



Negative emotions predict elevated interleukin-6 in the United States but not in Japan



Yuri Miyamoto^{a,*}, Jennifer Morozink Boylan^a, Christopher L. Coe^b, Katherine B. Curhan^c, Cynthia S. Levine^c, Hazel Rose Markus^c, Jiyoung Park^d, Shinobu Kitayama^d, Norito Kawakami^e, Mayumi Karasawa^f, Gayle D. Love^g, Carol D. Ryff^g

^a Department of Psychology, University of Wisconsin, 1202 West Johnson Street, Madison, WI 53706, United States

^b Harlow Center for Biological Psychology, University of Wisconsin, 22 N. Charter Street, Madison, WI 53715, United States

^c Department of Psychology, Stanford University, Jordan Hall, Building 420, 450 Serra Mall, Stanford, CA 94305, United States

^d Department of Psychology, University of Michigan, 530 Church Street, Ann Arbor, MI 48109, United States

^e Department of Mental Health, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

^f Department of Communication, Tokyo Woman's Christian University, 2-6-1 Zenoukuji, Suginami-ku, Tokyo 166-8585, Japan

^g Institute on Aging, University of Wisconsin, 2245 Medical Science Center, 1300 University Avenue, Madison, WI 53706, United States

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ABSTRACT

Previous studies conducted in Western cultures have shown that negative emotions predict higher levels of pro-inflammatory biomarkers, specifically interleukin-6 (IL-6). This link between negative emotions and IL-6 may be specific to Western cultures where negative emotions are perceived to be problematic and thus may not extend to Eastern cultures where negative emotions are seen as acceptable and normal. Using samples of 1044 American and 382 Japanese middle-aged and older adults, we investigated whether the relationship between negative emotions and IL-6 varies by cultural context. Negative emotions predicted higher IL-6 among American adults, whereas no association was evident among Japanese adults. Furthermore, the interaction between culture and negative emotions remained even after controlling for demographic variables, psychological factors (positive emotions, neuroticism, extraversion), health behaviors (smoking status, alcohol consumption), and health status (chronic conditions, BMI). These findings highlight the role of cultural context in shaping how negative emotions affect inflammatory physiology and underscore the importance of cultural ideas and practices relevant to negative emotions for understanding of the interplay between psychology, physiology, and health.

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1. Introduction

Numerous studies have shown that negative emotions are associated with worse health, such as cardiovascular disease (e.g., Kubzansky and Kawachi, 2000), cancer (e.g., Penninx et al., 1998), and even mortality (e.g., Pinquart and Duberstein, 2010). One of the biological pathways believed to mediate this linkage between negative emotions and health is inflammation (Everson-Rose and Lewis, 2005; Kiecolt-Glaser et al., 2002). Prior studies have shown that stress, depressive moods, and negative emotions lead to increased levels of pro-inflammatory cytokines (Bower et al., 2007; Carroll et al., 2011; Dickerson et al., 2004; Howren et al., 2009; Kiecolt-Glaser et al., 2007; Marsland et al., 2008; Stewart et al., 2009; Suarez, 2003), and an activation of inflammatory processes is involved in the development and pathogenesis of various health problems, such as diabetes (Kristiansen and Mandrup-Poulsen,

2005) and cardiovascular disease (Ridker et al., 2000). However, most previous studies have been conducted within Western cultural contexts and thus less is known about whether these pathways extend to other populations and cultural contexts.

Cultures vary in their ideas and practices relevant to emotions (Mesquita and Leu, 2007; Tsai, 2007). Historically, Western cultures have valued and encouraged the pursuit of positive emotions, but construed negative emotions as something to be avoided, and often as signs of an inability to control one's life (Kotchemidova, 2005; Ryan and Deci, 2001). In many Asian cultures, on the other hand, there is a philosophical tradition of dialectical thinking, where reality is considered to be constantly changing and comprised of opposites (Peng and Nisbett, 1999). For example, happiness and unhappiness are assumed to coexist and complement each other (Miyamoto and Ma, 2011; Spencer-Rodgers et al., 2010). Thus, the existence of negative emotions or hardship is accepted and even recognized as necessary for self-improvement (Heine et al., 1999). Reflecting cultural differences in such beliefs, cross-cultural research has shown that Easterners are more likely

* Corresponding author. Tel.: +1 608 890 1035.

E-mail address: ymiyamoto@wisc.edu (Y. Miyamoto).

than Westerners to perceive there are some desirable aspects of negative emotions (Eid and Diener, 2001). For example, compared to the case in Western cultures, in Eastern cultures, negative emotions are more likely to be a source of motivation to improve the self (Uchida and Kitayama, 2009) and to invite sympathy and social support from surrounding people (Kitayama and Markus, 2000). In contrast, Westerners are more likely than Easterners to view negative emotions as unacceptable and to be avoided (Bastian et al., 2012).

Trying to avoid or reduce negative thoughts or emotions may contribute to the detrimental effects on mental health (Hayes et al., 1996). Indeed, growing evidence suggests that acceptance and observation of negative emotions, facilitated by strategies encouraged by mindfulness training rooted in Eastern religious and philosophical tradition (Kabat-Zinn, 1990; Segal et al., 2002), leads not only to better mental health, but also to better physical health outcomes (e.g., Davidson et al., 2003; Kabat-Zinn et al., 1985). These findings suggest that in Eastern cultural contexts, where negative emotions are less likely to be perceived as unacceptable or to be avoided and are more likely to be accepted as a component of normal reality, adverse health concomitants may be less evident compared to Western cultural contexts.

Cross-cultural studies provide some supporting evidence. A balance between moderate amounts of positive and negative emotion is associated with fewer physical symptoms in Japan than in the United States (Miyamoto and Ryff, 2011), indicating that moderate amounts of negative emotion, coupled with positive emotions, are not maladaptive for health in Japanese adults. Furthermore, Curhan et al. (2013) found that negative emotions are more closely associated with worse self-reported physical health in the United States than in Japan, independent of the effect of positive emotions. These findings suggest that negative emotions may result in poorer health in the United States, but perhaps have more minimal association in Japan.

Despite the extant evidence, little is known about whether these conclusions extend to biomarkers of health. Many previous studies conducted in Western cultures indicate chronic life stress and depressive moods can elevate inflammatory physiology, specifically shown by focusing on the pleiotropic pro-inflammatory cytokine, Interleukin-6 (IL-6; Howren et al., 2009; Kiecolt-Glaser et al., 2002; Marsland et al., 2008; Stewart et al., 2009). Thus, a central question is whether this research conducted in Western cultures will generalize to Eastern cultural contexts. It is possible the findings will not, given Eastern views of negative emotions as accepted and inevitable parts of reality, in contrast to the Western views of negative emotions as distressing, problematic, and maladaptive. In Eastern cultural contexts, negative emotions may not be as physiologically costly and thus not be predictive of elevated inflammatory markers and physiological dysregulation.

We hypothesized that negative emotions (after taking into account demographic and health control variables) would predict higher IL-6 among American adults who perceive the experience of the negative as problematic and maladaptive. Conversely, we predicted a link between negative emotions and IL-6 would be weaker among Japanese adults, because negative emotion is more typically construed as acceptable and a natural part of reality.

2. Materials and methods

2.1. Participants

American respondents were a subset from the Midlife in the United States (MIDUS) survey, which began in 1995–1996. It is a national probability sample recruited through random digit dialing. The survey included a telephone interview and a self-adminis-

tered questionnaire. Using the same assessments, a follow-up survey was conducted about 9–10 years later (MIDUS II). In addition, biological data were collected from a subset of the MIDUS II respondents, who traveled to one of three General Clinical Research Centers (GCRC) for an overnight visit. The present analyses included 1044 participants for whom IL-6 data were available (474 males, 570 females; $M = 55.21$ years). The parallel survey, the Midlife in Japan (MIDJA), was conducted in 2008 with participants randomly selected from the Tokyo metropolitan area and completed a self-administered questionnaire. A subset of the MIDJA respondents was recruited to participate in biological data collection ($N = 382$; 168 males, 214 females; $M = 54.24$ years). These respondents visited a medical clinic near the University of Tokyo. Serum specimens were frozen and shipped to the United States for analysis. Although American respondents were slightly better educated ($M = 14.58$ years of education) than were the Japanese respondents ($M = 13.62$ years of education), $t(1418) = 6.61$, $p < .001$, both samples were comparable in terms of age, $t(1424) = 1.30$, $p = .19$, and gender composition, $\chi^2(N = 1426) = 0.23$, $p = .63$.

2.2. Negative emotion

The measures of emotions were collected as part of comprehensive self-administered questionnaires in both MIDUS II and MIDJA, which were completed prior to biological data collection. Participants were asked to rate how much of the time during the past 30 days they felt each emotion (for details about the sources, see Mroczek and Kolarz, 1998) using a 5-point rating scale: *none of the time* (1), *a little of the time* (2), *some of the time* (3), *most of the time* (4), and *all the time* (5). The negative emotions included the following 6 items: so sad nothing could cheer you up, nervous, restless or fidgety, hopeless, that everything was an effort, and worthless. Cronbach's alphas were .85 and .86, for Americans and Japanese, respectively. Participants' responses to six items were averaged to compute a negative emotion score.

Following Mroczek and Kolarz (1998), retrospective report over 30 days was used. In support of this approach, Feldman Barrett (1997) showed that the average of momentary report of negative (positive) emotions over 90 days strongly predicted the retrospective report of negative (positive) emotions. However, individual differences have been observed in the discrepancy between momentary and retrospective report of emotions (Robinson and Clore, 2002). Specifically, individuals high on neuroticism tend to report experiencing more negative emotions in their retrospective report than in their momentary report, whereas individuals high on extraversion tend to report experiencing more positive emotions in their retrospective report than in their momentary report (Feldman Barrett, 1997). We thus controlled for neuroticism and extraversion to rule out the possibility that cultural differences in the health correlate of negative emotions were due to personality differences in retrospective reporting of emotions.

2.3. IL-6

Frozen blood samples were shipped on dry ice from the 3 GCRC sites and from Tokyo to a single testing laboratory. Serum IL-6 levels were determined by high-sensitivity enzyme-linked immunosorbent assay (ELISA) (Quantikine, R&D Systems, Minneapolis, MN), with a lower sensitivity of detection at 0.16 pg/mL. All values were quantified in duplicate; any value over 10 pg/mL was re-run in diluted sera to fall on the standard reference curve.

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