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Associations of depressive symptoms, trait hostility, and gender with C-reactive protein and interleukin-6 response following emotion recall

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Abstract

Objective—Depressive symptoms moderate the effect of trait hostility on circulating levels of C-reactive protein (CRP) and interleukin-6 (IL-6). We extended these findings by examination of the effects of depressive symptoms and hostility on changes in CRP and IL-6 in response to an acute laboratory stressor.

Methods—The study included 307 men and 218 women, affording the opportunity to examine moderation by gender. Regression analyses were performed to examine depressive symptoms, hostility ratings, gender, and their interactions as predictors of CRP and IL-6 response to an emotion recall task. Analyses were adjusted for age, race, body mass index, and pre-recall task levels of either CRP or IL-6.

Results—The product term for depressive symptoms $\times$ hostility $\times$ gender was not significantly related to CRP nor IL-6 response. However, depressive symptoms $\times$ hostility did interact to predict CRP response ($p = .002$); those with the combination of high symptoms of depression and hostility had the largest CRP response. The depressive symptoms $\times$ gender interaction was also a predictor of both CRP ($p = .001$) and IL-6 ($p = .04$) response; for each inflammatory marker depressive symptoms were significantly associated with higher CRP response in women, as compared to men. Hostility did not moderate depressive symptoms, nor gender for IL-6.

Conclusions—Our findings extend prior research by suggesting that, broadly speaking, depression is related to inflammatory markers, however this relation appears complex. Depression seems to be related to inflammation more strongly among hostile individuals, and more strongly among women than among men.

Keywords

C-reactive protein; Interleukin-6; Anger Recall; Depressive Symptoms; Hostility; Gender

Introduction

Heightened levels of CRP and IL-6 are associated with coronary artery disease (CAD) in healthy individuals, predict the incidence of future events in CAD patients, are associated with the prevalence and severity of CAD (1–4), and predict mortality independent of traditional risk factors (5). Elevated levels of C-reactive protein (CRP) and interleukin-6 (IL-6) also predict the development of type 2 diabetes mellitus (6). Thus, CRP and IL-6 are important biomarkers of cardiovascular and metabolic disease and continued research examining their mechanistic role in pathogenesis is needed.

Both depressive symptoms and trait hostility are associated with CAD (7) and metabolic dysregulation (8), yet the mechanisms promoting these relations are not thoroughly understood. A growing number of studies have reported that both depressive symptoms and hostility are associated with increased circulating levels of CRP and IL-6 (9–12). Such evidence indicates that increased inflammation may be one of the mechanisms by which depressive symptoms and hostility confer increased risk for disease.

Depressive symptoms and hostility often co-occur. More importantly, and germane to the present study, it has been suggested that their negative health effects may potentiate one another (13). Results from the Air Force Health Study (14) indicate that when these traits co-occur there is an increased risk of coronary heart disease. Although the specific pattern of findings has been somewhat inconsistent, several recent studies have examined the potential interactive effects of depressive symptoms and hostility with respect to the prediction of increased circulating levels of CRP and/or IL-6. Two studies have now shown that significant effects of hostility on CRP and/or IL-6 are only present in those who have higher levels of depressive symptoms (9,11). However, conflicting results have been reported by Miller et al. (12), such that increased hostility was associated with IL-6, but only among those with *few* symptoms of depression. In light of the sparse and somewhat conflicting findings, additional research in this area is needed.

It is well known that the immune system responds acutely to psychological stress. Results of a recent meta-analysis (15) indicate that laboratory induced stress is associated with pre to post stress increases in circulating levels of CRP and IL-6. Increased stress responsivity has been posited as one of the pathophysiological effects of negative emotions and trait hostility (16). Thus, examination of the interactive effects of depressive symptoms and hostility with regard to stress reactive changes in circulating levels of CRP and IL-6 would complement and extend existing research in this area. As noted by Steptoe et al. (15) very few studies of inflammatory response to acute stress have examined the moderating effects of psychological factors. Furthermore, the majority of studies reviewed consisted of small samples (i.e., only one study consisted of more than 100 participants), thus few had sufficient power to provide adequate tests of interactive effects.

The present study was conducted to address some of the above noted gaps in the exiting literature that has focused on understanding the potential mechanisms linking CRP and IL-6 to disease. Results from recent studies indicate that depressive symptoms moderate the influence of hostility on circulating levels of CRP and/or IL-6 such that the effect of hostility on these markers is only present for those who have symptoms of depression (9,11). We wished to extend these findings by examining whether or not these relations apply to acute stress related changes in CRP and IL-6, in addition to their circulating levels. Because the influence of hostility and depressive symptoms on health outcomes has been frequently shown to vary by gender (e.g., 17–19), and unlike the majority of prior research in this area the present study contained a large number of both men and women, we also examined gender as an additional moderator.

Methods

Participants—Individuals between the ages of 18 to 55 were recruited to take part in the Family Heart Study. Data collection for the present paper took place from 8/2004 to 9/2008. The study was designed to identify genetic variants that interact with the environment to affect expression and clustering of psychosocial and biobehavioral characteristics (endophenotypes) that increase risk of cardiovascular disease (CVD), with a focus on the characteristic of hostility. Sibling pairs were recruited via community based ads. Individuals who reported that they were suffering from any major medical condition (e.g., cancer, heart disease, arthritis, diabetes) or psychiatric disorder (e.g., bipolar disorder, schizophrenia, memory loss) or who were pregnant, planning to become pregnant, or were breast feeding were excluded from the study. Individuals taking psychotropic medications (e.g., antidepressants, antianxiety), St. John's Wort, antihypertensive medication (with the exception of HCTZ); who used or had a history of recreational drug use were also excluded from the study. Participants who were the first family member to volunteer were screened for their level of hostility and individuals who were high or low on hostility were further recruited to participate in the study. The screening instrument used was the 27-item Cook-Medley (19,20). The cutpoints for low and high hostility levels were 9 or below and 14 or above, respectively. Next, participants were asked to contact their brother(s) and/or sister(s) who might also qualify for and be interested in the study. If they agreed, they were told they should contact us by phone and arrangements were made for them to enroll in the study. Relatives who agreed to participate were not screened regarding their level of hostility prior to their inclusion in the study. Participants who did not have a family member who qualified to take part in the study were not enrolled. The study was conducted at Duke University Medical Center, and all subjects gave informed consent prior to their participation in the study using a form approved by the Duke University Medical Center Institutional Review Board and were compensated \$275 for study completion. The study sample, comprised of individuals who were qualified to participate and completed the stress reactivity protocol, consisted of 570 individuals. The present sample is comprised of between 492 to 525 individuals who had complete data for the specific analyses of interest (i.e., CRP and/or IL-6 pre and post emotional stress and covariates). The current hypotheses do not involve genetic analyses, and our hypotheses are not concerned with sib-pair relation. The potential within sib-pair correlation, however, was accounted for in a mixed models approach using sib-pair as a clustering identifier for the random effect in all analyses.

Study Procedure—Following the phone screen, assessments were carried out over 2 days in the Duke Clinical Research Unit (CRU). On day one, qualified participants: 1) signed an informed consent and completed a psychosocial battery, including assessment of symptoms of depression and trait ratings of hostility, 2) had blood drawn for genetic testing, 3) completed a physical health screening by the study nurse, and 4) received information regarding study procedures that required participants to fast between midnight and day 2 of the study. On day 2 of the study individuals arrived at the CRU in a fasting state by 9:00 a.m., at which time an indwelling catheter was inserted. From 9:30 to 11:30 participants completed an oral glucose tolerance test (not reported here). At noon a 10-minute rest period occurred prior to the initiation of the emotion recall tasks (see below) during which time blood was drawn, via the indwelling catheter, for assessment of baseline CRP and IL-6. Blood was sampled again for assessment of CRP and IL-6 at the completion of the recall tasks approximately 1 hour later.

Emotion Recall Protocol—Per study protocol requirements no caffeine, nicotine, or alcohol was consumed for a minimum of 12 hours prior to the emotion recall task. During the protocol minute to minute blood pressure (BP) readings were gathered via a Dynamap XL 9300 (Johnson & Johnson Health Care System, Inc.). Similar to prior studies (21,22) anger and sadness recall periods lasted 5 minutes with a 10 minute rest period between. For the emotion

recall periods, participants were asked to think of an incident that made them very angry toward another person, and that still makes them angry right now when they think about it. They were then asked to visualize that experience in their mind, recalling in detail what happened. Next participants were asked to verbally recount the entire story, including how they felt at that time. For the first minute, they were asked to visualize the (anger or sadness) incident and then for the next four minutes they were asked to describe the situation. Blood pressures were taken throughout the five minute period; one during the first visualization minute and four during the telling of the episode. The same protocol was followed for the sadness task that followed, substituting the recall of an incident that made them extremely sad. Participants also completed a visual analog scale at baseline and at the completion of the recall tasks to assess change in emotional responding for related emotions (e.g., “angry” and “depressed”).

Measures

CRP and IL-6—Plasma inflammatory markers were measured by enzyme-linked immunosorbent assay (ELISA) using a commercially available kit. Cytokines were measured using ELISA *in vitro*. IL-6 kits were purchased from R and D Systems (Minneapolis, MN), and all plates were run according to manufacturer’s protocol, without exception. The mean r-squared value for all ELISA plates was 0.990. Samples were run in duplicate, and any that exceeded 20% CV between duplicates was retested with a fresh aliquot. CRP kits were purchased from Bio-Quant, Inc. (San Diego, CA), and all plates were run according to manufacturer’s protocol, without exception. The mean r-squared value for all ELISA plates was 0.990. Manufacturer’s control samples were run with each plate, CV did not exceed 20% between duplicates in any case, nor did they exceed 10% difference from the label value. Any results that exceed 10.0 mg/L were retested at a higher dilution to bring results within assay range. Values over 10.0 are real results and not extrapolated. The CRP assay was conducted under conditions of high sensitivity (hsCRP) to provide greater discrimination between atherosclerotic risk in a non-clinical population. Serum levels of CRP mg/L > 10 are likely to be reflective of an infection or trauma and therefore may not indicate cardiovascular risk (23). Extreme outliers (i.e., individuals at or above the 99th percentile) for CRP and IL-6 were removed prior to analyses, this resulted in the removal of 23 participants and no participants with CRP mg/L > 10. CRP and IL-6 were not normally distributed, thus both measures were log transformed prior to analyses.

Symptoms of Depression—Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) (24). The CES-D is a widely used 20-item self-report scale designed to measure depressive symptomatology (i.e., depressive affect, well-being, somatic complaints, and interpersonal concerns) in a general population. Items are scored on a 4-point scale (0–3), with the total score ranging between 0–60. Higher scores represent depressive responses and a score of 16 or greater is generally considered suggestive of a depressive disorder.

Trait Hostility—The 50-item Cook-Medley Hostility (HO) questionnaire (25) has been extensively used in health psychology and is generally believed to primarily reflect cynicism and mistrust (26). A rational analysis of item content (20) has led to the refinement of the full scale down to 27 items that in some studies have been a better predictor of health outcomes than the full scale (19,20). We used this abbreviated version containing three item subsets: Cynicism, Hostile Affect, and Aggressive Responding. The items are rated true or false with higher scores reflecting greater levels of trait hostility. The questionnaire has a range of 0–27.

Age, Race, Gender, and Body Mass Index (BMI)—Age was represented in years. Race was coded African American=0, Caucasian=1; gender, women=0, men=1. BMI was calculated

as weight in kilograms divided by height in meters squared. Table 1 presents sample characteristics.

Statistical Analyses

Regression analyses were conducted to examine the interaction of depressive symptoms, hostility, and gender as predictors of change in Log-CRP and Log-IL-6. Age, race, BMI, and baseline level of the inflammatory marker (either Log-CRP or Log-IL-6) were adjusted in all analyses. Initial models included a 3-way interaction term for depressive symptoms $\times$ hostility $\times$ gender, along with appropriate 2-way and main effect terms. Thus, the initial overall model for each inflammatory marker was as follows: Log-CRP (or Log-IL-6) at the end of the stress protocol was regressed on age, race, BMI, baseline Log-CRP (or baseline Log-IL-6), depressive symptoms, hostility, gender, depressive symptoms $\times$ hostility, depressive symptoms $\times$ gender, hostility $\times$ gender, depressive symptoms $\times$ hostility $\times$ gender. When nonsignificant, the 3-way interaction term was dropped from initial model and 2-way terms (for depressive symptoms $\times$ gender; and hostility $\times$ gender) were examined. Similarly, in the absence of a significant 3-way interaction, nonsignificant 2-way interactions were removed prior to examination of the final model. All analyses were carried out using SAS (Cary, NC) PROC MIXED with maximum likelihood estimation. Mixed models allowed for us to account for potential within-sib-pair correlation, using sib-pair as a clustering identifier for the random effect in all analyses.

Results

Primary Analyses

CRP—The depressive symptoms $\times$ hostility interaction was a significant predictor of Log-CRP response ($p = .002$); those with the combination of high symptoms of depression and hostility had the largest increase in Log-CRP response to acute stress. In addition, the depressive symptoms $\times$ gender interaction was a significant predictor of Log-CRP response ($p = .001$); women with higher symptoms of depression had larger increases in stress related Log-CRP response, as compared to other groups. Figure 1(a & b) graphically depicts the form of these interactions. The ΔR^2 , i.e., the variance explained by the inclusion of significant interaction terms was $= .01$. Table 2 presents the results of the final regression model for change in Log-CRP.

Of the covariates modeled, only baseline Log-CRP level was positively associated with Log-CRP response ($p = .001$). The 3-way, as well as the hostility $\times$ gender interaction, were not significant predictors of Log-CRP response ($p = .06$ and $p = .29$, respectively).

IL-6—The depressive symptoms $\times$ gender interaction was also significantly related to Log-IL-6 ($p = .04$); for women higher depressive symptoms were associated with a greater Log-IL-6 response as compared to those with lower depressive symptoms, and for men the opposite pattern was found (see Figure 2). The ΔR^2 associated with inclusion of the interaction term was $= .01$.

With regard to covariates BMI ($p = .03$) and baseline levels of IL-6 ($p = .001$) were positively associated with Log-IL-6 response, whereas age ($p = .46$) and race ($p = .91$) were unrelated to Log-IL-6. Remaining interactions examined, i.e., the 3-way ($p = .57$), hostility $\times$ gender ($p = .36$), and depressive symptoms $\times$ hostility ($p = .49$), were not related to IL-6 response.

Additional Analysis

We also examined relations among Log-CRP, Log-IL-6, hostility, and depressive symptoms. Associations between baseline levels of Log-CRP and Log-IL-6, adjusted for sibship, were

significant ($r = .24$, $p = .01$). Changes in Log-CRP and Log-IL-6 in response to acute stress, however, were unrelated ($r = .01$, $p < .98$). Hostility was positively associated with depressive symptoms, adjusted for sibship ($r = .30$, $p = .01$). Finally, in the present sample models adjusted for sibship, age, race, gender, and BMI baseline Log-CRP and Log-IL-6 were not significantly related to ratings of hostility or depressive symptoms, nor their product terms (p 's $> .10$).

Secondary Analyses

Changes in emotion from pre to post recall tasks were assessed using a Visual Analog Scale. Participants had significantly higher ($p = .001$) ratings of negative emotions (i.e., the mean for ratings of "tense, sad, upset, angry, depressed, frustrated, disgusted, agitated, irritated") from pre to post task emotion recall periods. Women had greater increases in negative emotion than men ($p = .001$). In secondary analyses we included adjustment for the mean negative emotion response (i.e., a mean of the change scores across negative emotions ratings). Change in negative emotion was significantly correlated with change in Log-CRP; those with increased negative emotional responses also had larger Log-CRP responses ($r = .11$, $p = .02$). The addition of change in emotion as a covariate in our adjusted models predicting Log-CRP response, however, did not alter either of the magnitude of the significant 2-way interactions (i.e., hostility $\times$ depressive symptoms nor gender $\times$ depressive symptoms), i.e., all p 's remained $< .01$. The change in negative emotion was not related to change in Log-IL-6 ($p > .54$), nor did the inclusion of negative emotional response in adjusted models significantly alter the relation between Log-IL-6 response and depressive symptoms for women and men, i.e., $p < .05$ was retained.

In parallel fashion to that for emotional responding, we also assessed cardiovascular reactivity (systolic and diastolic blood pressure, and heart rate: SBP, DBP, HR) from pre to post recall. During emotion recall participants had significant increases for SBP ($p = .001$), DBP ($p = .001$), and HR ($p = .001$). DBP reactivity did not vary by gender ($p > .02$), but women had significantly greater SBP ($p = .02$) and HR ($p = .001$) reactivity as compared to men. Changes in SBP, DBP, and HR were not associated with changes in Log-CRP nor Log-IL-6 (p 's $> .05$), and the inclusion of these measures of reactivity, in adjusted analyses, did not alter any of the primary analyses in any material way (i.e., each significant 2-way interaction remained so and the size of the effect remained similar).

Anger and sadness recall periods were averaged across tasks in order to reduce the number of additional analyses conducted. However, when analyses were conducted by task for anger and sadness recall separately, the type of task did not meaningfully alter the results of the mediation analyses (i.e., nothing previously significant became non-significant, nor did anything previously non-significant become significant and effect sizes remained similar).

Discussion

The present findings suggest that psychological constructs potentiate effects of acute exposure to a negative emotional stressor to cause an increase in circulating inflammatory markers for certain individuals, and in particular for women with depressive symptoms. Women in the present sample who had higher levels of depressive symptoms had larger baseline adjusted responses to the emotional stressor for both log-CRP and Log-IL-6, as compared to other groups. In addition, for women and men alike, individuals who had a combination of high ratings of hostility and depressive symptoms had increased CRP response to the stressor.

To our knowledge only two studies (28,29) have examined gender as a moderator of acute stress related changes in CRP and/or IL-6, and only one of these examined psychosocial constructs as a moderator of these potential relations (29). In a study of 20 men and 20 women, IL-6 increased from baseline to recovery during an acute stress protocol, but men showed a

peak response earlier than women (28). In a sample of 125 men and 205 women from the Whitehall II cohort Steptoe et al. (29) examined socioeconomic status (SES), along with moderation by gender, as predictors of IL-6, TNF-alpha, and interleukin-1 receptor antagonist (IL-1RA) responses to Stroop mirror tracing tasks. Although no association was found for SES, women showed greater increases in IL-6 and IL-1RA, as compared to men. In the present sample we also found, as did Steptoe et al. (29), that women had greater IL-responses. However, this appears to have been driven primarily by women who had higher depression scores, as indicated by our statistical interaction.

As previously noted, several studies have reported associations between CRP and/or IL-6 and the combination of hostility and depressive symptoms (9,11,12,30). In a recent study of 316 healthy adults it was shown that hostility was positively related to plasma levels of CRP and IL-6 only among participants with higher depressive symptoms (11). In another sample of 127 healthy individuals a composite score representing greater anger, hostility, and depressive symptoms was associated with elevated circulating levels of CRP (30). Similarly, among 90 healthy men the interaction of depressive symptoms and hostility ratings was significantly associated with circulating levels of IL-6, such that those with higher hostility ratings in combination with higher depression ratings had higher levels of IL-6, as compared to the remaining 3 groups (9). These findings, in combination with the present findings, suggest that it is important to consider how these two related emotions may work in unison to increase levels of inflammation. However, it should be noted that unlike the present study, these prior studies focused only on circulating levels of these inflammatory markers and did not include responses to acute stress, and they did not consider moderation by gender.

Our secondary analyses examining pre to post task emotional responses provide evidence for the effectiveness of the recall protocol with regard to increasing the subjective emotional experiences of anger and sadness. Additionally, participants who had rated more intense subjective responses to the negative emotional stressor had increased CRP responses to the protocol. Our findings, however, provided no support for the notion that these subjectively rated increases in negative emotions are linked to an underlying mechanism that may partially account for the present patterns of findings with regard to psychological constructs, CRP, and/or IL-6 responses from pre to post emotion recall. In this regard our findings are similar to those of another study that reported the lack of an association between pre to post changes in arousal of negative emotion and changes in IL-6 as moderated by a measure of insulin resistance (31); however, unlike the present study this sample was comprised of 58 men and no women.

Similarly, while our secondary analyses also suggest that the task resulted in significant increases in levels of SBP, DBP, and HR they offer no support for the theory that acute increases in cardiovascular responding may be responsible for acute IL-6 and/or CRP responses from pre to post emotion recall. This finding contrasts with a prior study that indicates IL-6 was positively related to heart rate, but not heart rate variability (32); however, in this previous study gender was controlled and not examined as a potential moderator of effects.

There are several plausible mechanisms that have been hypothesized to account for the association between negative emotional states (e.g., depressive symptoms and hostility) and acute increases in inflammatory responding, see (15). It is possible that acute stressful emotional reactions result in increased levels of inflammatory markers such as IL-6 via stimulation created by neuroendocrine and autonomic nervous system responding. At present animal models support this notion (33) however there are few studies that have demonstrated this process in humans (34). Since IL-6 induces production of CRP in the liver, stress might contribute to increases in CRP via its effects on IL-6 levels. Acute stress can also induce peripheral blood mononuclear cells to migrate from the marginal pool resulting in an increased number of circulating cells. Thus, the acute enlargement in the number of cells producing

inflammatory markers (e.g. IL-6), rather than increased production on a per-cell basis, may be responsible for the increase in inflammatory makers during times of stress. Another potential mechanism for stress induced increases in inflammatory responses is associated with changes in plasma volume. Acute negative emotional responding has been shown to stimulate reductions in plasma volume (35) and increase hemoconcentration (36). During times of stress plasma is forced from capillary beds into interstitial spaces. Since cytokines and CRP are unable to migrate passively through the endothelium the result is an increase in concentration in these inflammatory molecules.”

It was somewhat surprising that hostility and depressive symptoms were not related to baseline levels of CRP and IL-6 in the present sample. We are aware, however, of two prior studies that have shown that hostility and/or depressive symptoms were unrelated to baseline measures of inflammation, yet were significant predictors of inflammatory markers over a period of several years (37,38). In a sample of healthy men C3, an inflammatory protein, was not significantly related to baseline measures of hostility, depression, or anger, but each of these emotional constructs were significant predictors of increases in C3 over a 10-year follow-up period (37). Similarly, (38) in a sample of older men and women baseline measures of IL-6 were not associated with depression ratings, yet depression ratings significantly predicted 6-year change in IL-6. Thus, baseline measures of cytokines and depression/hostility were not related in the present study, yet change in cytokines and depression/hostility ratings were related; and similar lack of relation had been shown in other studies. While purely speculative, it is possible that acute stress related changes in cytokine levels provide a more sensitive measure, as compared to basal levels.

We also might have expected a significant relation between our measures of change for IL-6 and CRP, as these measures were significantly correlated at baseline. However, others have reported lack of relations among measures of IL-6 and CRP e.g. (39). One likely explanation for the lack of correlation for these measures of change is that they had a differential time course of response across the experimental protocol.

There are several limitations of this study that should be noted. The present data were collected in a healthy sample and may not generalize to the various clinical samples (e.g., multiple sclerosis and rheumatoid arthritis patients) that have been examined in this line of research e.g. (40,41). A score of 16 or above is considered indicative of clinical depression and only 13% of the present sample had scores in this range. Thus, as with comparisons to samples with physical disorders, the present results may not apply in samples of clinically depressed patients. In addition, the time period between our initial and final blood draw was approximately 1 hour. A longer or shorter time period between assessment of baseline and recovery measures of CRP and IL-6 may have yielded a different pattern of results, as suggested by prior research that reported the peak IL-6 response during an acute stressor was earlier for men as compared to women (28). Thus, it is possible that the present findings for depression may have been weaker in men because their inflammatory marker levels had substantially recovered by the posttask assessment. In addition, the emotional recall task used as a stressor in the present study differs from some of the tasks used in other studies, e.g., mental arithmetic. Thus it is possible that our pattern of findings may not generalize to less emotionally related stressors. Finally, it should be noted that, although the present sample in entirety represents the normal range of hostility, approximately half of the sample was preselected to be high or low on this construct. Therefore, while unlikely, it is possible that the selection procedure may limit the generalizability of the present findings.

The present results contribute to the literature examining the effects of acute psychological stress on circulating inflammatory markers in substantial ways. They add to the small existing literature that indicates psychosocial characteristics like depressive symptoms and hostility

interact to effect acute stress related changes in CRP and IL-6. In addition, due to our large sample size we had the opportunity to examine moderation by gender with regard to associations among depressive symptoms, hostility, and changes in inflammatory markers. We conclude that it is important to consider gender differences, as the associations of emotion-related constructs with markers of inflammation may be particularly important in women. As Steptoe et al. point out (15), at this point, the clinical relevance of acute change in inflammatory markers remains unclear. Mounting evidence, however, suggests that these markers respond significantly to acute psychological stressors and that these responses are potentiated by psychosocial characteristics. The direct causal role of CRP per se in CHD pathogenesis has recently been called into question (42); however, the causal role of inflammation in CHD has not been negated (43). Our findings indicate, therefore, that future research in this area may contribute to our understanding of the role played by inflammatory processes in mediating the relationship between psychosocial factors and cardiovascular disease.

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Abbreviations

CAD	Coronary Artery Disease
CRP	C-reactive protein
CRU	Duke Clinical Research Unit
IL-6	interleukin-6
DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
HR	Heart Rate

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a.

b.

Figure 1.

Figure 1(a). Regression results for Log-CRP response (adjusted for baseline Log-CRP, age, race, and body mass index): High and low values for depressive symptoms and hostility were based on a participant at the 25th and at the 75th percentile for the distribution.

Figure 1(b). Regression results for Log-CRP response (adjusted for baseline Log-CRP, age, race, and body mass index): High and low values for depressive symptoms were based on a participant at the 25th and at the 75th percentile for the distribution.

$p = .04$

Figure 2.

Regression results for Log-IL-6 response (adjusted for baseline Log-IL-6, age, race, and body mass index): High and low values for depressive symptoms were based on a participant at the 25th and at the 75th percentile for the distribution

Table 1

Sample Characteristics

Characteristic	Total n = 525	Women n = 307	Men n = 218
Age, mean (SD) *	30.3 (9.0)	32.0 (9.5)	28.0 (7.4)
Body Mass Index, mean (SD)	26.1 (5.5)	26.1 (5.9)	26.1 (4.9)
Race, n (%) Caucasian	356 (67.4%)	194 (62.6%)	162 (72.3%)
Gender, n (%) Women	310 (58.5%)	---	---
CES-D, mean (SD)	8.9 (7.5)	8.4 (7.5)	9.6 (7.4)
Cook-Medley Hostility, mean (SD) *	10.4 (5.1)	9.9 (4.7)	11.2 (5.3)
Baseline Serum C-reactive Protein (mg/L) *	1.97 (2.2)	2.29 (2.3)	1.55 (1.8)
Post Task Serum C-reactive Protein (mg/L) *	2.01 (2.2)	2.33 (2.4)	1.58 (1.9)
Baseline Serum interleukin-6 (pg/ml) *	1.72 (1.8)	1.90 (1.9)	1.47 (1.7)
Post Task Serum interleukin-6 (pg/ml) *	2.20 (2.5)	2.53 (2.8)	1.74 (2.0)

*
p < .05.

Table 2

Regression results for final models for Log-CRP and Log-IL-6.

Effect	Estimate	Standard Error
<u>Log-CRP post Recovery</u>		
Intercept	−0.002	0.052
BMI	0.002	0.001
Race (African American)	0.001	0.018
Age	0.001	0.001
Baseline Log-CRP	1.000	0.008
Hostility	−0.020	0.012
Depressive symptoms	−0.071	0.023
Gender (Female)	−0.060	0.025
Depressive Symptoms × Gender	0.060	0.017
Hostility × Gender	0.023	0.001
<u>Log-IL-6 post Recovery</u>		
Intercept	0.068	0.185
BMI	0.013	0.001
Race (African American)	−0.038	0.074
Age	−0.003	0.004
Baseline Log-IL-6	0.740	0.040
Hostility	−0.063	0.031
Depressive Symptoms	−0.040	0.048
Gender	0.022	0.091
Depressive Symptoms × Gender	0.127	0.060

Note: Scores for depressive symptoms and hostility were standardized 1 SD.