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Autonomy, Positive Relationships, and IL-6: Evidence for Gender-Specific Effects

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Abstract

Objectives—A body of evidence indicates that women value relationship-centered aspects of well-being more than men do, while men value autonomy-centered aspects of well-being more than women do. The current study examined whether gender moderates relations between autonomy and positive relationships and interleukin-6 (IL-6), a cytokine associated with inflammatory processes. Aspects of well-being consistent with gender-linked values were expected to be most health-protective such that positive relationships would predict lower IL-6 only or more strongly in women, and autonomy would predict lower IL-6 only or more strongly in men.

Methods—In the first study, a sample of 119 older adults (55% female) living in Kentucky were visited in their homes for interviews and blood draws. In the second study, a sample of 1,028 adults (45% female) living across the United States (U.S.) underwent a telephone interview followed by a visit to a research center for blood draws.

Results—In the Kentucky sample, autonomy was quadratically related to IL-6 such that average autonomy predicted higher IL-6; this effect was stronger in men, providing support for our hypothesis only at above average levels of IL-6. In the U.S. national sample, more positive relationships were associated with lower IL-6 in women only. When the national sample was restricted to match the Kentucky sample, higher autonomy was associated with lower IL-6 in men only.

Conclusions—Results provide preliminary evidence for gender-specific effects of positive relationships and autonomy on IL-6. Further work is needed to establish the generalizability of these effects to different ages, cultures, and health statuses.

A strong body of evidence suggests that women value relationships and relationship-related values more than do men, whereas men value autonomy and autonomy-related values more than do women. In a cross-cultural study that included 127 samples from 70 countries, men consistently reported valuing power, stimulation, achievement, and self-direction more than women; in contrast, women reported assigning greater value to benevolence and universalism than men (Schwartz & Rubel, 2005). Such a pattern has been repeatedly demonstrated across a wide range of ages and cultures (Badger, Simpson, & Jenson, 1998; Beutel & Marini, 1995; Caricati, 2007; Ferssizidis et al., 2010; Jensen, McGhie, & Jensen, 1991; Marini, Fan, Finley, & Beutel, 1996; Knafo & Spinath, 2011; Schartz & Rubel-Lifschitz, 2009; Stimpson, Neff, Jensen, & Newby, 1991; Weisgram, Bigler, & Liben, 2010). It should be noted that men and women do not construe the meanings of these values

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in different ways, suggesting that such gender differences are not due to differences in the way men and women define such values (Struch, Schwartz, & van der Kloot, 2002).

Two well-studied aspects of eudaimonic psychological well-being, *positive relationships* and *autonomy*, reflect values associated with gender (Ryff & Keyes, 1995). *Positive relationships* have been defined as the degree to which the quality—and not just the size—of one's social network is adequate for providing resources in a variety of situations (Ryff & Keyes, 1995). Congruent with their greater preference for relationship-promoting values, women report more positive relationships (Ryff & Keyes, 1995; Ryff, Lee, Essex, & Schutte, 1994; Ryff, 1989). *Autonomy* is characterized by self-determination, independence, resistance to social pressures to think and act in certain ways, and the use of personal standards for the measurement of one's own behavior. Consistent with their greater endorsement of autonomy-centered values, men tend to report greater autonomy and related traits than women, though these differences appear to be less robust (Cross & Madson, 1997; Ryff, Lee, Essex, & Schutte, 1994).

Well-being in areas consistent with one's gender-linked values (e.g., autonomy in men) may be more health-protective than well-being in other areas (e.g., positive relationships in men). In one study of 76 American adolescents with Type 1 diabetes, daily interpersonal conflict was more strongly associated with poor metabolic control among girls than among boys (Helgeson, Lopez, & Karmarck, 2009). In another study of 888 Swedish adults, becoming unemployed was associated with greater somatic complaints among men only, whereas family status (i.e., being single or divorced) was the strongest predictor of somatic complaints among women (Isaksson, Johansson, Ballagh, & Sjoberg, 2004). Finally, several studies have provided evidence that work stress has a greater negative impact than marital stress on cardiovascular health among men, whereas the opposite appears to be true for women (Orth-Gomer et al., 2000; Smith & Brown, 1991; Theorell, Perski, Orth-Gomer, Hamsten, & de Faire, 1991). Thus, aspects of psychosocial functioning that reflect gender-linked values may be more or less relevant to health depending on one's gender.

Interleukin-6 as a Biomarker for Physical and Psychological Well-Being

Interleukin-6 (IL-6) is a pleiotropic cytokine that has been associated with the pathogenesis of a variety of diseases. Levels of IL-6 predict adverse health outcomes such as cardiovascular events, osteoporosis, systemic lupus, prostate cancer, and Alzheimer's disease (e.g., Eriksson et al., 2011; Papanicolaou, Wilder, Manolagas, & Chrousos, 1998; Ridker, Rifai, Stampfer, & Hennekens, 2000). IL-6 also correlates with negative psychosocial states such as depression, anxiety, and stress (Dentino et al., 1999; Gruenewald et al., 2009; Petersen et al., 2008; Howren, Lamkin, & Suls, 2009; Penninx et al., 2003). IL-6 may be a mechanism linking interactions among gender, psychological functioning, and outcomes such as somatic complaints and cardiovascular health.

Some evidence links psychological well-being to lower IL-6 in both genders. In a large sample of American men and women (ages 35–86), positive relationships were associated with lower IL-6, though only at lower levels of education (Morozink, Friedman, Coe, and Ryff, 2010). Social integration, support, and engagement also predicted lower IL-6 in women with cancer (Lutgendorf, Anderson, Sorosky, Buller, & Lubaroff, 2000; Costanzo et al., 2005; Lutgendorf, Russell, Ullrich, Harris, & Wallace, 2004). In two studies of older (ages 61–91) women, positive relationships predicted lower IL-6, even in the presence of poor sleep (Friedman et al., 2005) or stressful transitions (Friedman et al., 2007). The one study to examine the association between autonomy and IL-6 failed to find a relationship in the sample as a whole, which included men and women (Morozink et al., 2010). No studies have examined the possibility that gender moderates the correlation of gender-linked aspects

of well-being with IL-6. Certain aspects of well-being may be more strongly associated with lower inflammation when consistent with gender-linked values. Additionally, known gender differences in positive relationships, autonomy, and IL-6 suggest the importance of investigating gender differences in links between these aspects of well-being and IL-6.

Recent meta-analytic evidence suggests that the relationship of autonomy to negative psychological functioning may be curvilinear, providing a potential explanation for the lack of significant links between autonomy and health or IL-6 in previous studies. The study in question, which included 63 societies and 420,599 individuals, demonstrated that, in addition to a protective main effect of autonomy, there was a quadratic association between autonomy and psychological symptoms such that the greatest symptoms were associated with moderate societal autonomy (Fischer and Boer, 2011). The authors do not provide an interpretation of this curvilinear effect; however, this pattern warrants consideration and further exploration in independent samples. We argue that individuals may benefit from social acquiescence at lower levels of autonomy and from self-directedness at higher levels of autonomy, while individuals may experience deleterious effects at moderate levels of autonomy, which may indicate greater conflict between one's own priorities and the priorities of others.

The Current Study: Gender, Well-being, and IL-6

No studies have examined the possibility that the associations of gender-linked well-being variables such as positive relationships and autonomy with IL-6 differ by gender. The current study therefore tested the hypothesis that gender moderates the associations of both positive relationships and autonomy with IL-6. It was predicted that positive relationships would be associated with lower IL-6 only or more strongly in women, and that autonomy would be associated with lower IL-6 only or more strongly in men. Additionally, because recent meta-analytic evidence suggests curvilinear effects of certain aspects of well-being on psychological health, quadratic effects were also considered.

Study 1: Older Adults in Kentucky

Method

Participants—Participants were 119 older adults living in the Lexington, KY area taking part in a study of psychosocial factors and immunity. The sample was 55% female and 96% Caucasian. Descriptive statistics can be found in Table 1. Participants were excluded if they had diseases or disorders affecting the immune system (e.g., autoimmune disorders, cancer), had undergone chemotherapy in the past 5 years, were taking immunomodulatory medications such as steroids or opiates, or were taking more than two of the following medication classes: antihypertensives, hormone replacement, thyroid supplements, and psychotropics. A power analysis revealed that this sample size would yield 80% power to detect a medium-sized effect (smallest *r* detectable with 80% power = .25) of the interaction between gender and well-being.

Measures

Demographics: Participants reported demographic variables and provided a list of prescription medications during a home interview.

Autonomy and Positive Relationships with Others (Scales of Psychological Well-being): The Scales of Psychological Well-being (SPWB; Ryff and Keyes, 1995) measure eudaimonic well-being; in contrast to hedonic well-being, which refers to one's happiness and pleasure, eudaimonic well-being refers to one's ability to flourish and fulfill one's

potential (Ryff & Singer, 2006). The 14-item subscale version was administered. The Autonomy subscale includes items such as, “My decisions are not usually influenced by what everyone else is doing,” and “I have confidence in my opinions, even if they are contrary to the general consensus”. The Positive Relations with Others subscale includes items such as, “I have not experienced many warm and trusting relationships with others” (reverse scored), and “I know that I can trust my friends, and they know they can trust me”. Response options ranged from 1 (“strongly disagree”) to 6 (“strongly agree”) with no “neutral” option. The Autonomy subscale demonstrated acceptable internal consistency (α = .73), while the Positive Relations with Others subscale demonstrated good internal consistency (α = .81).

Interleukin-6: Study nurses drew blood following the interview visit (median interval = 1.5 months). Blood draw was deferred if the participant was acutely ill. Sera were frozen at −80°C and later thawed for analysis at the University of Kentucky General Clinic Research Center. High-sensitivity ELISA kits (R&D Systems, Minneapolis, MN) were utilized according to the manufacturer’s specifications. The mean intra-assay coefficient of variance was 1.9%, and the mean inter-assay coefficient of variance was 4.5%. IL-6 results were log10 transformed to achieve normality.

Data analysis: Log10 IL-6 was regressed on the covariates age, BMI, statin medication use, and beta-blocker use, and the predictors gender, Positive Relationships or Autonomy, and the interaction between Positive Relationships or Autonomy and gender. Covariates were used in these models based on (1) robust relationships to IL-6 that (2) were not hypothesized to play a substantive role (O’Connor et al., 2009; Segerstrom, 2009). The established threshold at which IL-6 becomes a risk factor for health problems in older adults is 3.19 mg/dL (Harris et al., 1999). Harris et al. (1999) reported that 27% of a nationally representative sample was at or above this threshold. The log10 value of 3.19 is .50; therefore, for significant effects, we also calculated the level of well-being at which predicted IL-6 would cross this threshold.

Results

Zero-order correlations can be found in Table 2. Higher IL-6 was significantly associated with male gender, older age, beta-blocker use, higher BMI, and lower scores on the Positive Relations with Others scale. Roughly 19.9% of the sample was above the cutoff for “risky” levels of IL-6 (3.19 pg/dL; .50 log10 pg/dL). This lower proportion of older adults above the risk threshold for IL-6 was expectable given that the sample was screened for general health. Although women had more Positive Relations with Others, gender was not associated with Autonomy.

Results of regression models testing study hypotheses are presented in Table 3. Autonomy was quadratically related to IL-6 such that average Autonomy was associated with the highest IL-6; although significant in both men and women, this pattern was significantly stronger in men. As shown in Figure 1, the apex of this quadratic relationship reached the risk threshold of .50 (log10 pg/ml) for men only (for comparison across samples, the scale midpoint—between “slightly disagree” and “slightly agree” is shown). Although Positive Relationships tended to be associated with lower IL-6, this effect was no longer statistically significant after inclusion of covariates and gender (β = −.12, t = −1.23, p = .22). The effect of Positive Relations with Others was not moderated by gender. Controlling for education did not impact the results of these regression analyses.

Discussion

Rather than a straightforward effect of autonomy, there appeared to be a curvilinear effect of autonomy that was stronger in men. Examination of the graph in Figure 1 reveals that, among participants with autonomy above the scale midpoint, the effect of autonomy was moderated by gender in the expected manner such that autonomy was more strongly associated with lower IL-6 in men. This may be thought of as partial support for our hypothesis. Among participants with autonomy below the average, the opposite pattern emerged, again moderated by gender: IL-6 increased as autonomy approached the scale midpoint, a pattern that was stronger in men. This opposite pattern for individuals with below-average autonomy was unexpected and is partially inconsistent with our hypothesis. However, it is consistent with recent meta-analytic evidence that moderate autonomy may be associated with poorer psychological health (Fischer & Boer, 2011). As mentioned previously, social acquiescence (i.e., low autonomy) may be protective for some individuals, whereas higher autonomy may be beneficial insofar as it represents the ability of the individual to act according to his or her own priorities. Moderate autonomy may represent greater conflict between one's own priorities and the priorities of others. Additionally, women reported more positive relationships, but men did not report greater autonomy. This sample characteristic may indicate that some men in Kentucky value autonomy less than men in the rest of the country, possibly due to more collectivistic norms in this region of the country (Vandello & Cohen, 1999).

As in previous work, positive relationships correlated with lower IL-6; this effect was nonsignificant after controlling for demographic and pharmacologic variables. Contrary to hypotheses, there was not a significant interaction between gender and positive relationships. Several potential explanations exist. Gender may not moderate the effect of positive relationships on IL-6. Relationships become central to emotion regulation in older age, and this effect may overtake gender-specific effects found in younger adults (Carstensen, Fung, & Charles, 2003). Additionally, a larger sample may be needed to detect significant interactive effects of this relatively small size ($\beta = -.17$). As noted before, this sample (n=119) yielded 80% power to detect only a significant medium ($r = .25$) interactive effect of gender and well-being.

Study 2: National Sample

In Study 1, both very high and very low autonomy were associated with lower IL-6, an effect that was stronger in men and consistent with previous findings that moderate autonomy may be associated with poorer psychological functioning (Fischer & Boer, 2011). However, questions remained about the generalizability of this finding to a more diverse population. Additionally, a larger sample was needed to detect small interactive effects. Therefore, we conducted a set of analyses identical to those in Study 1 using a sample of adults from the Mid-life Development in the United States (MIDUS-II) study. Our hypotheses remained unchanged.

Method

Participants—Participants were 1,028 (45% female) adults living across the United States taking part in the MIDUS-II study. Ninety percent of participants were Caucasian, 4.6% were African American, 1.6% were Native American, and all other categories comprised fewer than 1% of the sample. Descriptive statistics can be found in Table 1. Though BMI and use of statin and beta-blocker medications were controlled for in statistical analyses, participants were not excluded on the basis of chronic health conditions or use of immunomodulatory medications. This sample size yields 80% power to detect a small interactive effect (smallest r detectable with 80% power = .08) of gender and well-being.

Measures

Demographics: Participants reported demographics and medication use during a telephone interview. For education, participants chose from the response options on the following scale: No School or Some Grade School (1–6), Eighth Grade/Junior High School (7–8), Some High School (9–12 with No Diploma or GED), GED, Graduated from High School, 1–2 Years of College with No Degree, 3 or More Years of College with No Degree, 2-Year College Degree, 4 or 5-Year College Degree, Some Graduate School, Master's Degree, Ph.D/M.D or Other Professional Degree.

Autonomy and Positive Relationships: Participants completed the version of the SPWB with 7-item subscales. Response options ranged from 1 ("strongly disagree") to 7 ("strongly agree") with 4 representing "neutral". Internal consistency was acceptable for both scales (Autonomy $\alpha = .71$; Positive Relations with Others $\alpha = .78$). These scales contain half as many items as the scales used in the first study; however, because the two versions used had virtually identical reliabilities, it is unlikely that this affected the results. For information about the 7-item subscales and how they compare to the 14-item subscales used in Study 1, see van Dierendonck (2004).

Interleukin-6: Blood draws occurred on the second morning (6:30–7:00 AM) of a stay at a clinical research center. The median time between completion of questionnaires and blood draws is unknown. Sera were frozen at −65 to −80 °C until shipment on dry ice to the MIDUS-II laboratory. IL-6 levels were determined using the high-sensitivity ELISA kit (R & D Systems, Minneapolis, MN). The intra-assay coefficient of variance was 4.09% and the inter-assay coefficient of variance was 13%. Because of the high inter-assay coefficient of variance, IL-6 values were standardized around the low-control plate value to control for the influence of inter-assay variability (C. Coe, personal communication, 2/10/12). A log10 transformation was applied to IL-6 to achieve normality.

Data analysis: Data analysis was performed as described for Study 1. The categorical education variable was recoded to a continuous years of education variable by assigning the median number of years associated with each category.

Results

Zero-order correlations can be found below the diagonal in Table 4. Higher IL-6 correlated with older age, female gender, higher BMI, lower education, and nonuse of statins and beta-blockers. Men had higher Autonomy, and women had more Positive Relations with Others.

Roughly 23% of this sample was at or above the threshold for "risky" levels of IL-6 (3.19 pg/dL; .50 log10 pg/dL). Results of regression models are presented in Table 5. As predicted, the association of Positive Relationships with Others with IL-6 was moderated by gender; women with more positive relationships had lower IL-6 (see Figure 2). The simple slope was significant for women ($\beta = -.01$, $t = -2.84$, $p = .005$) but not for men ($\beta = .003$, $t = 1.31$, $p = .19$). Based on the simple slope for women, the risk threshold of .50 (log10 pg/ml) would be reached with a score 1.93 standard deviations below the mean. There were no significant main or moderated effects of Autonomy on IL-6. Post-hoc analyses revealed that the three-way interactions of autonomy and gender with age, race, and education were not significant. Controlling for education and race did not influence results.

Creation of a Restricted Sample—The results of Study 1 differed from those found in the larger national sample. There were no longer any effects of Autonomy on IL-6, and a gender-specific effect of Positive Relationships with Others emerged. The Kentucky and national samples differed on several key demographic variables—most notably, the

Kentucky sample was comprised of older adults (65 years or older), a subset of adults that may differ in important ways from younger adults. To determine whether sample differences influenced results, the national sample was restricted to match the ranges (though not matched on means) of key demographic and IL-6-related variables in the Kentucky sample. The restricted variables (and associated ranges) are as follows: age (65–83 years), education (7–22 years), BMI (18.07–45.89), race (Caucasian), and marital status (married). The resulting sample consisted of 235 older adults (42% female). This sample was both adequately powered to detect small interactive effects (like the national sample) and comprised of older adults (like the Kentucky sample).

Descriptive statistics can be found in Table 1. Roughly 21% of this restricted national sample was at or above the threshold for "risky" levels of IL-6 (3.19 pg/dL; .50 log10 pg/dL). Although the ranges of demographic and IL-6-related variables were equivalent across the Kentucky and restricted national samples, there were some small mean differences: the restricted national sample was younger ($t(350) = 9.01$, $p < .001$), more educated ($t(352) = 5.35$, $p < .001$), had a higher proportion of men ($\chi^2(1) = 5.61$, $p = .02$), and had a higher proportion of participants using beta-blockers ($\chi^2(1) = 72.14$, $p < .001$) and statins ($\chi^2(1) = 9.54$, $p < .01$). There were no significant differences between the two samples in BMI or IL-6. Because the Autonomy and Positive Relationships response scales differed slightly between the two samples, the Kentucky data were transformed to match the scaling of the national sample. T-tests comparing the means of these variables revealed that the restricted national sample had higher Autonomy ($t(349) = -5.36$, $p < .001$) but not more Positive Relationships with Others ($t(349) = -1.29$, $p = .19$).

Regression Analyses in the Restricted National Sample—Zero-order correlations can be found above the diagonal in Table 4. IL-6 was not significantly correlated with any other variable. Men had higher Autonomy and women had more Positive Relations with Others. Results of regression models in this restricted sample are presented in Table 6. Positive Relationships with Others predicted lower IL-6 regardless of gender ($\beta = -.01$, $t = -1.99$, $p = .04$). Additionally, consistent with our hypothesis, a linear effect of Autonomy on IL-6 was moderated by gender such that higher Autonomy was associated with lower IL-6 in men (Interaction $\beta = .01$, $t = 2.26$, $p = .02$; see Figure 3, which includes delineation of the "neutral" scale midpoint). The simple slope for Autonomy was significant for men ($\beta = -.01$, $t = 2.13$, $p = .03$) but not women ($\beta = .003$, $t = .45$, $p = .65$). Based on the simple slope for men, the risk threshold of .50 (log10 pg/ml) would be reached at 2.73 standard deviations below the sample mean of Autonomy.

Discussion

In the full US national sample, there was no longer an effect of autonomy—moderated or unmoderated—on IL-6. However, positive relationships and gender interacted to predict IL-6: positive relationships were associated with lower IL-6 in women only. When the national sample was restricted to match the Kentucky sample, the effect of autonomy on IL-6 was again moderated by gender; higher autonomy predicted lower IL-6 in men only, this time in a linear fashion. Therefore, the gender-moderated effect of autonomy in the restricted national sample was consistent with the pattern of associations between gender, autonomy, and IL-6 in individuals above the scale midpoint in the Kentucky sample. As in the Kentucky sample, positive relationships were associated with lower IL-6 regardless of gender. In addition, the fact that the pattern of results in the restricted national sample was similar to the pattern of results in the Kentucky sample is consistent with the notion that sample characteristics—and not merely inadequate statistical power—were responsible for differences in the effects observed in the Kentucky and *full* national samples.

General Discussion

Across cultures and ages, women value relationships more than do men, whereas men value autonomy more than do women (see Schwartz and Rubel, 2005). We hypothesized that well-being consistent with the values characteristic of one's gender should be most health protective. Accordingly, the present studies investigated the possibility that the associations of certain aspects of well-being with IL-6, a cytokine associated with inflammatory processes, would be moderated by gender. Results indicate that gender differences in the associations between gender-linked aspects of well-being and IL-6 may exist. Further, they provide tentative support for the hypothesis that well-being conforming to gender-linked values is more robustly associated with lower IL-6. While the observed effects were not identical across samples, several consistencies emerged that may help to generate more specific hypotheses for testing in future independent samples. Most notably, the results presented in the current studies highlight the possibility of gender-specific health effects for different aspects of well-being.

Autonomy, Gender, and IL-6

Zero-order correlations between autonomy and IL-6 were nonsignificant in every sample. However, in two samples of older adults, autonomy was only or more strongly associated with IL-6 in men. In a sample of older adults in Kentucky, we found a quadratic effect in which average responses near the midpoint of the autonomy scale were associated with the highest levels of IL-6, a pattern that was stronger in men. Though these findings are more consistent with recent meta-analytic findings (Fischer & Boer, 2011) than with our original hypothesis, our hypothesis was supported when one considers only those in the sample with levels of autonomy located mainly above the scale midpoint. In a larger, younger national sample, we found no main or moderated effects of autonomy on IL-6. We then created a restricted national sample by matching the full national sample to the Kentucky sample on key demographic ranges. In this national sample of older adults, which was characterized by higher average levels of autonomy than the Kentucky sample, we found a more straightforward gender-specific effect of autonomy; for men only, average responses to autonomy items falling near the scale midpoint (corresponding to −2 *SD* below the sample mean) were associated with higher IL-6, and as autonomy increased, IL-6 decreased. Though not quadratic, this pattern of results is actually consistent with previous findings and the pattern found in the Kentucky sample; that is, "neutral" autonomy was associated with higher IL-6 (Fischer & Boer, 2011). Further testing with independent samples is needed to clarify the nature of the relationship between autonomy and IL-6 and the potential role of gender in moderating this relationship.

Additionally, differing sample characteristics may have contributed to the fact that the interactive effect of autonomy and gender found in Kentucky was quadratic, while the interactive effect found in the restricted national sample was linear. Autonomy was uncorrelated with gender in the Kentucky sample, and autonomy was lower in the Kentucky sample than in the restricted national sample. Post-hoc analyses revealed that differences in autonomy between the two samples of older adults were driven by significantly higher levels of autonomy in men from the restricted national sample compared to men from the Kentucky sample. This could be related to the fact that individuals in Kentucky tend to embrace a more collectivist mindset, which has been associated with lower levels of autonomy, especially in men (Vandello & Cohen, 1999).

These results replicate and extend recent meta-analytic findings indicating a similar deleterious effect of moderate autonomy (Fischer and Boer, 2011). Such effects may represent beneficial effects of both social acquiescence and high autonomy, accompanied by a potential deleterious effect of moderate autonomy, which may represent greater conflict

between one's own priorities and the priorities of others. Further, the present study provides the first evidence that these effects may be especially robust in older men, who may benefit from retaining independence or interdependence despite decreases in physical functioning (Fiori, Consedine, & Magai, 2008). While the three-way interaction of autonomy, gender, and age was not significant in these samples, this possibility should be further explored.

To our knowledge, these are the first studies to examine gender-specific effects of autonomy on IL-6. Results are consistent with evidence for gender differences in health responses to autonomy-related life events. For example, a large Swedish study found that becoming unemployed is associated with health complaints among men only (Isaksson, Johansson, Ballagh, & Sjoberg, 2004) and that work stress has a stronger negative effect on cardiovascular health in men than in women (Theorell, Perski, Orth-Gomer, Hamstein, & de Faire, 1991). Higher IL-6 may be one pathway through which autonomy and related outcomes produce such health effects in men.

Positive Relationships, Gender, and IL6

We found some evidence that positive relationships are more strongly associated with lower IL-6 in women; in a large national sample of adults, positive relationships were associated with lower IL-6 in women only. In fact, zero-order correlations between positive relationships and IL-6 were not significant in this national sample. In the two samples of older adults, there were small associations between greater positive relationships and lower IL-6 that were not moderated by gender.

Gender-specific effects of positive relationships were not present in the two samples of older adults. Though post-hoc power analyses revealed inadequate power to detect a small interactive effect in the Kentucky sample, the restricted national sample *was* adequately powered. Therefore, sample characteristics may instead be responsible for the lack of gender-specific effects of positive relationships in the older adult samples. For example, higher education in the older adult samples may have diminished effects of positive relationships, which may be present only at lower levels of education such as those found in the national sample (Morozink et al., 2010). Alternatively, the importance of positive relationships for older adults specifically may have overwhelmed gender-specific effects, which may be more evident in younger samples (Carstensen, Fung, & Charles, 2003). Finally, some *combination* of demographic differences may be responsible for inconsistencies across samples. Further testing in independent samples is needed before firm conclusions about moderation by gender can be drawn.

Results are nonetheless consistent with evidence that positive relationships predict lower IL-6 among women (e.g., Friedman et al., 2007). To our knowledge, this was the first study to investigate whether gender moderates effects of positive relationships on IL-6. Evidence for gender-specific protective effects of positive relationships parallels evidence that interpersonal conflict, marital stress, and single or divorced marital status are more robustly associated with poor health outcomes in women than in men (Helgeson, Lopez, & Karmarck, 2009; Isaksson, Jhansson, Ballagh, & Sjoberg, 2004; Therell, Perski, Orth-Gomer, Hamstein, & de Faire, 1991). Higher IL-6 may represent one pathway through which less positive relationships are associated with greater health risk in women.

Limitations and Future Directions

Testing our hypotheses in multiple groups, we observed several differences in effects across samples. However, the current study was not explicitly designed to examine such factors. Future studies must clarify these effects by using specific designs and methods to examine the effects of culture and aging.

Another set of limitations concern barriers to making comparisons across samples. First, because IL-6 follows a diurnal slope, failure to control for time of day in the Kentucky sample may have introduced error variance and reduced statistical power. Second, the Kentucky sample completed home interviews, whereas the national sample completed telephone interviews. However, previous studies have not found large differences between telephone and in-person survey methods, even when questions asked are of a sensitive nature (Aneshensel, Frerichs, Clark, & Yokopenic, 1982; Fenig, Levav, Kohn, & Yelin, 1993). Third, different versions of the same scale were used to measure well-being in the two samples. However, reliabilities of the two scale forms were virtually identical.

Finally, although many cytokines are involved in the dynamics of inflammation, the current study examined a single cytokine—IL-6—as an indicator of inflammatory processes. On the other hand, IL-6 is a robust indicator of health risk, especially in older adults. Additionally, most effects did not exceed the established risk threshold. However, increased inflammation stemming from failure to achieve valued states may be particularly important for people with other risk factors such as heart disease, cancer, or advanced frailty.

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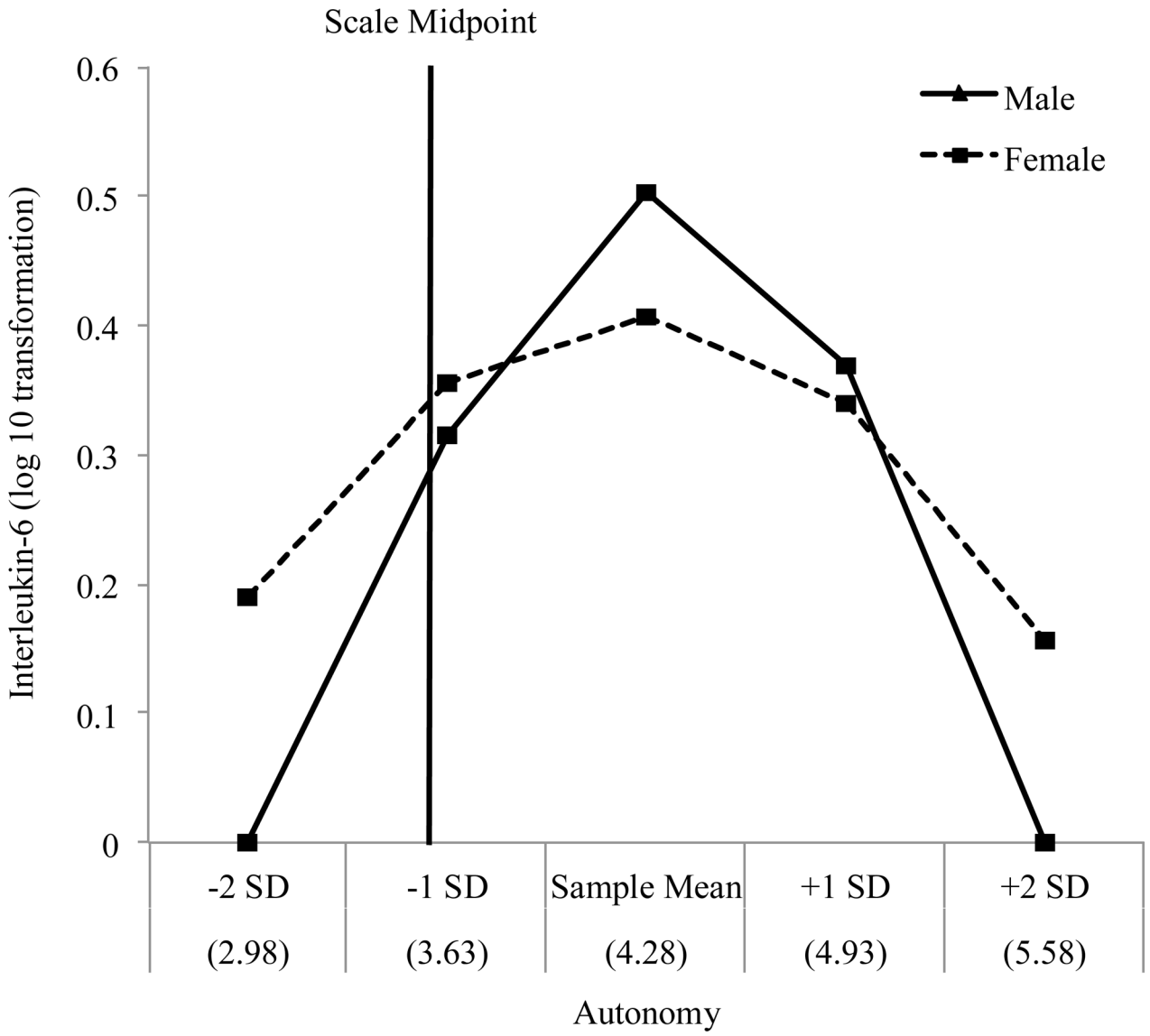

Figure 1.
The moderating effect of gender on the quadratic relationship between Autonomy and IL-6 in a sample of older adults living in Kentucky.

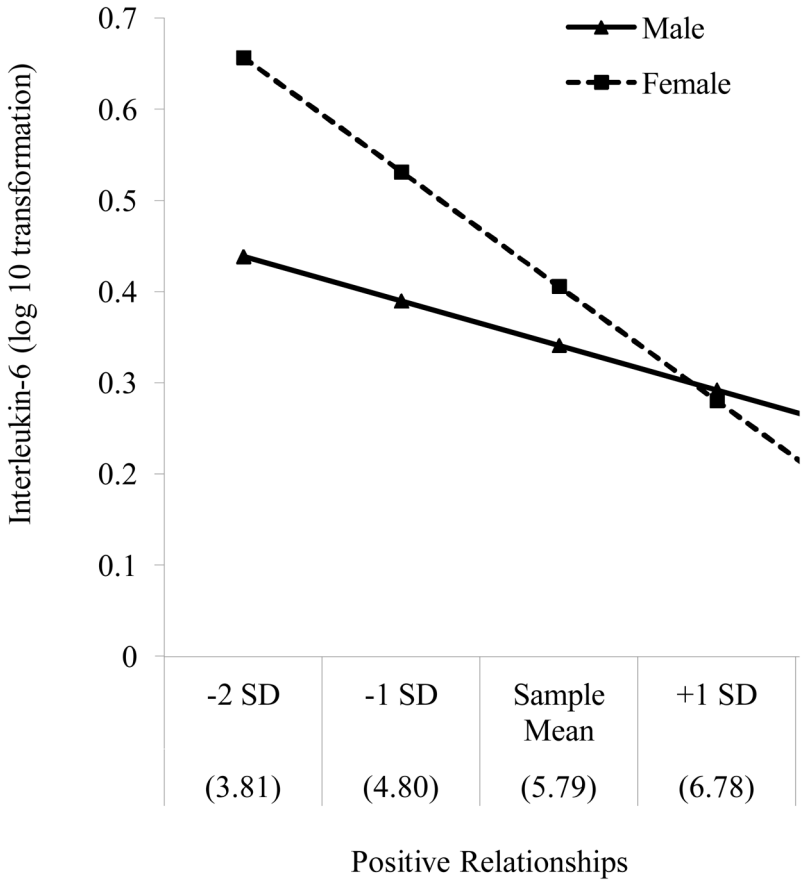

Figure 2.
The moderating effect of gender on the relationship between Positive Relationships and IL-6 in a US national sample of adults. The range of the x axis of the graph has been adapted so that the figure displays predicted levels of IL-6 only at obtainable levels of Positive Relationships scores (i.e., a maximum of 7).

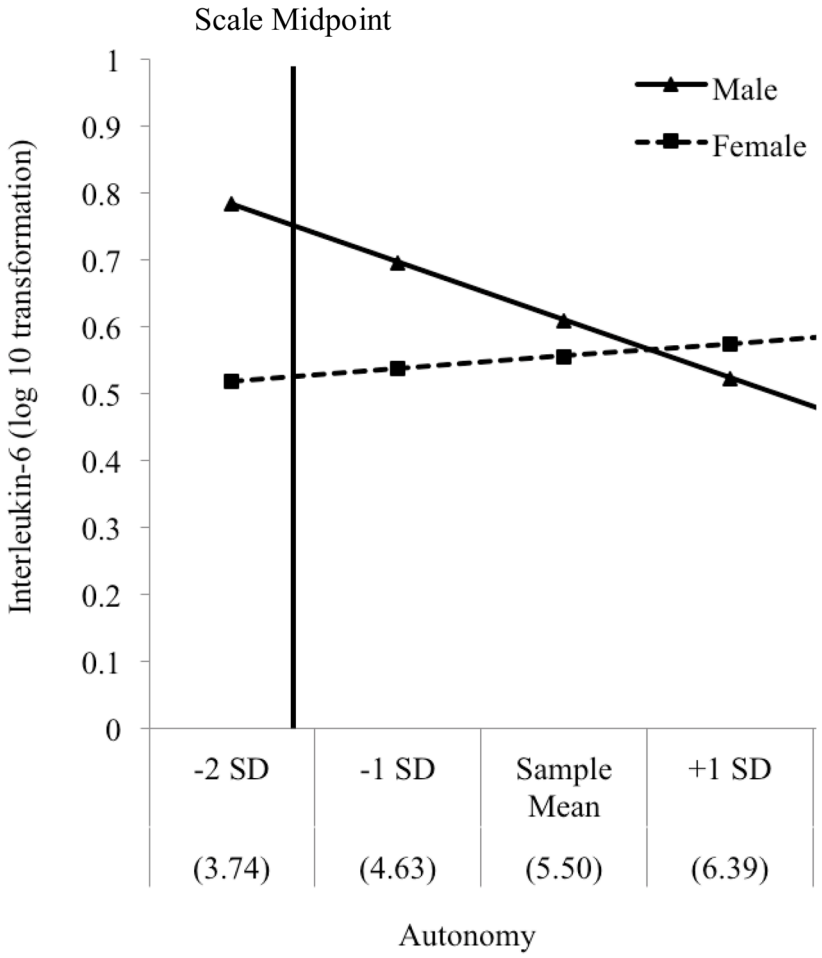

Figure 3.
The moderating effect of gender on the relationship between Autonomy and IL-6 in a US national sample of older adults. The range of the x axis of the graph has been adapted so that the figure displays predicted levels of IL-6 only at obtainable levels of Autonomy scores (i.e., a maximum of 7).

Table 1

Means and Standard Deviations for Variables across the 3 Samples

	Mean (SD)		
Variable	**Kentucky Sample (n = 119)**	**Full U.S. Sample (n = 1,208)**	**Restricted U.S. Sample (n = 235)**
Age	75.14 (5.71)[a]	54.50 (11.71)	68.97 (6.14)[b]
BMI	28.69 (5.35)	29.77 (6.62)	28.95 (4.94)
Interleukin-6 (IL-6)	2.94 (3.08)	3.25 (3.24)	3.83 (3.93)
Level of Education	16.08 (2.45)	14.30 (2.61)	15.53 (2.62)
Autonomy	4.28 (.65)[a†]	5.31 (.99)[††]	5.50 (.89)[b††]
Positive Relationships	5.13 (.63)[†]	5.79 (.99)[††]	6.10 (.81)[††]

Note. SD, standard deviation. Differing superscripts indicate significant mean differences between the Kentucky and Restricted U.S. samples. Raw (untransformed) IL-6 values are presented.

[†]indicates that responses were chosen from a 1–6 range, while

[††]indicates that responses were chosen from a 1–7 range. T-tests comparing differences in average scores on well-being scales were performed only after variables were rescaled to make response scales identical; however, this table presents average well-being values in their original scale.

Table 2

Correlations among Primary Study Variables in Study 1 (Kentucky Sample; N = 119)

Variable	1	2	3	4	5	6	7	8	9
1. Age									
2. Gender	−.25*								
3. BMI	−.17	−.17							
4. Education	−.09	−.12	−.19*						
5. Statin Use	−.08	−.03	.18*	−.08					
6. Beta-Blocker Use	.21*	−.03	.03	−.08	−.27*				
7. Autonomy	−.02	.05	−.08	.05	−.002	−.03			
8. Positive Relationships	−.20*	.33*	−.10	−.02	−.09	−.09	.39*		
9. Interleukin-6 (IL-6)	.18*	−.11	.30*	−.17	−.07	.21*	−.03	−.18*	

Note.

* $p < .05$. Gender was coded 0 = male and 1 = female.

Table 3

Linear regression of log interleukin-6 on Positive Relationships, Autonomy, and their interactions with gender in a sample of older adults in Kentucky

Variable	*β*	*p*	Total R^2	R^2 Δ	*p*
Model 1: IL-6 (log10 transformation)					
Step 1			.17	.17	<.01
Gender	−.01	.92			
Age	.18	.08			
Body Mass Index (BMI)	.33	<.01			
Statin Use	−.01	.91			
Beta-blocker Use	.16	.11			
Step 2			.18	.01	.22
Positive Relationships	−.12	.22			
Step 3			.18	.002	.59
Positive Relationships x Gender	−.17	.59			
Step 4			.18	.001	.77
Positive Relationships^2	−.02	.77			
Step 5			.19	.001	.74
Positive Relationships^2 x Gender	−.04	.75			
Model 2: IL-6 (log10 transformation)					
Step 1			.17	.17	<.01
Gender	−.01	.92			
Age	.18	.07			
Body Mass Index (BMI)	.33	<.01			
Statin Use	−.01	.91			
Beta-blocker Use	.16	.11			
Step 2			.17	.003	.58
Autonomy	−.05	.58			
Step 3			.17	.001	.70
Autonomy x Gender	−.12	.70			
Step 4			.17	.000	.85
Autonomy^2	−.02	.85			

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Variable	β	p	Total R^2	R^2 Δ	p
Step 5			.21	.04	.04
Autonomy^2 x Gender	.69	.04			

Note.

$^{*}p < .05$. For R^2 values, an asterisk indicates that the F value for the ANOVA of the full model at that step is significant. For ΔR^2, an asterisk indicates that the inclusion of that step's novel predictor produced an F value than was significantly greater than that of the previous model.

Table 4

Correlations among Primary Study Variables in Study 2 (Full Sample below diagonal, N = 1,028; Restricted Sample above diagonal, N = 235)

Variable	1	2	3	4	5	6	7	8	9
1. Age	--	−.11	−.26*	−.01	−.03	.03	.01	.01	.09
2. Gender	−.05	--	−.08	−.09	.23*	−.02	−.15*	.27*	−.12
3. BMI	−.05*	.01	--	−.04	−.06	−.24*	.07	−.002	.15
4. Education	−.08*	−.08*	−.09*	--	.00	−.01	.02	−.02	−.002
5. Statin Use	−.27*	.16*	−.14*	.08*	--	.26*	−.05	.04	−.17
6. Beta-Blocker Use	−.28*	−.02	−.18*	.06*	.38*	--	−.04	−.02	−.17
7. Autonomy	.01	−.12*	.04	.08*	.09*	−.05*	--	.35*	−.02
8. Positive Relationships	−.01	.14*	−.05	.06*	−.04*	−.05*	.38*	--	−.14
9. Interleukin-6 (IL-6)	.20*	.11*	.34*	−.10*	−.10*	−.24*	.01	.04	--

Note.

* $p < .05$. Gender was coded 0 = male and 1 = female.

Table 5

Linear regression of log interleukin-6 on Positive Relationships, Autonomy, and their interactions with gender in a US national sample of adults

Variable	β	p	Total R^2	R^2 Δ	p
Model 1: IL-6 (log10 transformation)					
Step 1			.19	.19	<.001
Gender	.07	.004			
Age	.007	<.001			
Body Mass Index (BMI)	.02	<.001			
Statin Use	.03	.28			
Beta-blocker Use	−.09	.007			
Step 2			.19	.002	.19
Positive Relationships	−.002	.19			
Step 3			.20	.01	.001
Positive Relationships x Gender	−.01	.001			
Step 4			.20	.000	.55
Positive Relationships^2	.000	.55			
Step 5			.20	.000	.69
Positive Relationships^2 x Gender	.000	.69			
Model 2: IL-6 (log10 transformation)					
Step 1			.19	.19	<.001
Gender	.07	.004			
Age	.007	<.001			
Body Mass Index (BMI)	.02	<.001			
Statin Use	.03	.28			
Beta-blocker Use	−.09	.007			
Step 2			.19	.002	.26
Autonomy	−.002	.26			
Step 3			.19	.000	.80
Autonomy x Gender	.001	.80			
Step 4			.19	.001	.45
Autonomy^2	.000	.45			

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Variable	*β*	*p*	Total R^2	R^2 Δ	*p*
Step 5			.19	.001	.47
Autonomy^2 x Gender	.000	.47			

Note.

$^{*}p < .05$. For R^2 values, an asterisk indicates that the *F* value for the ANOVA of the full model at that step is significant. For ΔR^2, an asterisk indicates that the inclusion of that step's novel predictor produced an *F* value than was significantly greater than that of the previous model.

Table 6

Linear regression of log interleukin-6 on Positive Relationships, Autonomy, and their interactions with gender in a restricted US national sample of older adults

Variable	β	p	Total R^2	R^2 Δ	p
Model 1: IL-6 (log10 transformation)					
Step 1			.09	.09	.04
Gender	−.05	.39			
Age	.01	.03			
Body Mass Index (BMI)	.004	.51			
Statin Use	−.11	.07			
Beta-blocker Use	−.07	.27			
Step 2			.12	.03	.05
Positive Relationships	−.01	.05			
Step 3			.12	.001	.73
Positive Relationships x Gender	.004	.74			
Step 4			.12	.000	.87
Positive Relationships^2	.000	.87			
Step 5			.14	.01	.13
Positive Relationships^2 x Gender	.003	.13			
Model 2: IL-6 (log10 transformation)					
Step 1			.09	.09	.04
Gender	−.05	.39			
Age	.01	.03			
Body Mass Index (BMI)	.004	.51			
Statin Use	−.11	.07			
Beta-blocker Use	−.07	.27			
Step 2			.10	.006	.38
Autonomy	−.004	.37			
Step 3			.13	.02	.04
Autonomy x Gender	.02	.04			
Step 4			.13	.004	.49
Autonomy^2	.000	.49			

Variable	β	p	Total R^2	R^2 Δ	p
Step 5			.13	.000	.91
Autonomy^2 x Gender	.000	.91			

Note.

$^{*}p < .05$. For R^2 values, an asterisk indicates that the F value for the ANOVA of the full model at that step is significant. For ΔR^2, an asterisk indicates that the inclusion of that step's novel predictor produced an F value than was significantly greater than that of the previous model.