Anxiety, Not Anger, Induces Inflammatory Activity: An Avoidance/Approach Model of Immune System Activation

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Psychological stressors reliably trigger systemic inflammatory activity as indexed by levels of proinflammatory cytokines. This experiment demonstrates that one’s specific emotional reaction to a stressor may be a significant determinant of whether an inflammatory reaction occurs in response to that stressor. Based on extant correlational evidence and theory, a causal approach was used to determine whether an avoidant emotion (anxiety) triggers more inflammatory activity than an approach emotion (anger). In an experimental design ($N = 40$), a 3-way Emotion Condition $\times$ Time $\times$ Analyte interaction revealed that a writing-based anxiety induction, but not a writing-based anger induction, increased mean levels of interferon-$\gamma$ (IFN-$\gamma$) and interleukin-1$\beta$ (IL-1$\beta$), but not interleukin-6 (IL-6) in oral mucous, $F(2, 54) = 4.64, p = .01, \eta^2_p = .15$. Further, self-reported state anxiety predicted elevated levels of proinflammatory cytokines, all $\Delta R^2 > .06$, $p < .04$, but self-reported state anger did not. These results constitute the first evidence to our knowledge that specific negative emotions can differentially cause inflammatory activity and support a theoretical model explaining these effects based on the avoidance or approach motivations associated with emotions.

Keywords: anxiety, anger, avoidance and approach motivation, inflammation

When confronted with an environmental stressor, people can react in different ways. Frustrating romantic partners, unexpected physical confrontations, or overwhelming work demands cause a variety of responses. Sometimes people cower in desperation, but sometimes they lash out in retaliation. Prior work has uncovered that such disparate emotional responses may relate differently to the immune system’s inflammatory response (Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004; Moons, Eisenberger, & Taylor, 2010). For example, the specific emotions of shame and fear have been explicitly linked to inflammatory responses (Dickerson et al., 2004; Moons et al., 2010). However, it is still unclear whether different emotions in fact differentially induce inflammatory activity. The current work tests whether anxiety causes a stronger inflammatory response than anger as reflected in proinflammatory cytokines.

Proinflammatory cytokines are immune system proteins that help initiate and coordinate inflammatory processes (Elenkov, Iezzoni, Daly, Harris, & Chrousos, 2005; Hanada & Yoshimura, 2002). Therefore, assessing mean levels of these cytokines provides an effective way of gauging the degree of inflammatory activity within an organism (e.g., Ohzato et al., 1992). In addition, proinflammatory cytokines are increased by both physical and psychological stress (Segerstrom & Miller, 2004), presumably because inflammatory responses proved adaptive for dealing with psychological stressors (see Maier & Watkins, 1998). For example, during interpersonal confrontations the potential for aggression can be a significant psychological stressor. Inflammatory response in the early stages, even before injury occurs, can facilitate healing of subsequent injury (Dhabhar, 2002). Thus, psychological activation of an inflammatory response can give an organism a jump-start on healing thereby potentially increasing survival.

Psychological processes can thus trigger inflammation, but proinflammatory cytokines can in turn significantly change behavior by inducing a set of “sickness behaviors” (Dantzer, O’Connor, Freund, Johnson, & Kelley, 2008). Reduced drinking and eating, reduced exploration, and increased social withdrawal are some of the classic behaviors caused by inflammation (Dantzer & Kelley, 1989). Many of these behaviors encourage the organism to limit energy expenditure and, consequently, enhance the resources available for healing or fighting infection (Maier & Watkins, 1998). However, social withdrawal may be advantageous in other ways. Even in the absence of infection, withdrawal behavior may benefit an organism facing a perceived stressor. For example, avoidance of unmanageable threats like predators, natural disasters, or aggressive conspecifics may on average enhance survival. Thus, the behavioral changes caused by inflammation could be advantageous for avoiding environmental stressors and associated injury.

Consistently triggering an inflammatory response to every situational stressor would be a costly enterprise. Not every stressful situation is accompanied by perceptions of potential injury and, relatedly, not every stressful situation warrants withdrawal. Specific emotions may offer a more precise way to activate inflam-
Emotions involve cognitive, behavioral, and physiological changes, which makes them excellent candidates for regulating stress responses across multiple systems. Specific emotions can also concisely describe the perceived nature of a given situation; anxiety-inducing situations are typically perceived in a very different way than angering situations.

Emotions and affective states exist on at least three orthogonal dimensions: valence, arousal, and motivational state (e.g., Kassam, Markey, Cherkassky, Loewenstein, & Just, 2013). Valence represents the positivity or negativity of the feeling, while arousal conveys the physiological activation or lack thereof coincident with the feeling. Motivational state refers to the tendency to either approach or avoid a given stimulus, goal, or aspect of the environment. Because these dimensions are orthogonal to one another, it is thus possible to distinguish between two broad classes of emotions based on their underlying motivational state: approach or avoidance.

Based on recent affective neuroscience work, Moons and colleagues (2010) proposed that emotions that are primarily avoidance-oriented may be particularly likely to trigger inflammatory activity compared with emotions that are primarily approach-oriented. Avoidance emotions like fear or anxiety can arise when people are uncertain and feel that they lack control (Lazarus, 1991; Smith & Ellsworth, 1985). Indeed, experiences of avoidance emotions like fear or anxiety are associated with perceptions of greater personal risk, the risk of potential injury, when compared with approach emotions like anger (Lerner & Keltner, 2001; Study 2). Thus, avoidance emotions like fear and anxiety signal that a situation is perilous, personal harm may be more likely, and healing may therefore be necessary. In such cases, people engage in withdrawal behavior induced by emotional states while their immune systems may adaptively and preemptively ready them to cope with potential injuries or infections (Dhabhar, 2002), given the increased likelihood of injury following avoidance emotions. It is also likely that this relationship is bidirectional; that is, inflammatory activity may produce avoidance-motivated states (Dantzer et al., 2008). Indeed, both avoidance motivation and inflammatory activity seem to share similar neural underpinnings, as evidenced by similar electroencephalogram (EEG) alpha-wave asymmetry (Master et al., 2009; Shields & Moons, 2015). As a consequence, the avoidance emotion of anxiety may increase inflammatory activity, facilitate subsequent physical healing, and increase motivation to avoid threats (Dantzer et al., 2008; Dhabhar, 2002).

In contrast, similarly negative and high-arousal approach emotions like anger arise when people feel certain and relatively in control of a situation (Lazarus, 1991; Smith & Ellsworth, 1985). Instead of avoiding the stressor, people who feel angry are motivated to approach and perhaps inflict harm or seek retribution (Carver & Harmon-Jones, 2009; Harmon-Jones & Allen, 1998; Harmon-Jones & Sigelman, 2001). Indeed, people feeling angry perceive relatively little risk (Lerner & Keltner, 2001). Although individuals who feel angry can also be injured in subsequent confrontations, the perceived personal risk of such injury is likely lower than for people who feel anxious and vulnerable. Assuming that, on average, people accurately assess their resources in relation to the demands of a situation, then people may suffer less harm in situations in which they feel angry than in situations in which they feel anxious. Demonstrating that the avoidance emotion of anxiety elicits a stronger inflammatory response than the approach emotion of anger would be consistent with this line of thought.

While previous literature has found associations between avoidance-motivated emotions such as fear and shame and increases in proinflammatory cytokines without finding similar associations between approach-motivated emotions and increases in cytokines (Dickerson et al., 2004; Moons et al., 2010), there are some discrepancies in the literature. In particular, some studies have indicated that anger may also induce an inflammatory state (e.g., Carroll et al., 2011; Puterman et al., 2014). These discrepancies, however, can be explained by differences in data analytic strategy. In particular, studies that found relationships between anger and induced inflammatory activity did not fully control for baseline anger (Carroll et al., 2011; Puterman et al., 2014), leaving changes in inflammatory activity to be driven by changes in affect without accounting for the variance that baseline affect explains in inflammatory markers. Thus, these methodological differences taken into consideration, previous literature tentatively suggests that acute increases in avoidance-motivated emotions increase inflammatory activity, while acute increases in approach-motivated emotions are less likely to do so.

**Present Research**

The current experiment specifically tested whether induced anxiety would cause a greater inflammatory response than induced anger. As such, this article contains three central hypotheses: (1) The anxiety and the anger induction will produce stress-related physiological arousal as measured by cardiovascular indices, but the level of arousal will not differ between emotions, given that both of these emotions are high-arousal and negatively valenced; (2) An experimental manipulation inducing anxiety will produce a significant inflammatory response, while the manipulation inducing anger will not; and (3) Individual differences in increased self-reported anxiety, but not increased self-reported anger, will significantly predict an inflammatory response.

**Method**

**Pilot Study**

Prior to the primary experiment discussed herein, a pilot study was conducted to confirm the validity of a commonly used guided writing emotion induction (e.g., Moons & Mackie, 2007; Strack, Schwarz, & Gschneidinger, 1985). In this task, undergraduates at the University of California, Davis, vividly described an unresolved situation that made them either very anxious or very angry in a 10-min essay. Subjects who reported anxiety and anger before and after the manipulation showed the expected pattern, \( F(1, 51) = 14.37, p < .001, \eta^2_p = .22 \). Reported anxiety increased from baseline in the anxiety condition (\( M_{pre} = 2.44, M_{post} = 3.14, t(51) = 2.47, p = .02, \eta^2_p = .11 \), but not in the anger condition (\( M_{pre} = 2.91, M_{post} = 2.82, t < 1 \). Conversely, reported anger increased in the anger condition (\( M_{pre} = 1.88, M_{post} = 3.48, t(51) = 5.12, p < .001, \eta^2_p = .34 \), but not in the

1 Data from one participant was excluded because they had accidentally participated previously.
anxiety condition \( (M_{pre} = 2.18, M_{post} = 2.72), t(51) = 1.63, p = .11 \). Therefore, this pilot study illustrates that the anxiety and anger inductions are effective in accomplishing their intended goals—that is, these inductions reliably induce the expected emotions.

**Participants and Design**

Sample size for the current study was determined a priori by a power analysis using G*Power 3.1 (Faul, Erdfelder, Buchner, & Lang, 2009). In particular, detecting a between-within analysis of variance (ANOVA) interaction effect of \( \eta_p^2 = .05 \) (the effect size of poststressor fear predicting IL-6 in a prior study; Moons et al., 2010) with two groups and two timepoints (a difference between the emotion induction conditions in cytokine changes over time) at 80% power requires a total sample size of 40 participants—20 per group. Thus, although the sample size used in this study was small, it was determined a priori by statistical methods and was nearly identical to other studies that have successfully investigated similar effects (e.g., Pruessner et al., 2013).

There were no interim analyses conducted, and data collection was stopped once 40 participants had completed the study. Thus, 40 healthy, nonsmoking undergraduate students (19 women, 21 men) from the University of California, Davis, participated in exchange for partial course credit during the fall quarter of 2011. The average age of the sample was 19 (range = 18–36). The sample was racially diverse with 48.7% Asian, 2.6% Black or African American, 17.9% Hispanic, and 30.8% White self-identified participants. Participants with the following conditions were excluded: mental or physical health problems; use of medications affecting cardiovascular, endocrine, or immune function; current treatment from a mental health professional; current use of tobacco, drugs, and engaging in strenuous activity for 2 hr prior to their session start time, and refrain from taking medication on the day of their experimental session. Upon entering the lab, participants confirmed their compliance with these instructions, provided informed consent, and were then randomly assigned to the anxiety (9 women; 11 men) or anger condition (10 women; 10 men). Research assistants that in any way came into contact with study participants were blind to study hypotheses. All procedures were approved by the institutional review board at the University of California, Davis.

**Procedure**

Participants reported to the laboratory at either 12:30 or 3:30 in the afternoon for 2-hr experiment sessions. Participants completed health questionnaires used in previous research (Moons et al., 2010; Taylor et al., 2010) to confirm eligibility and assess their health-related behaviors. Specifically, participants reported the number of servings of caffeinated and alcoholic beverages they consumed in the past 7 days on average to assess habitual caffeine and alcohol intake that can affect the accuracy of assays (Crews et al., 2006; O’Connor & Irwin, 2010; Ohta, Lukashev, Jackson, Fredholm, & Sitkovsky, 2007). Because adipose tissue contributes strongly to levels of cytokines (Mohamed-Ali et al., 1997; O’Connor et al., 2009), participants also reported their height and weight from which a body mass index (BMI) was calculated. Because sleep and diurnal variations in the endocrine and immune systems can impact proinflammatory cytokine levels (Petrovsky, McNair, & Harrison, 1998; Vgontzas et al., 2005), participants also reported whether they napped before their session. Five participants—two in the anger-induction condition and three in the anxiety-induction condition—indicated that they napped. Analysis revealed that these participants’ inflammatory markers significantly differed from those of the other participants, \( p = .055 \). Thus, these participants were excluded from all analyses examining proinflammatory cytokines.

To assess autonomic arousal and sympathetic nervous activity (SNS) activity, electrocardiograph (ECG) and impedance cardiograph (ZKG) signals were recorded continuously with a Biopac Systems Inc (Goleta, CA). MP150 unit, using a standard lead II electrode configuration for electrocardiogram (ECG) and a tetrapolar aluminum-mylar tape electrode system (for ZKG). Blood pressure was continuously recorded using an automated continuous noninvasive arterial pressure (CNAP) blood pressure device that obtained readings via cuffs placed around participants’ non-dominant upper arm and fingers. The ECG and ZKG signals were scored using Biopac’s Acqknowledge 4.1.1 (Biopac Systems Inc.) program, which produced ensemble-averaged values for 1-min epochs. Both conditions were expected to result in increased physiological arousal as reflected by increased heart rate (HR) and mean arterial pressure (MAP), and in increased activation of the SNS as reflected by decreased pre-ejection period (PEP), a well-validated measure of SNS activation (Sherwood et al., 1990). Parasympathetic nervous system (PNS) activity was assessed via high-frequency heart rate variability (HF HRV), a relatively pure measure of PNS activity (Berntson et al., 1997). Equivalent cardiovascular reactivity and recovery can help establish that differences in cytokine reactivity are not because of pure differences in arousal—leaving anger and anxiety to differ primarily in approach or avoidance.

Standard protocols for manually identifying each epoch’s Q points and B points on the ECG and dZ/dt waveforms, respectively, were used to gauge PEP values (Berntson et al., 1997; Berntson, Quigley, & Lozano, 2007). Heart rate and heart rate variability were derived from the continuous ECG signals. HF HRV was derived from the R to R peak interval variations for each epoch using the Acqknowledge program, which uses the Welch periodogram and least squares detrending methods. After sensors were equipped, participants completed personality questionnaires unrelated to the current study for 15 min to allow all participants to acclimate to the environment and equipment. The average of the last 2 min of this acclimation period was used to establish baseline HR, MAP, PEP, and HF HRV.

Participants then provided baseline oral mucosal transudate (OMT) samples, which can be used to assess markers of immune system activation (Nishanian, Aziz, Chung, Detels, & Fahey, 1998). An OnSure Oral Specimen Collection Device (Bethlehem, PA) was used. An absorbent pad was placed between the lower cheek and gum for 2 min to obtain OMT samples. Following the general format of the Positive and Negative Affective Schedule (Watson, Clark, & Tellegen, 1988), participants then used 7-point scales anchored by 1 (not at

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2 The timing of the session had no significant main effect or interactions with condition.
all) and 7 (very much) to report their emotions. Embedded among other questions, baseline reports of anxiety (anxious, worried), \( r = .53 \), and anger (angry, hostile), \( r = .37 \), were provided by participants in this questionnaire (cf. Moons et al., 2010).3

Participants then completed the pilot-tested emotion induction. Participants were prompted to write with the following instructions, “Please write an essay in the space provided below. Please remember, relive, and vividly recall a negative event that makes you feel extremely [anxious/angry]. Choose an event that has not been resolved and is still a source of [worry/frustration] for you. Please give as much detail as necessary to vividly describe the situation and try to describe your feelings. You will have 10 minutes to complete this task. You must write for the full 10 minutes. The study will automatically continue when the 10 minutes is over. Please begin.” Participants thus wrote for 10 min about either an unresolved anxiety-inducing situation or angering situation.4 Cardiovascular activity was monitored continuously during the 10-min induction. After this period, participants completed postinduction reports of anxiety, \( r = .46 \), and anger, \( r = .78 \), embedded among other items using the same scale that they used preinduction. Cardiovascular activity was also monitored during the 5 min following the emotion induction to examine cardiovascular recovery. Participants wrote an essay about their future plans during recovery to ensure that observed cardiovascular changes during the induction were not because of the action of writing an essay rather than to the emotion content of the essay. Exactly 20 min after the end of the emotion induction essay period, participants provided postinduction OMT samples. This timepoint for postinduction OMT samples (30 min after beginning the emotion induction essay) was chosen following Dickerson et al. (2004), who found significant differences in OMT cytokine activity 30 min after beginning a self-blame essay in three different study sessions. Participants were then debriefed, thanked, and dismissed.

Cytokine Assays

Inflammatory activity was assessed by examining baseline and postemission induction levels of three proinflammatory cytokines that have been typically sensitive to acute stress manipulations (Segerstrom & Miller, 2004; Steptoe, Hamer, & Chida, 2007): interferon-γ (IFN-γ), interleukin-1β (IL-1β), and interleukin-6 (IL-6). IFN-γ exerts a direct proinflammatory effect and drives the activity of other proinflammatory cytokines (Dinarello, 2000). IL-1β has been strongly linked to sickness behaviors in both experimental animal models and supportive work in humans (Dantzer, 2001; Watkins & Maier, 2002). IL-6 is a commonly examined marker of systemic inflammation that also relates to psychological variables. For example, Moons et al. (2010) examined OMT samples, a technique used by several labs (e.g., Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004; Goodin et al., 2012; Slavich, Way, Eisenberger, & Taylor, 2010), and uncovered a significant positive association between IL-6 and self-reported levels of fear. The current experiment allowed for a similar test of IL-6—along with IL-1β and IFN-γ—and self-reported anxiety, a different avoidance emotion.

Immediately after collection of OMT samples, the absorbent pad was stored in a stabilizing buffer and kept frozen until the fluid and buffer were extracted by centrifugation at the time of testing. All samples were assayed in duplicate at the Pathogen Detection Core Laboratory of the California National Primate Research Center. Commercially available reagents were used according to the manufacturer’s instructions. Protein concentrations for each oral fluid sample were determined using the Bio-Rad Protein Assay (Hercules, CA), which is a Bradford-based method assay using Coomassie Brilliant Blue G-250. Human IFN-γ, IL-1β, and IL-6 levels in the oral fluid samples were measured using quantitative Lumiplex multiplex bead reagents from Life Technologies (Carlsbad, CA). This multiplexed micro bead immunoassay uses specific antibody pairs to capture and detect each cytokine and is quantitated by a Biotin-Streptavidin-RPE fluorescence signal. Using results from the protein and cytokine assays, pg/ml concentrations for each analyte in each sample were calculated. Following Dickerson and colleagues (2004), all analyses were conducted on the ratio of the inflammatory analyte value to the total protein concentration in the sample to account for flow-rate and attain a more reliable estimate of inflammatory marker levels. 12.5% of IFN-γ samples fell below the limit of detection (.07), leaving four participants in the anger-induction condition and two participants in the anxiety-induction condition with missing IFN-γ values. Similarly, 5% of IL-6 samples fell below the limit of detection (.05), leaving two participants in the anger-induction condition and one participant in the anxiety-induction condition with missing values. Intrassay CV for IFN-γ, IL-1β, and IL-6 were 6.04%, 23.6%, and 21.68%, respectively. Interassay CV for IFN-γ, IL-1β, and IL-6 were 3.77%, 5.99%, and 2.82%, respectively.

Data Reduction and Analytic Strategy

Missing values were handled through listwise deletion in respective analyses.5 Of the 35 participants who did not nap (and were retained in cytokine analyses), four participants in the anger induction condition and two participants in the anxiety induction condition had missing cytokine data. A computer error for one participant in the anger induction condition caused the loss of that participant’s pre- and postinduction emotion self-reports (this par-

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3 Two participants had outlying values (scores greater than 3 SDs in absolute value from the mean) for self-reported anger at Time 1—there were no outliers on either of the self-reports at Time 2. Aside from improving the correlation between self-reported anger and hostility at time one, \( r = .51 \), excluding these outliers did not influence the results. Excluding these scores from analyses regressing postinduction cytokines on self-reported emotions did not alter the results.

4 Essay character length, \( t(38) = 0.91, p = .37, d = 0.30 \), and word count, \( t(38) = 1.00, p = .32, d = 0.32 \), did not differ between conditions. Essays in both conditions described mostly social problems or conflict. Two blind coders assessed essay content, including participants’ references to themselves, other people, level of perceived social evaluation, and general level of negativity. No condition differences emerged except that anxious essays referenced others more than anger essays, \( p = .04 \). Including this variable as a covariate in the described ANOVA examining cytokines strengthened the overall pattern; it made the emotion condition effect on IL-1β significant rather than marginal.

5 Analyses handling missing values using iterative robust model-based imputation (Templ, Kowarik, & Filzmoser, 2011) instead of listwise deletion produced identical results, with two exceptions. First, the change in IL-1β between pre- and postinduction for the anxiety induction condition became significant rather than marginal, \( p = .04 \). Second, the effect of self-reported postinduction anger on IL-6 became significant—rather than marginal, as it is in the reported analyses—indicating that increases in anger reduced levels of IL-6, \( \beta = -.40, p = .003 \).
ticipant did not have missing cytokine data), leaving 39 individuals with complete pre- and postinduction emotion self-report data. Because data absence varied by cytokine, not all analyses had the same number of observations—sample size in each analysis can be inferred from the respective degrees of freedom, considering covariates. Figure 1 provides an illustration of missing data.

We chose an a priori basis to control for habitual caffeine intake, BMI, and habitual alcohol use in analyses that included covariates. Controlling for participant race/ethnicity, habitual nicotine use (only one participant in our sample infrequently smoked cigarettes; none regularly smoked), and habitual exercise frequency did not alter any of the reported results. All cytokine values were log-transformed before analysis to normalize distributions.

Results

Data absence did not significantly alter random assignment, χ²(1) = 0.46, p = .50. Groups did not differ on baseline affective (ps > .64), cardiovascular (ps > .25), or inflammatory markers (ps > .79), nor did the groups differ on any covariate (ps > .38), all ps uncorrected. Table 1 displays means and SEs for each of the baseline measures and covariates by group. Table 2 displays zero-order correlations among baseline and postinduction cytokine levels and emotion reports.

Manipulation Check

To examine whether the emotion inductions were both and equivalently related to autonomic arousal and reactivity, a 2 (Emotion Condition: anxiety or anger) × 2 (Time: baseline, postinduction) × 2 (Emotion Self-Report: anxiety or anger) mixed-model ANOVA was conducted. The hypothesized three-way interaction was significant, F(1, 37) = 4.80, p = .04, η²p = .12, indicating that the self-reported emotions differentially changed over time by condition. Planned contrasts illustrated the expected pattern driving this three-way interaction: These differences were because of a significant difference between conditions on postinduction anger and anxiety, F(1, 37) = 4.49, p = .04, η²p = .11, without a corresponding significant difference between emotion conditions on preinduction anger and anxiety, F(1, 37) = 0.38, p = .54, η²p = .01.

Cardiovascular Reactivity

To examine whether the emotion inductions were both and equivalently related to autonomic arousal and reactivity, a 2 (Emotion Condition: anxiety or anger) × 3 (Time: baseline, induction, and recovery) × 4 (Cardiovascular Index: HR, PEP, MAP, and HRV) mixed-model ANOVA was conducted. The hypothesized main effect of time was significant, F(2, 66) = 12.92, p < .001, η²p = .25, indicating that the emotion inductions significantly altered cardiovascular activity over time. This main effect was qualified by a significant Cardiovascular Index × Time interaction, F(6, 228) = 6.30, p < .001, η²p = .14, indicating that the cardiovascular indices differed in change across time—demonstrating the expected decreases of PEP and HF HRV but increases in MAP and HR during the emotion induction. Tests of the quadratic pattern of change across time were also all significant, all ps < .007, indicating that changes in cardiovascular measures returned to baseline during recovery. It is important, however, that the main effect of emotion condition and all interactions of emotion condition with other variables were nonsignificant, all ps > .32. Post hoc pairwise comparisons using Tukey’s HSD confirmed that no cardiovascular index differed at any timepoint between emotion condition, all ps > .24. In short, both emotion inductions significantly increased physiological arousal (HR, MAP) and SNS activity (decreased PEP) from baseline and marginally decreased PNS activity (HF HRV), and all indicators returned to baseline levels during the postinduction recovery period. Table 3 provides

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anxiety induction</th>
<th>Anger induction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline anxiety</td>
<td>2.65 (0.34)</td>
<td>2.42 (0.35)</td>
</tr>
<tr>
<td>Baseline anger</td>
<td>1.45 (0.21)</td>
<td>1.53 (0.21)</td>
</tr>
<tr>
<td>Baseline IFN-γ (log)</td>
<td>0.74 (0.54)</td>
<td>0.95 (0.55)</td>
</tr>
<tr>
<td>Baseline IL-1β (log)</td>
<td>1.36 (0.17)</td>
<td>1.42 (0.18)</td>
</tr>
<tr>
<td>Baseline IL-6 (log)</td>
<td>1.18 (0.44)</td>
<td>1.19 (0.46)</td>
</tr>
<tr>
<td>Baseline heart rate</td>
<td>71.93 (2.63)</td>
<td>74.40 (2.63)</td>
</tr>
<tr>
<td>Baseline HF HRV</td>
<td>4.52 (0.28)</td>
<td>4.43 (0.28)</td>
</tr>
<tr>
<td>Baseline mean arterial pressure</td>
<td>80.87 (2.46)</td>
<td>77.74 (2.46)</td>
</tr>
<tr>
<td>Baseline pre-ejection period</td>
<td>126.28 (3.91)</td>
<td>119.83 (3.91)</td>
</tr>
<tr>
<td>Habitual caffeinated drinks/day</td>
<td>1.05 (0.20)</td>
<td>0.74 (0.21)</td>
</tr>
<tr>
<td>Habitual alcoholic drinks/day</td>
<td>0.60 (0.25)</td>
<td>0.42 (0.25)</td>
</tr>
<tr>
<td>BMI</td>
<td>22.43 (0.63)</td>
<td>21.63 (0.63)</td>
</tr>
</tbody>
</table>

Note. IFN = interferon; IL = interleukin; HF HRV = high-frequency heart rate variability; BMI = body mass index. Groups did not differ on any baseline measure or covariate, all ps > .25, uncorrected.
the pattern of cardiovascular indices across phases of the experiment.

**Proinflammatory Cytokine Reactivity**

To examine whether inflammatory markers increased from baseline to postinduction in the anxiety condition, a 2 (Emotion Condition: anxiety or anger) × 2 (Time: baseline and postinduction) × 3 (Analyte: IL-1β, IL-6, and IFN-γ) mixed-model ANOVA was conducted. The hypothesized Emotion Condition × Time interaction was significant, F(1, 27) = 5.61, p = .04, η² = .14, and reflected the expected pattern. On average, proinflammatory cytokine levels in the anxiety condition were similar at baseline (M = 1.10, SE = .34) to after the anger induction (M = 1.63, SE = .35), t(27) = 2.29, p = .03, η² = .16, 95% confidence interval (CI) [0.05, 0.13]. However, proinflammatory cytokine levels in the anger condition were similar at baseline (M = 1.19, SE = .35) and after the anger induction (M = 1.01, SE = .36), t(27) = .69, p = .47, η² = .02, 95% CI [−0.71, 0.35].

The two-way interaction was qualified by a significant Emotion condition × Time × Analyte 3-way interaction, F(2, 54) = 4.64, p = .01, η² = .15. The 3-way interaction was driven by the hypothesized pattern of results emerging for IFN-γ and IL-1β, but not for IL-6 (Figure 2). This interaction and pattern of results held even while controlling for BMI, caffeine intake during the preceding week, and alcohol consumption during the preceding week, F(2, 46) = 5.08, p = .01, η² = .18.

IFN-γ levels in the anxiety condition increased from baseline (M = 0.74, SE = 0.54) to after the anxiety induction (M = 1.81, SE = 0.53), t(27) = 2.53, p = .02, η² = .19. However, IFN-γ levels in the anger condition were similar at baseline (M = 0.95, SE = 0.55) and after the anger induction (M = 0.47, SE = 0.55), t(27) = 1.10, p = .28, η² = .04. Similarly, IL-1β levels tended to increase in the anxiety condition from baseline (M = 1.36, SE = 0.17) to after the anxiety induction (M = 1.61, SE = 0.18), t(27) = 1.96, p = .06, η² = .13. However, IL-1β levels in the anger condition were similar at baseline (M = 1.42, SE = 0.18) and after the anger induction (M = 1.47, SE = 0.19), t < 1, p = .68, η² < .01. In contrast, IL-6 levels in the anxiety condition did not differ between baseline (M = 1.18, SE = 0.44) and after the anxiety induction (M = 1.48, SE = 0.46), t(27) = 1.05, p = .30, η² = .04. In addition, IL-6 levels in the anger condition also did not differ between baseline (M = 1.19, SE = 0.46) and after the anger induction (M = 1.08, SE = 0.48), t < 1, p = .70, η² < .01.

In sum, anxiety appeared to cause the expected inflammatory response overall, although the effect was primarily driven by IFN-γ and IL-1β. A weighted contrast confirmed that examining only IFN-γ and IL-1β also produced the hypothesized Condition × Time interaction, F(1, 27) = 5.92, p = .02, η² = .18. Thus, compared with IFN-γ and IL-1β, IL-6 was more resistant to mean-level changes.

**Reported Anxiety and Anger Associations With Inflammatory Activity**

Analyses were conducted to examine whether inflammatory activity was predicted by overall levels of self-reported anxiety, but not by self-reported anger. Following the analytic strategy of Moons and colleagues (2010), a series of three regressions were conducted to examine how each analyte related to self-reported anxiety and anger. Caffeine intake, alcohol intake, BMI, baseline levels of the target analyte, baseline anxiety, and baseline anger were entered as covariates in each regression examining whether postinduction anxiety and anger predicted postinduction levels of the target analyte.

As shown in Table 4, postinduction levels of IFN-γ were positively associated with self-reported anxiety, β = .39, t(20) = 2.418, p = .03, but not with self-reported anger, β = −.18, t(20) = −1.262, p = .22. Further, postinduction levels of IL-1β were positively associated with self-reported anxiety, β = .47, t(24) = 3.03, p = .006, but not with self-reported anger, β = −.02, t(24) = −.17, p = .87. Finally, postinduction levels of IL-6 were also positively associated with self-reported anxiety, β = .55, t(21) = 3.22, p = .004, but not with self-reported anger, β = −.30, t(21) = −2.072, p = .051, although a trend in the opposite direction emerged. Thus, anxiety was consistently associated with greater levels of all three markers of inflammatory activity whereas anger was unrelated to any indicators of inflammation.

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6. Participant gender did not moderate any results.

7. Proinflammatory cytokines were not significantly related to any cardiovascular measures, all ps > .108, uncorrected. This lack of association could be because of the small sample size, or it could be because both anger and anxiety elevated cardiovascular measures, yet anxiety seems to be especially closely linked with β-adrenergic receptor occupation and NF-KB activation (see Discussion).
Table 3

Patterns of Cardiovascular Indices Across Baseline, Emotion Induction, and Recovery Phases Across Emotion Condition and by Emotion Condition

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Induction</th>
<th>Recovery</th>
<th>( F )</th>
<th>( p )</th>
<th>( \eta^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>73.17 (1.86)*</td>
<td>76.60 (1.94)*</td>
<td>73.50 (1.92)*</td>
<td>18.56</td>
<td>&lt;.001</td>
<td>.33</td>
</tr>
<tr>
<td>Anxiety</td>
<td>71.93 (2.63)</td>
<td>75.58 (2.75)</td>
<td>72.17 (2.71)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anger</td>
<td>74.40 (2.63)</td>
<td>77.63 (2.75)</td>
<td>74.82 (2.71)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP</td>
<td>79.31 (1.74)*</td>
<td>82.27 (1.74)*</td>
<td>77.21 (1.97)*</td>
<td>6.14</td>
<td>.03</td>
<td>.14</td>
</tr>
<tr>
<td>Anxiety</td>
<td>80.87 (2.46)</td>
<td>81.61 (2.45)</td>
<td>76.84 (2.79)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anger</td>
<td>77.74 (2.46)</td>
<td>82.94 (2.45)</td>
<td>77.59 (2.79)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEP</td>
<td>123.05 (2.77)*</td>
<td>119.74 (3.24)*</td>
<td>121.47 (3.18)*</td>
<td>4.97</td>
<td>.009</td>
<td>.12</td>
</tr>
<tr>
<td>Anxiety</td>
<td>126.28 (3.91)</td>
<td>123.73 (4.58)</td>
<td>123.48 (4.50)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anger</td>
<td>119.83 (3.91)</td>
<td>115.76 (4.58)</td>
<td>119.46 (4.50)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HF HRV</td>
<td>4.48 (.20)*</td>
<td>4.24 (.15)*</td>
<td>4.55 (.16)*</td>
<td>3.68</td>
<td>.03</td>
<td>.09</td>
</tr>
<tr>
<td>Anxiety</td>
<td>4.52 (.28)</td>
<td>4.46 (.21)</td>
<td>4.61 (.22)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anger</td>
<td>4.43 (.28)</td>
<td>4.02 (.21)</td>
<td>4.50 (.22)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. HR = heart rate in beats per minute; MAP = mean arterial pressure in mmHg; PEP = pre-ejection period in milliseconds (ms); HF HRV = high-frequency heart rate variability in ms\(^2\) (natural log transformed). The \( F \) column provides the analysis of variance (ANOVA) \( F \) value for the omnibus main effect of time. Means within a row that do not share the same superscript are significantly different at \( p < .05 \). Pairs of means indicated by * are marginally different at \( p < .10 \).

**Discussion**

Anxiety, but not anger, significantly increased inflammatory activity as revealed by IFN-\( \gamma \) and IL-1\( \beta \) levels. This is the first causal evidence that specific emotions elicit differential inflammatory responses. Further, self-reported levels of anxiety were consistently associated with greater inflammatory activity whereas self-reported anger was not. Thus, within this experiment, both experimental and correlational evidence indicate that anxiety has a privileged link to inflammatory activity. Together, these results provide evidence that anxiety more readily triggers an inflammatory response than anger.

Unlike IFN-\( \gamma \) and IL-1\( \beta \), mean levels increases in IL-6 were not found in the anxiety condition; however, self-reported anxiety was associated with higher levels of IL-6. One explanation for the lack of an anxiety induction effect on IL-6, and a weak effect on IL-1\( \beta \) is that the intraassay %CV for these two analytes were considerably larger than for IFN-\( \gamma \). Although individual inflammatory markers may genuinely function differently, in this case, differences in assay quality may explain the divergent effects observed across the three examined analytes. Importantly, if IFN-\( \gamma \) is statistically analyzed alone, the hypothesized interaction still emerges, thus the similar albeit weaker pattern of means observed for IL-1\( \beta \) and IL-6 bolster the effects observed for IFN-\( \gamma \), which had the best assay quality.

One interesting feature of this work is the magnitude of the effects. All of the significant effects were medium to large, accounting for at least 7% of the variance in the dependent variables. This offers strong evidence for the importance of distinct emotions when considering the ties between physiology and affect. Even without a direct or current threat to the self, simply recalling an anxiety-inducing situation was sufficient to activate an inflammatory response. This finding suggests that emotion-induced inflammatory activity may be fairly common, as these effects simply require an intrapsychic trigger and no obvious environmental stimulus. Future work can examine whether the impact of emotions on inflammatory activity is stronger when facing a current stressor.

The emotion induction essay was also sufficient to cause increased autonomic activity. HR, MAP, PEP, and HF HRV together demonstrated equivalent changes in SNS and PNS activity across both emotion conditions. This indicates that a physiological reaction was successfully induced in both conditions, and that variations in sheer magnitude of arousal are unlikely explanations of the observed differences in inflammatory activity. That is, it is difficult to argue that the anxiety induction was simply more powerful than the anger induction in triggering an autonomic stress response.

What might explain these similar autonomic but disparate immune system findings? Recent work has shown that anxiety seems to be closely linked to activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-KB) (Antoni et al., 2012; Koo, Russo, Ferguson, Nestler, & Duman, 2010), which is a rapid-acting transcriptional factor responsible for increased synthesis and eventual circulation of proinflammatory cytokines under stress (Bierhaus et al., 2003). NF-KB activation is accomplished through occupation of \( \beta \)-adrenergic receptors by norepinephrine (Bierhaus et al., 2003; Powell et al., 2013) and, notably, one study has linked state anxiety, but not state anger, with increased occupation of \( \beta \)-adrenergic receptors after controlling for relevant covariates (Yu, Kang, Ziegler, Mills, & Dimsdale, 2008). State anxiety may be particularly linked to \( \beta \)-adrenergic receptor occupation because, while anger and anxiety are associated with relatively similar brain activity (Phan et al., 2002), minor differences in activity in both the hypothalamus (Folkow & Von Euler, 1954; Robinson, Culberson, & Carmichael, 1983) and medulla oblongata (Matsui, 1965) differentially stimulate the adrenal medulla to produce either norepinephrine or epinephrine—both of which are associated with SNS activity. Thus, while anger and anxiety may appear similar on broad measures, such as subcortical hemodynamic responses or SNS activity, it is possible for them to be differentially associated with catecholamine release. As such, anxiety may be disproportionately associated with norepinephrine circulation, \( \beta \)-adrenergic receptor occupation, and thus NF-KB activation, leading to a heightened inflammatory response. This proposed
mechanism is speculative, but it provides an avenue for future research examining the potential differential contributions of various emotions to NF-κB induction or norepinephrine production. Several studies have related emotions to inflammatory activity; however, the majority of work has examined how trait-level anger or anxiety, for example, relate to inflammatory profiles (Graham et al., 2006; Marsland, Prather, Petersen, Cohen, & Manuck, 2008; Sjögren, Leanderson, Kristenson, & Ernerudh, 2006; Suarez, 2004; Suarez, Lewis, Krishnan, & Young, 2004), typically showing greater inflammatory activity associated with more negative trait levels.

Figure 2. Estimated marginal mean level in interferon-γ (IFN-γ; top panel), interleukin-1β (IL-1β; middle panel), and interleukin-6 (IL-6; bottom panel) at baseline assessment and 20 min after induction of either anxiety or anger (N = 28). IFN-γ and IL-1β significantly and marginally increased, respectively, from baseline to postinduction in the anxiety-induction condition, but not in the anger induction. Changes in IL-6 were not significant in either condition. SE bars depicted.
emotion. Although informative, these studies do not address the current question regarding how acute responses to specific stressors may induce adaptive inflammatory responses. Having high levels of trait negative emotion is arguably almost always dysfunctional because chronic negative emotions are largely insensitive to situational changes and thus are not tailored to deal effectively with any particular short-term problem. Further, if chronic negative affect is linked to chronically elevated inflammatory activity, trait negative emotions may mostly contribute to dysregulation of the immune system and deleterious outcomes (Brydon & Steptoe, 2005; McEwen, 1998; Steptoe et al., 2007). However, state emotions are tailored to specific situations and provide short-term changes in physiology that may prove advantageous when dealing with specific environmental stressors. If, as suggested in Moons et al. (2010), inflammatory activity triggered by avoidance emotions is adaptive, then this would presumably be particularly applicable to acute emotional reactions.

Although few studies have compared how multiple emotions relate to inflammatory activity, some work is supportive of the avoidance/approach model of emotion-induced inflammatory activity. For example, aside from the supportive data of Moons et al. (2010), inflammatory activity has been differentially related to peoples’ self-reported feelings of shame and guilt (Dickerson et al., 2004). Shame is an avoidance emotion associated with a strong desire to withdraw from others and was significantly associated with greater inflammatory activity. In contrast, guilt is an approach emotion associated with attempts to repair an action or mistake and was not related to inflammatory activity. Similarly, Shields and Moons (2015) found that the commonly observed neural signature of avoidance motivation—frontal EEG alpha asymmetry—predicted circulating cytokine levels, and that this relationship held even while controlling for covariates.

There are inconsistencies in the literature (e.g., Carroll et al., 2011; Puterman et al., 2014), but these discrepancies may be explained by differences in analytic strategy. We concur that trait anger is likely dysfunctional and probably linked to chronically elevated inflammatory activity. As a consequence, if baseline anger is shaped heavily by trait anger on average, then statistically controlling for baseline anger teases apart the effects associated with trait anger and the effects associated with state anger. In other words, if baseline anger is not controlled for then trait anger is conflated with state changes in anger and inflammation, which can lead to an apparent association between reactive state anger and inflammation that is actually driven by the confounded effect of trait anger. Studies linking greater anger with greater inflammatory activity did not fully control for baseline anger, leaving changes in inflammatory activity to be driven by both trait and state influences. However, all studies that either controlled for baseline affect or experimentally induced emotions have produced consistent results: avoidance-oriented emotions and motivational states relate to inflammatory activity.

Thus, in conjunction with Moons et al. (2010) and Dickerson et al. (2004), it now appears that the largely avoidant emotions of fear, shame, and anxiety have been linked to elevated inflammatory activity, whereas the approach emotions of anger and guilt have not. However, prior research commonly used nonspecific stressors rather than eliciting a specific emotion response (Carroll et al., 2011; Dickerson et al., 2004; Moons et al., 2010) and could thus not rule out the influence of covarying individual differences that could influence inflammatory activity. In addition, prior to Moons et al., such distinct emotion effects had not been framed in terms of avoidance or approach motivations. The current experiment induced specific emotion states to establish causality and provided support for an avoidance/approach framework of emotion-induced inflammatory activity. Future work can provide further evidence to support, refine, or refute this theoretical framework.

Our results are consistent with the body of research looking at the relation between proinflammatory cytokines and a similarly avoidance-oriented affective state, depressed mood (Dowlati et al., 2010). Experimental and correlational evidence support the idea that inflammatory activity can lead to depressed mood (Slavich & Irwin, 2014). Our results, however, suggest that this relationship may be bidirectional: The avoidance system may induce inflammatory activity and thus underlie some similarities in these emotion-related inflammatory states. Future research could thus attempt to elucidate whether experimental inductions of depressed mood (e.g., Berna et al., 2010) increase proinflammatory cytokines in a similar manner to induced anxiety.

An avoidance/approach model of emotion-induced inflammatory activity has practical implications for health. According to this model, people who regularly respond to stressors with avoidance emotions will experience more frequent occurrences of acute inflammatory activity. In contrast, people who regularly respond to stressors with approach emotions may show far less activation of their immune system across time. To the extent that frequent

| Table 4 Regression Results for Postinduction Anxiety and Anger Predicting Postinduction Levels of Interferon (IFN)-γ, Interleukin (IL)-1β, and IL-6 |
|-----------------|----------------|----------------|-----------------|----------------|----------------|
| Variable        | b (SE)         | β (SE)         | t (SE)          | p (SE)         | ΔR² (SE)       |
| IFN-γ            |                |                |                 |                |                |
| Anxiety         | .733           | .246           | .513            | 2.976          | .006           |
| Anger           | −.152          | .202           | −.120           | −.754          | .457           |
| IL-1β            |                |                |                 |                |                |
| Anxiety         | .186           | .061           | .431            | 3.077          | .004           |
| Anger           | .001           | .047           | .004            | −.030          | .976           |
| IL-6             |                |                |                 |                |                |
| Anxiety         | .513           | .148           | .474            | 3.473          | .002           |
| Anger           | −.254          | .145           | −.231           | −1.751         | .090           |

Note: Analyses controlled for baseline cytokine levels, baseline anxiety, and baseline anger.
activation of the immune system contributes to physiological dysregulation (Brydon & Steptoe, 2005; Steptoe et al., 2007), repeated episodes of emotion-induced inflammatory activity may be predictive of future health outcomes. Indeed, over time, physiological dysregulation driven by inflammatory activity leads to or is associated with the onset or worsening of many mental disorders, such as schizophrenia (Müller & Schwarz, 2006), depression (Slavich & Irwin, 2014), and bipolar disorder (Goldstein, Kemp, Soczynska, & McIntyre, 2009), and of many physical illnesses, such as autoimmune disorders (Stojanovich & Marisavljevic, 2008), cancer (Reuter, Gupta, Chaturvedi, & Aggarwal, 2010), and Alzheimer’s disease (Rubio-Perez & Morillas-Ruiz, 2012). It is important because many of these health outcomes may be brought about or exacerbated by a tendency to experience avoidance-oriented emotions and motivational states (O’Donovan, Slavich, Epel, & Neylan, 2013), psychological assessments of how people regularly respond to stressors may be predictive of health outcomes.

However, it would be imprudent to assume that all negative avoidance emotions always elicit inflammatory activity and negative approach emotions never do. Important differences in emotion regulation, psychosocial factors like variations in levels of perceived social support, and physiological features like dysregulation in immune system activity are just a few of the potentially important moderators of how emotions impact inflammatory processes. The duration of the stressor (Segerstrom & Miller, 2004) and the severity of the emotional experience (O’Donovan et al., 2010) could also play important roles in how distinct emotions relate to physiological outcomes. More work is needed to understand the qualifiers and boundaries of the emotion-induced inflammatory response demonstrated here.

The current data represent a single manner by which emotions can be triggered; however, there are countless triggers of emotional experiences. By demonstrating that recalling an emotional event is sufficient to elicit differential inflammatory activity, these findings will hopefully spur further investigation of other emotion elicitors. Understanding the distinct characteristics of specific emotion elicitors and the idiosyncratic ways in which people can respond to them can provide a more comprehensive understanding of when emotion will change inflammatory activity. However, the goal of the current work was to show that regardless of the antecedent determinants of how people come to experience emotions like anger and anxiety, those emotional experiences can have considerably different consequences for inflammatory activity. Still, some might argue that the anxiety or anger experienced for an emotion-eliciting autobiographical memory differs from anxiety or anger induced by a less-prompted stimulus. However, meta-analyses of neuroimaging studies have shown that autobiographical emotion induction produces nearly equivalent neural activity to emotions induced by other, more natural means—such as viewing or hearing emotionally laden pictures or words, respectively (Phan, Wager, Taylor, & Liberzon, 2002). Notably, the primary differences between these types of induction methods include autobiographical memory producing greater activity in the anterior cingulate cortex (ACC) and insula, both of which are areas that are thought to contribute to an inflammatory response (Slavich, Way, Eisenberger & Taylor, 2010). In other words, if anger were to elicit an inflammatory response, it would be more likely to do so during autobiographical recall than any other experimentally studied modality. The lack of effect of induced anger on a proinflammatory cytokine response found within this study, then, is suggestive evidence for its absence.

It should also be noted that increases in autonomic arousal, self-reported anxiety, and cytokines observed in the anxiety induction condition were less than is typically observed in studies using socioevaluative stressors (Kelly, Tyrka, Anderson, Price, & Carpenter, 2008; Steptoe, Hamer, & Chida, 2007; von Dawans, Kirschbaum, & Heinrichs, 2011). The observed increases in self-reported anger in the anger induction condition, however, were similar to increases in self-reported anger in response to a socioevaluative stressor (Kelly et al., 2008; Lupis, Lerman, & Wolf, 2014). As such, because anger increases were similar in magnitude to increases in anger following a socioevaluative stressor while anxiety increases were lesser in magnitude than is observed in response to a socioevaluative stressor, the lesser cytokine increases observed in this study could arguably be due solely to lesser increases in anxiety. Thus, rather than the small effects in the anxiety induction condition being a limitation of this study, they actually provide support for the idea that avoidance-related emotions drive inflammatory responses to stress.

Inflammatory markers derived from OMT samples are clinically significant and relate to outcomes like social stress (Deinzer et al., 2004; Weik, Herforth, Kolb-Bachofen, & Deinzer, 2008), depression (Johannsen, Rydmark, Söder, & Åsberg, 2007; Waschul et al., 2003), and physical health (Giannopoulou, Kamma, & Mombelli, 2003). However, OMT estimates of inflammatory activity tend to be modestly correlated with levels from blood samples (Fernandez-Botran, Miller, Burns, & Newton, 2011; Nishanian et al., 1998). Thus, there may be some miscalibration when trying to infer the absolute levels of cytokines circulating in the vasculature. However, in many cases, researchers are most interested in relative rather than absolute increases or decreases in inflammatory activity. Because these relative differences are captured by OMT samples, this methodology can provide a useful noninvasive assessment of inflammatory response. Further, for experimental designs like the current one, any inconsistency in cytokine estimates between OMT and blood samples would be similarly present in both experimental conditions and, consequently, cannot explain the observed differences across emotion induction conditions.

This experiment only included one baseline assessment of cytokine levels and one assessment 30 min after the beginning of the emotion induction. One possibility is that anger may also elicit an inflammatory response that appears more gradually and reaches its peak later than an anxiety-induced inflammatory response. Future research protocols can include multiple assessments of postinduction proinflammatory cytokine levels in an attempt to map the time-course of inflammatory responses to different emotions.

As a final limitation, the use of an undergraduate sample as well as the extensive exclusion criteria of this study warrant replication in a larger, more ecologically valid sample. While the exclusion criteria employed in this study are important for determining the effects of single-variable manipulations or predictors on inflammatory activity (O’Connor et al., 2009), it is possible that inflammatory activity could respond differently to induced emotions in individuals with psychiatric disorders or similar conditions. Hopefully, by first establishing that distinct emotions do indeed elicit differences in inflammatory activity, such detailed assessment of individual differences and moderators will be encouraged.
The idea that the avoidance system drives changes in inflammatory markers opens up novel and interesting avenues for future research beyond clarifying the methodological limitations discussed above. For example, this framework suggests that greater right frontal EEG asymmetry—the neural signature of avoidance motivation—should predict circulating inflammatory markers. While there is some correlational evidence of this effect in dispositional states (Master et al., 2009; Shields & Moons, 2015), our framework suggests that experimental manipulations of avoidance motivation per se should not only produce greater right-frontal EEG asymmetry but also increases in proinflammatory cytokines. Similarly, our framework suggests that inducing positive avoidance-oriented emotions would increase levels of proinflammatory cytokines; however, at least some increase in physiological arousal, as was observed in this study, may be necessary, which creates such an unusual combination of factors (i.e., high arousal and avoidant positive emotion) that we are unable to identify a candidate positive emotion.

More speculatively, given the correlational evidence obtained in Moons et al. (2010) and the marginal inverse relationship of poststressor anger to IL-6 obtained here, it may be the case that approach emotions decrease levels of proinflammatory cytokines. Thus, it is possible that valence alone is not wholly responsible for the effects that positive emotions have in decreasing proinflammatory cytokine levels (Dockray & Steptoe, 2010). That is, approach motivation may also play a role in decreasing inflammatory activity during these emotional states. Future research could test this hypothesis by comparing the decreases in proinflammatory cytokine levels caused by strongly approach-related positive affect, such as happiness, versus less approach-oriented positive affective states.

Conclusion

Much research has been devoted to understanding how proinflammatory cytokines induce various emotional or motivational states (e.g., Dantzer, 2001; Dowlati et al., 2010). However, the research presented here examines the reverse causal path, how emotional states lead to inflammatory activity. Although these results face limitations, they offer additional preliminary support for the approach/avoidance model of emotion-induced inflammatory activity, where the experience of avoidance-oriented emotions—such as fear or anxiety—in particular is, in part, responsible for stress-induced inflammatory activity. As such, interventions designed to attenuate the effects of stress on health might benefit from employing methods attempting to shift emotional reactions from avoidance-oriented emotions to approach-oriented emotions.

Specific emotions seem to provide a window into inflammatory activity. Indeed, the effects demonstrated here suggest that emotions are so proximally linked to inflammatory activity that assessing emotions, rather than other psychological or behavioral variables, may provide a particularly clear view of underlying inflammatory processes. The benefits of this robust association between emotions and inflammatory activity are also evident in the precision with which inflammatory processes can be predicted. Simply considering global stress or overall negative affect excludes the unique inflammatory signature of specific negative emotions. In sum, the current work encourages the examination of specific emotions when further investigating the interaction of psychological and inflammatory processes. Hans Selye said that “Every stress leaves an indelible scar, and the organism pays for its survival after a stressful situation by becoming a little older.” Although negative emotional reactions likely do leave scars across various psychological and biological systems, in terms of the immune system, some emotional reactions may cut deeper than others.

References


ANXIETY CAUSES INFLAMMATION


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