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Divergent associations of adaptive and maladaptive emotion regulation strategies with inflammation

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Abstract

Background—Recent work suggests effective emotion regulation may protect against risk of developing coronary heart disease (CHD), but the mechanisms remain unknown. Strategies for regulating emotions vary in how effectively they mitigate potentially toxic effects of stressful life experiences, and therefore may be differentially associated with CHD risk. In this study we examined emotion regulation strategies of reappraisal and suppression in relation to inflammation, a biological state associated with both stress and CHD. We hypothesized that suppression would be associated with elevated inflammation and reappraisal would be associated with lower inflammation.

Methods—We studied $n=379$ adult offspring (mean age=42.2 years) of Collaborative Perinatal Project participants, a national cohort of pregnant women enrolled in 1959–1966. Validated measures of two emotion regulation strategies were examined: reappraisal and suppression. Inflammation was measured as plasma C-reactive protein (CRP) levels. We fit multiple linear regression models predicting CRP while controlling for demographic, socioeconomic and health factors, including depressive symptoms, measured across the life course.

Results—A one standard deviation increase in reappraisal was associated with significantly lower CRP ($b = -0.18$, $se=0.06$, $p<0.01$) controlling for demographics. This relation was somewhat attenuated in life course models, with adulthood body mass index partially explaining the association. A one standard deviation increase in suppression was associated with significantly higher CRP ($b=0.21$, $se=0.05$, $p<0.001$) and this association was not substantively attenuated with further covariate adjustment.

Conclusion—Adaptive emotion regulation was associated with lower levels of inflammation and maladaptive emotion regulation was associated with higher levels of inflammation. If these associations are confirmed by prospective and experimental studies, such evidence may provide insight into novel targets for interventions to promote health and reduce cardiovascular risk.

Keywords

Emotion regulation; inflammation

INTRODUCTION

Accumulating evidence suggests both positive and negative emotional factors are related to inflammation, with high levels of distress associated with greater inflammatory risk (Everson-Rose & Lewis, 2005; Miller, Chen, & Cole, 2009) and positive affect associated with lower levels of inflammation (Steptoe, O'Donnell, Badrick, Kumari, & Marmot, 2008; Steptoe, Wardle, & Marmot, 2005). As a result, investigators have posited that capacity to regulate emotions, a critical component of healthy psychological functioning, also matters for physical health (Kubzansky, Park, Peterson, Vokonas, & Sparrow, 2011; Rozanski & Kubzansky, 2005; Taylor, Lerner, Sage, Lehman, & Seeman, 2004). Emotion regulation is a higher order feature of emotional functioning that involves the monitoring and management of emotional experience and response (Gross & John, 2003; John & Gross, 2004). Recent models linking emotion regulation to health posit that maladaptive regulatory strategies increase the risk of adverse health outcomes whereas adaptive strategies may protect health, beyond simply marking the absence of maladaptive functioning (Rozanski & Kubzansky, 2005).

Emotion regulation is not primarily an inborn trait. Rather, it is a set of strategies learned through socialization and experience over time, with childhood being a key period of development (John & Gross, 2004). Gross and John (2003; 2004) have suggested that reappraisal and suppression are commonly used regulatory strategies. Reappraisal, considered an adaptive strategy, involves altering how to think about an emotion-eliciting situation in order to change its emotional impact. For example, reappraising a job interview as an opportunity to impress and excel rather than as an anxiety provoking event may help to minimize the otherwise deleterious ramifications of the anxiety. Suppression, considered a maladaptive emotion regulation strategy, involves inhibiting emotional expression in response to an emotion eliciting event. Emotions are generally functional and adaptive processes that allow individuals to confront multiple challenges in a flexible manner. Suppression of emotion may impair the ability to effectively meet such challenges.

Evidence on the effects of these strategies in relation to psychological outcomes and physiologic activation suggest that suppression may be maladaptive while reappraisal may be health promoting. Specifically, experimental work has found that suppression of emotion leads to heightened sympathetic nervous system activation (Gross & Levenson, 1993, 1997). This suggests a physiologic cost of suppression, potentially by increasing wear and tear on the cardiovascular system over time. Also, habitual suppression of emotion is associated with more rumination, more depressive symptoms (Gross & John, 2003; John & Gross, 2004), less positive affect, and heightened cortisol reactivity in response to stressors (Lam, Dickerson, Zoccola, & Zaldivar, 2009). In contrast, reappraisal is associated with optimism and fewer depressive symptoms (Gross & John, 2003). Extrapolating from these findings and prior work on emotion and health (Consedine, Magai, & Bonanno, 2002), we would expect a maladaptive strategy like suppression to be associated with greater risk of chronic inflammation, and a more adaptive strategy like reappraisal to be associated with reduced risk. As emotion regulation strategies are largely learned during childhood and employed over the life course (John & Gross, 2004; Shonkoff & Phillips, 2000), the potential risk and protective effects of emotion regulation may accumulate and influence disease risk over time.

Though the capacity to regulate emotions may influence health, there has been little direct examination of this question. Indirect evidence comes from studies of distress or positive psychological functioning. For example, dysregulated emotion is a core feature of many forms of psychopathology and persistently high levels of distress (a marker of poorly regulated emotion) is associated with elevated inflammation (Elovainio, et al., 2009; Ford &

Erlinger, 2004; Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002; Liukkonen, et al., 2006; Pitsavos, et al., 2006; Ranjit, et al., 2007; Suarez, 2004) as well as related adverse health conditions like coronary heart disease (Kubzansky, 2007). Positive psychological factors such as emotional vitality (Kubzansky & Thurston, 2007) and optimism (Kubzansky, Sparrow, Vokonas, & Kawachi, 2001) are associated with reduced risk of coronary heart disease, and such factors are characterized in part by effective emotion regulation (Gross & John, 2003; Kubzansky & Thurston, 2007). To our knowledge, no studies have examined specific forms of emotion regulation like suppression and reappraisal in relation to inflammation. One prospective study of 1122 males (mean age=60.3 years) found a 20% reduced risk of incident coronary heart disease associated with high levels of self regulation (i.e. ability to manage impulses, feelings and behaviors with emotion regulation being a central feature) over 13 years of follow-up (Kubzansky, et al., 2011). While this study demonstrated the relation between higher order regulatory capacity and health outcome, the specific forms of regulation as well as mechanisms driving the association remain unknown and the potential influence of early life factors was not addressed. Another study among 181 Finnish adults observed cross-sectional protective associations for aspects of effective emotion regulation (i.e. mood repair and mood maintenance) and a positive association for emotion dysregulation (i.e. emotional ambivalence) with risk of metabolic syndrome at age 42. However, there was no control for potential confounding in this study, and it is unknown whether the associations would be maintained over time and net of demographic, socioeconomic, and early life health factors.

We build on this emerging research and examine one set of biological processes through which emotion regulation may influence cardiovascular health. In a US sample of males and females, we examine the relationship between two forms of emotion regulation (suppression, reappraisal) and a biomarker of inflammation (C-reactive protein; CRP). CRP was selected as the outcome as it has received much recent attention for its role as a marker of the pathophysiology of various health conditions, including cardiovascular disease (C Reactive Protein Coronary Heart Disease Genetics Collaboration, 2011; Danesh, et al., 2004; Miller, et al., 2009; Pearson, et al., 2003), and also because it may be associated with a range of psychosocial factors, including depression (Howren, Lamkin, & Suls, 2009), chronic (Janicki-Deverts, Cohen, Matthews, & Cullen, 2008) and acute stress (Steptoe, Hamer, & Chida, 2007). We hypothesized that suppression, a maladaptive emotion regulation strategy, would be associated with higher levels of inflammation whereas reappraisal, an adaptive emotion regulation strategy, would be associated with lower levels of inflammation. While it is possible for suppression to be appropriate in some situations, and for reappraisal to not always be beneficial, prior work has suggested that overall these strategies have more deleterious and adaptive consequences respectively (Gross & John, 2003). Given the hypothesis of accumulating risk associated with these tendencies, we therefore posit that the general categorizing of these strategies as either adaptive or maladaptive is appropriate when studying their relation to health. We test study hypotheses while controlling for demographic and childhood factors that may confound emotion regulation and CRP relations. These covariates were chosen based on theoretical and empirical considerations. Emotion regulation strategies are largely formed during childhood and are shaped in part by aspects of the socioeconomic environment, cognitive ability and health status (Shonkoff & Phillips, 2000). As these factors may also influence inflammation, we test study hypotheses while controlling for them (as measured during childhood) in order to assess emotion regulation and CRP associations net of early life factors. We also adjust for adulthood factors (educational attainment, smoking, body mass index, depressive symptoms) as potential mediators as past work has documented associations with CRP and they could potentially explain emotion regulation and CRP associations (Howren, et al., 2009; Pearson, et al., 2003; Pollitt, et al., 2007). To our knowledge, this is the first study to directly assess whether emotion regulation is associated with inflammation.

METHODS

Study Population

The sample comes from the Boston and Providence offspring of participants in the Collaborative Perinatal Project (CPP). Pregnant women enrolled in the CPP between 1959–1966 (Broman, Nichols, & Kennedy, 1975; Niswander & Gordon, 1972). The original aims of the CPP were to identify the neurodevelopmental consequences of pregnancy and delivery complications. Women were enrolled during pregnancy, and their offspring were regularly assessed from birth through age 7 years. Detailed medical and social histories were obtained from mothers at enrollment. Information on child birth outcomes and subsequent health and development were obtained several times during the first year of life, and again at age 7.

The New England Family Study (NEFS) was established to locate and interview the now adult CPP offspring from the Providence and Boston sites. The current sample comes from a recent project designed to examine the pathways linking education and health, described in detail elsewhere (Almeida, et al., 2010). Briefly, participants were sampled from a larger NEFS study ($n=1674$ (Gilman, et al., 2008)) oversampling racial/ethnic minorities and those with low and high levels of education attainment as required by the aims of that project ($n=914$). Accordingly, those selected were significantly less likely to be white and less likely to have a college degree compared to those not selected. Of the selected, 898 were eligible (e.g. living, not incarcerated), and 618 participated. Individuals participated in a three-hour interview where informed consent, extensive socioeconomic, health and psychological information (including an assessment of emotion regulation) were collected. Trained study personnel obtained blood samples and anthropomorphic measurements from participants following extensive quality procedures supervised by medical personnel. Human subjects committees at the Harvard School of Public Health and Brown University approved the study protocol.

Of the 618 participants interviewed, we excluded 42 participants who were not interviewed in person (and therefore ineligible for physiological assessments including blood samples and anthropometry measures), resulting in 576 eligible participants. Of these, 430 participants provided a blood sample, and 416 had usable plasma samples that were assayed for CRP. Individuals with CRP levels $>10\text{mg/L}$ were removed from the sample ($n=16$) as such levels may be indicative of current infection. A complete case analysis yielded an analytic sample of $n=379$.

Measures

Emotion Regulation—Emotion regulation involves the monitoring and management of emotional experience and response (Gross & John, 2003; John & Gross, 2004). Two emotion regulation strategies were examined in the adults, as assessed by the Emotion Regulation Questionnaire (ERQ) (Gross & John, 2003; John & Gross, 2004). The ERQ has 10 items with two subscales comprised of five items each, measuring suppression and reappraisal. Reappraisal is defined as altering how to think about an emotion eliciting situation in order to change its emotional impact. Suppression is defined as inhibiting emotional expression in response to an emotion eliciting event. To improve interpretability of reappraisal and suppression scores, raw items were summed and scale scores were standardized to have mean=0 and standard deviation=1. Primary analyses treated reappraisal and suppression continuously. To assess the possibility of threshold effects, additional analyses examined each emotion regulation strategy score categorized into tertiles according to the distribution of scores in the sample. The ERQ has been validated and has good psychometric properties (Gross & John, 2003; John & Gross, 2004). In this sample internal

consistency reliability was high for both subscales with reappraisal $r=0.86$ and suppression $r=0.78$.

Inflammation—The outcome variable was plasma concentration of C-reactive protein (CRP). CRP concentrations were determined using an immunoturbidimetric assay on the Hitachi 917 analyzer (Roche Diagnostics - Indianapolis, IN), using reagents and calibrators from DiaSorin (Stillwater, MN). This assay has a sensitivity of 0.03 mg/L. The day-to-day variabilities of the assay at concentrations of 0.91, 3.07 and 13.38 mg/L are 2.81, 1.61 and 1.1%, respectively. CRP levels ranged from 0.07mg/L to 80.10 mg/L in this sample. CRP was (natural) log transformed due to skewed distribution and examined continuously. Also, CRP was dichotomized according to the CDC/American Heart Association criteria for high and low cardiovascular disease risk (High risk: CRP ≥ 3 mg/L; low risk: CRP<3mg/L) (Pearson, et al., 2003) to consider clinically relevant levels of inflammation.

Covariates—Factors assessed during childhood and adulthood were included as covariates to determine whether emotion regulation was associated with inflammation net of health and socioeconomic status across the life course, or whether relevant adulthood factors could partially explain the associations.

Demographic factors included age, gender, race (white, not white), and original CPP study location (Boston, Providence). Childhood factors were assessed during childhood; all measures were obtained when children were 7 years of age, unless otherwise indicated. Child health was captured by measures of being born small for gestational age (SGA), body mass index (BMI), and physical health. Child intelligence was measured by intelligence quotient (IQ). Childhood social environment was assessed by socioeconomic status (SES). SGA was calculated as whether or not the child's birthweight (obtained at birth) was less than or equal to the 10th percentile for gestational age at delivery. BMI was calculated as the ratio of weight in kilograms to the square of height in meters (kg/m^2) as obtained by study personnel. Weight and height were measured as part of a scheduled study visit using standard instruments for the time. Child IQ was assessed using the Wechsler Intelligence Scale for Children (Wechsler, 1949) (scores were standardized to have a mean=100, standard deviation=15). Child health was a summary measure indicating whether or not the child experienced one or more chronic physical health condition from birth to age 7 as identified by a study pediatrician or maternal report. Categories of health conditions included: abnormalities of the liver, cardiovascular conditions, hematologic conditions (e.g. anemia), lower respiratory tract abnormality (e.g. asthma), neoplastic disease, neurologic abnormality, and prolonged/recurrent hospitalization. Childhood SES was assessed with an index adapted from the US Bureau of the Census which reflects the education, occupation and household income of the head of household (Myrianthopoulos & French, 1968) (scores range from 0–100, low-high).

Adulthood factors included current smoking, depressive symptoms, education attainment, and BMI. Current smoking was assessed as “Do you smoke cigarettes now? (yes/no)”. Depressive symptoms were assessed via the 10-item Center for Epidemiologic Studies of Depression scale (Radloff, 1977) (CES-D; $r=0.88$). Education attainment was assessed as self reported total years of education. Adulthood BMI was calculated as the ratio of weight in kilograms to the square of height in meters (kg/m^2) using measurements obtained by study personnel.

Analysis

First, those who had an available blood sample ($n=430$) were compared to those who were excluded due to missing samples ($n=188$) to determine whether there were any significant

differences by age, race, gender, education, reappraisal and suppression using chi-square and independent t-tests. Second, means and frequencies of participant characteristics were generated for the full sample, and also according to tertiles of reappraisal and suppression scores. Also, associations for participant characteristics and tertiles of emotion regulation were evaluated with analysis of variance and χ^2 tests. Bivariate associations with CRP were assessed for participant characteristics via Pearson's correlations and independent sample t-tests for continuous and categorical variables respectively. Next, three multiple linear regression models were fit separately for reappraisal and suppression to assess the association between emotion regulation and CRP. The demographics model included the emotion regulation measure plus age, race, and gender. The childhood model additionally included SGA, child BMI, child IQ, child health and child SES. The life course model additionally included adult current smoking, adult depressive symptoms, education attainment and adult BMI. The life course model was designed to consider adult covariates that could potentially be on the pathway between emotion regulation and inflammation. For example, individuals with more maladaptive emotion regulation strategies may have higher BMI which might lead to more inflammation (Appleton, et al., 2011; Howren, et al., 2009). Because the data for these covariates are cross-sectional we do not formally test potential mediation and acknowledge that the direction of effects could be reversed (i.e. BMI may influence effective emotion regulation).

The strategy of modeling blocks of variables separately was taken to allow for the examination of coefficient changes with the addition of related sets of covariates. A study site variable was included in all models to adjust for potential differences between original CPP locations. Models were fit in SAS 9.1 using PROC GENMOD to adjust variance estimates for the presence of multiple siblings from the same mother in the sample. Analyses were gender-pooled as formal tests for interaction and stratified analyses suggested no gender specific relations for emotion regulation and CRP, which is congruent to what others have observed (Gross & John, 2003; John & Gross, 2004). Also, as CRP was (natural) log transformed, coefficients were exponentiated and percent change in CRP for reappraisal and suppression scores were reported (UCLA Academic Technology Services Statistical Consulting Group, 2011).

Additional analyses were conducted to evaluate the possibility of non-linear relations between levels of emotion regulation and CRP, to assess clinically relevant levels of CRP, and to identify adulthood factors that could potentially explain emotion regulation and CRP relations. To assess whether there was a non-linear or threshold effect in the association between emotion regulation and CRP, suppression and reappraisal were categorized as tertiles and linear regression models were refit. To assess the association between emotion regulation and clinically relevant levels of CRP, models were refit with logistic regression using CRP dichotomized according to the CDC/American Heart Association criteria for high and low cardiovascular disease risk (Pearson, et al., 2003). When significant associations for emotion regulation were attenuated in life course models, adulthood factors associated with emotion regulation and CRP were removed and life course models were refit to determine whether that factor helped to explain the association.

RESULTS

Descriptive statistics

No significant differences were observed comparing participants who did and did not provide a blood sample by gender, race, education, reappraisal or suppression (all p 's > 0.05), although those who provided a sample were significantly younger than those who did not ($M = 0.9$ years, $p < 0.001$). Table 1 summarizes participant characteristics for the full sample and also by tertiles of reappraisal and suppression scores. Participants were mostly

white, more likely to be female, were on average 42 years old and had average CRP values of 1.7 mg/L. CRP was graded across levels of emotion regulation, with lower CRP associated with more reappraisal ($p < 0.01$) and higher CRP associated with more suppression ($p < 0.10$). Individuals high in reappraisal were more likely to be female, had fewer depressive symptoms and lower adulthood BMI (p 's < 0.01). Individuals high in suppression were more likely to be male, smoke, had less education, more depressive symptoms and had lower SES as children (p 's < 0.05). In bivariate analyses, minority individuals ($t = -2.08$, $p < 0.05$) and those with lower childhood SES ($r = -0.14$, $p < 0.01$), lower education attainment ($r = -0.12$, $p < 0.05$), and higher adult BMI ($r = 0.49$, $p < 0.001$) had significantly higher CRP. Adulthood depressive symptoms were marginally associated with CRP ($r = 0.09$, $p < 0.10$). Although some covariates were not associated with emotion regulation or CRP measures, all factors were included in the regression models to be conservative.

There was little overlap in use of suppression and reappraisal strategies in this sample. There was no correlation among suppression and reappraisal scores ($r = -0.06$, $p = 0.28$). Nine percent of participants had high reappraisal and high suppression scores, 50% had high scores for either reappraisal or suppression and had low/mid scores for the other strategy, and 41% had low/mid suppression and reappraisal scores. Also, when in the same linear regression model for CRP, suppression and reappraisal were both significantly associated with CRP (data not shown). These associations suggest that the two emotion regulation strategies are largely independent of one another, which is consistent with other empirical work (Gross & John, 2003).

Emotion regulation and CRP

Table 2 summarizes the results from the multiple linear regression models with CRP as a continuous outcome. After controlling for demographic and childhood factors, reappraisal was associated with significantly lower CRP ($b = -0.18$, $se = 0.06$, $p < 0.01$). Specifically, a one standard deviation increase in reappraisal was associated with a 16% decrease in CRP concentrations. Further adjustment for adulthood pathway factors somewhat attenuated the coefficient but the association remained significant. Significant associations were also observed for suppression, but in the opposite direction. After controlling for demographic and childhood factors, suppression was associated with significantly higher CRP ($b = 0.20$, $se = 0.05$, $p < 0.001$). Specifically, a one standard deviation increase in suppression was associated with a 22% increase in CRP concentrations. Further adjustment for adulthood pathway factors only slightly attenuated the coefficient and the association remained highly significant. Adulthood BMI was the only covariate significantly associated with CRP in the adjusted models (reappraisal $= 0.07$, $se = 0.01$, $p < 0.001$; suppression $= 0.08$, $se = 0.01$, $p < 0.001$).

Additional analyses

Emotion regulation and non-linear relations with CRP—Results from categorical emotion regulation models underscore the primary findings and suggest a dose-response relationship rather than a threshold effect with CRP (Table 3). Compared to the lowest reappraisal tertile, high reappraisal had significantly lower CRP ($b = -0.43$, $se = 0.14$, $p < 0.01$). Specifically, high reappraisal was associated with a 35% decrease in CRP concentrations as compared to low reappraisal. This association was maintained when childhood factors were added to the model, and attenuated to marginal significance when adulthood pathway factors were also included in the model. For suppression, the highest tertile was significantly associated with elevated CRP as compared to the lowest suppression tertile in all models (full multivariate $b = 0.35$, $se = 0.12$, $p < 0.01$). Specifically, high suppression was associated with a 42% increase in CRP concentrations as compared to low suppression.

Emotion regulation and clinically relevant CRP—Approximately 16% of the sample had CRP concentrations consistent with the CDC/American Heart Association's cut-point for being at high risk of cardiovascular disease. After controlling for demographics and childhood factors, a one standard deviation increase in reappraisal was marginally associated with 0.79 lower odds (95% CI: 0.69, 1.02, $p < 0.10$) of having high risk CRP; this trend was attenuated with inclusion of adulthood pathway factors (Table 4). For suppression, a one standard deviation increase was significantly associated with 44% (95% CI: 1.10, 1.90, $p < 0.01$) increased odds of having high risk CRP, controlling for demographics and childhood factors. This association was largely maintained even after including pathway covariates.

A more detailed assessment of the emotion regulation and CRP relationship—

As the associations for reappraisal and suppression with CRP were somewhat attenuated with the addition of adulthood pathway factors to the life course linear models, adulthood factors (smoking, depressive symptoms, education, BMI) were evaluated separately to identify which factor may be most relevant to the effect (thereby serving as a potential pathway variable between emotion regulation and CRP). Adulthood BMI was the only adult factor significantly associated with CRP in life course models. Removing adulthood BMI and refitting the life course models yielded significant associations for continuously measured reappraisal ($b = -0.16$, $se = 0.06$, $p < 0.01$) and the high reappraisal tertile ($b = -0.37$, $se = 0.14$, $p < 0.01$) with CRP. Thus, the attenuation in the coefficients for reappraisal in the life course model compared to the demographics only and childhood models was due to adulthood BMI, which indicates that adulthood BMI could play a role in the association between reappraisal and CRP. For suppression, removing adulthood BMI did not yield dramatically different coefficients, suggesting BMI may not be as significant a factor in the relation between suppression and CRP.

DISCUSSION

The results of this study indicate that reappraisal (adaptive emotion regulation) was associated with lower levels of inflammation whereas suppression (maladaptive emotion regulation) was associated with elevated inflammation when measured continuously. These relationships were largely maintained after controlling for demographic, socioeconomic and health factors measured across the life course including major determinants of CRP. With regard to high risk CRP levels, while the relative risk estimates sometimes achieved only marginal statistical significance, the consistency of effects across models, relatively narrow confidence intervals, and maintenance of effects after adjusting for multiple potential confounders suggest that associations with suppression and reappraisal should not be dismissed. Analyses with tertiles of reappraisal and suppression underscored results from linear models and suggest the likelihood of dose-response relationships. These findings are important as this study is the first to examine relationships between specific emotion regulation strategies and CRP, a potential risk marker for cardiovascular disease.

Results from this study are consistent with and extend findings from emerging epidemiological examinations of emotion regulation and cardiovascular health (Kinnunen, Kokkonen, Kaprio, & Pulkkinen, 2005; Kubzansky, et al., 2011) as well as other work examining relations among behavioral aspects of emotion regulation (e.g. written emotional disclosure) with a variety of health indicators (Frattaroli, 2006; Pennebaker & Beall, 1986).

Despite the cross-sectional nature of the emotion regulation and CRP analyses, there is some evidence to suggest that adulthood BMI may mediate the relation between reappraisal and CRP rather than that BMI affects both reappraisal and inflammation. Theory and empirical work indicate that emotion regulation strategies are largely formed during childhood and are employed over the life course (John & Gross, 2004). Moreover, recent work has found poor

self regulation measured in childhood to be associated with adulthood CRP, with adulthood (but not childhood) BMI significantly mediating the association (Appleton, et al., 2011). Similarly, in the present study childhood BMI did not predict either emotion regulation strategy, nor did it alter the association between emotion regulation and CRP. Such findings suggest that early life BMI cannot account for the observed relationships in adulthood. While there is likely a bidirectional relationship between emotion regulation and BMI in adulthood, findings from prior work generally suggest emotion regulation capacity may influence adult BMI in a meaningful way and is not simply an artifact of the relation between BMI and inflammation. Future work with temporally distinct measures should more rigorously evaluate this possibility.

Adult BMI appears to be one pathway by which emotion regulation is associated with CRP. Somewhat surprisingly, depressive symptoms did not help to explain the emotion regulation and CRP associations. Effective emotion regulation is an important component of healthy psychological functioning and poor emotion regulation may result in worse mental health, including more depressive symptoms. As many studies have observed associations for depressive symptoms and CRP (Howren, et al., 2009), and poor emotion regulation is associated with factors associated with increased risk of depression (e.g. high negative emotion, rumination, less coping) (Gross & John, 2003), we expected depressive symptoms would be on the pathway between emotion regulation and CRP. Instead, these findings suggest that emotion regulation may influence CRP through pathways other than depressive symptoms in this sample. It is possible that a more fine-grained assessment of both positive and negative emotions would provide a more comprehensive test of possible emotion-relation pathways by which regulatory strategies influence inflammation. We recommend future work obtain temporally distinct measures of regulation, emotion and inflammation and test such potential pathways.

A number of other plausible behavioral and physiologic mechanisms may help explain how emotion regulation could influence inflammation. The ability to regulate emotions effectively may increase health promoting behaviors such as engaging in more opportunities for rest and restoration (Rozanski & Kubzansky, 2005), or improved problem solving and mobilization of social support (Eisenberg, Hofer, & Vaughan, 2007). Those who are distressed (i.e. have poorly regulated emotion) are more likely to abuse substances, eat poorly, and get less exercise (Kiecolt-Glaser, et al., 2002). Plausible physiologic mechanisms include heightened hypothalamic-pituitary-adrenal axis (HPA) and sympathetic nervous system (SNS) activity. For example, several studies have found psychosocial stress and chronically elevated negative emotions to be associated with higher levels of inflammation and other markers of HPA dysregulation (e.g. elevated cortisol) (Matthews, et al., 2010; Miller, et al., 2009). Experimental studies have demonstrated that suppression leads to greater sympathetic nervous system activation as measured by increased skin conductance, decreased finger pulse amplitude, shortened pulse transmission time (Gross & Levenson, 1993) and enhanced sympathetic activation of the cardiovascular system (Gross & Levenson, 1997). Such heightened HPA and SNS activity and resultant stress hormones (e.g. corticosteroids, catecholamines) initiate an inflammatory response characterized by the production of a number of inflammatory markers including CRP (Black & Garbutt, 2002).

Also, as suppression and reappraisal are utilized at different points during an emotion generative process (Gross & John, 2003; John & Gross, 2004), the timing of use of each strategy may influence physiologic activation and inflammatory risk. Reappraisal is employed *before* the emotion occurs, thereby preventing and reducing the intensity of negative emotions (Gross & John, 2003; John & Gross, 2004). As such, HPA or SNS dysregulation may be avoided, potentially leading to lower levels of CRP. On the other hand, suppression strategies are employed *after* the emotion has occurred to modify the

behavioral manifestations of the emotion (Gross & John, 2003; John & Gross, 2004). Though perhaps appearing outwardly tranquil, chronic negative emotions along with HPA and SNS dysregulation may continue unchecked, potentially contributing to increased inflammation. Moreover, suppression has been found to require significant mental exertion (Consedine, et al., 2002). Thus, the act of suppression may further tax body systems and contribute to elevations in systemic inflammation.

This study has some limitations. First, it was a cross-sectional examination of emotion regulation and CRP measured at a single time point. Although the development of emotion regulation strategies largely occurs during childhood (John & Gross, 2004) which is temporally prior to our measure of CRP, we cannot rule out the possibility that inflammation influences emotion regulation. We recommend future work test these associations prospectively using multiple assessments of temporally distinct measures of emotion regulation and CRP. Also, while we control for a well characterized set of potential confounders from across the life course, it is possible that confounding by unmeasured variables (e.g. genetic factors, emotional reactivity) is influencing the observed relationships. For example, individuals with highly reactive temperaments would have to work harder to effectively regulate their emotions than those who are less emotionally reactive; it is as yet unclear whether emotional reactivity and emotion regulation are likely to have independent, synergistic, or overlapping effects on health and biology. Future work is advised to account for such factors.

This study has a number of strengths. First, we examined an objective measure of inflammation as the study outcome. Biomarkers are not subject to reporting biases and can provide insight into physiologic mechanisms through which psychosocial functioning may influence health. Also, we used a validated measure of emotion regulation that has good psychometric properties. Finally, we controlled for a well characterized set of potential confounders measured across the life course, which improves confidence that observed relationships are not spurious.

This study adds to the growing evidence base that healthy psychological functioning may buffer and maintain health whereas poor psychological functioning may contribute to poor health. However, in considering emotion regulation, we do not put forth yet another psychological risk or protective factor to be studied. Instead, as a higher order construct that encompasses positive and negative emotions, considering emotion regulation in relation to health may help to organize the sometimes disparate literature linking aspects of both positive and negative psychological functioning to health (Kubzansky, et al., 2011). Also, the relationships observed in this study have significant implications for intervention as reappraisal and suppression are learned strategies and not innate traits (John & Gross, 2004). Therefore, it may be possible to teach individuals how to manage their emotions effectively which may not only improve psychological functioning, but may also protect physical health as well.

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Table 1
 Characteristics of the full sample and according to tertiles of reappraisal and suppression

Characteristic	Full sample %/Mean (SD)	Reappraisal			Suppression		
		High (n=138)	Middle (n=126)	Low (n=115)	High (n=124)	Middle (n=135)	Low (n=120)
C-reactive protein, mg/L	1.7 (2.0)	1.3 (1.7)	1.8 (1.9)	2.1 (2.4)	2.0 (1.9)	1.6 (2.0)	1.5 (2.0)
Demographic factors							
Gender, female, %	57.5	68.1	57.1	45.2	44.4	57.8	70.1
Race, not white, %	19.5	24.6	19.8	13.0	25.8	14.8	18.3
Age, years	42.2 (1.7)	42.4 (1.8)	42.1 (1.7)	42.2 (1.7)	42.3 (1.7)	42.3 (1.8)	42.1 (1.7)
Childhood factors							
Small for gestational age, %	10.6	13.8	11.1	6.1	13.7	6.7	11.7
Socioeconomic status	54.2 (23.2)	54.5 (23.0)	55.7 (23.7)	52.2 (22.8)	47.7 (23.6)	56.6 (21.8)	58.1 (22.9)
Chronic condition, %	17.7	17.4	14.3	21.7	15.3	17.8	20.0
Body mass index, kg/m ²	16.0 (1.6)	16.0 (1.5)	16.1 (1.8)	16.0 (1.4)	16.0 (1.3)	16.0 (1.6)	16.1 (1.6)
Intelligence quotient	102.2 (13.7)	100.9 (13.0)	102.6 (15.1)	103.3 (12.8)	100.5 (14.8)	102.9 (13.3)	103.3 (12.8)
Adulthood factors							
Depressive symptoms, CES-D	1.6 (0.54)	1.5 (0.52)	1.6 (0.50)	1.7 (0.60)	1.7 (0.63)	1.6 (0.51)	1.4 (0.44)
Smokers, %	26.4	22.5	28.6	28.7	35.5	23.0	20.8
Education, years	13.6 (2.6)	13.8 (2.6)	13.6 (2.5)	13.3 (2.6)	13.1 (2.3)	13.7 (2.9)	13.9 (2.5)
Body mass index, kg/m ²	29.1 (7.6)	27.6 (6.1)	29.2 (7.7)	30.6 (8.6)	30.0 (7.5)	29.0 (8.7)	28.2 (5.9)

Note: The p values were generated from analysis of variance (continuous variables) and ² (categorical variables) tests. SD=Standard deviation; CES-D= Centers for Epidemiologic Studies of Depression Scale.

+
p<0.10

*
p<0.05

**
p<0.01

p<0.001

Table 2

Multiple linear regression models (b, se) for the association between emotion regulation and (natural log) C-reactive protein

Emotion Regulation	Demographics	Childhood	Life Course
Reappraisal	−0.18 ** (0.06)	−0.18 ** (0.06)	−0.10 * (0.05)
Suppression	0.21 *** (0.05)	0.20 *** (0.05)	0.15 ** (0.05)

Note: Demographic model controls for study site, age, race, gender. Childhood model controls for demographics plus child factors (born small for gestational age, socioeconomic status, physical health, child BMI, IQ). Life course model controls for demographics, child factors and adult factors (depressive symptoms, smoking, education, adult BMI). Coefficients represent change in (ln)CRP per one standard deviation change in reappraisal or suppression score.

*
p<0.05

**
p<0.01

p<0.001

Table 3

Multiple linear regression models (b, se) for the association between tertiles of emotion regulation and (natural log) C-reactive protein

Emotion Regulation	Demographics	Childhood	Life Course
Reappraisal			
High	-0.43 ** (0.14)	-0.42 ** (0.14)	-0.22 + (0.13)
Middle	-0.12 (0.14)	-0.11 (0.14)	-0.01 (0.12)
Low	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>
Suppression			
High	0.44 ** (0.14)	0.41 ** (0.14)	0.35 ** (0.12)
Middle	0.13 (0.14)	0.13 (0.14)	0.08 (0.12)
Low	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>

Note: Demographic model controls for study site, age, race, gender. Childhood model controls for demographics plus child factors (born small for gestational age, socioeconomic status, physical health, child BMI, IQ). Life course model controls for demographics, child factors and adult factors (depressive symptoms, smoking, education, adult BMI). Coefficients represent change in (ln)CRP per tertile of reappraisal or suppression scores as compared to the lowest tertile.

+
p<0.10

*
p<0.05

**
p<0.01

p<0.001

Table 4

Multiple logistic regression models (Odd Ratios, 95% confidence interval) for the association between emotion regulation and high risk C-reactive protein

Emotion Regulation	Demographics	Childhood	Life Course
Reappraisal	0.79 ⁺ (0.61, 1.02)	0.79 ⁺ (0.61, 1.02)	0.90 (0.68, 1.20)
Suppression	1.43 ^{**} (1.10, 1.89)	1.44 ^{**} (1.10, 1.90)	1.39 ⁺ (0.98, 1.97)

Note: Demographic model controls for study site, age, race, gender. Childhood model controls for demographics plus child factors (born small for gestational age, socioeconomic status, physical health, child BMI, IQ). Life course models controls for demographics, child factors and adult factors (depressive symptoms, smoking, education, adult BMI). Odds ratios represent the odds of having high-risk CRP per standard deviation change in reappraisal or suppression scores.

⁺
p<0.10

^{*}
p<0.05

^{**}
p<0.01

^{***}
p<0.001