baseline and the follow-up hyperactivity scores as predictors of IMT. Baseline hyperactivity remained an independent predictor of IMT after adjustment for childhood and adulthood risk factors ($\beta = 0.10$, $p = .044$ in the fully adjusted model). However, the hyperactivity follow-up score became a nonsignificant predictor of IMT after adjustment for childhood and adulthood risk factors ($\beta = 0.09$, $p = .086$). BMI in adulthood accounted for this attenuation (p in the fully adjusted model = .017).

With a view to illustrating the significance of hyperactivity for IMT, the women were categorized into tertiles based on their average hyperactivity score. Figure 1 shows that the women who had the lowest average level of hyperactivity as children had a mean IMT of 0.53 mm as adults, compared with a mean IMT of 0.56 in the women with the highest

TABLE 1. Characteristics of the Study Group (N = 708)

Study Variable	Men (N = 310), Mean (SD)	Women (N = 398), Mean (SD)	p Value[a]
Childhood temperament			
Negative emotionality			
Baseline[b]	1.06 (0.11)	1.06 (0.14)	.761
Follow-up[c]	1.36 (0.52)	1.24 (0.36)	<.001
Average level[d]	0.08 (0.85)	−0.07 (0.76)	.017
Hyperactivity			
Baseline[e]	2.09 (0.57)	2.09 (0.61)	.958
Follow-up[e]	2.02 (0.62)	1.98 (0.55)	.339
Average level	2.06 (0.50)	2.03 (0.48)	.486
Sociability			
Baseline[f]	2.44 (0.74)	2.53 (0.68)	.106
Follow-up[f]	2.53 (0.71)	2.56 (0.69)	.577
Average level	2.48 (0.60)	2.54 (0.54)	.183
Childhood risk factors			
LDL cholesterol (mmol/L)			
Baseline	3.39 (0.72)	3.57 (0.77)	.001
Follow-up	3.09 (0.74)	3.26 (0.80)	.002
Average level	3.23 (0.69)	3.42 (0.73)	.001
Systolic blood pressure (mm Hg)			
Baseline	107.0 (10.2)	107.3 (10.3)	.671
Follow-up	110.4 (9.7)	109.4 (9.4)	.156
Average level	108.7 (8.3)	108.4 (7.8)	.567
Body mass index (kg/m^2)			
Baseline	16.0 (1.7)	15.8 (1.7)	.359
Follow-up	16.8 (2.4)	16.9 (2.4)	.751
Average level	16.4 (1.9)	16.4 (2.0)	.843
Parental occupational status			
Baseline[f]	1.89 (0.76)	1.90 (0.73)	.341
Follow-up[f]	1.89 (0.76)	1.86 (0.75)	.877
Average level[f]	1.89 (0.73)	1.88 (0.70)	.433
Parental educational level			
Baseline[f]	2.18 (0.71)	2.15 (0.73)	.665
Follow-up[f]	2.15 (0.76)	2.12 (0.75)	.748
Average level[f]	2.17 (0.70)	2.13 (0.72)	.140
Adulthood risk factors			
Intima-media thickness (mm)	0.57 (0.09)	0.55 (0.07)	.006
LDL-cholesterol (mmol/L)	3.17 (0.86)	3.03 (0.75)	.024
Systolic blood pressure (mm Hg)	120.1 (12.5)	111.2 (11.7)	<.001
Body mass index (kg/m^2)	24.9 (4.1)	24.0 (4.4)	.003
Smoking (daily smokers, %)	31	21	.002
Participants' educational level[f]	2.18 (0.53)	2.15 (0.52)	.695

[a] Indicates difference between genders, χ^2 for categorical variables (i.e., smoking, occupational status, and educational level) and F ratio for continuous variables.
[b] Range of scale is 1 to 2.
[c] Range of scale is 1 to 5.
[d] Based on standardized negative emotionality scores.
[e] Range of scale is 1 to 4.
[f] Range of scale is 1 to 3.

average score in childhood (p of the difference = .014). The association of hyperactivity with IMT showed a significant linear trend (p = .014).

DISCUSSION

The current study examined whether childhood temperament was able to predict carotid artery IMT in adulthood 21 years later and whether the well-documented risk factors of atherosclerosis, i.e., cholesterol levels, blood pressure, BMI, smoking, and SES, play a role in this association. It was found that of the IMT risk factors, childhood temperament predicted adulthood smoking in both genders, and in women, BMI, SBP, and educational level, as well. In women, temperament predicted adulthood IMT after adjustment for childhood and adulthood IMT risk factors (to be given in Table 3). This suggests that temperament may contribute to the development of IMT in two ways: it influences risk factors such as smoking and BMI, and it may have a direct effect on IMT through a mechanism that is not considered in the present study.

All temperament factors used in the study, hyperactivity, negative emotionality and low sociability, correlated with risk factors, whereas only hyperactivity correlated with IMT. This

TABLE 2. Summary of the Significant Associations Between Childhood Temperament and Risk Factors for Carotid Artery Intima Media Thickness Measured in Adulthood

Predictor	Risk Factor in Adulthood							
	Men (N = 310)				Women (N = 398)			
	p^a		β	p	p^a		β	p
Negative emotionality								
Baseline					.004	Smoking	0.14	.005
						Educational level	−0.14	.005
Follow-up					<.001	Body mass index	0.15	<.001
						Smoking	0.18	<.001
						Educational level	−0.12	.014
Average level					<.001	Body mass index	0.09	.037
						Smoking	0.20	<.001
						Educational level	−0.17	.001
Hyperactivity								
Baseline	.012	Smoking	0.13	.024				
		Systolic BP	−0.11	.044				
Follow-up					.007	Smoking	0.14	.006
						Body mass index	0.09	.035
Average level	.022	Smoking	0.19	.001	.002	Body mass index	0.09	.030
						Smoking	0.11	.024
						Educational level	−0.12	.017
						Systolic BP	0.11	.023
Sociability								
Baseline					.027	Systolic BP	−0.12	.015
						Educational level	0.10	.039
Follow-up					.015	Body mass index	−0.12	.006
						Educational level	0.16	.001
Average level	.045	Smoking	−0.20	<.001	.002	Body mass index	−0.13	.003
						Educational level	0.16	.001
						Systolic BP	−0.12	.013

BP = blood pressure.

[a] Significance level in the multivariate model; only significant values are listed. Educational level is adjusted for parental educational level; body mass index is adjusted for childhood body mass index; systolic blood pressure is adjusted for childhood systolic blood pressure.

TABLE 3. Age-Adjusted Regression Coefficients of Childhood Temperament in Predicting Carotid Artery Intima Media Thickness in Adulthood[a]

Predictor	Men (N = 310)				Women (N = 398)			
	β	t Value	p	R^{2b}	β	t Value	p	R^{2b}
Negative emotionality								
Baseline	−0.04	−0.63	.532	0.07	−0.01	−0.15	.882	0.01
Follow-up	−0.04	−0.64	.524	0.07	−0.00	−0.07	.941	0.01
Average level	−0.04	−0.78	.435	0.07	−0.01	−0.15	.884	0.01
Hyperactivity								
Baseline	0.04	0.64	.524	0.07	0.11	2.17	.031	0.02
Follow-up	0.05	0.86	.388	0.07	0.11	2.11	.036	0.02
Average level	0.05	0.89	.373	0.07	0.13	2.59	.010	0.03
Sociability								
Baseline	−0.05	−0.90	.369	0.07	0.02	0.45	.650	0.01
Follow-up	−0.10	−1.81	.071	0.08	−0.04	−0.72	.469	0.01
Average level	−0.09	−1.63	.104	0.08	−0.01	−0.18	.860	0.01

[a] Each row represents a separate regression analysis.

[b] Variance explained by age and the temperament variable.

was in line with our hypothesis. Even though statistically significant, the associations were not very strong, but given the long follow-up incorporating several developmental transitions, the finding is notable. Furthermore, the findings on temperament were confirmed in the next study phase 3 years later.

TABLE 4. Multivariate Hierarchical Regression Analyses of Childhood Hyperactivity, Average Levels of Childhood Risk Factors, and Adulthood Risk Factors in Predicting Intima Media Thickness in Women (N = 398)

Predictor	Step 1				Step 2				Step 3			
	β	t Value	p	R^2	β	t Value	p	R^2	β	t Value	p	R^2
Childhood risk factors												
Age, years	0.10	2.01	.040		0.09	1.67	.095		0.10	1.86	.064	
LDL cholesterol (mmol/L)					−0.03	−0.52	.601		−0.05	−0.75	.451	
Systolic blood pressure (mm Hg)					0.10	1.88	.061		0.07	1.15	.252	
Body mass index (kg/m^2)					−0.03	−0.44	.662		−0.10	−1.50	.134	
Parental occupational status					0.02	0.26	.794		0.03	0.47	.638	
Parental educational level					−0.02	−0.33	.740		−0.03	−0.45	.652	
Adulthood risk factors												
LDL cholesterol (mmol/L)									0.02	0.31	.756	
Systolic blood pressure (mm Hg)									0.09	1.56	.119	
Body mass index (kg/m^2)									0.15	2.40	.017	
Smoking									−0.06	−1.24	.216	
Participants' educational level									0.02	0.30	.767	
Hyperactivity, average level	0.13	2.59	.010		0.13	2.60	.010		0.11	2.24	.026	
				0.028				0.039				0.074

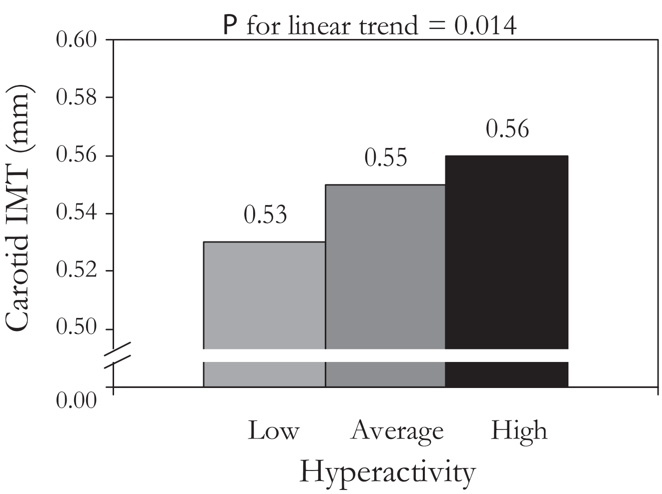

Figure 1. Means of carotid artery intima media (IMT) thickness in women at the 21-year follow-up examination according to tertiles of hyperactivity (average score) in childhood.

Although the variance accounting for IMT by hyperactivity was relatively small (7%), the association appears to be of clinical significance because there is a strong linear relationship between those variables, i.e., IMT increases as a function of hyperactivity, mean IMT being 0.53 mm and 0.56 mm for the female groups of low and high childhood hyperactivity, respectively. For healthy young women, this is a distinct difference. Studies in older adults have shown that every 0.1-mm increase in IMT increases the risk of subsequent cardiovascular events by about 50% (11). Thus, in our study, the difference of 0.03 mm between high and low hyperactivity groups would imply about a 15% to 20% difference in subsequent cardiovascular risk. However, rather than providing a clinically useful estimate of future cardiovascular risk, we believe that the value of our finding is that it provides insight into a mechanism that can account for the involvement of the temperament dimension in the pathophysiology of stress-related cardiovascular disease.

The linear nature of the association between hyperactivity and IMT suggests the absence of threshold beyond which all girls are at a similar risk. The absence of a threshold effect, in turn, suggests that interventions that succeed in reducing hyperactivity in children even to a slight degree may be beneficial in terms of future cardiovascular health. Räikkönen et al. (40) found a "threshold effect" for anger among women: anger correlated with IMT, but after a certain threshold, the level of anger did not play any role. This suggests that interventions are not effective until the level of anger falls below this threshold.

Our finding of a gender-related difference in the role of temperament is noteworthy. Despite only slight gender differences in the levels of temperament scores, temperament played a different role in men and women. The effect was stronger in women whose temperament factors predicted adulthood smoking, a low educational level, higher SBP, and a high BMI, whereas in the men, temperament systematically predicted only smoking. Furthermore, a direct effect of childhood hyperactivity on adulthood IMT was found only in women.

This result is in line with our previous findings derived from the same database: in those studies in which gender was treated separately, hyperactivity was a greater risk for girls. In subjects aged 3 to 9 years, hyperactivity and low sociability were associated with high levels of apoB in girls, whereas this was not true in boys (20). In addition, children, adolescents, and young adults with parental CHD were compared in terms of temperament with their one-to-one matched controls without parental CHD. One significant difference was found: the girls with parental CHD characteristically showed a higher level of hyperactivity (41).

The present finding is also in line with the findings of previous studies. According to the literature, gender-related differences in temperament, if any, are rather small, but because of environmental expectations, the same temperamental factors play different roles in boys and girls (28,29). Interaction between environmental demands and individual temperament drives human development: healthy development occurs when the two are in balance. This phenomenon is called "goodness of fit," whereas "poorness of fit" refers to an imbalance in personal capacities and environmental expectations. A high activity level as such may be problematic. It has been previously shown that parents and teachers sometimes fail to recognize a highly active child as normal. High activity is even less accepted in girls than it is in boys (42), which may also explain our finding of a gender-related role of hyperactivity as a risk factor.

Hyperactivity may later result in a chronic stress. Long-term stress has been suggested to underlie both BMI (43) and IMT (44). Inability to cope with a stress has also been associated with smoking (45). Hyperactivity may increase a girl's stress proneness because of the poorness of fit between her individual temperament and her environmental role expectations. Moreover, because of her temperament she may also create her own stressful environment. There is abundant evidence that a child's negative emotionality and hyperactivity increase its mother's all-round negative attitude toward it, including emotional distance, lack of sensitivity, and strict disciplinary style (46). Early childhood experiences such as a lack of parental warmth and inappropriate handling are associated with alterations in neuroendocrine responses, reflected in stress vulnerability and overactivity of physiological stress systems in adulthood (47,48).

Atherosclerosis is known to originate in childhood. The present findings suggest that behavioral risk factors for atherosclerosis may originate as early, i.e., also in childhood. Further, traditional cardiovascular risk factors, such as smoking and high body mass, may be a link through which early life behavioral factors affect later atherosclerosis. Focusing on childhood behavioral risk factors is as important as decreasing the level of somatic risk factors of CHD. All activities aimed at reducing the poorness of fit between individual characteristics and environmental expectations are of preventive value.

Summary

We investigated whether childhood temperament, i.e., hyperactivity, negative emotionality, and sociability, was able to predict carotid IMT and its risk factors in adulthood after a follow-up period of 21 years. The subjects ($n = 708$) were derived from the population-based sample of the Cardiovascular Risk in Young Finns study and were aged 3 to 9 years at the baseline. We found that childhood temperament predicted adulthood smoking and SBP in both genders and educational level and BMI in women. Furthermore, childhood hyperactivity predicted adulthood IMT after adjustment for childhood and adulthood risk factors for IMT in women. This suggests that temperament may contribute to the development of IMT in two ways: indirectly through risk factors and, in women, directly through a mechanism that is not considered in the present study. These findings are in accordance with previous findings suggesting that, despite the apparent absence of gender-related differences in temperament, the same temperament factors play different roles in boys and girls.

REFERENCES

1. Berenson GS, Srinivasan SR, Bao W, Newman WP III, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults: the Bogalusa Heart Study. N Engl J Med 1998;338:1650–6.
2. Järvisalo MJ, Jartti L, Näntö-Salonen K, Irjala K, Rönnemaa T, Hartiala JJ, Celermajer DS, Raitakari OT. Increased aortic intima-media thickness: a marker of preclinical atherosclerosis in high-risk children. Circulation 2001;104:2943–7.
3. Pauciullo P, Iannuzzi A, Sartorio R, Irace C, Covetti G, Di Costanzo A, Rubba P. Increased intima-media thickness of the common carotid artery in hypercholesterolemic children. Arterioscler Thromb 1994;14:1075–9.
4. Mahoney LT, Lauer RM, Lee J, Clarke WR. Factors affecting tracking of coronary heart disease risk factors in children: the Muscatine Study. Ann N Y Acad Sci 1991;623:120–32.
5. Porkka KV, Viikari JS, Taimela S, Dahl M, Åkerblom HK. Tracking and predictiveness of serum lipid and lipoprotein measurements in childhood: a 12-year follow-up: the Cardiovascular Risk in Young Finns Study. Am J Epidemiol 1994;140:1096–110.
6. Webber LS, Srinivasan SR, Wattigney WA, Berenson GS. Tracking of serum lipids and lipoproteins from childhood to adulthood: the Bogalusa Heart Study. Am J Epidemiol 1991;133:884–99.
7. Haapanen A, Koskenvuo M, Kaprio J, Kesäniemi YA, Heikkilä K. Carotid arteriosclerosis in identical twins discordant for cigarette smoking. Circulation 1989;80:10–6.
8. Poli A, Tremoli E, Colombo A, Sirtori M, Pignoli P, Paoletti R. Ultrasonographic measurement of the common carotid artery wall thickness in hypercholesterolemic patients: a new model for the quantitation and follow-up of preclinical atherosclerosis in living human subjects. Atherosclerosis 1988;70:253–61.
9. Burke GL, Evans GW, Riley WA, Sharrett AR, Howard G, Barnes RW, Rosamond W, Crow RS, Rautaharju PM, Heiss G. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Stroke 1995;26:386–91.
10. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam Study. Circulation 1997;96:1432–7.
11. Chambless LE, Heiss G, Folsom AR, Rosamond W, Szklo M, Sharrett AR, Clegg LX. Association of coronary heart disease incidence with carotid arterial wall thickness and major risk factors: the Atherosclerosis Risk in Communities (ARIC) Study, 1987–1993. Am J Epidemiol 1997;146:483–94.
12. Hodis HN, Mack WJ, LaBree L, Selzer RH, Liu CR, Azen SP. The role of carotid arterial intima-media thickness in predicting clinical coronary events. Ann Intern Med 1998;128:262–9.
13. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults: Cardiovascular Health Study Collaborative Research Group. N Engl J Med 1999;340:14–22.
14. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease. Arterioscler Thromb 1991;11:1245–9.
15. Buss AH, Plomin R. A Temperament Theory of Personality Development. New York: Wiley; 1975.
16. Appels A, Golombeck B, Gorgels A, de Vreede J, van Breukelen G. Behavioral risk factors of sudden cardiac arrest. J Psychosom Res 2000;48:463–9.
17. Björntorp P, Rosmond R. The metabolic syndrome: a neuroendocrine disorder? Br J Nutr 2000;83(suppl 1):49–57.
18. Lovallo WR. Stress and Health: Biological and Psychological Interactions. Thousand Oaks, CA; 1997.
19. Wachs TD, Kohnstamm GA. Temperament in Context. London: Lawrence Erlbaum Associates; 2001.
20. Räikkönen K, Keltikangas-Järvinen L, Solakivi T. Behavioral coronary risk indicators and apolipoproteins A-I and B in young Finnish children: cross-sectional and predictive associations. Prev Med 1990;19:656–66.
21. Ravaja N, Keltikangas-Järvinen L. Temperament and metabolic syndrome precursors in children: a three-year follow-up. Prev Med 1995;24:518–27.

22. Keltikangas-Järvinen L, Räikkönen K, Lehtimäki T. Dependence between apolipoprotein E phenotypes and temperament in children, adolescents and young adults. Psychosom Med 1993;55:155–63.
23. Pulkki-Råback L, Elovainio M, Kivimäki M, Raitakari O, Keltikangas-Järvinen L. Temperament in childhood predicts body mass in adulthood: the Cardiovascular Risk in Young Finns Study. Health Psychol 2005;24: 307–15.
24. Katainen S, Räikkönen K, Keltikangas-Järvinen L. Adolescent temperament, perceived social support, and depressive tendencies as predictors of depressive tendencies in young adulthood. Eur J Pers 1999;13:183–207.
25. Keltikangas-Järvinen L, Heinonen K. Childhood roots of adulthood hostility: family factors as predictors of cognitive and affective hostility. Child Dev 2003;74:1751–68.
26. Räikkönen K, Keltikangas-Järvinen L. Childhood hyperactivity and the mother-child relationship as predictors of risk Type A Behavior in adolescence: A six year follow-up. Pers Individ Dif 1992;13:321–7.
27. Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. Circulation 1999;99:2192–217.
28. Kerr M. Culture as a context for temperament: suggestion from the life courses of shy Swedes and Americans. In: Wachs TD, Kohnstamm GA, eds. Temperament in Context. Mahwah, NJ: Lawrence Erlbaum Associates; 2001:139–52.
29. Kerr M, Tremblay RE, Pagani L. Boys' behavioral inhibition and the risk of later delinquency. Arch Gen Psychiatry 1997;54:809–16.
30. Åkerblom HK, Viikari J, Uhari M, Räsänen L, Byckling T, Louhivuori K, Pesonen E, Suoninen P, Pietikäinen M, Lähde PL, Dahl M, Aromaa A, Sarna S, Pyörälä K. Atherosclerosis precursors in Finnish children and adolescents, 1: general description of the cross-sectional study of 1980, and an account of the children's and families' state of health. Acta Paediatr Scand Suppl 1985;318:49–63.
31. Åkerblom HK, Viikari J, Raitakari OT, Uhari M. Cardiovascular Risk in Young Finns Study: general outline and recent developments. Ann Med 1999;31(suppl 1):45–54.
32. Raitakari OT, Juonala M, Kähönen M, Taittonen L, Laitinen T, Mäki-Torkko N, Järvisalo MJ, Uhari M, Jokinen E, Rönnemaa T, Åkerblom HK, Viikari JSA. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. JAMA 2003;290:2277–83.
33. Wells E. Behavioral patterns of children in school. Vitality Health Stat 1980;113.
34. Buss AH, Plomin R. Temperament: Early Developing Personality Traits. Hillsdale, NJ: Erlbaum; 1984.
35. Katainen S, Räikkönen K, Keltikangas-Järvinen L. Childhood temperament and mother's child-rearing attitudes: stability and interaction in a three-year follow-up study. Eur J Pers 1997;11:249–65.
36. Räikkönen K, Katainen S, Keskivaara P, Keltikangas-Järvinen L. Temperament, mothering, and hostile attitudes: a 12-year longitudinal study. Pers Soc Psychol Bull 2000;26:3–12.
37. Lynch J, Kaplan GA, Salonen R, Salonen JT. Socioeconomic status and progression of carotid atherosclerosis. Arterioscler Thromb Vasc Biol 1997;17:513–9.
38. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502.
39. Uhari M, Nuutinen EM, Turtinen J, Pokka T, Kuusela V, Åkerblom HK, Dahl M, Kaprio EA, Pesonen E, Pietikäinen M, Salo MK, Viikari J. Blood pressure in children, adolescents and young adults. Ann Med 1991;23:47–51.
40. Räikkönen K, Matthews KA, Sutton-Tyrrell K, Kuller LH. Trait anger and the metabolic syndrome predict progression of carotid atherosclerosis in healthy middle-aged women. Psychosom Med 2004;66:903–8.
41. Räikkönen K, Keltikangas-Järvinen L, Pietikäinen M. Type A behaviour and its determinants in children, adolescents and young adults with and without parental coronary heart disease: a case control study. J Psychosom Res 1991;35:273–80.
42. Bates J. Temperament and parent-child relations as interacting factors in children's behavioral adjustment. In: Molfese V, Molfese D, eds. Temperament and Personality Development across the Life Span. London: Lawrence Erlbaum Associates; 2000:141–76.
43. Räikkönen K, Hautanen A, Keltikangas-Järvinen L. Association of stress and depression with regional fat distribution in healthy middle-aged men. J Behav Med 1994;17:605–16.
44. Hintsanen M, Kivimäki M, Elovainio M, Pulkki-Råback L, Keskivaara P, Juonala M, Raitakari OT, Keltikangas-Järvinen L. Job strain and early atherosclerosis: the Cardiovascular Risk in Young Finns Study. Psychosom Med. In press.
45. Kassel JD, Shiffman S, Gnys M, Paty J, Zettler-Segal M. Psychosocial and personality differences in chippers and regular smokers. Addict Behav 1994;19:565–75.
46. Keltikangas-Järvinen L. Psychology and the risk for cardiovascular disorder: a developmental perspective. In: Bäckman L, von Hofsten C, eds. Psychology at the Turn of the Millennium. Vol 1. Hove: Psychology Press; 2002:335–53.
47. Steptoe A. Stress effects, overview. In: Fink G, ed. Encyclopedia of Stress. Vol 3. San Diego: Academic Press; 2000.
48. De Bellis MD. Developmental traumatology: the psychobiological development of maltreated children and its implications for research, treatment, and policy. Dev Psychopathol 2001;13:539–64.