Relations of Trait Depression and Anxiety to Low Lipid and Lipoprotein Concentrations in Healthy Young Adult Women

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Objective: Recent evidence suggests that naturally occurring low cholesterol concentrations (<4.14 mmol/liter) are associated with depression as well as poor psychological health. For the most part, these associations have been observed in men. The current study assessed the relation of naturally occurring low lipid and lipoprotein concentrations to trait measures of depression and anxiety in 121 healthy young adult women. **Methods:** Fasting lipid samples were collected at the same time as health history. Trait depression and anxiety were assessed using the Neuroticism, Extraversion, Openness-Personality Inventory (NEO-PI) depression subscale and Spielberger's Trait Personality Inventory (STPI) anxiety subscale. Analyses were conducted using both univariate and multivariate procedures. **Results:** NEO depression was inversely associated with total cholesterol ($p = .027$), triglycerides ($p = .012$), and the ratio of total cholesterol to high-density lipoprotein cholesterol ($p = .059$). Similarly, STPI anxiety was inversely associated with total cholesterol ($p = .002$), low-density lipoprotein cholesterol ($p = .016$), triglycerides ($p = .024$), and ratio of total cholesterol to high-density lipoprotein cholesterol ($p = .075$). These associations were significant after adjustment for age, body mass index, physical activity, oral contraceptive use, and hostility. Neither depression nor anxiety was associated with high-density lipoprotein cholesterol. Univariate analyses indicated that women with low total cholesterol concentrations (<4.14 mmol/liter), relative to those with moderate to high cholesterol levels, were more likely to have higher scores on the NEO depression subscale (27 of 69 (39%) vs. 10 of 52 (19%)) and STPI anxiety subscale (24 of 69 (35%) vs. 11 of 52 (21%)). **Conclusions:** In healthy young adult women, low lipid and lipoprotein concentrations are inversely associated with trait measures of depression and anxiety. These findings are independent of age, body mass index, physical activity, and other factors known to influence lipid concentrations. **Key words:** depression, anxiety, lipids, lipoproteins, women.

TC = total cholesterol; NIM = nonillness-related mortality; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; OC = oral contraceptive; Ho = Cook-Medley hostility scale; NEO-PI = Neuroticism, Extraversion, Openness-Personality Inventory; STPI = Spielberger's Trait Personality Inventory; BMI = body mass index.

INTRODUCTION

Recent evidence has indicated an inverse association between low TC levels and NIM in both men and women (1). The association between low TC and NIM has led researchers to examine whether naturally occurring low TC levels, frequently defined as concentrations below 4.14 mmol/liter, are associated with psychological factors, such as depression and other affective disorders, that may contribute to suicide and traumatic death (2, 3). A number of large epidemiological studies have shown that naturally occurring low TC is inversely associated with depression (4–7). In contrast, the number of studies examining the relationship between anxiety and lipid levels are few and, for the most part, have indicated a positive association in samples of individuals diagnosed with anxiety disorders (8). For both anxiety and depression, the majority of studies have been conducted in men, with very few studies examining these relationships in women.

Although the findings of an association between depression and low lipid concentrations are compelling, the results are equivocal. Inconsistencies among results, however, may be due to various limiting factors. For example, the strongest evidence comes from a study of elderly subjects, specifically men over the age of 70 years (4). It is clear that in this age group, general ill health and preexisting medical conditions can influence TC as well as depression. As Morgan et al. (4) showed, poor physical health and related factors can moderate the relationship between TC and depression. Although some studies (5) have attempted to control for these factors by using multivariate statistics, it is difficult to untangle the potential association between current health and depression in the elderly.

A second limiting factor is the relatively small number of individuals with naturally occurring levels of TC under 4.14 mmol/liter. For example, in the preliminary study by Morgan et al. (4), only 8% of the 1020 male participants had TC levels below 4.14 mmol/liter. Similarly, in the Multiple Risk Factors Intervention Trial (7), only 6% of the 350,977 men had TC levels below 4.14 mmol/liter. Although large sample sizes increase the power to detect differences between groups, a skewed distribution in which there are few individuals with low TC can prevent adequate testing of the hypothesis.

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A third limitation is the omission of important and relevant psychological variables, such as anxiety and hostility, that may explain the depression–cholesterol association. It is well known that depression is strongly and positively associated with anxiety, which seems to be positively related to lipid levels in clinical populations (8). Similarly, depression is also related to hostility, which has been shown to be positively associated with serum lipid concentrations (9–11). Inclusion of hostility is particularly important given that emerging evidence suggests that specific aspects of hostility, such as aggression and impulsivity, may be associated with low cholesterol concentrations (12). To date, only one study has examined the concomitant relations of depression, anxiety, and hostility to lipids, with results indicating no associations (13). Thus, a more concise test of the hypothesis of an association between low TC levels and poor psychological well-being should include measures of hostility and anxiety as well as depression.

Lastly, the majority of studies have examined only the relation of depression to TC. For the most part, few studies have included other lipid and lipoprotein constituents, such as LDL-C, HDL-C, and triglycerides. Inclusion of these additional measures may lead to a better determination of the degree to which depression and anxiety are associated with low lipid and lipoprotein concentrations.

Given the interrelationships among anxiety, depression, and hostility and their relevance to NIM (14), the current study assessed the relation of trait depression, anxiety, and hostility to serum lipid concentrations. To avoid the potential impact of health problems and preexisting medical conditions on lipid levels, we examined these relationships in 121 healthy young adult women. To test more thoroughly the hypothesis that depression and anxiety are associated with low lipid and lipoprotein levels, TC, LDL-C, HDL-C, triglycerides, and the ratio of TC to HDL-C were assessed.

METHODS

Subjects were 121 healthy adult women between the ages of 18 and 27 years ($X = 21$ (± 2.3) years) recruited through advertisements placed in local newspapers. Subjects were enrolled in a study of the independent and combined effects of psychological factors and OC use on cardiovascular risk factors in premenopausal women. As part of the enrollment criteria, participants were required to score in the upper (>18) and lower (<11) quartiles of age- and race-appropriate norms of the Cook and Medley (15) hostility scale (Ho), which is composed of 50 items derived from the Minnesota Multiphasic Personality Inventory. Additional inclusion criteria for participation included no history of major illnesses, no current medication use for acute or chronic illnesses or for treatment of hypercholesterolemia, nonsmoker, and no clinical history or treatment for depression or anxiety. Of the 121 women in this sample, 47% were current OC users, defined as continuous use of OC for 6 months or more before study participation. Eighty-two percent reported exercising weekly on a regular basis for an average of 5 hours/week, with most subjects doing some kind of aerobic exercise. Of the 121 subjects, 103 (85%) were white, 12 (10%) were black, two (<2%) were Hispanic, and four (3%) were Asian. Additional subject characteristics are shown in Table 1.

Assessment

Trait depression was assessed using a subscale of the NEO Personality Inventory (16), a self-report instrument frequently used to measure normal personality traits. The NEO depression scale measures the tendency of individuals to experience depressive affect or mood. Scores from this scale, however, do not indicate depressive symptomatology. The scale is composed of eight items with five response choices: strongly disagree, disagree, neutral, agree, and strongly agree. Scores range from 0 to 32. High scores are indicative of individuals who are prone to feelings of guilt, sadness, hopelessness, and loneliness. Representative items from the depression subscale include the following: "I am seldom sad or depressed," "sometimes I feel completely worthless," and "sometimes things look pretty bleak and hopeless to me." Costa and McCrea (16) have reported an α coefficient of 0.84 and a 6-month test–retest reliability of 0.80. The NEO depression scale is positively correlated with the Center for Epidemiologic Studies depression scale ($r = 0.59$), a measure of depressive symptomatology (16).

Trait anxiety was assessed using the trait anxiety subscale of the STPI (17). The anxiety scale measures an individual's enduring tendencies to experience anxious moods and anxiety states. The STPI anxiety subscale is composed of 10 items. Each item has four response choices: almost never, sometimes, often, and almost always. Subjects are instructed to respond to the questions as they feel in general. STPI anxiety scores range from 10 to 40, with high scores indicating higher trait anxiety. The scale has high internal reliability (Cronbach $\alpha = 0.80–0.85$) (18) and good test–retest reliability (10-year $r = 0.63$) (19).

Subjects also completed a series of questionnaires pertaining to medical and psychological health history, past medication use, physical activity, and self-rated health status. For physical activity, subjects were asked if they exercised on a regular basis.

Lipid Determination

Blood samples were collected in the morning after a 12-hour fast. TC, HDL-C, and triglycerides were determined by enzymatic methods. LDL-C was calculated by using the following formula: LDL cholesterol = TC − (HDL cholesterol − triglycerides/5) (20).

TABLE 1. Characteristics of Study Population

	Mean	SD
Age (yr)	21.1	2.4
BMI (kg/cm^2)	21.8	2.3
Lipids (mmol/liter)		
TC	4.09	0.70
LDL-C	2.38	0.58
HDL-C	1.29	0.27
Triglycerides	0.94	0.48
TC/HDL-C ratio	3.33	0.85
STPI anxiety score	19.5	5.5
NEO depression score	14.4	5.4

Statistical Analyses

Univariate analyses were performed using χ^2 tests. Given the lack of normative data, anxiety groups were established by grouping subjects scoring in the upper quartile (ie, high group) and subjects scoring in the remaining three quartiles (ie, moderate-to-low group). For depression groups, an a priori cutoff score of >17 was used. According to published norms, scores above 17 are considered high to very high for young women (16). TC groups were established using an a priori criterion of <4.14 mmol/liter (low TC group) and ≥4.14 mmol/liter (moderate-to-high TC group).

Multivariate analyses were conducted using the general linear model procedures as described in the SAS statistical procedures manual (21). Significant multivariate results were followed up by individual multiple regressions for each outcome variable. Given the strong association between NEO depression and STPI trait anxiety (r = 0.79) in this sample, two separate sets of analyses were performed to avoid the effects of multicollinearity. For these analyses, TC, LDL-C, HDL-C, and triglyceride concentrations and the TC/HDL-C ratio were treated as continuous outcome variables. Depression and anxiety scores were treated as continuous predictor variables with age, BMI, physical activity, OC status, and hostility as control variables. Among the control variables, physical activity, OC status, and hostility were treated as dichotomous variables. The remaining control variables were treated as continuous variables.

RESULTS

Univariate Analyses

χ^2 tests were conducted to examine the interdependent relationships between depression, anxiety, and TC groups. In this sample, 30.6% of the subjects scored above 17 on the NEO depression scale. Results indicated a significant relationship between depression and the TC groups ($\chi^2(1) = 5.53$, $p = .019$). The relative odds ratio was 2.70 (95% CI, 1.18–6.20). Among women with TC levels below 4.14 mmol/liter ($N = 69$), 39% had scores above 17. For women with TC levels of 4.14 mmol/liter and above ($N = 52$), only 19% scored high or very high on trait depression. Table 2 presents the distribution of subjects across depression and TC groups.

A similar χ^2 analysis was performed to compare subjects who scored in the top quartile of the STPI anxiety scale to those in the remaining quartiles. Results indicated a marginally significant relationship between anxiety and TC ($\chi^2(1) = 3.69$, $p = .055$) with an odds ratio of 2.41 (95% CI, 0.98–5.92). The distribution of subjects was such that among women with TC below 4.14 mmol/liter ($N = 69$), 35% scored in the top quartile on the STPI anxiety scale. Among women with TC of 4.14 mmol/liter and above ($N = 52$), 21% scored in the top quartile.

Because of the known effects of OC use on lipids and lipoproteins, a controlled comparison of the relationship between depression and TC groups stratifying for OC use was conducted. Results of a Mantel-Haenszel test indicated a significant relationship for both groups. Moreover, the result of the test of homogeneity of the odds ratios was not significant($\chi^2(1) = 0.602$), implying that the relationship between depression and TC groups was the same regardless of the level of OC use. Results of a Mantel-Haenszel test of the relationship between anxiety and TC were similar.

Multivariate Analyses

NEO Depression. Multivariate analysis indicated a significant effect for NEO depression ($F(5,105) = 2.69$, $p = .0205$). Results of independent multiple regression showed that after controlling for age, BMI, physical activity, OC status, and Ho status, NEO depression significantly predicted TC ($\beta = -0.03$, $p = .027$), and triglycerides ($\beta = -0.02$, $p = .012$) (see Table 3). NEO depression was marginally significant in predicting the ratio of TC/HDL-C ($\beta = -0.03$, $p = .059$). NEO depression was not a significant predictor of LDL-C ($\beta = -0.02$, $p = .122$) and HDL-C ($\beta = -0.002$, $p = .75$). Inspection of the regression coefficients indicated that depression was inversely associated with TC, triglycerides, and the TC/HDL-C ratio.

In these analyses, results also showed that the Cook-Medley Ho scale significantly predicted TC ($\beta = 0.27$, $p = .049$) and LDL-C ($\beta = 0.22$, $p = .058$). Inspection of adjusted means indicated that women with high Ho scores had higher TC levels relative to women with low Ho scores (mean ± SE for high and low Ho groups, 4.19 ± 0.11 vs. 3.93 ± 0.10, respectively).

STPI Anxiety. Multivariate analyses showed a significant effect for STPI anxiety ($F(5,105) = 2.70$, $p = .0246$). Independent multiple regression analysis indicated that after controlling for age, BMI, OC use, physical activity, and Ho status, STPI anxiety significantly predicted TC ($\beta = -0.04$, $p = .002$), triglycerides ($\beta = -0.02$, $p = .024$), and LDL-C ($\beta = -0.03$, $p = .016$) (see Table 4). STPI anxiety was marginally significant in

TABLE 2. Prevalence of High Anxiety and Depression Scores Among TC Groups

Group	TC (mmol/liter)	*N*	High Depressive Mood Score (%)	High Anxiety Score (%)
Low	<4.14	69	27 (39)	24 (35)
Moderate to high	≥4.14	52	10 (19)	11 (21)

TABLE 3. Regression Coefficients for Models With Depression Scores

	TC		LDL-C		Triglycerides		TC/HDL-C Ratio	
	Coefficient (SE)	*p*	Coefficient (SE)	*p*	Coefficient (SE)	*p*	Coefficient (SE)	*p*
Age	−0.003 (0.03)	.893	0.009 (0.02)	.697	−0.03 (0.02)	.169	0.0071 (0.03)	.827
BMI	0.03 (0.02)	.189	0.03 (0.02)	.142	0.005 (0.02)	.771	0.03 (0.03)	.367
Physical activity	0.11 (0.17)	.518	0.09 (0.14)	.554	0.06 (0.12)	.601	0.15 (0.20)	.469
OC use	0.47 (0.12)	<.001	0.24 (0.11)	.033	0.25 (0.09)	.004	0.03 (0.15)	.870
Hostility	0.27 (0.13)	.049	0.22 (0.12)	.058	0.05 (0.09)	.606	0.25 (0.16)	.137
Depression	−0.03 (0.01)	.027	−0.02 (0.01)	.122	−0.02 (0.009)	.012	−0.03 (0.02)	.059

predicting the TC/HDL-C ratio ($\beta = -0.03$, $p = .075$). STPI anxiety was not a significant predictor of HDL-C. Inspection of the regression coefficients indicated that STPI anxiety was inversely associated with TC, LDL-C, and triglycerides.

In these analyses, results also indicated that the Cook-Medley Ho score significantly predicted TC ($\beta = 0.32$, $p = .018$) and LDL-C ($\beta = 0.26$, $p = .024$). Inspection of adjusted means indicated that women with high Ho scores had higher TC and LDL-C levels (mean ± SE for TC and LDL-C, 4.18 ± 0.12 and 2.47 ± 0.10, respectively) relative to the low Ho group (3.87 ± 0.14 and 2.22 ± 0.12, respectively).

DISCUSSION

Findings from the current study support the general hypothesis that naturally occurring low lipid and lipoprotein concentrations are associated with trait measures of depression and anxiety. Among young healthy women, trait measures of depression and anxiety were negatively and significantly related to TC, LDL-C, and triglyceride concentrations as well as the TC/HDL-C ratio. Adjustment for age, BMI, physical activity, hostility, and OC use did not influence these associations. Among women with TC levels below 4.14 mmol/liter, 39% had high to very high NEO depression scores. Similarly, among women with TC levels below 4.14 mmol/liter, 35% scored in the upper quartile of the STPI anxiety scale. Among women with TC levels of 4.14 mmol/liter and above, only 19 and 21% scored high on the depression and anxiety scales, respectively.

The current findings directly contrast results from a recent study of 2307 young (18–30 years) healthy black and white women (13). In that study, Markovitz et al. examined group differences on various paper-and-pencil measures of hostility, anxiety, and depressive symptoms in women with TC levels above and below 3.62 mmol/liter, in women with LDL-C levels above and below 1.97 mmol/liter, and in women with triglyceride concentrations above and below 0.45 mmol/liter. In both univariate and multivariate analyses using these groupings, Markovitz et al. failed to find any lipid-related group differences on trait measures of hostility and anxiety as well as on a measure of depressive symptoms. It is possible that the divergence between the observations made in this study and those of Markovitz et al. is due to differences in grouping strategies. The analyses conducted by Markovitz et al. compared subjects in the lowest 10% of lipids values (eg, TC < 3.62 mmol/liter) to the remainder of the cohort. In the case of TC levels, this strategy assumes that individuals with TC levels between 3.62 and 4.14 mmol/liter are significantly different from those with TC levels below 3.62 mmol/liter in terms of anxiety and depression. In the current sample, tests of this assumption failed to indicate significant differences between women with TC levels below 3.62 mmol/liter and women with TC levels above 3.62 and below 4.14 mmol/liter on the STPI anxiety (mean for lowest vs. low TC groups, 20.5 vs. 20.7, respectively)

TABLE 4. Regression Coefficients for Models With Anxiety Scores

	TC		LDL-C		Triglycerides		TC/HDL-C Ratio	
	Coefficient (SE)	*p*	Coefficient (SE)	*p*	Coefficient (SE)	*p*	Coefficient (SE)	*p*
Age	−0.009 (0.03)	.730	0.006 (0.02)	.801	−0.031 (0.02)	.110	0.002 (0.03)	.960
BMI	0.03 (0.02)	.173	0.03 (0.02)	.125	0.003 (0.02)	.861	0.02 (0.03)	.408
Physical activity	0.05 (0.16)	.763	0.04 (0.14)	.774	0.05 (0.12)	.644	0.13 (0.21)	.515
OC use	0.48 (0.12)	<.001	0.24 (0.11)	.026	0.26 (0.09)	.003	0.04 (0.15)	.801
Hostility	0.32 (0.13)	.018	0.26 (0.12)	.024	0.04 (0.09)	.652	0.25 (0.16)	.132
Anxiety	−0.04 (0.01)	.002	−0.03 (0.01)	.016	−0.02 (0.01)	.024	−0.03 (0.02)	.075

and NEO depression (15.1 vs. 16.5, respectively) scales. It seem likely, therefore, that the absence of significant associations in the Markovitz et al. study is due to the strategies used to establish low-lipid groups.

Another recently published study reported a negative association between TC and depressive symptoms in 300 healthy women (age 30–65 years). Horsten et al. (22) found that women with TC levels at or below 4.7 mmol/liter reported nearly twice as many depressive symptoms as women with higher TC levels. Interestingly, these results were not replicated when TC was used as a continuous variable. In the current study, both NEO depression and STPI anxiety are significantly associated with TC whether it is entered as a dichotomized variable (using 4.14 mmol/liter as an a priori cutoff) or as a continuous variable. The discrepancy between the current findings and those of Horsten et al. thus focuses on the linear effect of TC on depression. It may be that differences in sample demographics may account, in part, for the contrasting findings. In the Horsten et al. study, women were older, and approximately 33% were smokers. In addition, 70% were postmenopausal, with approximately 28% of those women receiving hormone replacement therapy. These factors may have contributed to the significantly greater range of TC concentrations. In the Horsten et al. study, TC concentrations ranged from 3.0 to 10.6 mmol/liter, with 41% of the sample having TC levels above 6.2 mmol/liter. As noted, Horsten et al. found that scores on a measure of depressive symptoms showed no linear relationship by decile TC groups. However, if the relationship between TC and depressive symptoms is examined only among the lowest six decile TC groups (women with TC levels of 3.0–6.2 mmol/liter), making it comparable to the TC range in the current study, there is the possibility of detecting a linear relationship between TC and depressive symptoms. Therefore, the difference between the findings of Horsten et al. (22) and those of the current study with respect to the linear effects of TC on depression may be due to the difference in the range of TC levels.

Although the current findings indicate significant negative associations between lipids and trait measures of depression and anxiety, they do not indicate causality and/or directionality. Various plausible explanations, however, have been proposed to explain the directionality of the relationships between depression, anxiety, and low lipid concentrations. First, it has been suggested that depression can lead to a loss of appetite and thus a reduction in weight and TC concentration (2). In this sample, however, BMI was positively but not significantly related to NEO depression ($r = 0.16$) and STPI anxiety ($r = 0.13$). Furthermore, a 1-year follow-up study of 20% of the sample indicated that weight was relatively stable ($r = 0.95$). Similarly, TC ($r = 0.83$), LDL-C ($r = 0.83$), HDL-C ($r = 0.89$), triglycerides ($r = 0.58$), and TC/HDL-C ratio ($r = 0.90$) were generally stable over the same 1-year period. Comparisons of means at time zero and 1 year later yielded a significant decrease only in HDL-C and a reduction in the TC/HDL-C ratio (due to a nonsignificant reduction in TC in conjunction with a significant reduction in HDL-C). If depressed and anxious subjects were to exhibit decreases in weight and TC subsequent to a reduction in caloric intake, these changes would more than likely be reflected in mean changes across the 1-year period. Although the current findings were statistically controlled for BMI, they do not completely exclude the possibility that depression leads to lower TC through a reduction in caloric intake. Evidence suggests that a reduction in caloric intake does not lead to reduced weight without an increase in metabolic rate (23). Thus, controlling for BMI alone does not completely rule out the possibility that reduced caloric intake among individuals prone to anxiety and depression contributes to lower TC.

A second hypothesis is that anxiety, depression, and low TC are all indicators of poor health in general (24). Poor health and/or existing medical conditions are known to lead to low TC (25) as well as anxiety and depression. In the current study, however, this is not a plausible explanation. All subjects rated their health status as either excellent or good, and all were screened for current and previous medical and psychological conditions. The fact that 82% of the women reported exercising on a weekly basis indicates the relatively good health of this sample. Lastly, all subjects were nonsmokers. Thus, it is not likely that poor health explains the relationships between lipids, depression, and anxiety.

Lastly, it has been hypothesized that low lipid levels may precede depression and anxiety. Engelberg (26) hypothesized that low TC levels may lead to a reduction of central serotonergic activity because of a reduced neuronal activity affecting receptor function. Low serotonin concentrations have been reported in depressed individuals (27, 28). Moreover, low serotonin concentrations have also been associated with anxiety (29), especially in depressed patients (30). Recently, researchers showed that men with naturally occurring low TC levels (<4.5 mmol/liter) exhibit lower plasma serotonin concentrations (31). That low TC levels are associated with a relative deficiency in serotonergic transmission, possibly due to reduced lipid content of brain cells, provides a biologically plausible explanation for the current observations of

negative associations between low cholesterol levels, depression, and anxiety.

It is noteworthy that scores on the Cook-Medley Ho scale were positively associated with TC and LDL-C concentrations even after controlling for depression and anxiety. These findings are consistent with those of a number of studies indicating that men and women who are characterized by frequent bouts of anger and an antagonistic and hostile personality have higher lipid levels (9–11). It has been suggested, however, that some aspects of hostility, specifically aggression, violence, and impulsivity, are associated with low lipid levels (32–34). One recent study showed that monkeys fed a low-fat, low-cholesterol diet exhibit more aggressive behaviors than those fed a high-fat, high-cholesterol diet (35). In humans, low TC has been observed in individuals who are prone to violence and aggressive conduct (32) as well as in incarcerated men and patients who are hospitalized for violent behavior (33, 34). Together, these data suggest that high and low lipid levels may be associated with hostility and hostile behaviors. However, another alternative is that impulsive and aggressive behaviors are associated with low cholesterol levels, whereas anger and antagonism are related to high lipid levels. Although anger, hostility, and aggression are interrelated, anger and hostility are not equivalent to aggression and impulsiveness (36). Thus, it may be that individuals who exhibit impulsive aggression and violent behavior to anger-arousing situations constitute a subgroup of hostile persons who are characterized by low TC concentrations. This possibility is consistent with the hypothesis that dysfunction of serotonergic systems underlies aggressive and impulsive behavior (35, 37). It is possible, therefore, that the variation in relationships between lipid levels and hostility is due to the degree to which physical aggression and violence are inhibited among hostile persons.

In the present study, high scores on trait measures of depression and anxiety were associated with naturally occurring low lipid and lipoprotein concentrations. The current study, however, did not address the question of whether lipid lowering is associated with the onset of depressive mood and anxiety states. The only conclusions that can be drawn from these data are that healthy individuals prone to depressive moods and anxiety exhibit low concentrations of lipids and lipoproteins. Although lipid-lowering trials have been successful in reducing TC by 10 to 20% (38), for the most part, the large clinical trials have not achieved TC levels below 4.14 mmol/liter (39). Although the present findings offer little insight into the relations of depression and anxiety to lipid lowering, one possibility that arises from these data is that individuals predisposed to or at risk for depressive moods and anxiety are more likely to undergo adverse psychological changes during lipid lowering. This testable hypothesis is consistent with reports of increased depressive mood among some individuals receiving cholesterol-lowering therapy (40). Thus, lipid lowering may be detrimental to psychological well-being, but only among individuals who are predisposed to episodes of depression and anxiety. If this is the case, it would be desirable to identify or screen for individuals at risk for depression and anxiety before any type of lipid-lowering therapy is implemented.

In summary, in young healthy women, naturally occurring low TC levels, specifically levels below 4.14 mmol/liter, as well as low LDL-C and triglyceride concentrations, are significantly and negatively associated with trait measures of depression and anxiety. These associations are observed even after controlling for factors known to affect lipid concentrations. These findings are potentially relevant in relation to observations of increased NIM in persons with spontaneously occurring low cholesterol levels as well as to observations of the increased frequency of depression and anxiety in women.

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REFERENCES

1. Jacobs D, Blackburn H, Higgins M, Reed D, Iso H, McMillan G, Neaton J, Nelson J, Potter J, Rifkind B, Rossouw J, Shekelle R, Yusuf S. Report of the Conference on Low Blood Cholesterol: mortality associations, October 9–10, 1990. Circulation 1992;86: 1046–60.
2. Wardle J. Cholesterol and psychological well being. J Psychosom Res 1995;39:549–62.
3. Murphy JM, Monson RR, Olivier DC, Sobol AM, Pratt LA, Leighton AH. Mortality risk and psychiatric disorders: results of a general physicians survey. Soc Psychiatry Psychiatr Epidemiol 1980;24:134–42.
4. Morgan RE, Palinkas LA, Barrett-Connor EL, Wingard DL. Plasma cholesterol and depressive symptoms in older men. Lancet 1993;341:75–9.
5. Brown SL, Salive ME, Harris TB, Simonsick EM, Guralnik JM, Kohout FJ. Low cholesterol concentrations and severe depressive symptoms in elderly people. BMJ 1994;308:1328–32.
6. Lindberg G, Larsson G, Setterlind S, Rastam L. Serum lipids and mood in working men and women. J Epidemiol Community Health 1994;48:360–3.
7. Neaton JD, Blackburn H, Jacobs D, Kuller L, Lee DJ, Sherwin R,

Shih J, Stamler J, Wentworth D. Serum cholesterol level and mortality findings for men screened in the Multiple Risk Factor Intervention Trial. Arch Intern Med 1992;152:1490–500.
8. Hayward C. Anxiety disorders and serum lipids. In: Hillbrand M, Spitz RT, editors. Lipids, health, and behavior. Washington DC: American Psychological Association; 1997. p. 69–79.
9. Dujovne VF, Houston BK. Hostility-related variables and plasma lipid levels. J Behav Med 1991;14:555–65.
10. Weidner G, Sexton G, McLellarn R, Connor SL, Matarazzo JD. The role of type A behavior and hostility in an elevation of plasma lipids in adult men and women. Psychosom Med 1987; 49:136–45.
11. Suarez EC, Bates MP, Harralson TL. The relation of hostility to lipids and lipoproteins in women: evidence for the role of antagonistic hostility. Ann Behav Med 1998;20:59–63.
12. Hillerbrand M, Spitz RT, Foster HG. Serum cholesterol and aggression in hospitalized male forensic patients. J Behav Med 1995;18:33–43.
13. Markovitz JH, Smith D, Raczynski JM, Oberman A, Williams OD, Knox S, Jacobs DR Jr. Lack of relation of hostility, negative affect, and high-risk behavior with low plasma lipid levels in the Coronary Artery Risk Development in Young Adults study. Arch Intern Med 1997;157:1953–9.
14. Apter A, van Praag HM, Plutchik R, Sevy S, Korn M, Brown SL. Interrelationship among anxiety, aggression, impulsivity, and mood: a serotonergically linked cluster? Psychiatry Res 1990;32: 191–9.
15. Cook WW, Medley DM. Proposed hostility and pharisaic: virtue scores for the MMPI. J Appl Psychol 1954;38:414–8.
16. Costa PT, McCrea RR. Personality in adulthood: a six-year longitudinal study of self-report and spouse ratings on the NEO Personality Inventory. J Pers Soc Psychol 1988;54:853–63.
17. Spielberger CD, Gorsuch RL, Lushene RE. STAI manual for the State-Trait Anxiety Inventory. Palo Alto (CA): Consulting Psychologists Press; 1970.
18. Smith TW, Frohm KD. What's so unhealthy about hostility? Construct validity and psychosocial correlates of the Cook and Medley Ho Scale. Health Psychol 1985;4:503–20.
19. Matthews KA, Owens JF, Kuller LH, Sutton-Tyrrell K, Jansen-McWilliams L. Are hostility and anxiety associated with carotid atherosclerosis in healthy postmenopausal women? Psychosom Med 1998;60:633–8.
20. Friedewald WT, Levy RI, Fredrickson DS. Estimation of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502.
21. SAS Institute. SAS user's guide. Statistics, version 5 edition. Cary (NC): SAS Institute; 1985.
22. Horsten M, Wamala S, Vingerhoets A, Orth-Gomer K. Depressive symptoms, social support, and lipid profile in healthy middle-aged women. Psychosom Med 1997;59:521–8.
23. Keesey RE. A set point analysis of the regulation of body weight. In: Stunkard AJ, editor. Obesity. Philadelphia: WB Saunders; 1980. p. 144–65.
24. Jacobs DR Jr. Why is low blood cholesterol associated with risk of nonatherosclerotic disease death? Annu Rev Public Health 1993;14:95–114.
25. Verdery RB. Hypocholesterolemia, hypolipoproteinemia, and risk of death. In: Hillbrand M, Spitz RT, editors. Lipids, health, and behavior. Washington DC: American Psychological Association; 1997. p. 247–62.
26. Engelberg H. Low serum cholesterol and suicide. Lancet 1992; 339:727–9.
27. Coccaro EF, Siever LJ, Klar HM, Maurer G, Cochrane K, Cooper TB, Mohs RC, Davis KL. Serotonergic studies in patients with affective and personality disorders: correlates with suicidal and impulsive behavior. Arch Gen Psychiatry 1989;46:587–99.
28. Delgado PL, Charney DS, Price LH, Aghajanian GK, Landis H, Heninger GR. Serotonin function and the mechanism of antidepressant action. Arch Gen Psychiatry 1990;47:411–8.
29. Kahn RS, van Praag HM, Wetzler S, Asnis GM, Barr G. Serotonin and anxiety revisited. Biol Psychiatr 1988;23:189–208.
30. Banki CM. Correlation of anxiety and related symptoms with cerebrospinal fluid 5-hydroxyindoleacetic acid in depressed women. J Neural Transm 1977;41:135–43.
31. Steegmans PH, Fekkes D, Hoes AW, Bak AA, van der Does E, Grobbee DE. Low serum cholesterol concentrations and serotonin metabolism in men. BMJ 1996;312:221.
32. Virkkunen M, Penttinen H. Serum cholesterol in aggressive conduct disorder: a preliminary study. Biol Psychiatr 1984;19: 435–9.
33. Santiago JM, Dalen JE. Cholesterol and violent behavior. Arch Intern Med 1994;154:1317–21.
34. Virkkunen M. Serum cholesterol levels in homicidal offenders: a low cholesterol level is connected with a habitual violent tendency under the influence of alcohol. Neuropsychobiology 1983;10:65–9.
35. Kaplan JR, Manuck SB, Fontenot MB, Muldoon MF, Shively CA, Mann JJ. The cholesterol-serotonin hypothesis: interrelationship among dietary lipids, central serotonergic activity, and behaviors in monkeys. In: Hillbrand M, Spitz RT, editors. Lipids, health, and behavior. Washington, DC: American Psychological Association; 1996. p. 139–66.
36. Averill JR. Anger and aggression: an essay on emotion and aggression. New York: Springer-Verlag; 1982.
37. Manuck SB, Flory JD, McCaffery JM, Matthews KA, Mann JJ, Muldoon MF. Aggression, impulsivity, and central nervous system serotonergic responsivity in a nonpatient sample. Neuropsychopharmacology 1998;19:287–99.
38. Muldoon MF, Manuck SB, Matthews KA. Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. BMJ 1990;301:309–14.
39. Larosa JC. Cholesterol lowering and noncardiovascular disease. In: Hillbrand M, Spitz RT, editors. Lipids, health, and behavior. Washington DC: American Psychological Association; 1997. p. 275–92.
40. Ketterer MW, Brymer J, Rhoads K, Kraft P, Goldberg D. Lipid lowering therapy and violent death: is depression a culprit? Stress Med 1994;10:233–7.