Negative affective responses to a speech task predict changes in interleukin (IL)-6 ☆

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ABSTRACT

Laboratory studies show that individuals differ appreciably in the magnitude of their inflammatory responses to acute psychological stress. These individual differences are poorly understood, yet may contribute to variation in stress-associated disease vulnerability. The present study examined the possibility that affective responses to acute stress contribute to these differences. For this purpose, 102 relatively-healthy community volunteers (mean age 50 years; 60% female; 91.2% white) performed an acute stress protocol and measures of affective state and serum levels of the proinflammatory cytokine, interleukin (IL)-6 were collected at the end of a 30-min resting baseline, a 5-min evaluative public speaking task, and a 30-min recovery period. Results of regression analyses, controlling for age, race, gender, menopausal status, and body mass index, revealed a positive association of task-related increases in anger and anxiety with increases in IL-6 (R^2 change = .08, p = .004; R^2 change = .08, p = .005, respectively). Further examination showed that these affective responses to the task were independent predictors of change in IL-6. Cardiovascular reactivity to the task did not explain the association. These results suggest that individuals who exhibit angry or anxious responses to acute challenge are more vulnerable to stress-related increases in markers of systemic inflammation, possibly rendering them more susceptible to inflammatory disease.

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1. Introduction

It is generally accepted that psychological stress contributes to susceptibility to immune-related disease (e.g., Black, 2003; Cohen and Hamrick, 2003; Rozanski et al., 1999; Schneiderman et al., 2008), yet not all similarly stressed individuals are equally likely to develop disease, suggesting that variability must exist either in psychological and/or biological vulnerability (Schneiderman et al., 2008). In this regard, laboratory studies show that individuals differ appreciably in the magnitude of their immune reactivity to acute stress, with some individuals exhibiting large inflammatory responses, as indexed by increases in circulating levels of inflammatory mediators, and others little or no response (Black, 2003; Cohen and Hamrick, 2003; Rozanski et al., 1999; Schneiderman et al., 2008; Steptoe et al., 2007). This interindividual variability is reproducible on retesting (Marsland et al., 1995, 2002), raising the possibility that individual differences in inflammatory reactivity to stress provide a marker of increased vulnerability to immune-related disease.

Current models of stress and disease suggest that individuals differ in their emotional reactions to environmental situations and that it is this emotional reactivity that drives physiologic responses (Holmes et al., 2006). In support of these models, negative emotional reactions to laboratory stress have been shown to co-vary with (1) larger cardiovascular (heart rate and blood pressure) responses (Feldman et al., 1999), (2) increased expression of beta2-integrins on monocytes, a marker of inflammatory activity (Greeson et al., 2009), (3) increased levels of the inflammatory marker interleukin (IL)-6 in oral fluids (Moons et al., 2010), and (4) increased stimulated production of IL-6 among male participants with higher insulin resistance (Suarez et al., 2006). Furthermore, cardiovascular reactivity and other more direct indices of sympathetic nervous system activation parallel (and predict) interindividual variability in the magnitude of many immune responses to acute stress (Manuck et al., 1991). However, to date, no studies have examined whether variability of circulating levels of inflammatory mediators in response to acute stress reflects individual differences in task-induced emotional activation, possibly as a function of emotionally-induced activation of the sympathetic nervous system (Feldman et al., 1999; Suarez et al., 1998; Suarez

and Williams, 1990). Thus, the purpose of the present study was to examine whether negative emotional responses (anger, anxiety) to a simulated public speaking task are associated with the magnitude of change in circulating levels of IL-6, and to explore whether cardiovascular responses to stress, an index of activation of the sympathetic nervous system, account for any observed associations.

2. Methods

2.1. Participants

Data for the present study were derived from the Vaccination and Immunity Project (VIP), a longitudinal study examining the association of psychosocial, physiologic and behavioral factors with antibody response to hepatitis B vaccination among a middle aged (40–60 years) community sample. Participants in the VIP project were recruited by mass mail solicitation in Allegheny County, Pennsylvania. Individuals were ineligible to participate if they smoked, had taken medications known to affect the endocrine, nervous, or immune systems in the past three months, or had a reported history or symptoms of systemic diseases known to affect these same systems. Data collection occurred over multiple laboratory sessions, and informed consent was obtained in accordance with approved protocol guidelines of the University of Pittsburgh Institutional Review Board.

For the present analyses, we used data collected at a laboratory session, which started between 7:00 and 9:00 AM, lasted approximately 1.5 h, and took place prior to the first hepatitis B vaccination on a day when the participant reported being 2 weeks free of symptoms of infection or antibiotic use. At this session, measurements of affect and peripheral IL-6 were obtained before and after participants performed a 5-min, videotaped public speaking task. The current analyses included data from 102 VIP participants (60% female; mean age = 50 years) on whom we had complete measures of affect and IL-6.

2.2. Procedures

Prior to the laboratory session, participants were asked to abstain from caffeine, beverages (other than water), and food for 12 h, from strenuous physical activity and non-prescription medications for 24 h, and from alcohol for 48 h. On arrival, participants completed a medical history interview, filled out questionnaires, and had measurements of height and weight taken. Next, an intravenous catheter was inserted into the antecubital fossa of one arm for the collection of blood samples, and an occluding cuff was placed on the other arm for automated measurement of heart rate (HR) and systolic and diastolic blood pressure (SBP and DBP; Critikon Dinamap 8100 Vital Signs Monitor, Tampa, FL). Following instrumentation, participants were seated for a 30-min resting period. Baseline recordings of blood pressure (BP) and HR were recorded every 90 s for the last 6 min of this rest period (4 readings) and 4 ml of blood was drawn for the determination of IL-6 levels. Participants then completed a measure assessing mood state across the baseline period. Following the baseline, participants performed a simulated public speaking task, consisting of 2 min of preparation for a speech defending themselves against an alleged transgression (shoplifting or traffic violation), followed by 3 min of videotaped speech delivery. We have previously demonstrated that this task elicits reproducible cardiovascular and immune responses (Marsland et al., 1995, 2002). HR and BP were measured every 90 s during speech preparation and performance, and a second 4 ml of blood was collected immediately after task completion. Following sample collection, mood was reassessed,

focusing on feelings during speech delivery. Participants then rested quietly for a 30 min period, with BP and HR recorded every 90 s during the final 6 min of this period (4 readings), a 4 ml blood sample drawn in the final minute, and mood during this period assessed.

2.3. Measures

2.3.1. Serum IL-6
Serum samples were stored at −80°C until analysis in batches. IL-6 levels were determined using a high sensitivity quantitative sandwich enzyme immunoassay kit (R & D Systems). Briefly, standards, controls and samples were added to a 96-well microplate pre-coated with monoclonal anti-IL-6 antibodies. Unbound substances were removed by washing and an enzyme linked polyclonal anti-IL-6 antibody was then added. This was followed by washing, incubation with a substrate solution and then with the amplifier solution. The intensity of the color that resulted was measured at 490 nm. The assay standard range is 0.15–10 pg/mL. IL-6 levels were extrapolated from a standard curve with linear regression from a log-linear curve. All samples were run in duplicate and the average inter- and intra- assay coefficients of variation were 7% and 5%, respectively. Natural log transformation was applied to normalize raw score distributions of the IL-6 values.

2.3.2. State affect
Affective state was assessed with a mood adjective rating scale derived from the POMS (McNair et al., 1971), with item selection based on Usala and Hertzog's (1989) factor analysis of item loading. Items assessed anxiety (e.g., tense, nervous, uneasy, on edge), anger (e.g., angry, resentful, hostile), depression (e.g., sad, unhappy, depressed), calm (e.g., relaxed, comfortable, calm, at ease), fatigue (e.g., tired, sluggish, sleepy, fatigued, worn out), vigor (e.g., lively, energetic, full of pep), and well-being (e.g., cheerful, happy, pleased). Participants rated their mood on a scale ranging from 0 (not at all) to 4 (extremely).

2.3.3. Covariates
Participant's age, gender, and race were determined through self-report. Body mass index (BMI) was calculated by dividing weight (kg) by height^2 (m^2). Menopausal status was determined through self-report of menstruation, with classification of pre-menopausal when subject reported regular, normal menstrual cycles ($n = 18$), peri- or post-menopausal when reporting either irregular or no menstrual cycle ($n = 42$).

2.4. Statistical analyses

SPSS for windows (version 17.0) was used for all analyses. First, Spearman and Pearson product–moment correlations were conducted to assess associations of covariates (age, gender, race, and BMI) with baseline IL-6. Next, to evaluate any main effects of the speech task on cardiovascular, affective, and inflammatory parameters, repeated-measures analyses of variance (ANOVAs) were conducted on each dependent variable, followed by Least Significant Difference (LSD) pairwise comparisons when indicated. For these analyses, mean HR and BP values were calculated for baseline, task, and post-task periods. When sphericity could not be assumed, Greenhouse–Geisser correction for repeated-measure ANOVA was used. Next, to test our primary hypothesis, Pearson product–moment correlations were used to assess associations of task-induced affective responses with the magnitude of concomitant cardiovascular and immune changes. For this purpose, we calculated baseline-adjusted change scores by regressing task measurements onto corresponding baselines and saving the residuals. On analysis of IL-6 responses, we focused on changes in circulating

levels of IL-6 from baseline to 30 min post-task given evidence that IL-6 responses to acute psychological challenge are delayed (Steptoe et al., 2007). We also ran a series of linear regression analyses entering covariates (age, gender, race, menopausal status, and BMI) in the first step, and baseline-to-task affective changes in the second step of a model predicting baseline-to 30 min post-task changes in IL-6. We did not adjust p values for multiple analyses.

3. Results

Participants were 102 adults (59.8% female; 91.2% Caucasian) with a mean age of 50.3 (SD = 5.1) years and BMI of 26.3 (SD = 3.8). An initial examination of associations between demographic/health characteristics, baseline affect, and baseline IL-6 revealed a significant association of IL-6 with BMI ($r = .50$, $p < .001$), but not with demographic characteristics or baseline affective states. Being female was positively associated with baseline fatigue ($r = .23$, $p = .02$) and anxiety ($r = .22$, $p = .03$), and negatively associated with baseline vigor ($r = -.23$, $p = .02$).

3.1. Effects of the speech task on mean affect, BP, HR, and IL-6

Mean values of affect, BP, HR, and IL-6 levels at baseline, task, and 30 min post-task are presented in Table 1. Repeated measures ANOVAs reveal a significant period main effect on analysis of anger ($F(1, 124) = 31.97$, $p < .001$), anxiety ($F(1, 133) = 82.23$, $p < .001$), depressive affect ($F(2, 165) = 6.04$, $p = .006$), and vigor ($F(2, 176) = 45.87$, $p < .001$), with levels increasing from baseline to task, and returning to baseline levels 30 min post-task. Decreases in fatigue ($F(2, 193) = 72.78$, $p < .001$), well-being ($F(2, 156) = 21.19$, $p < .001$), and calm ($F(2, 168) = 111.17$, $p < .001$) from baseline to task were also observed. In regard to cardiovascular parameters, significant period main effects were observed for SBP ($F(1, 135) = 193.23$, $p < .001$), DBP ($F(1, 157) = 231.69$, $p < .001$), and HR ($F(1, 129) = 109.53$, $p < .001$), with task values being significantly higher than baseline and 30 min post-task levels. Finally, there was a trend towards a period main effect on analysis of IL-6 levels ($F(1, 144) = 3.08$, $p = .066$), with pairwise comparisons revealing a significant increase in IL-6 from task to 30 min post-task ($p = .04$), but no significant change from baseline to task, or from baseline to 30 min post-task .

3.2. Factors that may contribute to variability in the magnitude of IL-6 responses to stress

Consistent with the findings of others (Steptoe et al., 2007), we observed considerable variability in the magnitude of change in IL-6 from baseline to 30 min post-task (mean change score = .04 pg/ml, SD = .32 pg/ml), suggesting that individuals vary

markedly in the magnitude of their inflammatory response to the task. To explore factors associated with this variability in IL-6 reactivity, we first examined associations of age, gender, race, and BMI with residualized changes in IL-6. Of these characteristics, only age was associated with IL-6 reactivity ($r = .21$, $p < .05$). Interestingly, age also predicted greater increases in depressive affect in response to the task ($r = .24$, $p < .05$). For women, we also examined the association of menopausal status with residualized changes in IL-6. Here, correlations revealed a significant association of greater IL-6 responses in peri-/post-menopausal women ($r = .25$, $p = .05$).

Preliminary bivariate analyses revealed expected associations of task-related increases in anger, anxiety, and depression with IL-6 reactivity ($r = .27$, $p < .01$; $r = .25$, $p < .02$; $r = .21$, $p < .05$, respectively) (See Table 2). No significant correlations were found between the other dimensions of affective reactivity and IL-6 change. As shown in Figs. 1 and 2, regression analyses showed that positive associations between angry and anxious responses to the task and IL-6 reactivity were retained after controlling for gender, age, race, BMI, and menopausal status (anger: $\beta = .29$; R^2 change = .08; $F(1, 94) = 8.91$, $p = .004$; anxiety: $\beta = .28$; R^2 change = .08; $F(1, 94) = 8.46$, $p = .005$), with a similar trend on analysis of depressive responses ($\beta = .16$; R^2 change = .024, $F(1, 93) = 2.45$, $p = .12$). In contrast, exploratory analyses revealed a tendency for calm responses to the task to be negatively associated with IL-6 responses ($\beta = -.16$; R^2 change = .024, $F(1, 93) = 2.48$, $p = .12$). No significant associations were observed between task-related changes in fatigue, vigor, or well-being and IL-6 reactivity.

In light of a significant association between the magnitude of angry and anxious responses to the task ($r = .45$, $p < .001$), we next examined whether these moods contributed independently to IL-6 reactivity. Here, we entered task-related change in anger (or anxiety) along with covariates in the first step, and change in anxiety (or anger) in the second step of a regression model predicting IL-6 reactivity. Results showed a small decrease in the association of angry responses and IL-6 reactivity with anxiety in the model (beta changed from .29 to .21), with a trend for an independent effect of anger ($p = .06$). Similarly, although including angry responses in the model reduced the anxiety effect size (beta changed from .28 to .18), there was a trend for an independent relationship between anxiety and IL-6 reactivity ($p = .08$). Overall, these analyses suggest that the association of angry and anxious responses to the speech task and IL-6 reactivity are largely independent. Indeed, entering both mood responses into the model together accounted for greater variance in IL-6 reactivity than either alone (R^2 change = .11, $F(2, 93) = 6.10$, $p = .003$).

Next, we examined whether gender moderated the association of affective reactivity with IL-6 responses to the task. Here, we entered task-related change in anger (or anxiety) along with gender, age, race, menopausal status, and BMI in the first step, and the interaction of gender with change in anger (or anxiety) in the second step of a regression model predicting IL-6 reactivity. Results showed no significant gender X anxiety interaction in the

Table 1
Mean blood pressure, heart rate, negative affect scores, and IL-6 levels at baseline, task, and 30-minute post-task intervals.

	Baseline	Task	30-min post-task
Systolic Blood Pressure (mm Hg)[a,b]	112.0 (14.0)	131.3(18.6)	114.9(14.6)
Diastolic Blood Pressure (mm Hg)[a,b]	71.1(9.3)	80.6(10.6)	71.9(8.9)
Heart Rate (bpm)[a,b]	60.3(7.4)	69.0(11.5)	60.5(8.0)
Anxiety[a,b]	1.06(1.6)	5.06(4.3)	1.46(2.0)
Anger[a,b]	.10(.5)	1.36(2.1)	.23(.7)
Depression[a,b]	.32(.9)	.64(1.1)	.35(.8)
IL-6 (pg/ml)[b]	1.22(.61)	1.20(.6)	1.26(.6)

[a] Difference significant at $p < .05$ for baseline to task.
[b] Difference significant at $p < .05$ for task to 30 min post-task.

Table 2
Correlations of baseline-to-task change in negative affect with concomitant change in cardiovascular measures and baseline-to-30-minute post-task change in serum IL-6.

	ΔIL-6	ΔHR	ΔSBP	ΔDBP
1. Δ Anxiety	.25[*]	.23[*]	.32[**]	.09
2. Δ Anger	.27[*]	−.03	.04	.04
3. Δ Depression	.21[*]	−.04	−.06	.01
4. Δ Heart rate	−.05	—	.47[**]	.23[*]
5. Δ Systolic BP	−.02	.47[**]	—	.65[**]
6. Δ Diastolic BP	−.07	.23[*]	.65[**]	—

All change scores were residuals adjusting for baseline levels.
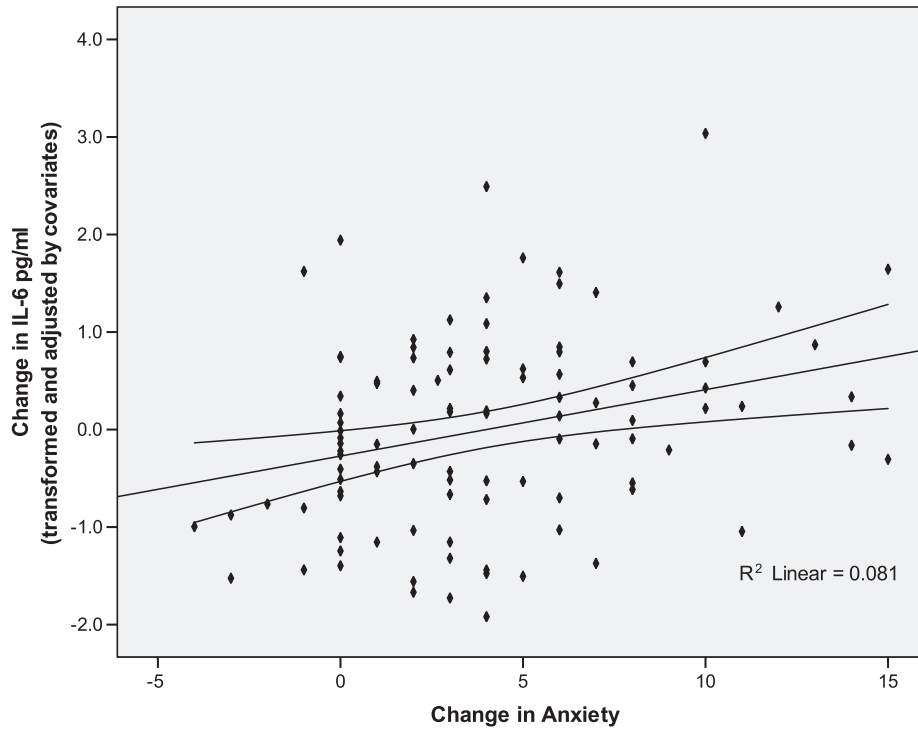[*] $p < .05$.
[**] $p < .001$.

Fig. 1. Association of anxious responses to the speech task with change in IL-6 from baseline to 30 min post-task with 95% mean prediction interval.
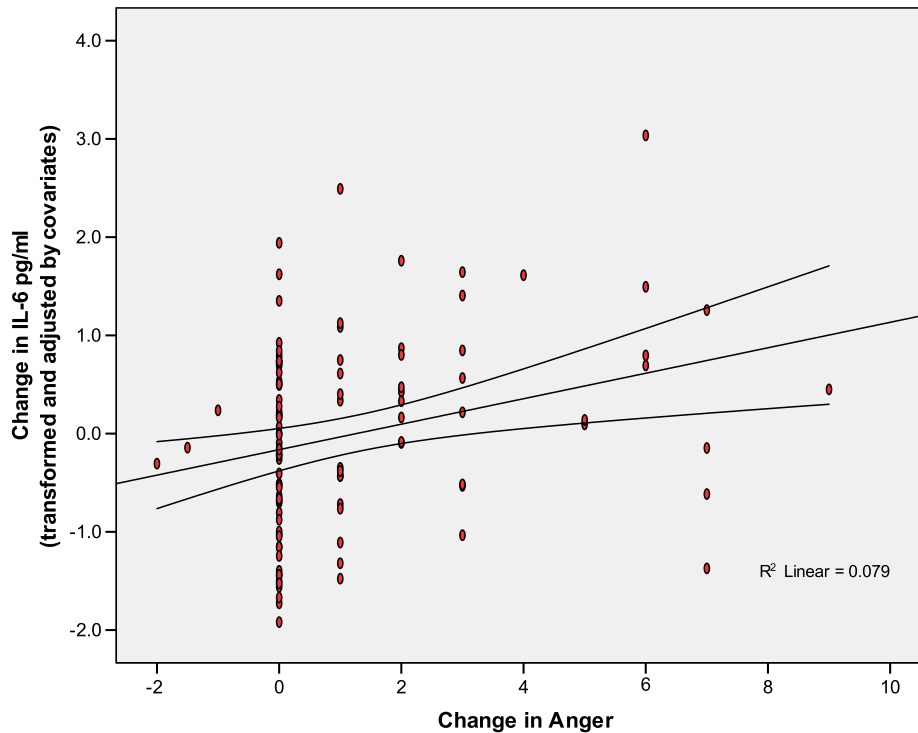

Fig. 2. Association of angry responses to the speech task with change in IL-6 from baseline to 30 min post-task with 95% mean prediction interval.

prediction of IL-6 reactivity. However, the interaction of gender with anger was marginally associated with IL-6 response (R^2 change = .028, p = .08). Further analyses broken down by gender revealed that angry responses to the task were positively associated with IL-6 reactivity for males (R^2 change = .16, p = .007), but not females (R^2 change = .02, p = .30).

3.3. Cardiovascular reactivity

Finally, we examined whether cardiovascular responses to the task accounted for the variance in IL-6 reactivity associated with affective responses. After adjusting for covariates, anxious responses to the speech task were significantly associated with

baseline-to-task increases in SBP ($r = .30$, $p = .003$) and HR reactivity ($r = .23$, $p = .03$), but not DBP. In contrast, there were no associations between anger and cardiovascular responses to the task. Moreover, cardiovascular responses were unrelated to IL-6 reactivity and entering SBP or HR reactivity into the regression model did not alter the magnitude of the association between anxious responses and IL-6 reactivity.

4. Discussion

Consistent with the findings of others, we observed widespread individual differences in the magnitude of change in circulating levels of IL-6 in response to acute psychological stress. The primary goal of the current study was to examine whether task-induced affective states contributed to this variability in inflammatory response. In our sample of relatively healthy, mid-life adults, angry and anxious responses to a simulated public speaking task were associated positively with changes in circulating levels of IL-6, as measured 30 min following the task. These associations were independent of age, race, BMI, menopausal status for women, and baseline levels of IL-6. In regard to gender, anxious reactions predicted increases in IL-6 for males and females; however, associations of task-induced anger with IL-6 were observed primarily among males. In sum, our findings provide initial evidence that affective responses to acute psychological stress contribute to heightened inflammatory responses. These findings are consistent with recent evidence that negative affective states result in activation of innate inflammatory pathways. For example, negative affective responses to an anger recall interview (ARI) are associated with increased beta2-integrin expression (Greeson et al., 2009) and monocyte-stimulated proinflammatory cytokine production among insulin resistant men (Suarez et al., 2006). Similarly, negative affective responses to the Trier Social Stress Test (TSST) have been positively associated with magnitude of inflammatory response, with perceived stress predicting increases in circulating levels of IL-1β (Yamakawa et al., 2009) and fear predicting increases in IL-6 in oral fluids (Moons et al., 2010). In contrast to the current findings, Moons et al. (2010) did not observe an association of anger in response to the TSST and inflammatory markers in oral fluids. Reasons for these discrepant findings are unclear, but may relate to the examination of oral versus circulating inflammatory markers or be a function of the timing of the assessment of affective state, with measures being taken immediately following the task in the current study and 30 min after the task in the Moons et al. (2010) study.

Interestingly, although we observed that angry and anxious responses to the speech task covaried, the positive associations of these activated negative emotions with inflammatory responses following acute challenge were largely independent. Stress-induced increases in depression and fatigue, which represent less physiologically activating negative moods than anxiety and anger, were not significantly associated with IL-6 reactivity after adjusting for covariates. Changes in positive affect (i.e., calm, vigor, and well-being) were also unrelated to the magnitude of IL-6 responses. These findings raise the possibility that activated negative emotional states contribute to the increase in circulating levels of IL-6 that follows acute psychological challenge. However, it is also possible that our failure to find more significant associations of depression, calm, vigor, fatigue, and well-being with IL-6 reflects the relatively small task-related changes in these affective states, when compared with anxiety and anger, limiting our ability to detect relationships.

Although there is growing evidence that circulating levels of IL-6 typically increase following acute psychological stress (see Steptoe et al., 2007 for review), mean effect sizes are modest (Steptoe et al., 2007), with a number of studies finding no significant IL-6 response to laboratory stress (e.g., Miller et al., 2005; Lutgendorf et al., 2004). The current findings are generally consistent with this literature and show a trend toward a mean increase in IL-6 from pre- to 30 min post-task. Our findings extend this literature by providing the first evidence to show that individual differences in affective response to the task are associated with the magnitude of this inflammatory response in healthy mid-life adults. We also provide initial evidence to suggest that there may be gender differences in the impact of acute affective states on systemic inflammation, with both sexes showing similar inflammatory responses to anxiety, but males showing greater responses to anger than females. Thus, inconsistencies across studies may reflect gender differences and/or heterogeneity of affective responses, with results varying as a function of the type or intensity of emotions induced by the laboratory task. It is also likely that neurological (Slavich et al., 2010) or genetic (Cole et al., 2010) vulnerabilities contribute to individual differences in affective and/or inflammatory responses. The clinical significance of the increases in systemic inflammation that follow acute laboratory challenge remains to be determined. In this regard, Brydon and Steptoe (2005) showed a positive association of magnitude of IL-6 response to acute laboratory stress with increases in blood pressure over a 3 year follow-up period; an effect that was independent of initial blood pressure, baseline IL-6, age, BMI, gender and smoking status. This raises the possibility that individuals prone to stress-induced increases in inflammation, possibly by virtue of their affective responses to environmental challenges, may be at greater risk for cardiovascular disease.

Several potential mechanisms may underlie associations of activated negative emotions and inflammatory responses to acute stress. Based on existing literature, we expected that negative emotional states would activate the sympathetic division of the autonomic nervous system, resulting in increases in circulating levels of IL-6 as the consequence of (1) activation of peripheral blood mononuclear cells (Bierhaus et al., 2003), (2) the release of IL-6 from adipocytes (Burysek and Houstek, 1997), and (3) procoagulant/proinflammatory responses elicited from damaged vascular walls under sheer stress (Moshage, 1997; Thrall et al., 2007; von Känel et al., 2001). However, in contrast to the findings of others (Owen and Steptoe, 2003), our analyses did not provide clear evidence for an association of cardiovascular responses to the stress task, an indirect measure of autonomic activity, with the magnitude of inflammatory response. Although anxious responses to the speech stressor were associated with concomitant increases in SBP and HR, this cardiovascular reactivity did not account for variability in IL-6 response associated with anxious mood. Moreover, there was no association of task-induced anger with cardiovascular reactivity in the current sample. Thus, our findings do not provide evidence that activation of the sympathetic nervous system drives the increase in peripheral inflammation associated with activated negative mood states. That said, measures of HR and BP provide an indirect measure of sympathetic activation, and it remains possible that a more direct measure of autonomic activation, such as circulating catecholamine levels, could yield a different pattern of results.

Given that stress-related increases in markers of peripheral inflammation are typically not detected until at least 30 min following the stressor, it is also possible that the kinetics of the autonomic response to stress are more influential than the peak stress response. For example, individuals who take longer to recover to baseline levels after a task may be at greater risk for inflammatory responses. In support of this possibility, delayed blood pressure recovery following acute stress has been positively associated with the magnitude of inflammatory response (Steptoe and Marmot, 2006). This delay in blood pressure recovery may be the result of

prolonged sympathetic activity, decreased parasympathetic activity, or greater peripheral damage as a consequence of prolonged blood pressure. In regard to the parasympathetic division of the autonomic nervous system, lower heart rate variability, an indirect measure of parasympathetic (vagal) control over variations in heart rate, accompanies both negative emotional states (Brosschot and Thayer, 1998; Friedman and Thayer, 1998) and inflammation (Frasure-Smith et al., 2009; Marsland et al., 2007). Thus, it is possible that stress-induced decreases in parasympathetic activation may contribute to associations of negative emotional states with markers of inflammation. Finally, activation of the hypothalamic-pituitary adrenal (HPA) axis may also play a role, as cortisol shows a delayed response to acute psychological stress that parallels the timing of the inflammatory response. In this regard, it has been proposed that individuals who are emotionally sensitive to psychological stressors may exhibit blunted cortisol responses to stress and thus increased activation of inflammatory processes (Burke et al., 2005).

Several limitations of the current research should be noted. First, the sample was healthy, nonsmoking, and free of medications affecting immune, nervous, and endocrine systems; thus, results may not generalize to clinical or at-risk samples. Second, analyses were based on affect and IL-6 reactivity from only one laboratory session – repeated assessments across time and situations would provide a more reliable measure of individual differences. In addition, our protocol did not include assessment of changes in IL-6 later than 30 min after the task. Given that increased inflammatory activity has been observed up to 2 h after acute stress, future work would benefit from exploring whether affective response predicts more sustained elevations in IL-6 (Steptoe et al., 2007). Finally, although relatively small increases in circulating markers of inflammation (i.e. CRP, IL-6) have been shown to predict increased disease risk (Libby and Ridker, 2004; Libby et al., 2002; Ward et al., 2009), the clinical significance of the small, transient, stress-induced increase in IL-6 remains to be determined.

In conclusion, the present findings suggest that individual differences in affective responses to a mildly stressful speaking task are associated with the magnitude of change in circulating IL-6 levels, a marker of systemic inflammatory activity. Gender may play a role in this relationship, with males showing greater inflammatory responses to acute anger than females, but both genders showing similar inflammatory responses to anxiety. Otherwise, positive associations of negative affective states with IL-6 were independent of demographic characteristics and cardiovascular reactivity. These results suggest that activated negative affect in response to acute stress is associated with stress-related increases in inflammation. Long-term or repeat activation of inflammatory pathways as a consequence of heightened negative affective responses to stressful situations in daily life may contribute to risk for inflammatory diseases.

Conflict of interest

All authors declare that there are no conflicts of interest.

Acknowledgment

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