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Feeling Bad Is Not Always Unhealthy: Culture Moderates the Link Between Negative Affect and Diurnal Cortisol Profiles

Jiyoung Park
University of Texas at Dallas

Shinobu Kitayama
University of Michigan

Yuri Miyamoto and Christopher L. Coe
University of Wisconsin, Madison

Prior research has demonstrated that the daily experience of negative affect is associated with increased levels of proinflammatory activity as evidenced by higher interleukin-6 among Americans but not among Japanese. This cultural difference may be driven by culturally divergent beliefs about negative affect as a source of threat to self-image versus as natural and integral to life. Here, we examined whether culture may moderate the relationship between negative affect and biological stress responses, with a focus on the hypothalamic-pituitary-adrenal (HPA) axis activity. By using culturally matched surveys of Americans ($N = 761$) and Japanese ($N = 328$), we found that negative affect was associated with a flattening of the diurnal cortisol slope among Americans after controlling for demographic variables, personality traits, sleep patterns, and health behaviors. In contrast, the association between negative affect and the HPA axis activity was negligible among Japanese. Moreover, we assessed biological health risk with biomarkers of both inflammation (interleukin-6 and C-reactive protein levels) and cardiovascular function (higher systolic blood pressure and total-to-HDL cholesterol ratio) and found that the relationship between negative affect and increased biological health risk, which was observed only among Americans, was mediated by the flattening of the diurnal cortisol rhythm. These findings suggest that cultural differences in how emotions are construed may make the experience of negative affect more or less stressful and differentially consequential for health.

Keywords: culture, negative affect, stress, diurnal cortisol profiles, biological health risk

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In her bestselling book, Judith Orloff (2010) advocated a view that one must liberate oneself from negative affect to achieve a healthy state of mind, body, and spirit. Embedded in this argument is a construal of negative affect as a harmful and problematic experience, causing potentially negative health consequences. Consistent with this view of negative affect as problematic, numerous studies have linked negative affect to increased health risk, including increased inflammatory activity (Panagiotakos et al., 2004), risk for cardiovascular disease (Kubzansky & Kawachi, 2000), and mortality (Pinquart & Duberstein, 2010). In a recent study, Miyamoto et al. (2013) assessed interleukin-6 (IL-6), a proinflammatory cytokine, as a marker of health risk and confirmed that there is a strong association between negative affect and IL-6 among Americans. Importantly, however, this linkage was absent among Japanese adults.

This cultural difference in the association between negative affect and IL-6 may be attributed to the distinct way that negative affect is construed in each culture—that is, whether negative affect is interpreted as a failure of self-control, and thus poses a threat to one's sense of self (in the United States), or is generally accepted as a natural aspect of life, and thus is not as threatening (in Japan). To date, however, little is known about whether negative affect is linked in a differential manner across cultures to biological stress responses known to react to self-threat (Dickerson, Gruenewald, & Kemeny, 2004). In the present analysis, we filled this gap by examining whether the degree to which negative affect is associated with increases in physiological stress responses is moderated by culture by comparing American and Japanese adults from two large, cross-culturally matched surveys. Specifically, we examined the regulation of the hypothalamic-pituitary-adrenal (HPA) axis, as reflected in diurnal cortisol profiles, which was employed as a

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Jiyoung Park, School of Behavioral and Brain Sciences, University of Texas at Dallas; Shinobu Kitayama, Department of Psychology, University of Michigan; Yuri Miyamoto and Christopher L. Coe, Department of Psychology, University of Wisconsin, Madison.

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Correspondence concerning this article should be addressed Jiyoung Park, School of Behavioral and Brain Sciences, University of Texas at Dallas, 800 West Campbell Road, Richardson, TX 75080. E-mail: j.park@utdallas.edu

neuroendocrine biomarker. Additionally, we also tested whether the Miyamoto et al. (2013) conclusion based on IL-6 levels would generalize to multiple biomarkers of both inflammation and cardiovascular function. We further examined the associations between diurnal cortisol profiles and these other biomarkers of health risk across the two countries.

Culturally Divergent Folk Theories of Negative Affect

The last two decades of cultural psychological research has documented substantial variation in how negative affect is viewed across cultures (e.g., Boiger, Mesquita, Uchida, & Feldman Barrett, 2013; Diener & Suh, 2000; Mesquita & Leu, 2007). Dating back to Greek philosophical traditions, Western beliefs about emotions have been based on a hedonic principle that people are motivated to maximize positive affect and minimize negative affect (Tatarkiewicz, 1976). The pursuit of positive affect is seen as the cardinal means to achieve well-being, and correspondingly, negative affect is construed as an adverse state to be avoided or otherwise controlled and held at bay (Bastian et al., 2012). These beliefs, in turn, have likely been reinforced by a broader idea of emotions as a manifestation of one's internal attributes (Chentsova-Dutton, Tsai, & Gotlib, 2010; Kitayama, Markus, & Kurokawa, 2000). Because emotions are construed as a reflection of the personal self, recurrent daily experiences of negative affect are interpreted as signaling an inability or failure to regulate problematic impulses or cope with environmental demands (Kotchemidova, 2005). Thus, they will pose a threat to one's sense of self, thereby eliciting biological stress responses. If repeatedly experienced, the physiological activation may gradually compromise health over time (Epel, McEwen, & Ickovics, 1998).

Although the view of negative affect as unwanted, and thus as a state to be avoided, is widely shared across Western cultures, such beliefs are less common and not as widely shared in Asian cultures. Indeed, Peng, Nisbett, and others have suggested that beliefs about emotions in East Asia may instead have their roots in dialectical thought traditions, including Buddhism, Confucianism, and Taoism (Peng & Nisbett, 1999; Spencer-Rodgers & Peng, 2017; Wilken & Miyamoto, 2017). The dialectical perspective holds that elements in opposite poles, such as positive affect and negative affect, are mutually dependent. Thus, they coexist in a state of balance rather than being mutually exclusive in a dualistic way (De Vaus, Hornsey, Kuppens, & Bastian, 2018; Miyamoto & Ma, 2011). Based on this perspective, negative affect is viewed as relatively transient, with the potential to be transformed in more positive directions, because both negative and positive affect are natural, cyclical, and interconnected on a continuum. In support of the hypothesized presence of this dialectical view of emotion in many Asian cultures, evidence shows that when asked to report on the frequency of their emotional experiences, whereas Westerners typically evince a strong negative association between positive and negative affect, Asians express a weaker or no association between them (Bagozzi, Wong, & Yi, 1999; Kitayama et al., 2000; Scollon, Diener, Oishi, & Biswas-Diener, 2005; Spencer-Rodgers, Peng, & Wang, 2010). Furthermore, Miyamoto and Ma (2011) showed that Asians endorse the dialectical view of emotions more strongly than do Americans of European family backgrounds. Building on this prior work, we hypothesized that adults in Japan would not feel either as threatened or stressed merely because they experienced negative affect. Appraising negative affect in these more neutral, nonthreatening ways may protect a person from its adverse effects on physiology and, thus, on long-term health (Jamieson, Mendes, & Nock, 2013).

The aforementioned study by Miyamoto et al. (2013), which found a reliable association between negative affect and IL-6 among Americans but not among Japanese, is consistent with this perspective. Moreover, Curhan et al. (2014) similarly observed that the association between negative affect and self-reported measures of health was significantly weaker among Japanese than among Americans. We further hypothesize that negative affect is unhealthy for Americans, as it poses a threat to their self-image and thus is aversive and stressful. In contrast, for many Asian cultures, negative affect may be relatively innocuous and thus is less likely to induce the perception of threat or the accompanying physiological stress responses. To date, however, no study has specifically examined the potential cultural difference in the association between negative affect and biological stress responses. The main aim of the present analyses was to address this gap by assessing the activity of the HPA axis, focusing on cortisol, the final hormone secreted into the bloodstream, which then diffuses into saliva.

HPA Axis Dysregulation as a Neuroendocrine Marker of Stress

Cortisol is the primary glucocorticoid released by the adrenal gland and is activated in response to a variety of stressful events, such as perceived threats to physical and psychological safety, including the subjective experience of self-threat (Dickerson et al., 2004). In healthy states, cortisol secretion follows a diurnal pattern such that cortisol is secreted in abundance at awakening (acutely peaking approximately 30 min afterward in response to awakening), which is then followed by a steady decline across the rest of the day. Cortisol secretion is adaptive in the face of acute stress because this hormone mobilizes the body's energy resources to meet the physiological demands of the stress. However, when the activation is prolonged, it can lead to a "wear and tear" dysregulation of other physiological systems of the body, consistent with the allostatic load models, including altered hormone feedback signals to and from the brain (McEwen, 2000). Indeed, evidence shows that sustained stress and recurrent daily demands alter the healthy daily rhythm. Specifically, the "wear and tear" caused by daily stress and threats has been shown to result in a less steep decline in cortisol levels across the day (Kirschbaum & Hellhammer, 1994).

If recurrent experience of negative affect is a source of stress (given its self-threatening nature of the experience), it should be associated with a flattening of the diurnal cortisol slope. Such an effect has been repeatedly observed in studies of Western populations (Adam, Hawkley, Kudielka, & Cacioppo, 2006; Polk, Cohen, Doyle, Skoner, & Kirschbaum, 2005). Given the Asian construal of negative affect as more transient, however, we expected that this association would be substantially attenuated among Japanese adults. The first aim of the current work was to test this prediction.

Extension to Biological Health Risk

The second aim of the current work was to examine the robustness of the Miyamoto et al. (2013) finding, which had been based on a single biomarker (the proinflammatory cytokine, IL-6), by testing multiple indicators of both inflammation and cardiovascular status. One additional inflammatory biomarker closely tied to cytokine activity is C-reactive protein (CRP), an acute phase reactant produced by the liver (Heinrich, Castell, & Andus, 1990). When elevated over a long period, proinflammatory activity gradually compromises blood vessels, leading to the buildup of plaque and poorer cardiovascular functioning, and can adversely affect the kidneys, which then raises blood pressure (Everson-Rose & Lewis, 2005). We therefore incorporated measures from other previous analyses (Kitayama et al., 2015, 2018) and included two indices of cardiovascular health (systolic blood pressure and lipid metabolism) in addition to the two blood biomarkers of inflammation (IL-6 and CRP). We anticipated that a composite measure of biological health risk defined by these four biomarkers would be significantly associated with negative affect among Americans but not among Japanese.

In addition, we explored whether the two associations we anticipated for Americans—that is, (a) between negative affect and the flattening of diurnal cortisol rhythm, and (b) between negative affect and biological health risk defined by increased levels of inflammation and cardiovascular dysfunction—might be related in a systematic way. As noted earlier, stress responses caused by threatening events, indexed by the HPA dysregulation evident in a flattened diurnal rhythm, may eventually increase biological health risk. Indeed, prior work has demonstrated that a dysregulation of the HPA axis contributes to increases in the levels of proinflammatory cytokines in peripheral circulation (Papanicolaou, Wilder, Manolagas, & Chrousos, 1998), which, in turn, catalyze the pathogenesis of cardiovascular disease (Kumari, Shipley, Stafford, & Kivimaki, 2011). In particular, among several key indications of cortisol hyper- and hypoactivity, the flattening of the diurnal cortisol slope has been shown to be most consistently linked to mental and physical health outcomes (Adam et al., 2017). Given its sensitivity to stress (Adam & Gunnar, 2001; Doane & Adam, 2010) as well as its associations with a variety of health problems (Doane et al., 2013; Kumari et al., 2009), the diurnal cortisol slope has been proposed by many as an important pathway linking stress to poor health outcomes (Adam & Kumari, 2009). Building on this evidence, we explored whether a flattening of the diurnal cortisol rhythm would statistically mediate the relationship between negative affect and biological health risk among Americans. We predicted that the evidence for this type of mediation would be negligible among Japanese because negative affect would be less likely to be as threatening or stressful for them.

Present Research

We tested our predictions using two large cross-culturally matched surveys of Americans (Midlife in the United States [MIDUS]) and Japanese (Midlife in Japan [MIDJA]; see http://midus.wisc.edu/ for more information). Our first aim (Aim 1) was to test the prediction that negative affect would be associated with a flattening of the diurnal cortisol slope among Americans, whereas this linkage would be either attenuated or absent among Japanese. Our second aim (Aim 2) was to test the generalizability of the Miyamoto et al. (2013) conclusions, based on Japanese who participated in the first wave of MIDJA (MIDJA I), by examining the relationship between negative affect and the composite index of four biomarkers of inflammation and cardiovascular status among Japanese who participated in the second wave (MIDJA II) 5 years later. Our final, exploratory aim was to test the potential mediating influence of the diurnal cortisol rhythm (i.e., slope) on the relationship between negative affect and biological health risk for both cultural groups as an initial step to better understand the path from negative affect to poor health.

Method

Participants

The American data were obtained from the MIDUS survey. The first wave of the survey was conducted in 1995 to 1996 based on a national probability sample of 7,108 adults (aged 25 to 74 years) recruited through random-digit dialing. A subset of respondents completed a follow-up survey in 2004 to 2006 (MIDUS II; N = 4,963). A random subsample of the MIDUS II respondents were recruited to complete the National Study of Daily Experiences (NSDE II; N = 2,022), which included assessments of cortisol samples over 4 days and nightly telephone interviews over 8 days (see Almeida, McGonagle, & King, 2009, for further details). The current analysis included a subset of the NSDE II respondents who traveled to one of three Clinical and Translational Research Centers (CTRCs) for additional blood and urine collections (n = 817; M_{age} = 58.47, SD_{age} = 11.48; 54.7% female). The time lag between the MIDUS II survey session and the biomarker session was approximately 24 months. In order to maximize the cultural contrast, we excluded a small subsampling of other racial groups (23 African Americans, five Native Americans, three Asian Americans, one multiracial, 22 others, and two missing), which left 761 European Americans (M_{age} = 58.71, SD_{age} = 11.52; 54.7% female).

The Japanese data were obtained from the companion survey conducted in Japan, MIDJA. The first wave of the MIDJA was conducted in 2008 among a probability sample of 1,027 Japanese adults (aged 30 to 79 years) recruited from and representative of all 23 wards of the Tokyo metropolitan area. The second wave of data was collected in 2012 among a subset of the MIDJA I respondents (MIDJA II; n = 657). Our analysis focused on a subsample of the MIDJA II respondents who provided daily saliva samples for cortisol assessments over 3 days and also completed a biomarker assessment by traveling to a clinic at the University of Tokyo (n = 328; M_{age} = 60.43, SD_{age} = 13.14; 52.4% female).[1] The interval

[1] Our analysis focused on the MIDJA II biomarker sample whereas Miyamoto et al. (2013) used the MIDJA I biomarker sample. The MIDJA II biomarker sample included a subsample of the MIDJA I biomarker sample [i.e., the sample included in the Miyamoto et al. analysis (n = 243)] and some additional participants from the first wave who only completed the survey session but not the biomarker session (n = 85). Thus, blood samples for biomarker assays were obtained from some of the same participants in each wave (which accounts for 75% of our Japanese sample), but notably from two different timepoints with a time lag of approximately five years. Hence, there is no overlap in the Japanese data between our study and the previous Miyamoto et al. publication.

between the survey session and the biomarker collection for MIDJA II was 18 to 20 months.

Because we used the publicly available data sets, the total sample size was not determined based on an a priori power analysis. However, building on prior evidence that the same sample size was sufficient to discern cultural differences in psychosocial correlates of biological health (Kitayama et al., 2015, 2018; Miyamoto et al., 2013; Yoo, Miyamoto, Rigotti, & Ryff, 2017), the current sample size was deemed adequate to test our predictions.[2]

Measures

Salivary cortisol measures. Participants self-collected saliva samples at home using Salivettes (Sarstedt, Rommelsdoft, Germany). American participants provided the saliva samples at four time points each day for 4 consecutive days (on Days 2 to 5 of the 8-day NSDE study period), including upon awakening, 30 min after waking, before lunch, and at bedtime, which resulted in up to 16 samples for each participant (four samples per day for 4 days). The saliva samples from Japanese participants were obtained using the same daily protocol (with the four collection time points each day), except that their samples were collected for 3 consecutive days instead of 4, which resulted in up to 12 samples for each participant (four samples per day for 3 days). Written logs of the collection times were obtained to ensure compliance with the scheduled saliva collection. The samples from both countries were frozen and shipped to the MIDUS Biocore lab in the United States, where they were assayed with a time-resolved immunoassay with fluorescence detection using commercially available kits (IBL, Hamburg, Germany). The samples were assayed in duplicate and the intraassay and interassay coefficients of variation were below 5%. Following an established procedure (e.g., Sin, Ong, Stawski, & Almeida, 2017), values were natural log-transformed because the distributions of cortisol responses were positively skewed for both cultural groups.

To estimate the diurnal cortisol slope, we performed a regression analysis for each participant with the time of the daily data collection as a predictor of natural-log transformed cortisol values (see Doane et al., 2013, and Kumari et al., 2011, for the same approach). The second saliva sample on each day (collected 30 min after waking) was excluded from the calculation of slopes to control for the effect of the cortisol awakening response. The resulting regression coefficient was used to represent each participant's diurnal cortisol decline, which was employed as our primary outcome variable.

Biological health risk. Following prior research (Kitayama et al., 2015, 2018), we assessed two biomarkers of inflammatory activity (IL-6 and CRP) and two biomarkers of cardiovascular health (systolic blood pressure [SBP] and the ratio of total-to-HDL cholesterol [T/HDL cholesterol]) to generate a single composite index of biological health risk. Frozen blood samples collected during the biomarker session were shipped from the three CTRC sites in the United States and from the clinic in Tokyo, Japan, to a testing laboratory in Madison, Wisconsin (MIDUS Biocore Laboratory) for IL-6 and CRP assays. High-sensitivity enzyme-linked immunosorbent assay was used to determine serum IL-6 levels (Quantikine; R&D Systems, Minneapolis, MN), with a lower sensitivity of detection at 0.16 pg/mL. All values were quantified in duplicate determinations, and any value over 10 pg/mL was rerun in diluted sera to fall on the standard reference curve. A BNII nephelometer (Dade Behring Inc., Deerfield, IL) was used to determine plasma CRP levels, utilizing a particle enhanced immunonephelometric assay. Resting levels of SBP were obtained during the clinic visit in a seated position and the two most similar readings out of three were averaged. American participants' cholesterol data (total and HDL) were assayed at Meriter Labs (Madison, WI) using a Cobas Integra analyzer (Roche Diagnostics, Indianapolis, IN), and Japanese participants' data were assayed at Showa Medical Science in Tokyo, Japan. In addition, for 100 Japanese participants, cholesterol levels were also determined at Meriter Labs, verifying that the cholesterol determinations by the two laboratories were virtually identical ($r > .9$).

Following the statistical approach used in prior research (Kitayama et al., 2015, 2018; Miyamoto et al., 2013), we log-transformed and adjusted a small number of outlier values to reduce skewness (see Data Processing and Analytic Strategies section for winsorization procedure). As shown in our previous work (Kitayama et al., 2015, 2018), the four biomarkers were positively correlated within each country (see Table 1). Furthermore, culture-wise principal component analyses showed that all four indices loaded on a single factor for both cultures, accounting for 40.6% and 45.2% of the variances for Americans and Japanese, respectively. A confirmatory factor analysis (CFA) also confirmed the one-factor structure and further demonstrated measurement equivalence of this construct across both cultural groups. When we tested a configural model in which the factor loadings were freely estimated for both cultural groups, the model showed an acceptable model fit, $\chi^2(4) = 22.41$, $p < .001$, comparative fit index (CFI) = .954, root mean square error of approximation (RMSEA) = .092. When we compared this model with a metric invariance model in which we constrained the factor loadings to be equal across the groups, the model fit was similarly acceptable, $\chi^2(7) = 26.50$, $p < .001$, CFI = .951, RMSEA = .072. The CFI value difference between the two models (ΔCFI = .003) was less than 0.01, which indicates that the four biomarkers, when collapsed, coherently represent biological health risk for both cultural groups (Cheung & Rensvold, 2002). We thus used the factor scores from the principal component analysis, after combining both cultural groups, as a single index of biological health risk.

Negative affect. Following Miyamoto et al. (2013), we assessed negative affect with the six-item scale developed by Mroczek and Kolarz (1998), which was administered during the survey session. Participants rated how much of the time during the past 30 days (1 = *none of the time*, 5 = *all the time*) they felt six negative emotions (i.e., "so sad nothing could cheer you up," "nervous," "restless or fidgety," "hopeless," "that everything was an effort," and "worthless"; αs = .84 and .87 for Americans and Japanese, respectively). We tested measurement equivalence of this construct across the two cultural groups by comparing two CFA models with and without constraining the factor loadings to be equal across the groups. The configural model provided a good model fit, $\chi^2(10) = 19.16$, $p = .038$, CFI = .997, RMSEA = .041.

[2] Post hoc power analyses revealed that the power for detecting a significant interaction effect (Culture × Negative Affect) on the diurnal cortisol slope ranged from 56% to 70%, depending on which covariates were used in models. We also achieved a power of 52% to 61% to detect the same interaction effect on biological health risk.

Table 1
Intercorrelations Among the Four Biomarkers for Americans and Japanese

Variables	*n*	1	2	3	4
Americans					
1. IL-6	754	—	.49***	.13***	.07*
2. CRP	752		—	.14***	.17***
3. SBP	760			—	.11**
4. T/HDL cholesterol	752				—
Japanese					
1. IL-6	326	—	.50***	.27***	.15**
2. CRP	326		—	.17**	.27***
3. SBP	328			—	.21***
4. T/HDL cholesterol	326				—

Note. All four biomarkers were winsorized to three standard deviations from the mean for each culture and were then log-transformed. IL-6 = Interleukin-6; CRP = C-reactive protein; SBP = systolic blood pressure; T/HDL cholesterol = total-to-HDL cholesterol.
* $p < .05$. ** $p < .01$. *** $p < .001$.

Importantly, the metric model showed no worse fit than the configural model, $\chi^2(15) = 31.78$, $p = .007$, CFI = .994, RMSEA = .045, with less than 0.01 difference in the CFI value (ΔCFI = .003), suggesting that the construct of negative affect has the same meaning to participants in both countries.

Covariates. We controlled for several variables that could influence the effects of negative affect on diurnal cortisol rhythms and/or biological health risk, including demographic variables, personality traits, sleep patterns, and health behaviors.

Demographic variables. Building on previous evidence that demographic variables such as gender (0 = *male*, 1 = *female*), age, and educational attainment are strong predictors of diurnal cortisol patterns (Adam & Kumari, 2009) as well as levels of inflammation and cardiovascular risk (Coe et al., 2011), we adjusted for the effects of these variables. Approximately a half of the participants were female (54.7% and 52.4% for Americans and Japanese, respectively). Participants' age ranged from 35 to 86 years for Americans and from 36 to 85 years for Japanese at the time of biological data collection. Educational attainment was measured as a number of years of education that each participant completed.

Personality traits. Following Miyamoto et al. (2013), we controlled for two personality traits known to affect retrospective reports of emotional experiences. Specifically, individuals who are high in neuroticism tend to report more experiences of negative affect retrospectively than concurrently, whereas those who are high in extraversion show the opposite tendency of reporting more positive (or less negative) affect retrospectively than concurrently (Barrett, 1997). We thus controlled for these traits to sharpen our focus on the health correlates of negative affect. Neuroticism was assessed with an abbreviated Big Five personality trait scale (Rossi, 2001). Participants rated the extent to which each of the four adjectives ("worrying," "nervous," "moody," and "calm" [reverse-coded]) described them using a 4-point scale (1 = *not at all*, 4 = *a lot*; αs = .74 and .49 for Americans and Japanese, respectively). We used the same scale to assess extraversion, using participants' ratings on five items ("friendly," "outgoing," "lively," "active," and "talkative"; αs = .78 and .84 for Americans and Japanese, respectively). As shown in our previous work (Kitayama et al., 2018), one reverse-coded item ("calm") of the neuroticism scale did not cohere well with the rest three items, which resulted in the low reliability among Japanese. Excluding this item improved the reliability (α = .63) and, furthermore, did not alter the results substantially.

Sleep patterns. The timing of the sleep–wake cycle has been linked to cortisol secretory patterns (Lasikiewicz, Hendrickx, Talbot, & Dye, 2008). Following an established procedure (e.g., Adam & Kumari, 2009), we thus controlled for two standard markers of the sleep–wake cycle—that is, average wake time and average sleep duration across the days of saliva cortisol sampling. These parameters were estimated on the basis of the written logs of the cortisol collection times provided by the participants. The time when participants provided the first saliva sample daily was recorded as "wake time" for each day. The duration of sleep was estimated based on the first saliva collection time (wake time) and the last saliva collection time (bed time) of each day; wake time was subtracted from bed time to create an index of "awake hours," and this index was subtracted from 24 hr to compute the index of sleep duration. The daily data were then collapsed across the days of saliva sampling (4 days for Americans and 3 days for Japanese) to create the average scores of wake time and sleep duration, respectively.

Health behaviors. We controlled for smoking status and alcohol consumption as two indices of risky health behaviors that have been linked to cortisol secretion as well as biological health risk (Huizink, Greaves-Lord, Oldehinkel, Ormel, & Verhulst, 2009; O'Connor et al., 2009). A dummy-coded variable was used to assess current smoking status (0 = *nonsmoking*, 1 = *smoking*). The average number of alcohol drinks consumed per week was used as an index of alcohol consumption.

Data Processing and Analytic Strategies

For all variables, we checked for outliers exceeding three standard deviations from the mean for each variable in each country. We found outlier values in the diurnal cortisol slope, all four biomarkers, two parameters of the sleep–wake cycle, and alcohol consumption. To minimize the effects of these outliers, the scores were winsorized and set at three standard deviations from the mean within each culture separately (Kitayama et al., 2015, 2018; Miyamoto et al., 2013). This approach, advocated by both Winsor and Tukey, preserves their rank placement, while lessening the need to exclude an outlier value that is known to be high, and thus enhances the rigor of the statistical modeling (Reifman & Keyton, 2010).

Aim 1 was to test whether the link between negative affect and the diurnal cortisol slope would be different between Japan and the United States. Aim 2 was to examine whether the cultural difference documented by Miyamoto et al. (2013) on the relationship between negative affect and IL-6 would extend to the relationship between negative affect and the composite index of biological health risk comprised of four biomarkers related to inflammation and cardiovascular status.

In each analysis, we tested a three-step multiple regression model that varied in the covariates that were included. In Model 1, we entered the main effects of culture and negative affect and the interaction between the two as predictors of diurnal cortisol slope (Aim 1) and biological health risk (Aim 2). Considering the heterogeneity of the participants in terms of the demographic characteristics, we also included three demographic variables (gender, age, and years of education) as well as two personality traits (neuroticism and extraversion) as covariates in this model. Model 2 included two measures of the sleep–wake cycle (average wake time and average sleep duration) as additional covariates. In Model 3, we additionally controlled for two indices of health behaviors (smoking status and alcohol consumption).

Finally, as an initial step toward probing the physiologic pathways through which negative affect influences biological health across cultures, we explored the possibility that the hypothesized cultural difference in the relationship between negative affect and biological health risk would be mediated by another cultural difference—the relationship between negative affect and diurnal cortisol slope—by performing a moderated mediation analysis.

Results

Cultural Differences in Key Variables

Before testing the main predictions, we first examined whether the two cultural groups differed in the key study variables, including negative affect, diurnal cortisol slope, and biological health risk. Table 2 provides descriptive summary statistics for these variables. Japanese reported higher levels of negative affect ($M = 1.72$, $SE = .03$, 95% confidence interval: CI [1.65, 1.78]) than did Americans ($M = 1.47$, $SE = .02$, 95% CI [1.43, 1.51]), $F(1, 1084) = 40.56$, $p < .001$, $\eta_p^2 = .04$. The decline of the cortisol slope for Japanese was less steep ($M = -.08$, $SE = .003$, 95% CI [−.08, −.07]) than that of Americans ($M = -.12$, $SE = .002$, 95% CI [−.12, −.11]), $F(1, 1085) = 141.27$, $p <$

Table 2
Descriptive Statistics for Key Study Variables for Americans and Japanese

Variables	Americans			Japanese		
	n	*M*	*SD*	*n*	*M*	*SD*
Demographic variables						
Gender (% female)	416	54.7		172	52.4	
Age	761	58.71	11.52	328	60.43	13.14
Years of education	758	14.61	2.43	326	13.67	2.43
Psychological variables						
Negative affect	759	1.47	.54	327	1.72	.66
Neuroticism	759	2.01	.63	328	2.05	.52
Extraversion	759	3.14	.57	328	2.47	.66
Sleep–wake cycle						
Average wake time	761	6.64	1.19	326	6.32	1.16
Average sleep duration	761	8.11	1.15	326	7.43	1.24
Health behaviors						
Smoking status (% yes)	79	10.4		44	13.4	
Alcohol consumption	760	2.74	4.38	322	5.96	8.19
Average cortisol levels						
At awakening	760	2.55	.59	326	2.84	.45
30 min after waking	760	2.91	.61	326	3.08	.61
Before lunch	761	1.77	.59	326	2.42	.41
At bedtime	760	.67	.88	326	1.55	.67
Average cortisol collection times						
At awakening	761	6.65	1.31	326	6.32	1.20
30 min after waking	760	7.29	1.34	326	6.96	1.15
Before lunch	761	12.72	1.25	326	12.24	.75
At bedtime	761	22.53	1.34	326	22.89	1.31
Diurnal cortisol rhythm						
Diurnal cortisol slope	761	−.12	.06	326	−.08	.04
Biomarkers						
IL-6	754	.31	.31	326	.04	.33
CRP	752	.13	.48	326	−.39	.50
SBP	760	2.12	.06	328	2.10	.06
T/HDL cholesterol	752	.55	.15	326	.51	.13
Biological health risk (factor score)	750	.28	.89	326	−.65	.94

Note. Average cortisol levels were natural log-transformed. The values on all four biomarkers (IL-6, CRP, SBP, and T/HDL cholesterol) were log-transformed. Biological health risk scores were obtained from a principal component analysis performed on both samples combined based on the four biomarkers, which yielded a single factor. IL-6 = Interleukin-6; CRP = C-reactive protein; SBP = systolic blood pressure; T/HDL cholesterol = total-to-HDL cholesterol.

.001, $\eta_p^2 = .12$. The two groups also differed in the composite index of biological health risk. As found similarly in previous analyses of IL-6 and CRP (Coe et al., 2011), this composite index was significantly higher among Americans ($M = .28$, $SE = .03$, 95% CI [.22, .35]) than Japanese ($M = -.65$, $SE = .05$, 95% CI [−.75, −.55]), $F(1, 1074) = 243.37$, $p < .001$, $\eta_p^2 = .19$. These differences between the two countries remained the same even after adjustments for the effects of all covariates included in Model 3.

Aim 1: Culture as a Moderator of the Link Between Negative Affect and Diurnal Cortisol Slope

Next, we examined whether the relationship between negative affect and the diurnal cortisol slope was moderated by culture by testing the three-step regression models that differed in which covariates were included. The results of this analysis are summarized in Table 3 (Part A). The interaction effect between culture and negative affect was significant in Model 1 when we controlled for three demographic variables and two personality traits, $b = -.011$, 95% CI [−.022, −.001], $t(1062) = -2.05$, $p = .040$, and in Model 2 when we additionally controlled for two parameters of the sleep–wake cycle, $b = -.013$, 95% CI [−.024, −.003], $t(1060) = -2.43$, $p = .015$. Notably, the conclusions remained the same even when we additionally controlled for two health behaviors in Model 3, $b = -.012$, 95% CI [−.023, −.001], $t(1058) = -2.23$, $p = .026$. We used Model 3 and tested a simple slope for each cultural group. As illustrated in Figure 1A, greater negative affect was linked to a flatter cortisol slope among Americans, $b = .017$, 95% CI [.009, .025], $t(1058) = 4.20$, $p < .001$. In contrast, this relationship was completely absent for the Japanese participants, $b = .005$, 95% CI –.004, .013], $t(1058) = 1.12$, $p = .264$.

Table 3
Regression Coefficients in Predicting (Part A) Diurnal Cortisol Slope and (Part B) Biological Health Risk as a Function of Culture and Negative Affect

Predictor variables	Model 1		Model 2		Model 3	
	b	*t* test	*b*	*t* test	*b*	*t* test
A. Diurnal cortisol slope						
Culture	.037	9.594***	.030	7.825***	.030	7.709***
Negative affect	.017	4.149***	.019	4.693***	.017	4.196***
Culture × Negative Affect	−.011	−2.054*	−.013	−2.430*	−.012	−2.234*
Gender	−.002	−.532	.001	.254	.001	.470
Age	.001	3.927***	.001	5.074***	.001	5.550***
Years of education	−.002	−3.467***	−.002	−3.653***	−.002	−3.077**
Neuroticism	−.003	−.985	−.003	−.970	−.003	−.924
Extraversion	.001	.527	.002	.806	.002	.732
Average wake time			.001	.364	.001	.448
Average sleep duration			−.010	−6.535***	−.010	−6.589***
Smoking status					.019	3.762***
Alcohol consumption					.000	−.659
R^2		.160		.199		.210
F for ΔR^2		25.340***		25.767***		7.113***
B. Biological health risk						
Culture	−1.031	−15.806***	−.988	−14.744***	−.957	−13.877***
Negative affect	.177	2.519*	.159	2.263*	.128	1.811[a]
Culture × Negative Affect	−.210	−2.224*	−.199	−2.111*	−.188	−2.000*
Gender	−.257	−4.838***	−.276	−5.173***	−.288	−5.155***
Age	.018	7.709***	.017	7.274***	.018	7.619***
Years of education	−.053	−4.859***	−.054	−4.917***	−.048	−4.375***
Neuroticism	−.083	−1.513	−.078	−1.425	−.070	−1.280
Extraversion	−.017	−.360	−.023	−.498	−.021	−.462
Average wake time			.023	.932	.024	.963
Average sleep duration			.050	1.953[a]	.051	1.985*
Smoking status					.286	3.348***
Alcohol consumption					−.010	−2.008*
R^2		.279		.285		.294
F for ΔR^2		50.879***		4.033*		7.008***

Note. *N*s = 1,071 and 1,059 for the analyses on diurnal cortisol slope and biological health risk, respectively. United States is coded as the referent group for the culture variable. Model 1 tested the main effects of culture and negative affect and the interaction between the two variables after controlling for three demographic variables (gender, age, and years of education) and two personality traits (neuroticism and extraversion). Model 2 included two measures of the sleep–wake cycle (average wake time and average sleep duration), and Model 3 additionally controlled for two indices of health behaviors (smoking status and alcohol consumption).
[a] $p < .10$.
* $p < .05$. ** $p < .01$. *** $p < .001$.

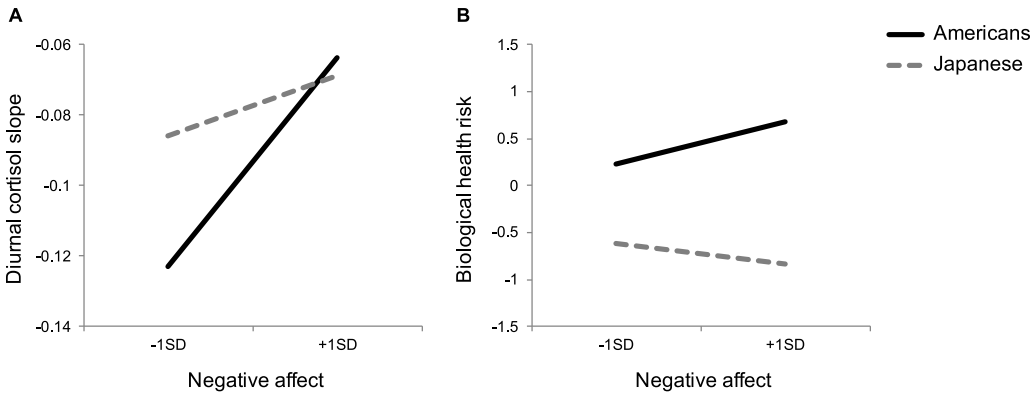

Figure 1. (A) Diurnal cortisol slope and (B) biological health risk as a function of negative affect for Americans (solid line) and Japanese (dotted line). Higher number on the *y*-axis indicates (A) a flatter diurnal cortisol slope and (B) greater biological health risk. Model 3 covariates (gender, age, years of education, neuroticism, extraversion, average wake time, average sleep duration, smoking status, and alcohol consumption) are controlled.

We next tested the awakening and evening cortisol samples separately to examine which cortisol response would be more important in accounting for the moderation of culture on the association between negative affect and the diurnal cortisol slope. The Culture × Negative Affect interaction was significant for the cortisol levels at awakening, regardless of the covariates included (for example, $b = .194$, 95% CI [.077, .312], $t(1057) = 3.25$, $p = .001$, in Model 3). In contrast, the same interaction was not significant for evening cortisol levels in all three models (for example, $b = .050$, 95% CI [–.123, .223], $t(1057) = .57$, $p = .572$ in Model 3). A subsequent simple slope analysis based on Model 3 showed that negative affect was linked to lower cortisol levels at awakening among Americans, $b = -.165$, 95% CI [−.253, −.077], $t(1057) = -3.68$, $p < .001$, whereas this relationship was not evident among Japanese, $b = .029$, 95% CI [−.066, .125], $t(1057) = .60$, $p = .547$. These results suggest that it was the more common occurrence of lower values in the morning, but not higher evening cortisol levels, that drove the significant relationship between negative affect and a flatter cortisol slope among Americans.

Aim 2: Culture as a Moderator of the Link Between Negative Affect and Biological Health Risk

Next, we tested whether culture also moderated the influence of negative affect on the composite index of biological health risk by following the same analytic steps used in the previous analyses. The key regression coefficients are summarized in Table 3 (Part B). The interaction between culture and negative affect was significant when we controlled for demographic variables and personality traits in Model 1, $b = -.210$, 95% CI [−.395, −.025], $t(1050) = -2.22$, $p = .026$, and sleep parameters in Model 2, $b = -.199$, 95% CI [−.384, −.014], $t(1048) = -2.11$, $p = .035$. Importantly, the interaction remained significant even when we additionally controlled for health behaviors in Model 3, $b = -.188$, 95% CI [−.372, −.004], $t(1046) = -2.00$ $p = .046$. A subsequent simple slope analysis based on Model 3 revealed that there was a marginal linkage between negative affect and increased biological health risk among Americans, $b = .128$, 95% CI [−.011, .267], $t(1046) = 1.81$, $p = .070$ (see Figure 1B). In contrast, this link was negligible among Japanese, $b = -.060$, 95% CI [−.209, .089], $t(1046) = -.79$, $p = .431$. Notably, the American slope was significant both in Model 1, $b = .177$, 95% CI [.039, .315], $t(1050) = 2.52$, $p = .012$, and Model 2, $b = .159$, 95% CI [.021, .297], $t(1048) = 2.26$, $p = .024$, indicating that only when we additionally controlled for the two health behaviors did the American effect become weaker. Furthermore, when we tested each of the four biomarkers separately, the results were generally consistent (see Figure S1 of the online supplemental materials), although the interaction did not reach statistical significance for CRP and SBP, and one specific pattern was nonsignificantly reversed (i.e., the effect of negative affect on SBP for Americans; see Table S1 of the online supplemental materials for regression coefficients on four biomarkers separately).[3]

[3] In an exploratory analysis, we tested whether culture moderated a relationship between negative affect and waist-to-hip ratio (WHR), an index of central obesity, as another health risk factor. When we adjusted for the effects of all covariates included in Model 3, there emerged a marginal interaction between culture and negative affect on this variable of adiposity, $b = –.013$, 95% CI [–.028, .001], $t(1056) = -1.77$, $p = .076$. Consistent with the patterns shown in the main analysis, greater negative affect was linked to higher WHR among Americans, $b = .012$, 95% CI [.001, .023], $t(1056) = 2.22$, $p = .027$. In contrast, the association was negligible among Japanese, $b = –.001$, 95% CI [–.013, .011], $t(1056) = –.14$, $p = .892$. Not surprisingly, given this pattern of results, the cultural moderation of the link between negative affect and biological health risk became weak when we additionally controlled for WHR, $b = –.134$, 95% CI [–.308, .039], $t(1044) = –1.52$, $p = .129$. This finding suggests that obesity may serve as a behavioral and metabolic pathway through which emotional experiences compromise biological health—a point that should be addressed in future work (see Yoo et al., 2017 for a similar argument). In contrast, the impact of the Culture × Negative Affect interaction on the diurnal cortisol slope remained significant with the inclusion of WHR as an additional covariate, $b = –.012$, 95% CI [–.022, –.001], $t(1055) = –2.16$, $p = .031$.

Exploratory Aim: Moderated Mediation

Finally, we explored whether the cultural difference in the relationship between negative affect and the diurnal cortisol slope might drive the cultural difference in the relationship between negative affect and biological health risk. If stress physiology, indexed by diurnal cortisol slope, is one of the mediating pathways through which negative affect leads to poor health, this pathway should be significant among Americans but not among Japanese. Specifically, among Americans, negative affect should be associated with a flattening of the diurnal cortisol slope, which, in turn, would be related to increased biological health risk. In contrast, among Japanese, the same mediating path should not be significant because their daily negative affect is not associated with either their diurnal cortisol profiles or biological health risk. This conclusion should be evidenced by a moderated mediation in which the effect of the mediating variable (diurnal cortisol slope) on the relationship between the predictor (negative affect) and the outcome variable (biological health risk) is dependent on the moderator (culture; Hayes, 2013).

We tested the moderated mediation model using Hayes's PROCESS Model 8, with 5,000 bias-corrected bootstrapping samples, using the same set of the covariates we had included in Model 3 for the prior analyses. As predicted, the indirect effect of diurnal cortisol slope on the relationship between negative affect and biological health risk was statistically significant among Americans (95% bias-corrected bootstrapping CI [.017, .074]). That is, negative affect was associated with a flatter diurnal cortisol slope, $b = .017$, 95% CI [.009, .025], $t(1046) = 4.25$, $p < .001$, and when negative affect and diurnal cortisol slope were entered simultaneously as predictors of biological health risk, the association between diurnal cortisol slope and biological health risk remained significant, $b = 2.249$, 95% CI [1.199, 3.299], $t(1045) = 4.20$, $p < .001$, whereas the relationship between negative affect and biological health risk became nonsignificant, $b = .089$, 95% CI [−.049, .228], $t(1045) = 1.26$, $p = .207$. In contrast, the comparable modeling of mediation was not significant among Japanese (95% bias-corrected bootstrapping CI [−.001, .031]) because there was no association between negative affect and diurnal cortisol slope, $b = .005$, 95% CI [−.003, .014], $t(1046) = 1.25$, $p = .213$. Consistent with this pattern of cultural difference in the indirect effects, the moderated mediation model was statistically significant (Hayes index = −.027, 95% bias-corrected bootstrapping CI [−.059, −.005]; see Figure 2).

Discussion

Negative affect has consistently been linked to adverse health outcomes in many studies of American and European adults (Kubzansky & Kawachi, 2000; Panagiotakos et al., 2004; Pinquart & Duberstein, 2010). The main contribution of our work is to challenge the generalizability of this finding to other cultural contexts outside of the West. Specifically, we tested whether daily experiences of negative affect would be linked to both (a) a dysregulation of HPA axis activity as indexed by a flattening of diurnal cortisol slope, and (b) prognostic risk factors for poor health, including proinflammatory activity (IL-6 and CRP) and cardiovascular status (SBP and T/HDL cholesterol). Replicating previous studies of Western populations (Adam et al., 2006; Polk et al., 2005), we found that greater negative affect was associated with a flattening of the diurnal cortisol slopes among Americans. We further showed that this relationship was driven by lower

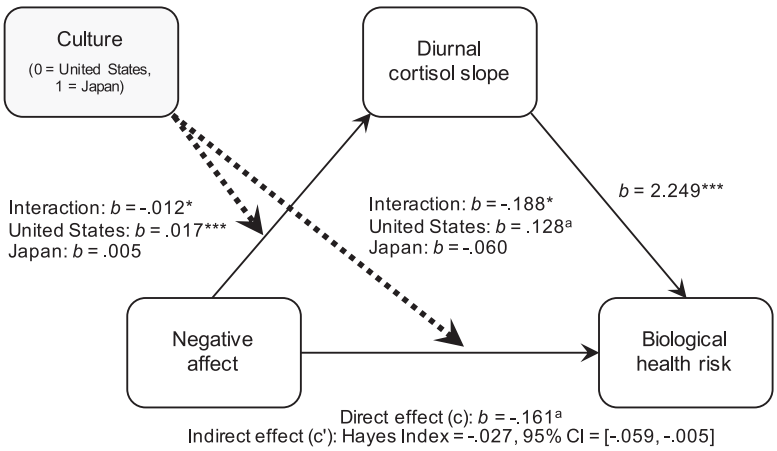

Figure 2. The effect of negative affect on biological health risk via diurnal cortisol slope, as moderated by culture (0 = United States, 1 = Japan). Unstandardized coefficients are shown. The values in the square bracket are 95% bias-corrected confidence interval (CI) from a bootstrap test with 5,000 replications; the moderated mediation (i.e., the mediated effect of diurnal cortisol slope on the link between negative affect and biological health risk, moderated by culture) is significant, as the CI does not include zero. The indirect effect of diurnal cortisol slope on the relationship between negative affect and biological health risk was statistically significant among Americans (95% bias-corrected bootstrapping CI [.017, .074]). In contrast, the comparable mediation was not significant among Japanese (95% bias-corrected bootstrapping CI [–.001, .031]). Model 3 covariates (gender, age, years of education, neuroticism, extraversion, average wake time, average sleep duration, smoking status, and alcohol consumption) are controlled. Statistical significance is indicated by asterisks (^{a} $p < .10$. * $p < .05$. *** $p < .001$). $N = 1{,}059$.

levels of cortisol at awakening, an effect that has been repeatedly linked to compromised health, including for both chronic fatigue syndrome and the experience of posttraumatic stress disorder in some cancer patients (Abercrombie et al., 2004; Gunnar & Vazquez, 2001). Moreover, extending Miyamoto et al. (2013), we showed that greater negative affect was linked to increased biological health risk among Americans by employing the composite index comprised of inflammatory, lipid, and blood pressure measures. In sharp contrast, the effects of negative affect on both the diurnal cortisol rhythm and biological health risk were negligible for Japanese.

Additionally, building on the substantial evidence that chronic stress responses, indexed by disturbances in daily cortisol secretion, are implicated in the etiology of inflammatory and cardiovascular diseases (Chrousos, 2009; Kumari et al., 2011), we explored the possibility that the cultural difference in the influence of negative affect on diurnal cortisol slopes might mediate another cultural difference we observed in the relationship between negative affect and biological health risk. Our analysis revealed that a flattening of diurnal cortisol slopes was the statistical mediator in the model of the association between negative affect and increased biological health risk among Americans. That is, for middle-aged and older American adults, greater negative affect was associated with a flatter diurnal cortisol slope, which, in turn, was linked to the measures of increased biological health risk. This result is consistent with the general conclusion that aberrant patterns of cortisol secretion are an important physiologic pathway through which chronic stress can lead to poor health (Gustafsson, Janlert, Theorell, & Hammarström, 2010). Our work extends this literature by suggesting that frequent daily experiences of negative affect, as a chronic stress signaling self-threat, might also exacerbate poor physical health through the same neuroendocrine pathways. In contrast, the same type of mediation appeared to be negligible for Japanese, consistent with the view that Asians are buffered against some of the harmful health consequences of negative affect because of their view of negative affect as fluctuating, momentary part of a natural cycle of both the self and external events, and thus not threatening or stressful.

We theorized that the cultural differences observed in the current analyses might be driven by a lower sense of self-threat posed by negative affect in Asian cultures that sanction a more dialectical (vs. hedonic) view of emotions (Peng & Nisbett, 1999; Spencer-Rodgers & Peng, 2017; Wilken & Miyamoto, 2017). This outlook might make recurrent daily experiences of negative affect less stressful. This view is supported in part by Miyamoto and Ma (2011; see also Miyamoto, Ma, & Wilken, 2017, for a review), who showed, in a series of studies, that Asians do indeed endorse dialectical views of emotions more strongly than Americans. They further showed that due to the Asian dialectical perspective on emotions, Asians are less motivated to engage in hedonic emotion regulation (i.e., upregulation of positive affect and downregulation of negative affect) compared with Americans, presumably because negative affect is less threatening to these individuals. It is noteworthy that our Japanese participants actually reported the experience of negative affect more often than did American participants, perhaps because of a greater acceptance of these experiences. At the same time, our analysis further suggests that Asians are less vulnerable to the physiological wear and tear caused by daily negative affect, possibly reflecting a reduced sense of self-threat. Future research should directly assess dialecticism (vs. hedonism) to test whether historical differences in these cultural traditions are responsible for modulating the health impact of negative affect as a self-threat.

Some limitations of the current work warrant discussion. First, one limitation of the current work is the lack of measures to assess underlying mechanisms for the observed cultural differences. In addition to systematically assessing the endorsement of dialectical versus hedonic views of negative affect, future research would also benefit from examining other potential theoretical explanations for our results. For example, it could be argued that negative affect is equally threatening to both cultural groups, but because of Asians' better emotion regulatory abilities (Mauss & Butler, 2010; Murata, Moser, & Kitayama, 2013), the effect of negative affect on physical health is attenuated among these individuals. Similarly, viewing negative affect as a transient, natural part of life may be an effective way of reappraising and coping with the experience of negative affect, which, in turn, may lessen its adverse health effects by facilitating quicker recovery from stress (Jamieson et al., 2013). These possibilities should be addressed in future research.

Second, our moderated mediation analysis conveyed that one potential pathway underlying the link between negative affect and biological health risk among Americans is through an influence of negative affect on daily cortisol rhythm. However, caution is warranted because we cannot exclude a possible reverse causation, namely, the possibility that physiological indices of increased biological health risk could themselves act on the HPA axis or influence the experience of negative affect, including symptoms like fatigue (e.g., Costanzo, Stawski, Ryff, Coe, & Almeida, 2012). Longitudinal follow-up evaluations would be needed to prospectively determine the dynamic relationships between these variables over time. In addition, we should acknowledge that our cross-sectional analysis was based on data collected at different time points in the two countries with a lag of approximately 7 years. Strictly speaking, then, the variation between the two surveys could be due to culture, potentially to global changes in economic or political events over time, or both. Future work would benefit from data collection in the United States and another Asian country that was obtained concurrently.

Third, it is also important to highlight that the level of biological health risk was much higher for Americans than for Japanese. Thus, it would be of value if future research could test whether the conclusions also apply to Asian immigrants in the United States, who are known to have more cardiovascular disease and Type 2 diabetes because of consuming a more Western diet and the increased prevalence of obesity (Yano et al., 2004). It would be important to show that the effects of culture persist even for Asians who are "Americanized" in diet and behavior, and thus show a corresponding shift in biological health risk, insofar as they retain a dialectical view of emotions as they assimilate across generations.

Fourth, our analysis utilized several different markers of physiology and health, ranging from cortisol secretion to the four biomarkers of inflammation, blood pressure, and lipid metabolism. Future research would benefit from also including indicators of neurobiological systems, such as the effect of negative emotional

experiences on the activity of the autonomic nervous system (Aschbacher et al., 2013). Following an initial lead reported by Mauss and Butler (2010), we could anticipate that negative affect would produce a cardiovascular profile of "threat" among Americans, whereas it might be evinced as "challenge" among Asians. These divergent patterns of autonomic reactivity could also lead to significant differences in the downstream effects on health (Epel et al., 1998; O'Donovan et al., 2012).

We started this article by referring to writings of Judith Orloff (2010), who advocated for the view that negative affect is unhealthy. Our findings suggest that negative affect may be unhealthy because of the pervasive cultural expectation of negative affect as harmful and problematic. Ironically then, best-selling authors such as Orloff and others might have contributed to the adverse health effect of negative affect by propagating this particular cultural perspective. Given this outlook, the experience of negative affect would convey added meaning about the self as being inadequate and incompetent, thereby serving as a signifier of threat to the self. Crucially, our analysis provides a number of compelling reasons to consider these questions in different cultures, including in Japan, where there is a more benign view of negative affect as transitory, integral to life, and even helpful for excelling and optimal performance.

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