Emotion

Positive Affect and Markers of Inflammation: Discrete Positive Emotions Predict Lower Levels of Inflammatory Cytokines

Jennifer E. Stellar, Neha John-Henderson, Craig L. Anderson, Amie M. Gordon, Galen D. McNeil, and Dacher Keltner

BRIEF REPORT

Positive Affect and Markers of Inflammation: Discrete Positive Emotions Predict Lower Levels of Inflammatory Cytokines

Jennifer E. Stellar
University of Toronto

Neha John-Henderson
University of Pittsburgh

Craig L. Anderson, Amie M. Gordon, Galen D. McNeil, and Dacher Keltner
University of California–Berkeley

Negative emotions are reliably associated with poorer health (e.g., Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002), but only recently has research begun to acknowledge the important role of positive emotions for our physical health (Fredrickson, 2003). We examine the link between dispositional positive affect and one potential biological pathway between positive emotions and health—proinflammatory cytokines, specifically levels of interleukin-6 (IL-6). We hypothesized that greater trait positive affect would be associated with lower levels of IL-6 in a healthy sample. We found support for this hypothesis across two studies. We also explored the relationship between discrete positive emotions and IL-6 levels, finding that awe, measured in two different ways, was the strongest predictor of lower levels of proinflammatory cytokines. These effects held when controlling for relevant personality and health variables. This work suggests a potential biological pathway between positive emotions and health through proinflammatory cytokines.

Keywords: proinflammatory cytokines, positive emotion, health

Negative affect reliably predicts poorer health, including risk of mortality, heart disease, and cancer (see Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002 for a review). One pathway by which negative emotions lead to poor health outcomes is through increasing inflammation, a response of the immune system (Moons, Eisenberger, & Taylor, 2010). Communication molecules called proinflammatory cytokines are essential in the coordination and promotion of inflammatory processes. Acute inflammatory activity is essential in responding adaptively to infection and injury. However, chronically elevated levels of proinflammatory cytokines in the absence of illness or injury can lead to negative health outcomes by stimulating the hypothalamic–pituitary–adrenal axis, increasing levels of C-reactive protein, and slowing muscle repair (Kiecolt-Glaser et al., 2002). Elevated levels of proinflammatory

cytokines have been implicated in the onset and progression of numerous chronic diseases including diabetes, cardiovascular disease, and depression (Cesari et al., 2003; Dowlati et al., 2010; Wellen & Hotamisligil, 2005). Although past research has focused on the relationship between proinflammatory cytokines and negative emotions, little is known about whether proinflammatory cytokines may be associated with positive emotions. We hypothesize that trait positive affect will be associated with lower levels of proinflammatory cytokines and explore whether certain discrete positive emotions are particularly predictive of reduced levels of these promoters of inflammation.

Stressful experiences and certain negative emotions, moods, and traits have been linked to higher systemic levels of proinflammatory cytokines (e.g., Kiecolt-Glaser et al., 2002). For example, self-reported fear elicited during the Trier Social Stress Task predicts elevated proinflammatory cytokines (Moons et al., 2010). Experiences of shame induced by writing about instances of self-blame on three separate days led to increases in proinflammatory cytokines pre- to posttask (Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004). Negative affect is also associated with proinflammatory cytokines in studies using trait measures, although this relationship is likely bidirectional (Messay, Lim, & Marsland, 2012). Clinical depression and anxiety are associated with higher levels of proinflammatory cytokines (Dowlati et al., 2010; O'Donovan et al., 2010), as is greater self-reported trait negative affect (Denollet, Vrints, & Conraads, 2008).

Although little is known about whether positive emotions are associated with levels of proinflammatory cytokines, there is rea-

son to believe that the two may have an inverse relationship. More generally, the experience of positive emotions leads to greater longevity and reduced morbidity (e.g., Pressman & Cohen, 2005). The capacity for positive emotions to promote faster recovery from stress (Folkman & Moskowitz, 2000) and help strengthen social ties (Fredrickson, 2003; Lyubomirsky, King, & Diener, 2005) point to possible mechanisms by which positive emotions lead to better health and reduced inflammatory activity.

The existing literature offers suggestive evidence that positive affect is associated with lower levels of proinflammatory cytokines. For instance, optimism (typically associated with greater positive affect) predicts lower levels of proinflammatory cytokine responses to a stressor (Brydon, Walker, Wawrzyniak, Chart, & Steptoe, 2009), and watching an amusing film temporarily decreases levels of proinflammatory cytokines (Mittwoch-Jaffe, Shalit, Srendi, & Yehuda, 1995). Moreover, women who frequently reported being very or extremely happy over the course of a day had lower levels of proinflammatory cytokines (Steptoe, O'Donnell, Badrick, Kumari, & Marmot, 2008).

Although these studies suggest an association between trait positive affect and reduced levels of proinflammatory cytokines, no research has examined the varying degree to which different positive emotions are associated with these promoters of inflammation. A discrete approach to emotions has proven fruitful in identifying specific negative emotions, such as shame and fear, which are particularly potent elicitors of proinflammatory cytokines (e.g., Dickerson et al., 2004). Assuming that trait positive affect is associated with reduced levels of proinflammatory cytokines, examining individual positive emotions may help identify emotion-specific mechanisms that help explain this relationship.

In this investigation, we present two studies that test the hypothesis that trait positive affect will be associated with reduced levels of inflammatory cytokines. In Study 2, we examine this relationship in more depth by exploring whether certain discrete positive emotions are stronger predictors of levels of proinflammatory cytokines.

Study 1

Participants

Ninety-four freshman undergraduates (30 males, 62 females, 2 declined to state) from a large West Coast university participated in this study for credit in a psychology class. The sample was 4% African American, 46% Asian American, 42% European American, 13% Latin American, and 8% other ethnicities.

Procedure

Participants arrived at the laboratory and completed background questionnaires on the computer. They provided a sample of oral mucosal transudate (OMT) approximately 15 min after they arrived at the laboratory. OMT is a filtrate of blood plasma that comes from the capillaries at the base of the crevice in between the teeth and gums, which then passes across the mucosa and gingival crevices and settles in the mouth. Participants were instructed to refrain from eating or drinking 1 hr before providing samples. An Orasure collective device (Epitope, Beaverton, OR) was placed between the lower cheek and gum for 2 min on the left side.

Samples were frozen and stored at −80 °C in a freezer in the laboratory. Levels of IL-6 were determined by an enzyme-linked immunosorbent assay (ELISA) using commercially available kits (R&D Systems, Minneapolis, MN). Samples from each individual were run in duplicate on the same plate. The intra-assay coefficient of variation (CV) was 8.5%, and the interassay CV was 9.6%. After the OMT collection, participants completed an activity for another experiment, were debriefed, and were released.

Measures

Body mass index. Participants provided their height and weight to calculate body mass index (BMI; $M = 22.72$, $SD = 3.65$). We included BMI as a covariate because past work has shown that it correlates positively with levels of interleukin-6 (IL-6) and weight varies greatly in the undergraduate population (Khaodhiar, Ling, Blackburn, & Bistrian, 2004).

Positive and Negative Affect Schedule. Participants reported how much they had experienced negative and positive affect over the course of the past month using 20 items (e.g., inspired, enthusiastic, hostile) on the Positive and Negative Affect Schedule (PANAS) ranging from 1 (*never*) to 5 (*always*; Watson, Clark, & Tellegen, 1988). The positive ($M = 3.46$, $SD = 0.68$) and negative ($M = 2.51$, $SD = 0.81$) subscales showed strong reliability (αs ≥ 0.87) and were negatively correlated, $r(94) = -0.23$, $p = .03$.

Results

The distribution of IL-6 was not normal; therefore, the values were log transformed in line with prior research (John-Henderson, Rheinschmidt, Mendoza-Denton, & Francis, 2014). In keeping with our hypotheses, a regression revealed that positive affect negatively predicted IL-6, controlling for BMI, $\beta = -.30$, $p = .004$.[1] In a second regression analysis, negative affect was not a significant predictor of IL-6, controlling for BMI, $\beta = .06$, $p = .71$. These results demonstrate that trait positive affect predicts lower levels of proinflammatory cytokines in a healthy sample.

Study 2

Participants

One hundred nineteen freshman undergraduates (36 males, 83 females) from a large West Coast university participated in this study for payment. The sample was 5% African American, 65% Asian American, 22% European American, 14% Latin American, and 4% other ethnicities.

Procedure

Participants took part in this study as part of a multisession longitudinal study. Participants completed background questionnaires on their home computers using a secure website. In a

---

[1] When including additional health-related covariates to predict IL-6 levels (whether participants had a chronic health condition, whether they smoked, and average hours of sleep), the overall pattern of results was the same. Thirteen of fourteen regression analyses remained significant, βs ≥ −0.20, ps ≤ .05; in Study 2, the PANAS positive affect became a marginally significant predictor, $\beta = -0.20$, $p < .06$.

follow-up session, participants came to the laboratory for a collection of OMT, which was conducted and assayed in the same manner as in Study 1.

Measures

BMI. BMI ($M = 22.5$, $SD = 3.7$) was collected for the same reason as Study 1.

PANAS. We used a validated, 10-item shortened version of the PANAS that assesses general positive and negative affect in the last month (Thompson, 2007). The positive ($M = 3.75$, $SD = 0.57$) and negative ($M = 2.26$, $SD = 0.66$) subscales showed strong reliability ($\alpha s \geq 0.72$) and were not correlated, $r(119) = -.04$, $p = .69$.

Dispositional Positive Emotions. The Dispositional Positive Emotions Scale (DPES) assesses the extent to which participants experience key positive emotions in their daily lives (Shiota, Keltner, & John, 2006). This scale focuses on seven positive emotions—amusement, awe, compassion, contentment, joy, love, and pride—with five to six items for each emotion. Participants marked their agreement on a 7-point Likert scale ranging from 1 (*strongly disagree*) to 7 (*strongly agree*) to statements such as "I feel wonder almost every day" (awe) and "I am an intensely cheerful person" (joy). The entire DPES scale ($M = 4.98$, $SD = 0.71$) and its seven subscales showed strong reliability ($\alpha s \geq 0.81$).

The Big Five Personality Inventory. The Big Five Personality Inventory (BFI; $M = 3.74$, $SD = 0.49$) measures five facets of personality, including agreeableness, conscientiousness, neuroticism, extraversion, and openness, using 44 items (John & Srivastava, 1999). Participants reported how much they agreed or disagreed from 1 (*strongly disagree*) to 5 (*strongly agree*) to 8–10 self-descriptive statements such as "is original." All subscales showed strong reliability ($\alpha s \geq 0.76$).

Results

Twelve participants did not complete both the online and laboratory session of the study, and two participants had IL-6 samples that did not produce viable results, which left a sample of 105. We log transformed the non-normal distribution of IL-6. In keeping with Study 1, positive affect, measured through the PANAS, negatively predicted levels of IL-6 controlling for BMI, $\beta = -0.21$, $p = .04$, whereas negative affect did not, $\beta = -0.02$, $p = .88$. In addition, our second measure of trait positive affect, the DPES, also negatively predicted IL-6 levels, controlling for BMI, $\beta = -0.25$, $p = .01$. These results suggest that greater trait positive affect predicts lower levels of proinflammatory cytokines.

To explore whether certain discrete positive emotions were more strongly associated with reduced levels of proinflammatory cytokines, we examined each of the seven subscales of the DPES in separate regressions controlling for BMI. Awe, joy, contentment, and pride negatively predicted IL-6 (see Table 1, column 1). Dispositional awe had the strongest relationship with IL-6 of any positive emotion. When applying a Bonferroni family-wise correction for multiple tests, only awe remained a significant predictor (significance threshold of $p = .007$). In addition, when all seven subscales of the DPES were simultaneously entered into a regression, only awe significantly predicted levels of IL-6 (see Table 1, column 2).

Table 1
Positive Emotions Predicting IL-6

DPES Subscale	IL-6	IL-6
Awe	−0.33***	−0.33**
Amusement	−0.02	0.16
Compassion	−0.09	0.05
Contentment	−0.20*	0.04
Joy	−0.23*	−0.11
Love	−0.10	−0.07
Pride	−0.21*	−0.009

Note. β values for positive emotions predicting IL-6 and controlling for participant's BMI. In column 1, emotions are separately entered into regressions and in column 2 they are simultaneously entered.
* $p < .05$. ** $p < .01$. *** $p < .001$.

To further explore this strong relationship between awe and proinflammatory cytokine levels, we examined a second measure of awe—participants' reports of experiencing awe the day they visited the laboratory. In the laboratory session, participants were asked how much they felt awe, wonder, and amazement that day, ranging from 1 (*not at all*) to 10 (*very much*). These three measures were combined into a composite of the daily experience of awe and showed a high reliability ($M = 6.35$, $SD = 1.58$; $\alpha = .88$). The more frequently participants reported feeling awe, wonder, and amazement that day, the lower their levels of IL-6, controlling for BMI, $\beta = -0.48$, $p < .001$.

Awe has been linked to the personality facet of openness and was correlated with openness in this study, $r(119) = 0.50$, $p < .01$ (Shiota et al., 2006). When controlling for openness to experience, dispositional awe and the amount of awe experienced that day continued to predict IL-6, $\beta = -0.33$, $p = .004$ and $\beta = -0.47$, $p < .001$, respectively.

General Discussion

Across two studies, trait positive affect predicted lower levels of the proinflammatory cytokine IL-6. Dispositional joy, contentment, pride, and awe each negatively predicted levels of IL-6. However, awe was the strongest predictor. This finding was replicated in a second analysis, in which the amount of awe experienced that day also predicted levels of IL-6.

Although our measure assessed affect over the past month to predict current levels of IL-6, our work cannot directly address questions of causality. Past research has shown that infecting individuals with influenza, which increases proinflammatory cytokine production, has led to reduced positive affect the next day (Janicki-Deverts, Cohen, Doyle, Turner, & Treanor, 2007). Therefore, it is possible and probably likely that there is a bidirectional relationship between positive affect and cytokine production.

Why would awe be such a potent predictor of reduced proinflammatory cytokines? One reason is that proinflammatory cytokines encourage social withdrawal and reduce exploration, which would serve the adaptive purpose of helping an individual recover from injury or sickness (Maier & Watkins, 1998). On the other hand, awe is associated with curiosity and a desire to explore, suggesting antithetical behavioral responses to those found during inflammation (Keltner & Haidt, 2003). In this sense, experiences of awe may be part of an integrated response that includes emo-

tional and biological responses that facilitate approach and social exploration. Alternatively, awe elicits feelings of interconnectedness with others (Keltner & Haidt, 2003) and may affect levels of cytokines through fostering social connection and supportive relationships (Kiecolt-Glaser, Gouin, & Hantsoo, 2010). In many ways awe lies on the opposite end of the spectrum from shame, a known elicitor of inflammatory activity (Dickerson et al., 2004).

We did not find a strong relationship between trait negative affect and IL-6 in either study. There are a few explanations for this lack of an association. Past work suggests that social stressors (i.e., social evaluation and rejection) and negative emotions that motivate social withdrawal (e.g., shame) are particularly strong elicitors of proinflammatory cytokine production (e.g., Dickerson et al., 2004; Slavich, Way, Eisenberger, & Taylor, 2010). These types of discrete emotions are not well represented in the PANAS. In addition, much of the literature on negative affect and proinflammatory cytokines is associated with state experiences. It may be that negative emotions exert the strongest influence on proinflammatory cytokines at the state, rather than trait, level. Much of the research that has been conducted on trait negative affect utilizes clinical samples, not healthy populations like our sample. To our knowledge, no studies have yet to identify an association between PANAS trait negative affect and proinflammatory cytokines within a healthy sample.

It is important to acknowledge that we measured levels of proinflammatory cytokines in OMT, not in blood, which most studies use when assessing proinflammatory cytokine levels. Research has shown that levels of proinflammatory cytokines in OMT are related to stressors and psychosocial risk factors and predict negative health outcomes (Dickerson et al., 2004; Saxton, John-Henderson, Reid, & Francis, 2011; Sjögren, Leanderson, Kristenson, & Ernerudh, 2006; Slavich et al., 2010). Given the above associations, although not a surrogate for measurements of systemic inflammatory activity in blood, measuring levels of proinflammatory cytokines in OMT appears to be a viable method.

The present research provides a potential biological pathway for the association between positive emotions and health. Positive emotions, especially awe, are associated with lower levels of proinflammatory cytokines. This research contributes to a growing body of work that demonstrates that positive emotions not only feel good, they are good for the body.

References

Brydon, L., Walker, C., Wawrzyniak, A. J., Chart, H., & Steptoe, A. (2009). Dispositional optimism and stress-induced changes in immunity and negative mood. *Brain, Behavior, and Immunity, 23,* 810–816. http://dx.doi.org/10.1016/j.bbi.2009.02.018

Cesari, M., Penninx, B. W., Newman, A. B., Kritchevsky, S. B., Nicklas, B. J., Sutton-Tyrrell, K., . . . Pahor, M. (2003). Inflammatory markers and onset of cardiovascular events: Results from the Health ABC study. *Circulation, 108,* 2317–2322. http://dx.doi.org/10.1161/01.CIR.0000097109.90783.FC

Denollet, J., Vrints, C. J., & Conraads, V. M. (2008). Comparing Type D personality and older age as correlates of tumor necrosis factor-α dysregulation in chronic heart failure. *Brain, Behavior, and Immunity, 22,* 736–743. http://dx.doi.org/10.1016/j.bbi.2007.10.015

Dickerson, S. S., Kemeny, M. E., Aziz, N., Kim, K. H., & Fahey, J. L. (2004). Immunological effects of induced shame and guilt. *Psychosomatic Medicine, 66,* 124–131. http://dx.doi.org/10.1097/01.PSY.0000097338.75454.29

Dowlati, Y., Herrmann, N., Swardfager, W., Liu, H., Sham, L., Reim, E. K., & Lanctôt, K. L. (2010). A meta-analysis of cytokines in major depression. *Biological Psychiatry, 67,* 446–457. http://dx.doi.org/10.1016/j.biopsych.2009.09.033

Folkman, S., & Moskowitz, J. T. (2000). Stress, positive emotion, and coping. *Current Directions in Psychological Science, 9,* 115–118. http://dx.doi.org/10.1111/1467-8721.00073

Fredrickson, B. L. (2003). The value of positive emotions. *American Scientist, 91,* 330–335. http://dx.doi.org/10.1511/2003.4.330

Janicki-Deverts, D., Cohen, S., Doyle, W. J., Turner, R. B., & Treanor, J. J. (2007). Infection-induced proinflammatory cytokines are associated with decreases in positive affect, but not increases in negative affect. *Brain, Behavior, and Immunity, 21,* 301–307. http://dx.doi.org/10.1016/j.bbi.2006.09.002

John, O. P., & Srivastava, S. (1999). The Big-Five trait taxonomy: History, measurement, and theoretical perspectives. In L. A. Pervin & O. P. John (Eds.), *Handbook of personality: Theory and research* (Vol. 2, pp. 102–138). New York, NY: Guilford Press.

John-Henderson, N. A., Rheinschmidt, M. L., Mendoza-Denton, R., & Francis, D. D. (2014). Performance and inflammation outcomes are predicted by different facets of SES under stereotype threat. *Social Psychological and Personality Science, 5,* 301–309. http://dx.doi.org/10.1177/1948550613494226

Keltner, D., & Haidt, J. (2003). Approaching awe, a moral, spiritual, and aesthetic emotion. *Cognition and Emotion, 17,* 297–314. http://dx.doi.org/10.1080/02699930302297

Khaodhiar, L., Ling, P. R., Blackburn, G. L., & Bistrian, B. R. (2004). Serum levels of interleukin-6 and C-reactive protein correlate with body mass index across the broad range of obesity. *Journal of Parenteral and Enteral Nutrition, 28,* 410–415. http://dx.doi.org/10.1177/0148607104028006410

Kiecolt-Glaser, J. K., Gouin, J. P., & Hantsoo, L. (2010). Close relationships, inflammation, and health. *Neuroscience and Biobehavioral Reviews, 35,* 33–38. http://dx.doi.org/10.1016/j.neubiorev.2009.09.003

Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., & Glaser, R. (2002). Emotions, morbidity, and mortality: New perspectives from psychoneuroimmunology. *Annual Review of Psychology, 53,* 83–107. http://dx.doi.org/10.1146/annurev.psych.53.100901.135217

Lyubomirsky, S., King, L., & Diener, E. (2005). The benefits of frequent positive affect: Does happiness lead to success? *Psychological Bulletin, 131,* 803–855. http://dx.doi.org/10.1037/0033-2909.131.6.803

Maier, S. F., & Watkins, L. R. (1998). Cytokines for psychologists: Implications of bidirectional immune-to-brain communication for understanding behavior, mood, and cognition. *Psychological Review, 105,* 83–107. http://dx.doi.org/10.1037/0033-295X.105.1.83

Messay, B., Lim, A., & Marsland, A. L. (2012). Current understanding of the bi-directional relationship of major depression with inflammation. *Biology of mood and anxiety disorders, 2,* 1–11.

Mittwoch-Jaffe, T., Shalit, F., Srendi, B., & Yehuda, S. (1995). Modification of cytokine secretion following mild emotional stimuli. *Neuroreport: An International Journal for the Rapid Communication of Research in Neuroscience, 6,* 789–792. http://dx.doi.org/10.1097/00001756-199503270-00021

Moons, W. G., Eisenberger, N. I., & Taylor, S. E. (2010). Anger and fear responses to stress have different biological profiles. *Brain, Behavior, and Immunity, 24,* 215–219. http://dx.doi.org/10.1016/j.bbi.2009.08.009

O'Donovan, A., Hughes, B. M., Slavich, G. M., Lynch, L., Cronin, M. T., O'Farrelly, C., & Malone, K. M. (2010). Clinical anxiety, cortisol and interleukin-6: Evidence for specificity in emotion-biology relationships. *Brain, Behavior, and Immunity, 24,* 1074–1077. http://dx.doi.org/10.1016/j.bbi.2010.03.003

Pressman, S. D., & Cohen, S. (2005). Does positive affect influence health? *Psychological Bulletin, 131,* 925–971. http://dx.doi.org/10.1037/0033-2909.131.6.925

Saxton, K. B., John-Henderson, N., Reid, M. W., & Francis, D. D. (2011). The social environment and IL-6 in rats and humans. *Brain, Behavior, and Immunity, 25,* 1617–1625. http://dx.doi.org/10.1016/j.bbi.2011.05.010

Shiota, M. N., Keltner, D., & John, O. P. (2006). Positive emotion dispositions differentially associated with Big Five personality and attachment style. *The Journal of Positive Psychology, 1,* 61–71. http://dx.doi.org/10.1080/17439760500510833

Sjögren, E., Leanderson, P., Kristenson, M., & Ernerudh, J. (2006). Interleukin-6 levels in relation to psychosocial factors: Studies on serum, saliva, and in vitro production by blood mononuclear cells. *Brain, Behavior, and Immunity, 20,* 270–278. http://dx.doi.org/10.1016/j.bbi.2005.08.001

Slavich, G. M., Way, B. M., Eisenberger, N. I., & Taylor, S. E. (2010). Neural sensitivity to social rejection is associated with inflammatory responses to social stress. *Proceedings of the National Academy of Sciences of the United States of America, 107,* 14817–14822. http://dx.doi.org/10.1073/pnas.1009164107

Steptoe, A., O'Donnell, K., Badrick, E., Kumari, M., & Marmot, M. (2008). Neuroendocrine and inflammatory factors associated with positive affect in healthy men and women: The Whitehall II study. *American Journal of Epidemiology, 167,* 96–102. http://dx.doi.org/10.1093/aje/kwm252

Thompson, E. R. (2007). Development and validation of an internationally reliable short- form of the positive and negative affect schedule (PANAS). *Journal of Cross-Cultural Psychology, 38,* 227–242. http://dx.doi.org/10.1177/0022022106297301

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54,* 1063–1070. http://dx.doi.org/10.1037/0022-3514.54.6.1063

Wellen, K. E., & Hotamisligil, G. S. (2005). Inflammation, stress, and diabetes. *The Journal of Clinical Investigation, 115,* 1111–1119. http://dx.doi.org/10.1172/JCI200525102