Health Psychology
2015, Vol. 34, No. 12, 1154–1165

0278-6133/15/$12.00 http://dx.doi.org/10.1037/hea0000240

Affective Reactivity to Daily Stressors Is Associated With Elevated Inflammation

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Objective: Inflammation increases the risk of chronic diseases, but the links between emotional responses to daily events and inflammation are unknown. We examined individual differences in affective reactivity to daily stressors (i.e., changes in positive and negative affect in response to stressors) as predictors of inflammatory markers interleukin-6 (IL-6) and C-reactive protein (CRP). ***Methods:*** A cross-sectional sample of 872 adults from the National Study of Daily Experiences (substudy of Midlife in the United States II) reported daily stressors and affect during telephone interviews for 8 days. Blood samples were obtained at a separate clinic visit and assayed for inflammatory markers. Multilevel models estimated trait affective reactivity slopes for each participant, which were inputted into regression models to predict inflammation. ***Results:*** People who experienced greater decreases in positive affect on days when stressors occurred (i.e., positive affect reactivity) had elevated log IL-6, independent of demographic, physical, psychological, and behavioral factors ($B = 1.12$, $SE = 0.45$, $p = .01$). Heightened negative affect reactivity was associated with higher log CRP among women ($p = .03$) but not men ($p = .57$); health behaviors accounted for this association in women. ***Conclusions:*** Adults who fail to maintain positive affect when faced with minor stressors in everyday life appear to have elevated levels of IL-6, a marker of inflammation. Women who experience increased negative affect when faced with minor stressors may be at particular risk of elevated inflammation. These findings add to growing evidence regarding the health implications of affective reactivity to daily stressors.

Keywords: daily stress, stress reactivity, inflammation, positive affect, negative affect

Inflammation is involved in the development and prognosis of chronic diseases—including cardiovascular and autoimmune diseases, and cognitive and functional decline—and increases the risk of mortality (Cohen, Harris, & Pieper, 2003; Danesh et al., 2004; Harris et al., 1999; Reuben et al., 2002; Weaver et al., 2002). Chronic stress is linked to elevated systemic inflammation and other adverse immunological changes that further contribute to sustained inflammation, such as delayed wound healing, prolonged infection, and glucocorticoid resistance (Cohen et al., 2012; Glaser & Kiecolt-Glaser, 2005; Kiecolt-Glaser et al., 2003; Miller, Cohen, & Ritchey, 2002; Segerstrom & Miller, 2004). Acute laboratory-based stressors elicit short-term increases in circulating inflammatory markers (Steptoe, Hamer, & Chida, 2007); while such changes in circulating inflammation in response to acute stress may be adaptive in certain contexts to prepare for possible injury and infection (Dhabhar & McEwen, 1997, 1999), the wear and tear of repeated exposure to minor stressors can be detrimental for long-term health (Aldwin, Jeong, Igarashi, Choun, & Spiro, 2014; McEwen & Seeman, 1999). The purpose of our study was to examine whether individual differences in emotional responses to

This article was published Online First June 1, 2015.

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Nancy L. Sin was supported by National Institute on Aging (NIA) Grant F32AG048698. Longitudinal follow-up of the Midlife in the United States (MIDUS) investigation was supported by NIA Grant P01-AG020166. The original MIDUS study was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development. We thank the staff of the Clinical Research Centers at the University of Wisconsin-Madison, UCLA, and Georgetown University for their support in conducting this study. The MIDUS Biomarker Project was supported by the following grants: M01-RR023942 (Georgetown), M01-RR00865 (UCLA) from the General Clinical Research Centers Program, and 1UL1RR025011 (University of Wisconsin-Madison) from the Clinical and Translational Science Award (CTSA) program of the National Center for Research Resources, National Institutes of Health. The funding sources had no involvement in the study design; data collection, analysis, or interpretation; nor the writing and submission of this article. The authors have no conflicts of interest to disclose.

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naturally occurring daily stressful events were associated with levels of inflammation.

Daily Experiences and Health

Daily stressors are routine challenges of everyday life, such as work deadlines, providing care for others, and interpersonal conflicts (Almeida, 2005). These minor occurrences refer to unexpected disruptions, as well as ongoing strains that stem from chronic or major stressors (e.g., divorce, unemployment, caregiving). Exposure to even minor stressors may contribute to inflammatory dysregulation and poorer health if the exposure or related psychological and cognitive stress responses are strong enough or frequent enough (Smyth, Zawadzki, & Gerin, 2013). Indeed, people who experience more frequent daily stressors tend to have higher levels of circulating and stimulated inflammatory markers, including interleukin(IL)-6 and C-reactive protein (CRP), compared with those who experience fewer daily stressors (Davis et al., 2008; Fuligni et al., 2009; Gouin, Glaser, Malarkey, Beversdorf, & Kiecolt-Glaser, 2012a, 2012b).

In contrast, positive aspects of everyday life may be protective for immune function (Steptoe, O'Donnell, Badrick, Kumari, & Marmot, 2008; Steptoe, Wardle, & Marmot, 2005). For example, individuals who report more frequent daily positive events tend to have relatively lower levels of inflammatory markers (Jain, Mills, von Känel, Hong, & Dimsdale, 2007; Sin, Graham-Engeland, & Almeida, 2015), and those who report greater positive emotions on a daily basis are more likely to show resistance to illness after exposure to a rhinovirus or influenza virus (Cohen, Alper, Doyle, Treanor, & Turner, 2006). Positive affect (PA) and negative affect (NA) are not fixed traits, however. Within-person variability in affect—such as fluctuations in response to external events—may increase susceptibility to poorer psychological and physical health, over and above the influences of average levels of affect (Cohen, Gunthert, Butler, O'Neill, & Tolpin, 2005; Gruber, Kogan, Quoidbach, & Mauss, 2013; Mroczek et al., 2013; Ong et al., 2013).

Emotional Reactions to Daily Stressors

Studies using daily diary or other intensive repeated-measures methodologies have examined the within-person coupling of daily events with affect, appraisals, or physical symptoms, in which participants serve as their own controls (Bolger & Zuckerman, 1995). In particular, affective reactivity to stressors is conceptualized as the magnitude of a person's change in affect on days when stressors occurred, compared with his or her stressor-free days. Although affective reactivity has traditionally been studied as an outcome of psychosocial or sociodemographic vulnerability factors (Almeida, 2005; Bolger, DeLongis, Kessler, & Schilling, 1989), recent work has utilized within-person measures of affective reactivity to reflect a person's trait-like pattern of responding to stress in everyday life and to predict between-person differences in outcomes (Cohen et al., 2005). Mounting evidence using this approach suggests that the frequency of daily stressors, in and of itself, may be less important than how an individual reacts to or appraises those stressors. Affective reactivity to daily stressors—but not exposure to stressors—increases the risk of mental disorders, chronic medical conditions, and mortality up to a decade later (Charles, Piazza, Mogle, Sliwinski, & Almeida, 2013; Mroczek et al., 2013; Piazza, Charles, Sliwinski, Mogle, & Almeida, 2013).

Research on emotional reactions to stressors has primarily focused on increases in psychological distress rather than decreases in positive psychological states, due to the prevailing tradition that defines mental health as the absence of illness (Ryff & Singer, 1998). PA frequently co-occurs with NA in the midst of stressful circumstances (Folkman, 1997; Folkman & Moskowitz, 2000; Ong, Bergeman, & Bisconti, 2004; Ong, Bergeman, Bisconti, & Wallace, 2006). Maintenance of PA may be critical for offsetting the detrimental influences of stress on mental and physical health (Zautra, Affleck, Tennen, Reich, & Davis, 2005; Zautra, Johnson, & Davis, 2005). For example, loss of PA in response to daily stressors predicted doubling of mortality risk among men in the Veterans Affairs Normative Aging Study, whereas stress-related increases in NA were not predictive of mortality (Mroczek et al., 2013). Thus, failure to maintain PA in the face of stressors may uniquely contribute toward dysregulation of physiological pathways that subsequently lead to poor health outcomes.

A number of psychological and behavioral factors may predispose individuals to have more pronounced affective reactions to stressful events, as well as important health-related outcomes. Neuroticism and trait NA have been shown to influence people's reactions to daily stressors and are both linked to elevated inflammation (Bolger et al., 1989; Marsland, Prather, Petersen, Cohen, & Manuck, 2008; Miyamoto et al., 2013), whereas positive dispositional characteristics (e.g., optimism) may be protective for stress reactivity and immune health (Brydon, Walker, Wawrzyniak, Chart, & Steptoe, 2009; Ikeda et al., 2011; Segerstrom, Taylor, Kemeny, & Fahey, 1998). Psychological distress—such as depressive symptoms, anxiety, and global perceived stress—is strongly implicated in inflammatory processes, and can both exacerbate as well as result from people's reactions to stressors in daily life (Glaser, Robles, Sheridan, Malarkey, & Kiecolt-Glaser, 2003; Kiecolt-Glaser et al., 2003). In addition, health behaviors have been shown to mediate the association between psychological factors and subsequent health outcomes (Duivis et al., 2011; Hoogwegt et al., 2013; Kubzansky & Thurston, 2007). Insufficient sleep, for example, may amplify negative emotional reactions to daily stressors (Zohar, Tzischinsky, Epstein, & Lavie, 2005), and individuals who have maladaptive responses to stressful situations may engage in risk behaviors to cope (e.g., smoking, excessive drinking) or fail to maintain optimal health behaviors such physical activity or sleep habits (Ong et al., 2013). Given their putative links to both stress reactivity and health, the current study will assess psychological and behavioral factors that may explain the associations of affective reactivity with inflammatory markers.

Aims of the Present Study

The primary objective of the current study was to evaluate individual differences in affective reactivity to daily stressors as predictors of the inflammatory markers IL-6 and CRP in a cross-sectional, national sample of adults. We hypothesized that people who experienced heightened PA and NA reactivity to stressors will have elevated IL-6 and CRP compared with people with lower affective reactivity, independent of mean affect levels. In contrast, the frequency of daily stressors was expected to be unrelated to inflammation. As a secondary objective, we examined whether

health behaviors, personality characteristics, and psychological distress were involved in the pathway between affective reactivity and inflammation. Furthermore, drawing on previous research regarding demographic disparities in daily stress processes and in inflammation (Almeida, Neupert, Banks, & Serido, 2005; Darnall & Suarez, 2009; Ranjit et al., 2007), exploratory analyses were conducted to test potential moderators—including age, gender, race, and income—of the associations between affective reactivity and inflammatory markers.

Methods

Participants and Design

The data for this study came from the second wave of the Midlife in the United States Study (MIDUS II), a national survey designed to investigate health and well-being in midlife and older adulthood. We used data from 3 linked projects within MIDUS: the parent study that surveyed psychosocial well-being, a daily diary study called the National Study of Daily Experiences, and an assessment of biomarkers and physiological functioning called the Biomarker Project. All participants completed the parent study first and were subsequently recruited for additional projects. Participants varied in the order and timing in which they completed the daily diary and the biomarker assessments: 38% of participants completed the diary protocol first, whereas 62% completed the biomarker assessment first. The interval between assessments was controlled for in the analyses.

The parent MIDUS II investigation (2004–2006) was comprised of 4,963 English-speaking adults aged 35 to 86 across the United States, and an additional 592 African Americans from Milwaukee. Participants in the parent study completed an in-depth interview and self-reported questionnaires. A random subsample of 2,022 MIDUS II respondents enrolled in the National Study of Daily Experiences, a daily diary study that consisted of telephone interviews on 8 consecutive evenings (Almeida, McGonagle, & King, 2009). Of these, 1,001 participated in the MIDUS Biomarker Project, during which they provided blood samples and were assessed for physical health and physiological function (Love, Seeman, Weinstein, & Ryff, 2010). Affective reactivity was calculated for all participants who had both stressor days (i.e., days on which a stressor occurred) and nonstressor days; 43 participants were excluded because they experienced stressors every day, and 70 were excluded because they experienced no stressors during the study. An additional 16 participants were excluded for missing data on income, leaving a final sample size of 872 for the primary analyses. Procedures were approved by Institutional Review Boards at participating sites, and all participants provided informed consent.

Daily Stressors and Affective Reactivity

Data on daily experiences were obtained during telephone interviews as part of the National Study of Daily Experiences. The Daily Inventory of Stressful Events (Almeida, Wethington, & Kessler, 2002) was used to assess whether each of 7 types of stressors occurred in the past 24 hr: argument, avoided an argument, stressor at work or school, stressor at home, discrimination, network stressor (i.e., stressful event that happened to a close friend or family member), and any other stressor. A day was categorized as a "stressor day" if the participant endorsed at least one stressor, or a "nonstressor day" if the participant indicated that no stressors occurred. *Stressor frequency* was defined as the percentage of interview days during which at least one stressor occurred (e.g., a person who experienced stressors on 2 of the 8 days had a stressor frequency of 25%).

Affect was assessed using scales developed for the MIDUS II Study (Kessler et al., 2002; Mroczek & Kolarz, 1998). Participants reported the frequency of emotions using a 5-point scale: 0 = *none of the time,* 1 = *a little of the time,* 2 = *some of the time,* 3 = *most of the time,* 4 = *all of the time*. The NA scale consisted of 14 items: *restless or fidgety, nervous, worthless, so sad nothing could cheer you up, everything was an effort, hopeless, lonely, afraid, jittery, irritable, ashamed, upset, angry,* and *frustrated*. The PA scale consisted of 13 items: *in good spirits, cheerful, extremely happy, calm and peaceful, satisfied, full of life, close to others, like you belong, enthusiastic, attentive, proud, active,* and *confident.* Daily NA and PA were calculated by averaging the items within each subscale, and then aggregating scores across interview days. During the 8 study days, Cronbach's alpha ranged from 0.83 to 0.87 for daily NA and from 0.92 to 0.95 for daily PA. Following prior work (Charles et al., 2013; Piazza et al., 2013), we controlled for *daily affect on nonstressor days* to distinguish between the affect people typically experienced and how they reacted on stressor days. We did not control for mean affect across all days because it overlaps with the concept of affective reactivity (which captures affect on stressor days).

Affective reactivity was defined as the change in levels of affect on days when stressors occurred, compared with one's typical affect on nonstressor days. Following procedures established in other daily stress studies (Bolger et al., 1989; Cohen et al., 2005), affective reactivity scores were computed for each participant using a two-level multilevel model in which the occurrence of a daily stressor (yes/no) was entered as a predictor of PA or NA on day d for person i:

Level 1 (day-level):

$$\text{Affect}_{di} = a_{0i} + a_{1i}(\text{Stressor Day}_{di}) + e_{di}$$

Level 2 (person-level):

$$a_{0i} = \beta_{00} + u_{0i}$$

$$a_{1i} = \beta_{10} + u_{1i}$$

At Level 1, a_{0i} is the intercept representing affect on nonstressor days, a_{1i} is the slope representing person i's change in affect on stressor days, and e_{di} is the residual representing day-to-day variability in affect for person i. At Level 2, β_{00} and β_{10} represent the sample average levels of affect and affective reactivity, respectively, and u_{0i} and u_{1i} are the variances reflecting person i's deviations from the sample average levels of affect and affective reactivity. These deviations were outputted from the multilevel model to calculate each person's PA reactivity and NA reactivity slopes. The slopes were subsequently entered as predictors of inflammatory markers in linear regression models for the primary analyses (Charles et al., 2013; Mroczek et al., 2013; Ong et al., 2013; Piazza et al., 2013). For example, a person with a PA

reactivity score of −0.16 (the sample mean) had a decrease of 0.16 (on a 0–4 scale) in PA on stressor days, compared with nonstressor days.

Inflammatory Markers

Participants traveled to one of 3 General Clinical Research Centers (UCLA, Georgetown, and University of Wisconsin-Madison) for the Biomarker Project, during which they completed a detailed medical history interview and provided fasting blood samples. The samples were frozen and shipped to the MIDUS II Biocore Lab, where they were stored in a −65°C freezer until assayed. The samples were assayed for six inflammatory markers: IL-6, CRP, fibrinogen, soluble IL-6 receptor, soluble E-selectin, and soluble intercellular adhesion molecule-1. For the current analysis, we focus on IL-6 and CRP due to their documented associations with chronic and acute stress (e.g., Gouin et al., 2012a; Kiecolt-Glaser et al., 2003; Steptoe, Hamer et al., 2007), as well as prognostic significance for long-term health, including cardiovascular disease and mortality (Danesh et al., 2004; Harris et al., 1999; Reuben et al., 2002). IL-6 was assayed at the MIDUS II Biocore Lab using high-sensitivity enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN). Intraassay and interassay coefficients of variation (CV) were <10%. CRP was analyzed at the Laboratory for Clinical Biochemistry Research at the University of Vermont using a particle enhanced immunonephelometric assay (BN II nephelometer; Dade Behring, Deerfield, IL). Intraassay CV was 2.3–4.4% and interassay CV was 2.1–5.7%. CRP data was missing for 3 individuals; therefore, the sample size for CRP analyses was 869. Data for IL-6 and CRP were natural log-transformed to correct for the non-normal distributions.

Covariates and Potential Explanatory Variables

Covariates. Demographic data on age, gender, race, and household income were obtained by a telephone survey as part of the parent MIDUS II Study. During the clinic visit for the Biomarker Project, participants reported medical comorbidities using a checklist of 20 physician-diagnosed chronic conditions (e.g., depression, heart disease, high blood pressure, diabetes). Current medication use was reported for blood pressure, cholesterol-lowering (e.g., statins), and corticosteroid medications. Height and weight were measured in the clinic and used to calculate body mass index (kg/m^2). The time interval in months between the daily diary and biomarker assessments was calculated by subtracting the date of blood draw from the date of the first daily diary interview; negative values refer to completion of biomarker assessment first, whereas positive values refer to completion of the daily diary first.

Health behaviors. Self-reported health behaviors were assessed during the same clinic visit as the blood draw. Regular exercise was measured with an item asking whether the participant engaged in regular exercise or physical activity of any intensity for 20 min or more at least 3 times per week (yes/no). A dummy-coded variable was used to control for current smoking status (yes/no). Participants rated their overall sleep quality during the past month using a 4-point scale (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989); responses were coded such that higher scores referred to better sleep quality. Three dummy-coded variables were created for the frequency of alcohol use in the past month: (a) never or <1 day per week in the past month, (b) 1–4 days per week, and (c) 5 or more days per week. Sleep quality was missing for one person.

Alternative analyses examined daily health behaviors, averaged across the 8 daily diary interviews. Each day, participants reported their minutes of vigorous physical activity, number of cigarettes smoked, sleep duration for the previous night, and number of alcoholic drinks. Average sleep duration was categorized as <7 hours, 7–8 hours, and >8 hours, based on prior literature regarding the nonlinear associations between sleep duration and health (Buxton & Marcelli, 2010). Five participants were missing data on daily smoking.

Psychological characteristics. We evaluated five key psychological factors that may be involved in stressor exposure and reactivity, perhaps by exacerbating (e.g., neuroticism, depressive symptoms, perceived stress, trait anxiety) or attenuating (e.g., optimism) affective and physiological stress responses. Neuroticism was assessed in the parent MIDUS II study by asking participants to rate themselves on 4 items (*moody, nervous, worrying, calm* [reversed]) using a 1–4 scale. Optimism was also assessed in the parent study, using the 6-item Life Orientation Test—Revised (Scheier, Carver, & Bridges, 1994). Three items were positively worded to measure optimism, and 3 items were negatively worded to measure pessimism; ratings were summed across the 6 items, with higher scores indicating more optimism. At the clinic visit for the biomarker assessment, perceived stress in the past month was measured using the 10-item Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983), depressive symptoms in the past week were assessed using the 20-item Center for Epidemiological Studies Depression Scale (Radloff, 1977), and trait anxiety was measured using the 20-item Spielberger Trait Anxiety Inventory (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). Four participants were missing data for neuroticism and optimism, and 5 participants were missing data for perceived stress, depressive symptoms, and/or anxiety.

Data Analysis

Descriptive statistics and correlations were run to examine relationships among daily stress processes, behavioral and psychological factors, and inflammatory markers. Next, affective reactivity scores—obtained from the multilevel models previously described—were evaluated as predictors of inflammatory outcomes (log IL-6 and log CRP) in a series of linear regression models. For the primary analysis, we controlled for stressor frequency, mean levels of NA and PA on nonstressor days, demographics, and the time interval between the daily diary and biomarker assessments. The next multivariate-adjusted model included physical health covariates: number of chronic medical conditions, body mass index, and medication use. Interactions between affective reactivity and demographic variables (age, gender, race, and income) were tested as predictors of log IL-6 and log CRP. For the secondary analyses, health behaviors were added, followed by psychological constructs, to examine whether they explained the associations between affective reactivity and inflammatory markers. Continuous variables were centered at the sample mean, except the time interval between assessments was centered at zero to indicate no lag. To aid in interpretability, the unstan-

dardized *B* estimates for PA reactivity were multiplied by −1 to represent higher levels of inflammation as a function of more pronounced PA reactivity. Analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

Results

Description of the Sample

Table 1 contains descriptive data for the sample of 872 adults. The sample was 57% female, with an average age of 58 years and median household income of $61,250. The racial composition of the sample was 82% White, 14% Black or African American, and 4% other races. Participants had, on average, 4 chronic medical conditions, body mass index of approximately 30, and about one third of the sample used blood pressure and cholesterol-lowering medications. The median lag between assessments was −6, indicating that the biomarker assessment was completed 6 months before the daily diary.

Collectively, the sample provided a total of 6,585 daily interviews. Participants completed an average of 7.6 out of 8 daily interviews ($SD = 0.89$). Stressors occurred on 43% of interview days ($SD = 22\%$), with a median of 4 stressors reported across 8 days of interviewing. People who experienced more frequent stressors tended to have lower mean PA, $r = -0.22$, $p < .001$, and higher mean NA, $r = .16$, $p < .001$, on nonstressor days, compared with people who had less frequent stressors. On nonstressor days, participants reported feeling PA close to "most of the time," whereas they reported low levels of NA (see Table 1). PA was significantly lower on stressor days ($M = 2.63$, $SD = 0.71$) versus nonstressor days ($M = 2.77$, $SD = 0.72$; paired $t_{(871)} = -11.04$, $p < .001$), whereas NA was significantly higher on stressor days ($M = 0.29$, $SD = 0.31$) versus nonstressor days ($M = 0.13$, $SD = 0.23$; paired $t_{(871)} = 21.22$, $p < .001$). Affect on nonstressor days was correlated with affective reactivity, such that people who had higher NA tended to experience relatively greater increases in NA when faced with stressors, $r = .67$, $p < .001$, whereas those with higher PA showed greater declines in PA when faced with stressors, $r = -0.51$, $p < .001$, perhaps because higher levels of PA allowed more latitude for downward movement. Thus, all analyses for affective reactivity were controlled for mean affect on nonstressor days.

Table 1
Participant Characteristics and Correlations With Inflammatory Biomarkers (N = 872)

Participant characteristics	Mean (*SD*) or *N* (%)	Pearson *r* correlations	
		Log IL-6	Log CRP
Demographics			
Age, years	57.85 (11.38)	0.23***	0.03
Female	496 (57%)	0.06†	0.19***
White race	718 (82%)	−0.17***	−0.18***
Household income, median (Q1, Q3)[a]	$61,250 ($32,250, $98,000)	−0.19***	−0.13***
Physical health and medication use			
Number of chronic conditions	4.15 (2.97)	0.24***	0.16***
Body mass index	29.66 (6.52)	0.36***	0.44***
Blood pressure medications	311 (36%)	0.25***	0.15***
Cholesterol medications	245 (28%)	0.11***	−0.02
Corticosteroid medications	32 (4%)	0.02	0.02
Daily stress and affect[b]			
Stressor frequency (% stressor days)	43% (22%)	−0.06†	−0.05
PA reactivity to stressors[c]	−0.16 (0.06)	0.07*	0.05
NA reactivity to stressors	0.17 (0.12)	0.02	0.05
PA on nonstressor days (range: 0–4)	2.77 (0.72)	−0.07*	−0.02
NA on nonstressor days (range: 0–4)	0.13 (0.23)	0.00	−0.02
Inflammatory markers[d]			
IL-6 (pg/mL), median (Q1, Q3)	2.06 (1.32, 3.41)	—	0.05***
CRP (mg/L), median (Q1, Q3)	1.36 (0.68, 3.42)	0.05***	—
Lag between assessments, median (Q1, Q3)[e]	−6 months (−9, 13)	0.06†	−0.08*

[a] Because of the non-normal distribution of household income, correlations and regression analyses were conducted using household income quintile. [b] Correlations of inflammatory markers with daily stress and affect were partialed for age due to the confounding effects of demographics. Affective reactivity and mean affect on nonstressor days were highly related. Therefore, the correlations of inflammatory markers with affective reactivity were further partialed for the corresponding mean affect on nonstressor days. Likewise, correlations of inflammatory markers with mean affect were partialed for both age and the corresponding measure of affective reactivity. [c] PA reactivity was a negative value indicating decreases in PA on stressor days. To aid in interpretability, correlation coefficients were multiplied by –1, such that positive correlations refer to higher levels of inflammation as a function of more pronounced PA reactivity. [d] The nontransformed median values for IL-6 and CRP are shown here. The data were natural log-transformed for correlations and multivariate analyses to normalize the distributions. [e] The time interval between assessments, in months, was calculated as (date of first daily diary interview—date of blood draw). Negative values refer to completion of biomarker assessment before the daily diary, whereas positive values refer to completion of the daily diary before the biomarker assessment.

† $p < 0.10$. * $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Table 1 shows correlations between key variables of interest and log-transformed inflammatory markers. Levels of inflammatory markers were lower among White and higher-income participants and were elevated among participants who were older, female, reported more chronic conditions, had higher body mass index, and who used blood pressure or cholesterol medications. Higher PA on nonstressor days was associated with lower IL-6, whereas PA reactivity (i.e., decreases in PA when faced with a daily stressor) was associated with higher IL-6.

Behavioral and Psychological Correlates of Daily Stress Processes and Inflammation

Table 2 shows Pearson correlation coefficients relating health behaviors and psychological measures to daily stress and inflammatory variables. Of the health behaviors measured at the biomarker assessment, regular exercise, sleep quality, and moderate alcohol use were associated with lower IL-6 and CRP, whereas smoking and low alcohol use were related to elevated inflammation. The health behaviors assessed in the daily diary interviews showed similar, albeit weaker, associations with inflammatory markers. Among the psychological constructs, only depressive symptoms and anxiety were significantly linked to elevated inflammation. Daily stress processes were strongly associated with all psychological constructs and with most of the health behavior measures. In particular, participants who had higher mean PA on nonstressor days reported relatively less psychological distress, more optimism, and better health behaviors, whereas affective reactivity, stressor frequency, and mean NA on nonstressor days were linked to poorer health behaviors and worse psychological functioning.

IL-6

As shown in Table 3, PA reactivity was significantly associated with elevated log IL-6, controlling for stressor frequency, NA reactivity, mean PA and NA on nonstressor days, demographics, and the time interval between assessments ($p = .03$). In addition, higher levels of PA on nonstressor days were associated with lower IL-6 ($p = .01$). NA reactivity, in contrast, was not predictive of IL-6, either before or after covariate adjustment. In a fully adjusted model that included body mass index, number of chronic conditions, and medication use, PA reactivity and mean PA remained significantly associated with IL-6 ($p = .01$ and $p = .007$,

Table 2
Psychological and Behavioral Constructs: Descriptives and Correlations With Daily Stress Processes and Inflammatory Markers

Psychological and behavioral variables	Mean (*SD*) or *N* (%)	Pearson *r* correlations						
		Mean PA	Mean NA	PA reactivity[a]	NA reactivity[a]	Stressor frequency	Log IL-6[b]	Log CRP[b]
Health behaviors from Biomarker Assessment ($n = 871$)								
Regular exercise	672 (77%)	0.02	−0.06†	−0.04	−0.07*	−0.01	−0.21***	−0.20***
Current smoker	112 (13%)	−0.13***	0.19***	0.09**	0.09*	0.01	0.08*	0.07*
Sleep quality (range: 0–3)	2.02 (0.69)	0.20***	−0.19***	−0.14***	−0.13***	−0.11**	−0.08*	−0.10**
Alcohol use frequency								
Alcohol use < 1 day/week	556 (64%)	−0.00	0.05	0.03	0.01	−0.05	0.12**	0.16***
Alcohol use 1–4 days/week	202 (23%)	0.01	−0.01	−0.11**	−0.08*	0.03	−0.09**	−0.11**
Alcohol use 5+ days/week	114 (13%)	−0.01	−0.06†	0.09**	0.09*	0.03	−0.06†	−0.10**
Daily health behaviors from daily interviews ($n = 867$)								
Physical activity, min	41.10 (58.06)	0.09*	−0.03	−0.07*	−0.05	0.06†	−0.10**	−0.10**
Cigarettes smoked	1.67 (5.17)	−0.16***	0.15***	0.07†	0.12***	0.05	0.08*	0.07*
Sleep duration, hr								
<7 hr	361 (41%)	−0.09**	0.06†	0.06†	0.07*	0.06†	0.05	0.06†
7–8 hr	391 (45%)	0.09**	−0.09**	0.03	−0.08*	0.01	−0.04	−0.08*
>8 hr	120 (14%)	−0.03	0.05	0.05	0.01	−0.09**	−0.01	0.03
Number of alcoholic drinks	0.53 (0.92)	−0.02	−0.04	0.03	0.05	0.03	−0.05	−0.11**
Psychological measures from Biomarker Assessment ($n = 867$)								
Depressive symptoms (range: 0–60)	8.39 (8.19)	−0.48***	0.49***	0.17***	0.23***	0.17***	0.10**	0.08*
Perceived stress (range: 10–50)	22.06 (6.28)	−0.42***	0.38***	0.16***	0.19***	0.22***	0.06†	0.04
Trait anxiety (range: 20–80)	33.98 (9.00)	−0.47***	0.45***	0.18***	0.23***	0.16***	0.08*	0.05
Psychological measures from self-administered questionnaire ($n = 868$)								
Neuroticism (range: 1–4)	2.03 (0.64)	−0.33***	0.31***	0.16***	0.21***	0.10**	−0.00	0.02
Optimism (range: 6–30)	23.97 (4.68)	0.30***	−0.27***	−0.16***	−0.16***	−0.07*	−0.06†	−0.02

[a] Affective reactivity was strongly related to mean affect on nonstressor days. Therefore, the correlations of psychological/behavioral variables with affective reactivity were partialed for the corresponding mean affect. PA reactivity was a negative value indicating decreases in PA on stressor days. To aid in interpretability, correlation coefficients for PA reactivity were multiplied by –1, such that positive correlations represent higher scores on the psychological/behavioral measures as a function of more pronounced PA reactivity. [b] Because of confounding with demographic factors, correlations with inflammation were partialed for age.
$^{\dagger} p < 0.10$. $^{*} p < 0.05$. $^{**} p < 0.01$. $^{***} p < 0.001$.

Table 3
Affective Reactivity to Stressors as Predictors of Log IL-6 (pg/mL)

Parameter	Affective reactivity		Physical health		Health behaviors		Psychological characteristics	
	B (*SE*)	*p*	*B* (*SE*)	*p*	*B* (*SE*)	*p*	*B* (*SE*)	*p*
Intercept	**1.204 (0.066)**	**<.001**	**1.008 (0.067)**	**<.001**	**1.056 (0.089)**	**<.001**	**1.063 (0.091)**	**<.001**
Lag between assessments[a]	**0.003 (0.001)**	**0.014**	**0.004 (0.001)**	**0.002**	**0.004 (0.001)**	**0.001**	**0.004 (0.001)**	**0.001**
Daily stress and affect								
Stressor frequency	−0.143 (0.115)	0.21	−0.179 (0.108)	0.10	−0.170 (0.107)	0.11	−0.147 (0.109)	0.18
PA reactivity[b]	**1.033 (0.478)**	**0.031**	**1.107 (0.445)**	**0.013**	**0.989 (0.446)**	**0.027**	**0.962 (0.457)**	**0.036**
PA on nonstressor days	**−0.121 (0.048)**	**0.012**	**−0.122 (0.045)**	**0.007**	**−0.116 (0.045)**	**0.010**	**−0.107 (0.048)**	**0.026**
NA reactivity[b]	−0.153 (0.297)	0.61	−0.263 (0.277)	0.34	−0.335 (0.275)	0.22	−0.228 (0.282)	0.42
NA on nonstressor days	−0.082 (0.155)	0.60	−0.049 (0.145)	0.74	−0.074 (0.145)	0.61	−0.075 (0.151)	0.62
Demographics								
Age	**0.016 (0.002)**	**<.001**	**0.012 (0.002)**	**<.001**	**0.013 (0.002)**	**<.001**	**0.013 (0.003)**	**<.001**
Gender (Ref: Male)	−0.056 (0.049)	0.25	−0.061 (0.047)	0.19	−0.062 (0.047)	0.19	−0.062 (0.048)	0.20
White race	**−0.356 (0.066)**	**<.001**	**−0.186 (0.063)**	**0.004**	**−0.157 (0.063)**	**0.014**	**−0.160 (0.065)**	**0.014**
Household income quintile	**−0.056 (0.018)**	**0.002**	**−0.046 (0.017)**	**0.007**	**−0.037 (0.017)**	**0.030**	**−0.038 (0.018)**	**0.034**
Physical health								
Body mass index			**0.037 (0.004)**	**<.001**	**0.035 (0.004)**	**<.001**	**0.035 (0.004)**	**<.001**
Number of chronic conditions			**0.019 (0.009)**	**0.032**	0.016 (0.009)	0.08	0.017 (0.009)	0.08
Cholesterol medications			0.007 (0.056)	0.89	0.010 (0.055)	0.85	−0.001 (0.056)	0.98
Corticosteroid medications			0.009 (0.120)	0.94	0.046 (0.120)	0.70	0.038 (0.12)	0.75
Blood pressure medications			0.096 (0.056)	0.09	0.090 (0.055)	0.11	0.088 (0.056)	0.12
Health behaviors at Biomarker Assessment								
Regular exercise					**−0.204 (0.055)**	**<.001**	**−0.194 (0.056)**	**0.001**
Current smoker					**0.157 (0.069)**	**0.023**	**0.146 (0.072)**	**0.042**
Subjective sleep quality					−0.007 (0.034)	0.84	−0.008 (0.036)	0.83
Alcohol use <1 day/week					0.065 (0.055)	0.24	0.059 (0.056)	0.30
Alcohol use 1–4 days/week					Reference		Reference	
Alcohol use 5+ days/week					0.033 (0.08)	0.68	0.031 (0.081)	0.70
Psychological characteristics								
Depressive symptoms							0.003 (0.005)	0.52
Perceived stress							−0.007 (0.006)	0.26
Trait anxiety							0.002 (0.005)	0.70
Neuroticism							−0.041 (0.048)	0.40
Optimism							0.000 (0.006)	0.99
R^2	0.12		0.24		0.26		0.26	

Note. Bold values refer to associations that are significant at $p < 0.05$. [a] The time interval between assessments, in months, was calculated as (date of first daily diary interview—date of blood draw). [b] For all participants, NA reactivity was a positive value representing *increases* in NA on days with stressors, compared with nonstressor days. For 99% of participants, PA reactivity was a negative value (indicating *decreases* in PA on stressor days). To aid in interpretability, the parameter estimate for PA reactivity was multiplied by –1 to represent higher IL-6 as a function of more pronounced PA reactivity.

respectively). Stressor frequency was not a significant predictor of IL-6 in any models (e.g., age- and gender-adjusted only, $B = -0.18$, $SE = 0.11$, $p = .10$), nor did it interact with affective reactivity. There were also no interactions between affective reactivity and demographic variables (i.e., age, gender, race, and income).

For the secondary analysis, health behaviors from the biomarker assessment were added to the model (see Table 3). The associations of PA reactivity and PA on nonstressor days with IL-6 persisted, whereas health behaviors (namely, regular exercise and smoking status) attenuated the association between chronic conditions and IL-6. Results were similar when health behaviors from the daily diary were entered instead (PA reactivity: $B = 1.04$, $SE = 0.45$, $p = .02$; PA on nonstressor days: $B = -0.11$, $SE = 0.05$, $p = .02$), in which daily physical activity and daily smoking were significant predictors of IL-6. Lastly, adding psychological characteristics to the model did not alter the associations of PA reactivity and PA on nonstressor days with IL-6. None of the psychological characteristics were significant in the model, and psychological characteristics did not interact with affective reactivity. Results were unchanged when psychological characteristics were entered before health behaviors.

CRP

PA reactivity and NA reactivity did not predict CRP when tested separately or together (fully adjusted model with demographic and physical health covariates: PA reactivity, $B = 0.61$, $SE = 0.68$, $p = .37$; NA reactivity, $B = 0.35$, $SE = 0.42$, $p = .41$; $R^2 = 0.26$). Stressor frequency and mean levels of affect also were not associated with CRP, either before or after controlling for covariates. PA reactivity did not interact with any variables. However, there was a significant NA Reactivity × Gender interaction ($B = -1.27$, $SE = 0.57$, $p = .025$ for interaction, controlling for stressor frequency, NA on nonstressor days, demographics, physical health, and time interval between assessments). As shown in

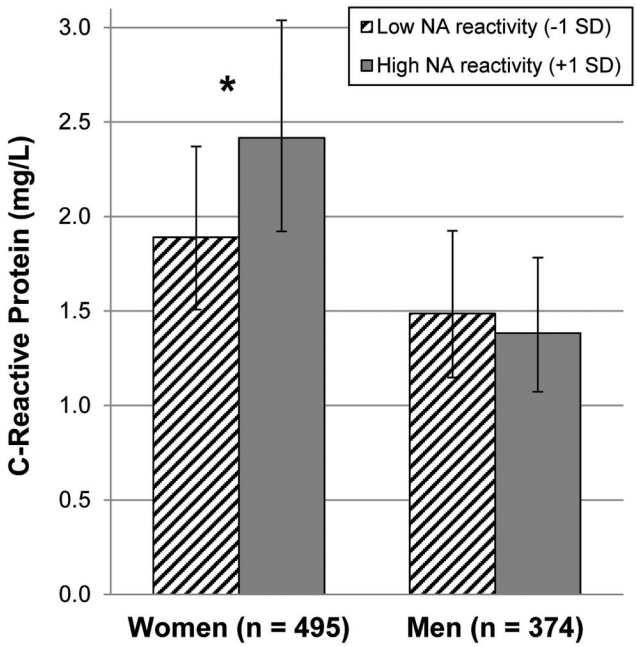

Figure 1. NA Reactivity × Gender interaction for CRP ($p = .025$ in fully adjusted model). For illustrative purposes, low and high NA reactivity are depicted as ±1 *SD* from the mean; error bars are 95% confidence intervals. Women who experienced greater increases in NA in response to daily stressors tended to have higher levels of CRP, compared with women with less NA reactivity ($p = .03$ for simple slope). NA reactivity was not related to CRP among men ($p = .57$ for simple slope).

Figure 1, women who experienced greater increases in NA on stressor days tended to have elevated CRP, compared with women with lower NA reactivity ($p = .03$ for simple slope); men did not differ in CRP based on their levels of NA reactivity ($p = .57$ for simple slope). The simple slope for women was reduced to nonsignificance ($p = .09$) after including health behaviors from the biomarker assessment to the model, particularly regular exercise ($B = -0.27$, $SE = 0.08$, $p = .001$) and current smoking ($B = 0.23$, $SE = 0.11$, $p = .03$; model $R^2 = 0.28$).

Discussion

Despite robust evidence linking chronic stress and acute laboratory-based stress with increased inflammation burden (Segerstrom & Miller, 2004; Steptoe, Hamer et al., 2007), little is known about the potential role of daily stress processes on circulating levels of inflammatory markers. The present study examined the associations of affective reactivity—reflecting how an individual generally reacts to daily stressors—with inflammatory markers IL-6 and CRP in a national sample of 872 midlife and older adults. People who experienced more pronounced decreases in PA on days when stressors occurred (as well as lower average daily PA) had elevated levels of IL-6, compared with those who were better able to maintain PA in the face of daily stressors. In addition, women who tended to experience greater increases in NA in reaction to daily stressors had higher CRP than women with less NA reactivity. Recent studies indicate that people's responses to minor stressors in everyday life are more consequential for mental and physical health than exposure to daily stressors per se (Charles et al., 2013; Cohen et al., 2005; Mroczek et al., 2013; O'Neill, Cohen, Tolpin, & Gunthert, 2004; Piazza et al., 2013). Our study adds to this growing literature by identifying inflammation as one of the key pathways whereby the emotional wear and tear of daily life may accumulate to influence long-term health outcomes. Furthermore, our findings highlight the important—but often overlooked—contributions of PA in naturalistic stress processes.

The Roles of Daily Stress and Affect in Inflammation

Previous studies have demonstrated associations between stress in everyday life and inflammation. For example, the frequency of daily stressors has been linked to higher circulating levels of IL-6 and CRP in adults and in healthy adolescents (Fuligni et al., 2009; Gouin et al., 2012a, 2012b). In our study, however, stressor frequency was not associated with inflammation. This finding is consistent with other studies that have used intensive idiographic methods and that have examined other aspects of stress processes beyond mere stressor exposure, including persistence of and changes in perceived stress. For example, a daily diary study of patients with rheumatoid arthritis showed that the perceived stressfulness of interpersonal relations across 30 days was associated with elevated lipopolysaccharide-stimulated production of IL-6 (Davis et al., 2008). In a study employing repeated weekly assessments of women with rheumatoid arthritis, increases in interpersonal stress in the current and prior week were associated with elevations in immune markers of disease activity (T-cell activation and soluble IL-2 receptor) during that week (Zautra et al., 1997). To our knowledge, the present study is the first to link affective reactivity to daily stressors with inflammation.

Although a growing body of research has documented the favorable inflammatory correlates of trait PA and other positive psychosocial attributes (Brouwers et al., 2013; Friedman, Hayney, Love, Singer, & Ryff, 2007; Friedman & Ryff, 2012; Steptoe et al., 2005), few empirical studies have examined PA during naturalistic stress. Our finding that daily stress-related declines in PA (but not increases in NA) predicted elevated IL-6 is consistent with theories regarding the unique benefits of PA, particularly in the context of stress (Folkman & Moskowitz, 2000; Fredrickson, 1998; Ong et al., 2006; Zautra, Reich, Davis, Potter, & Nicolson, 2000). PA is thought to serve multiple health-protective functions during stress, such as counteracting the physiological aftereffects of negative emotions (Fredrickson, Mancuso, Branigan, & Tugade, 2000; Ong & Allaire, 2005), reducing inflammatory and cardiovascular responses to acute stressors (Aschbacher et al., 2012; Steptoe, Gibson, Hamer, & Wardle, 2007; Steptoe et al., 2005), and promoting adaptive coping skills and positive reappraisal (e.g., benefit-finding; Folkman & Moskowitz, 2000; Tugade & Fredrickson, 2004). A limitation of our PA measure was that it did not offer the ability to group items into meaningful subscales for comparing low- versus high-arousal positive emotions. Further work is needed to understand how specific positive emotions or dimensions of PA relate to inflammatory outcomes.

Much of the research relating affect and stress to health has focused on global levels of these constructs, for example, by utilizing single-administration questionnaires. Yet, variability and dynamic changes in affect are important for mental and physical

functioning, independent of mean levels of affect. High variability in affect may be a signal of emotional instability or difficulty in regulating one's emotions. People with affective disorders show greater variability in NA, disturbances in PA, and more emotional reactivity to daily stressors, compared with healthy controls (Myin-Germeys et al., 2003; Peeters, Berkhof, Delespaul, Rottenberg, & Nicolson, 2006). However, less is known regarding the influence of within-person PA processes on subsequent mental and physical health outcomes (Mroczek et al., 2013; O'Neill et al., 2004; Ong et al., 2013).

Differential Associations, Moderators, and Mechanisms

Our results raise the question of why PA reactivity and NA reactivity were differentially related to IL-6 and CRP. Because of the cross-sectional design of this study and the interval (spanning months) between daily diary and biomarker assessments, our measures of affective reactivity and inflammatory markers are perhaps best considered to be trait-like constructs. PA reactivity may have been more stable than NA reactivity and therefore easier to capture its association with IL-6, assessed months before or after the daily diary. Indeed, prior research has described differences in how people regulate PA versus NA in their daily lives (Cohen et al., 2005; O'Neill et al., 2004; Scott, Sliwinski, & Blanchard-Fields, 2013; Zautra, Affleck et al., 2005). The temporal stability of PA reactivity to daily stressors is unclear, yet NA reactivity has been shown to vary within-person over time (e.g., it increases during periods of higher perceived stress; Sliwinski, Almeida, Smyth, & Stawski, 2009) and is perhaps more influenced by situational factors or the specific nature of the stressors. Similarly, although IL-6 is the primary signal for CRP release from the liver, IL-6 appears to be more responsive to dynamic processes in daily life, such as stress, circadian rhythms, and exercise (Steptoe, Hamer et al., 2007). Further, the literature on acute stress-induced changes in CRP is less robust compared with IL-6 and other inflammatory cytokines (Slavish, Graham-Engeland, Smyth, & Engeland, 2015; Steptoe, Hamer et al., 2007). Thus, the robust link between PA reactivity and IL-6 was consistent with previous evidence regarding the stress responsiveness of IL-6. It is possible that an association may emerge between NA reactivity to daily stressors and IL-6 in future research when these are assessed concurrently.

Despite the robust effects of sex and gender on immunity, few investigations have examined sex or gender differences in the link between psychological stress and immune responsivity (for review, see Darnall & Suarez, 2009). In line with several prior studies, we found that stress-related increases in NA were associated with higher levels of CRP among women but not men. Following acute psychological stressors, women have shown greater increases in stimulated cytokine production and poorer recovery of T-lymphocyte and natural killer cell counts to baseline levels, relative to men (Owen, Poulton, Hay, Mohamed-Ali, & Steptoe, 2003; Prather et al., 2009). The pathways underlying these gender disparities are unclear but may be related to sex-steroid hormones as well as differential patterns of rumination, coping responses, or other behavioral factors (e.g., diet, exercise, and sleep) in reaction to stress (Darnall & Suarez, 2009; Nolen-Hoeksema, Larson, & Grayson, 1999). Our findings suggest that women with higher NA reactivity tended to have elevated CRP because they were less physically active and more likely to smoke, compared with women with lower NA reactivity. Given the higher rates of autoimmune disorders and psychological stress in women (Matud, 2004), additional work is needed to disentangle the pathways underlying gender disparities in affective and inflammatory responses to stress.

We evaluated a range of psychological and behavioral factors as potential mechanisms or confounders. Psychological characteristics (i.e., neuroticism, optimism, perceived stress, depressive symptoms, and anxiety) were strongly related to daily stress and affect constructs, but they did not predict inflammation in the multivariate models. Although exercise and smoking—assessed either at the biomarker assessment or every day during daily interviews—mediated the link between NA reactivity and CRP in women, they only slightly attenuated but did not fully mediate the relationship between PA reactivity and IL-6. Dysregulation of the hypothalamic-pituitary-adrenal axis should be examined as a potential physiological mediator in future work. In particular, heightened affective reactivity to stressors may elicit the secretion of glucocorticoid hormones, such as cortisol, which normally terminate the inflammatory cascade. With prolonged exposure to stress, the immune system can become less sensitive to cortisol, resulting in poor regulation of inflammatory responses (Cohen et al., 2012; Miller et al., 2002).

Limitations and Future Directions

Several limitations should be considered when interpreting the results of this study. The daily diary measures were obtained from end-of-day reports and therefore did not provide information about affective responses during the stressful moments. Ecological momentary assessments would be better suited for examining reactions to stress as they occur, as well as for modeling within-day variation in affective and stress processes. In addition, although we controlled for the time interval between the daily diary and biomarker assessments, the cross-sectional design of this study does not allow us to draw causal conclusions. Psychological stress is often conceptualized as a risk factor for increased inflammation, yet a reverse association exists whereby high levels of proinflammatory cytokines contribute to sickness behaviors that are characteristic of depression (Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008; Raison, Capuron, & Miller, 2006). Longitudinal studies with repeated assessments of naturalistic stress processes and inflammation are needed to understand the directionality and time-course of these relationships. Longitudinal designs may reveal, for example, whether affective reactivity to daily stressors pile up over time to influence subsequent inflammation, in addition to the mechanisms underlying these effects.

Conclusion

Hassles and minor frustrations are common in day-to-day living. Our findings suggest that how people react to daily stressors may matter more for inflammatory outcomes than the frequency of such stressors. In particular, results suggest that those who tend to experience a dampening of PA in response to stress may have an increased risk of physiological dysregulation. Further investigations of microlevel, naturalistic emotional processes will be valuable for understanding how people adapt to the challenges of daily

life and may have implications for improving health and well-being.

References

Aldwin, C. M., Jeong, Y.-J., Igarashi, H., Choun, S., & Spiro, A., III. (2014). Do hassles mediate between life events and mortality in older men? *Experimental Gerontology, 59,* 74–80. http://dx.doi.org/10.1016/j.exger.2014.06.019

Almeida, D. M. (2005). Resilience and vulnerability to daily stressors assessed via diary methods. *Current Directions in Psychological Science, 14,* 64–68. http://dx.doi.org/10.1111/j.0963-7214.2005.00336.x

Almeida, D. M., McGonagle, K., & King, H. (2009). Assessing daily stress processes in social surveys by combining stressor exposure and salivary cortisol. *Biodemography and Social Biology, 55,* 219–237. http://dx.doi.org/10.1080/19485560903382338

Almeida, D. M., Neupert, S. D., Banks, S. R., & Serido, J. (2005). Do daily stress processes account for socioeconomic health disparities? *The Journals of Gerontology: Series B: Psychological Sciences and Social Sciences, 60,* 34–39.

Almeida, D. M., Wethington, E., & Kessler, R. C. (2002). The daily inventory of stressful events: An interview-based approach for measuring daily stressors. *Assessment, 9,* 41–55. http://dx.doi.org/10.1177/1073191102009001006

Aschbacher, K., Epel, E., Wolkowitz, O. M., Prather, A. A., Puterman, E., & Dhabhar, F. S. (2012). Maintenance of a positive outlook during acute stress protects against pro-inflammatory reactivity and future depressive symptoms. *Brain, Behavior, and Immunity, 26,* 346–352. http://dx.doi.org/10.1016/j.bbi.2011.10.010

Bolger, N., DeLongis, A., Kessler, R. C., & Schilling, E. A. (1989). Effects of daily stress on negative mood. *Journal of Personality and Social Psychology, 57,* 808–818. http://dx.doi.org/10.1037/0022-3514.57.5.808

Bolger, N., & Zuckerman, A. (1995). A framework for studying personality in the stress process. *Journal of Personality and Social Psychology, 69,* 890–902. http://dx.doi.org/10.1037/0022-3514.69.5.890

Brouwers, C., Mommersteeg, P. M. C., Nyklíček, I., Pelle, A. J., Westerhuis, B. L. W. J. J. M., Szabó, B. M., & Denollet, J. (2013). Positive affect dimensions and their association with inflammatory biomarkers in patients with chronic heart failure. *Biological Psychology, 92,* 220–226. http://dx.doi.org/10.1016/j.biopsycho.2012.10.002

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

Buxton, O. M., & Marcelli, E. (2010). Short and long sleep are positively associated with obesity, diabetes, hypertension, and cardiovascular disease among adults in the United States. *Social Science & Medicine, 71,* 1027–1036. http://dx.doi.org/10.1016/j.socscimed.2010.05.041

Buysse, D. J., Reynolds, C. F., III, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research, 28,* 193–213. http://dx.doi.org/10.1016/0165-1781(89)90047-4

Charles, S. T., Piazza, J. R., Mogle, J., Sliwinski, M. J., & Almeida, D. M. (2013). The wear and tear of daily stressors on mental health. *Psychological Science, 24,* 733–741. http://dx.doi.org/10.1177/0956797612462222

Cohen, H. J., Harris, T., & Pieper, C. F. (2003). Coagulation and activation of inflammatory pathways in the development of functional decline and mortality in the elderly. *The American Journal of Medicine, 114,* 180–187. http://dx.doi.org/10.1016/S0002-9343(02)01484-5

Cohen, L. H., Gunthert, K. C., Butler, A. C., O'Neill, S. C., & Tolpin, L. H. (2005). Daily affective reactivity as a prospective predictor of depressive symptoms. *Journal of Personality, 73,* 1687–1714. http://dx.doi.org/10.1111/j.0022-3506.2005.00363.x

Cohen, S., Alper, C. M., Doyle, W. J., Treanor, J. J., & Turner, R. B. (2006). Positive emotional style predicts resistance to illness after experimental exposure to rhinovirus or influenza a virus. *Psychosomatic Medicine, 68,* 809–815. http://dx.doi.org/10.1097/01.psy.0000245867.92364.3c

Cohen, S., Janicki-Deverts, D., Doyle, W. J., Miller, G. E., Frank, E., Rabin, B. S., & Turner, R. B. (2012). Chronic stress, glucocorticoid receptor resistance, inflammation, and disease risk. *Proceedings of the National Academy of Sciences of the United States of America, 109,* 5995–5999. http://dx.doi.org/10.1073/pnas.1118355109

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior, 24,* 385–396. http://dx.doi.org/10.2307/2136404

Danesh, J., Wheeler, J. G., Hirschfield, G. M., Eda, S., Eiriksdottir, G., Rumley, A., . . . Gudnason, V. (2004). C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *The New England Journal of Medicine, 350,* 1387–1397. http://dx.doi.org/10.1056/NEJMoa032804

Dantzer, R., O'Connor, J. C., Freund, G. G., Johnson, R. W., & Kelley, K. W. (2008). From inflammation to sickness and depression: When the immune system subjugates the brain. *Nature Reviews Neuroscience, 9,* 46–56. http://dx.doi.org/10.1038/nrn2297

Darnall, B. D., & Suarez, E. C. (2009). Sex and gender in psychoneuroimmunology research: Past, present and future. *Brain, Behavior, and Immunity, 23,* 595–604. http://dx.doi.org/10.1016/j.bbi.2009.02.019

Davis, M. C., Zautra, A. J., Younger, J., Motivala, S. J., Attrep, J., & Irwin, M. R. (2008). Chronic stress and regulation of cellular markers of inflammation in rheumatoid arthritis: Implications for fatigue. *Brain, Behavior, and Immunity, 22,* 24–32. http://dx.doi.org/10.1016/j.bbi.2007.06.013

Dhabhar, F. S., & McEwen, B. S. (1997). Acute stress enhances while chronic stress suppresses cell-mediated immunity in vivo: A potential role for leukocyte trafficking. *Brain, Behavior, and Immunity, 11,* 286–306. http://dx.doi.org/10.1006/brbi.1997.0508

Dhabhar, F. S., & McEwen, B. S. (1999). Enhancing versus suppressive effects of stress hormones on skin immune function. *Proceedings of the National Academy of Sciences of the United States of America, 96,* 1059–1064. http://dx.doi.org/10.1073/pnas.96.3.1059

Duivis, H. E., de Jonge, P., Penninx, B. W., Na, B. Y., Cohen, B. E., & Whooley, M. A. (2011). Depressive symptoms, health behaviors, and subsequent inflammation in patients with coronary heart disease: Prospective findings from the heart and soul study. *The American Journal of Psychiatry, 168,* 913–920. http://dx.doi.org/10.1176/appi.ajp.2011.10081163

Folkman, S. (1997). Positive psychological states and coping with severe stress. *Social Science & Medicine, 45,* 1207–1221. http://dx.doi.org/10.1016/S0277-9536(97)00040-3

Folkman, S., & Moskowitz, J. T. (2000). Positive affect and the other side of coping. *American Psychologist, 55,* 647–654. http://dx.doi.org/10.1037/0003-066X.55.6.647

Fredrickson, B. L. (1998). What good are positive emotions? *Review of General Psychology, 2,* 300–319. http://dx.doi.org/10.1037/1089-2680.2.3.300

Fredrickson, B. L., Mancuso, R. A., Branigan, C., & Tugade, M. M. (2000). The undoing effect of positive emotions. *Motivation and Emotion, 24,* 237–258. http://dx.doi.org/10.1023/A:1010796329158

Friedman, E. M., Hayney, M., Love, G. D., Singer, B. H., & Ryff, C. D. (2007). Plasma interleukin-6 and soluble IL-6 receptors are associated with psychological well-being in aging women. *Health Psychology, 26,* 305–313. http://dx.doi.org/10.1037/0278-6133.26.3.305

Friedman, E. M., & Ryff, C. D. (2012). Living well with medical comorbidities: A biopsychosocial perspective. *The Journals of Gerontology: Series B: Psychological Sciences and Social Sciences, 67,* 535–544. http://dx.doi.org/10.1093/geronb/gbr152

Fuligni, A. J., Telzer, E. H., Bower, J., Cole, S. W., Kiang, L., & Irwin, M. R. (2009). A preliminary study of daily interpersonal stress and C-reactive protein levels among adolescents from Latin American and European backgrounds. *Psychosomatic Medicine, 71,* 329–333. http://dx.doi.org/10.1097/PSY.0b013e3181921b1f

Glaser, R., & Kiecolt-Glaser, J. K. (2005). Stress-induced immune dysfunction: Implications for health. *Nature Reviews Immunology, 5,* 243–251. http://dx.doi.org/10.1038/nri1571

Glaser, R., Robles, T. F., Sheridan, J., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2003). Mild depressive symptoms are associated with amplified and prolonged inflammatory responses after influenza virus vaccination in older adults. *Archives of General Psychiatry, 60,* 1009–1014. http://dx.doi.org/10.1001/archpsyc.60.10.1009

Gouin, J.-P., Glaser, R., Malarkey, W. B., Beversdorf, D., & Kiecolt-Glaser, J. (2012a). Chronic stress, daily stressors, and circulating inflammatory markers. *Health Psychology, 31,* 264–268. http://dx.doi.org/10.1037/a0025536

Gouin, J.-P., Glaser, R., Malarkey, W. B., Beversdorf, D., & Kiecolt-Glaser, J. K. (2012b). Childhood abuse and inflammatory responses to daily stressors. *Annals of Behavioral Medicine, 44,* 287–292. http://dx.doi.org/10.1007/s12160-012-9386-1

Gruber, J., Kogan, A., Quoidbach, J., & Mauss, I. B. (2013). Happiness is best kept stable: Positive emotion variability is associated with poorer psychological health. *Emotion, 13,* 1–6. http://dx.doi.org/10.1037/a0030262

Harris, T. B., Ferrucci, L., Tracy, R. P., Corti, M. C., Wacholder, S., Ettinger, W. H., Jr., . . . Wallace, R. (1999). Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. *The American Journal of Medicine, 106,* 506–512. http://dx.doi.org/10.1016/S0002-9343(99)00066-2

Hoogwegt, M. T., Versteeg, H., Hansen, T. B., Thygesen, L. C., Pedersen, S. S., & Zwisler, A.-D. (2013). Exercise mediates the association between positive affect and 5-year mortality in patients with ischemic heart disease. *Circulation: Cardiovascular Quality and Outcomes, 6,* 559–566. http://dx.doi.org/10.1161/CIRCOUTCOMES.113.000158

Ikeda, A., Schwartz, J., Peters, J. L., Fang, S., Spiro, A., III, Sparrow, D., . . . Kubzansky, L. D. (2011). Optimism in relation to inflammation and endothelial dysfunction in older men: The VA Normative Aging Study. *Psychosomatic Medicine, 73,* 664–671. http://dx.doi.org/10.1097/PSY.0b013e3182312497

Jain, S., Mills, P. J., von Känel, R., Hong, S., & Dimsdale, J. E. (2007). Effects of perceived stress and uplifts on inflammation and coagulability. *Psychophysiology, 44,* 154–160. http://dx.doi.org/10.1111/j.1469-8986.2006.00480.x

Kessler, R. C., Andrews, G., Colpe, L. J., Hiripi, E., Mroczek, D. K., Normand, S. L. T., . . . Zaslavsky, A. M. (2002). Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological Medicine, 32,* 959–976. http://dx.doi.org/10.1017/S0033291702006074

Kiecolt-Glaser, J. K., Preacher, K. J., MacCallum, R. C., Atkinson, C., Malarkey, W. B., & Glaser, R. (2003). Chronic stress and age-related increases in the proinflammatory cytokine IL-6. *Proceedings of the National Academy of Sciences of the United States of America, 100,* 9090–9095. http://dx.doi.org/10.1073/pnas.1531903100

Kubzansky, L. D., & Thurston, R. C. (2007). Emotional vitality and incident coronary heart disease: Benefits of healthy psychological functioning. *Archives of General Psychiatry, 64,* 1393–1401. http://dx.doi.org/10.1001/archpsyc.64.12.1393

Love, G. D., Seeman, T. E., Weinstein, M., & Ryff, C. D. (2010). Bioindicators in the MIDUS national study: Protocol, measures, sample, and comparative context. *Journal of Aging and Health, 22,* 1059–1080. http://dx.doi.org/10.1177/0898264310374355

Marsland, A. L., Prather, A. A., Petersen, K. L., Cohen, S., & Manuck, S. B. (2008). Antagonistic characteristics are positively associated with inflammatory markers independently of trait negative emotionality. *Brain, Behavior, and Immunity, 22,* 753–761. http://dx.doi.org/10.1016/j.bbi.2007.11.008

Matud, M. P. (2004). Gender differences in stress and coping styles. *Personality and Individual Differences, 37,* 1401–1415. http://dx.doi.org/10.1016/j.paid.2004.01.010

McEwen, B. S., & Seeman, T. (1999). Protective and damaging effects of mediators of stress. Elaborating and testing the concepts of allostasis and allostatic load. *Annals of the New York Academy of Sciences, 896,* 30–47. http://dx.doi.org/10.1111/j.1749-6632.1999.tb08103.x

Miller, G. E., Cohen, S., & Ritchey, A. K. (2002). Chronic psychological stress and the regulation of pro-inflammatory cytokines: A glucocorticoid-resistance model. *Health Psychology, 21,* 531–541. http://dx.doi.org/10.1037/0278-6133.21.6.531

Miyamoto, Y., Boylan, J. M., Coe, C. L., Curhan, K. B., Levine, C. S., Markus, H. R., . . . Ryff, C. D. (2013). Negative emotions predict elevated interleukin-6 in the United States but not in Japan. *Brain, Behavior, and Immunity, 34,* 79–85. http://dx.doi.org/10.1016/j.bbi.2013.07.173

Mroczek, D. K., & Kolarz, C. M. (1998). The effect of age on positive and negative affect: A developmental perspective on happiness. *Journal of Personality and Social Psychology, 75,* 1333–1349. http://dx.doi.org/10.1037/0022-3514.75.5.1333

Mroczek, D. K., Stawski, R. S., Turiano, N. A., Chan, W., Almeida, D. M., Neupert, S. D., & Spiro, A., III. (2013). Emotional reactivity and mortality: Longitudinal findings from the VA Normative Aging Study. *The Journals of Gerontology: Series B: Psychological Sciences and Social Sciences*. Advance online publication.

Myin-Germeys, I., Peeters, F., Havermans, R., Nicolson, N. A., DeVries, M. W., Delespaul, P., & Van Os, J. (2003). Emotional reactivity to daily life stress in psychosis and affective disorder: An experience sampling study. *Acta Psychiatrica Scandinavica, 107,* 124–131. http://dx.doi.org/10.1034/j.1600-0447.2003.02025.x

Nolen-Hoeksema, S., Larson, J., & Grayson, C. (1999). Explaining the gender difference in depressive symptoms. *Journal of Personality and Social Psychology, 77,* 1061–1072. http://dx.doi.org/10.1037/0022-3514.77.5.1061

O'Neill, S. C., Cohen, L. H., Tolpin, L. H., & Gunthert, K. C. (2004). Affective reactivity to daily interpersonal stressors as a prospective predictor of depressive symptoms. *Journal of Social and Clinical Psychology, 23,* 172–194. http://dx.doi.org/10.1521/jscp.23.2.172.31015

Ong, A. D., & Allaire, J. C. (2005). Cardiovascular intraindividual variability in later life: The influence of social connectedness and positive emotions. *Psychology and Aging, 20,* 476–485. http://dx.doi.org/10.1037/0882-7974.20.3.476

Ong, A. D., Bergeman, C. S., & Bisconti, T. L. (2004). The role of daily positive emotions during conjugal bereavement. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 59,* P168–P176.

Ong, A. D., Bergeman, C. S., Bisconti, T. L., & Wallace, K. A. (2006). Psychological resilience, positive emotions, and successful adaptation to stress in later life. *Journal of Personality and Social Psychology, 91,* 730–749. http://dx.doi.org/10.1037/0022-3514.91.4.730

Ong, A. D., Exner-Cortens, D., Riffin, C., Steptoe, A., Zautra, A., & Almeida, D. M. (2013). Linking stable and dynamic features of positive affect to sleep. *Annals of Behavioral Medicine, 46,* 52–61. http://dx.doi.org/10.1007/s12160-013-9484-8

Owen, N., Poulton, T., Hay, F. C., Mohamed-Ali, V., & Steptoe, A. (2003). Socioeconomic status, C-reactive protein, immune factors, and responses to acute mental stress. *Brain, Behavior, and Immunity, 17,* 286–295. http://dx.doi.org/10.1016/S0889-1591(03)00058-8

Peeters, F., Berkhof, J., Delespaul, P., Rottenberg, J., & Nicolson, N. A. (2006). Diurnal mood variation in major depressive disorder. *Emotion, 6,* 383–391. http://dx.doi.org/10.1037/1528-3542.6.3.383

Piazza, J. R., Charles, S. T., Sliwinski, M. J., Mogle, J., & Almeida, D. M. (2013). Affective reactivity to daily stressors and long-term risk of reporting a chronic physical health condition. *Annals of Behavioral Medicine, 45,* 110–120. http://dx.doi.org/10.1007/s12160-012-9423-0

Prather, A. A., Carroll, J. E., Fury, J. M., McDade, K. K., Ross, D., & Marsland, A. L. (2009). Gender differences in stimulated cytokine production following acute psychological stress. *Brain, Behavior, and Immunity, 23,* 622–628. http://dx.doi.org/10.1016/j.bbi.2008.11.004

Radloff, L. S. (1977). The CES-D Scale a Self-Report Depression Scale for research in the general population. *Applied Psychological Measurement, 1,* 385–401. http://dx.doi.org/10.1177/014662167700100306

Raison, C. L., Capuron, L., & Miller, A. H. (2006). Cytokines sing the blues: Inflammation and the pathogenesis of depression. *Trends in Immunology, 27,* 24–31. http://dx.doi.org/10.1016/j.it.2005.11.006

Ranjit, N., Diez-Roux, A. V., Shea, S., Cushman, M., Ni, H., & Seeman, T. (2007). Socioeconomic position, race/ethnicity, and inflammation in the multi-ethnic study of atherosclerosis. *Circulation, 116,* 2383–2390. http://dx.doi.org/10.1161/CIRCULATIONAHA.107.706226

Reuben, D. B., Cheh, A. I., Harris, T. B., Ferrucci, L., Rowe, J. W., Tracy, R. P., & Seeman, T. E. (2002). Peripheral blood markers of inflammation predict mortality and functional decline in high-functioning community-dwelling older persons. *Journal of the American Geriatrics Society, 50,* 638–644. http://dx.doi.org/10.1046/j.1532-5415.2002.50157.x

Ryff, C. D., & Singer, B. (1998). The contours of positive human health. *Psychological Inquiry, 9,* 1–28. http://dx.doi.org/10.1207/s15327965pli0901_1

Scheier, M. F., Carver, C. S., & Bridges, M. W. (1994). Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): A reevaluation of the Life Orientation Test. *Journal of Personality and Social Psychology, 67,* 1063–1078. http://dx.doi.org/10.1037/0022-3514.67.6.1063

Scott, S. B., Sliwinski, M. J., & Blanchard-Fields, F. (2013). Age differences in emotional responses to daily stress: The role of timing, severity, and global perceived stress. *Psychology and Aging, 28,* 1076–1087. http://dx.doi.org/10.1037/a0034000

Segerstrom, S. C., & Miller, G. E. (2004). Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychological Bulletin, 130,* 601–630.

Segerstrom, S. C., Taylor, S. E., Kemeny, M. E., & Fahey, J. L. (1998). Optimism is associated with mood, coping, and immune change in response to stress. *Journal of Personality and Social Psychology, 74,* 1646–1655. http://dx.doi.org/10.1037/0022-3514.74.6.1646

Sin, N. L., Graham-Engeland, J. E., & Almeida, D. M. (2015). Daily positive events and inflammation: Findings from the National Study of Daily Experiences. *Brain, Behavior, and Immunity, 43,* 130–138. http://dx.doi.org/10.1016/j.bbi.2014.07.015

Slavish, D. C., Graham-Engeland, J. E., Smyth, J. M., & Engeland, C. G. (2015). Salivary markers of inflammation in response to acute stress. *Brain, Behavior, and Immunity, 44,* 253–269. http://dx.doi.org/10.1016/j.bbi.2014.08.008

Sliwinski, M. J., Almeida, D. M., Smyth, J., & Stawski, R. S. (2009). Intraindividual change and variability in daily stress processes: Findings from two measurement-burst diary studies. *Psychology and Aging, 24,* 828–840. http://dx.doi.org/10.1037/a0017925

Smyth, J., Zawadzki, M., & Gerin, W. (2013). Stress and disease: A structural and functional analysis. *Social and Personality Psychology Compass, 7,* 217–227.

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory STAI (Form Y).* Palo Alto, CA: Consulting Psychologists Press.

Steptoe, A., Gibson, E. L., Hamer, M., & Wardle, J. (2007). Neuroendocrine and cardiovascular correlates of positive affect measured by ecological momentary assessment and by questionnaire. *Psychoneuroendocrinology, 32,* 56–64. http://dx.doi.org/10.1016/j.psyneuen.2006.10.001

Steptoe, A., Hamer, M., & Chida, Y. (2007). The effects of acute psychological stress on circulating inflammatory factors in humans: A review and meta-analysis. *Brain, Behavior, and Immunity, 21,* 901–912. http://dx.doi.org/10.1016/j.bbi.2007.03.011

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

Steptoe, A., Wardle, J., & Marmot, M. (2005). Positive affect and health-related neuroendocrine, cardiovascular, and inflammatory processes. *Proceedings of the National Academy of Sciences of the United States of America, 102,* 6508–6512. http://dx.doi.org/10.1073/pnas.0409174102

Tugade, M. M., & Fredrickson, B. L. (2004). Resilient individuals use positive emotions to bounce back from negative emotional experiences. *Journal of Personality and Social Psychology, 86,* 320–333. http://dx.doi.org/10.1037/0022-3514.86.2.320

Weaver, J. D., Huang, M.-H., Albert, M., Harris, T., Rowe, J. W., & Seeman, T. E. (2002). Interleukin-6 and risk of cognitive decline: MacArthur studies of successful aging. *Neurology, 59,* 371–378. http://dx.doi.org/10.1212/WNL.59.3.371

Zautra, A. J., Affleck, G. G., Tennen, H., Reich, J. W., & Davis, M. C. (2005). Dynamic approaches to emotions and stress in everyday life: Bolger and Zuckerman reloaded with positive as well as negative affects. *Journal of Personality, 73,* 1511–1538. http://dx.doi.org/10.1111/j.0022-3506.2005.00357.x

Zautra, A. J., Hoffman, J., Potter, P., Matt, K. S., Yocum, D., & Castro, L. (1997). Examination of changes in interpersonal stress as a factor in disease exacerbations among women with rheumatoid arthritis. *Annals of Behavioral Medicine, 19,* 279–286. http://dx.doi.org/10.1007/BF02892292

Zautra, A. J., Johnson, L. M., & Davis, M. C. (2005). Positive affect as a source of resilience for women in chronic pain. *Journal of Consulting and Clinical Psychology, 73,* 212–220. http://dx.doi.org/10.1037/0022-006X.73.2.212

Zautra, A. J., Reich, J. W., Davis, M. C., Potter, P. T., & Nicolson, N. A. (2000). The role of stressful events in the relationship between positive and negative affects: Evidence from field and experimental studies. *Journal of Personality, 68,* 927–951. http://dx.doi.org/10.1111/1467-6494.00121

Zohar, D., Tzischinsky, O., Epstein, R., & Lavie, P. (2005). The effects of sleep loss on medical residents' emotional reactions to work events: A cognitive-energy model. *Sleep: Journal of Sleep and Sleep Disorders Research, 28,* 47–54.

Received October 21, 2014
Revision received April 14, 2015
Accepted April 18, 2015 ■