Associations Between Health-Related Self-Protection, Diurnal Cortisol, and C-Reactive Protein in Lonely Older Adults

Rebecca Rueggeberg, PhD, Carsten Wrosch, PhD, Gregory E. Miller, PhD, and Thomas W. McDade, PhD

Objectives: The aim of this study was to examine whether health-related self-protection (e.g., using positive reappraisals or avoiding self-blame) prevents lonely older adults from exhibiting increases in diurnal cortisol secretion and higher levels of C-reactive protein (CRP). **Methods:** This longitudinal study (n = 122) examined diurnal cortisol levels (area under the curve) at baseline and 2-year follow-up. Levels of CRP were measured at 6-year follow-up. The main predictors included baseline levels of loneliness and health-related self-protection. **Results:** Among lonely participants, baseline self-protection predicted an amelioration of 2-year increases in diurnal cortisol volume ($\beta = -.34$, $p = .03$) and lower levels of CRP at 6-year follow-up ($\beta = -.42$, $p = .006$). These significant associations were not found among nonlonely participants ($\beta < .14$, $p = .33$). In addition, mediation analyses demonstrated that the buffering effect of self-protection on lonely older adults' levels of CRP at 6-year follow-up was statistically mediated by 2-year changes in cortisol volume ($\beta = -.16$, $p = .06$). **Conclusions:** These findings suggest that lonely older adults may ameliorate biologic disturbances if they engage in self-protection to cope with their health threats. **Key words:** diurnal cortisol, C-reactive protein, loneliness, self-protection. Aging.

AUC = area under the curve; **CRP** = C-reactive protein; **BMI** = body mass index; **SES** = socioeconomic status.

INTRODUCTION

Feelings of loneliness are increasingly recognized to compromise quality of life (1,2). Such adverse consequences of loneliness are likely to be especially pronounced in older adulthood (3) when most individuals experience a normative loss of resources and increasing health threats (4,5). Indeed, lonely older adults may find managing health-related threats particularly challenging, and the stress that ensues may contribute to patterns of biologic dysregulation (e.g., cortisol disturbance or heightened systemic inflammation). However, theory and research also suggest that older adults can cope with health threats and prevent such problems if they engage in self-protective control strategies (5,6). Some examples of self-protective control strategies are positive reappraisals, where a person focuses on positive aspects in the context of a problem, and the avoidance of self-blame for the occurrence of a health problem itself. In the current research, we tested these ideas using four waves of data from a longitudinal study of older adults. We expected that self-protective strategies would prevent lonely older adults, over time, from exhibiting increases in cortisol output and heightened systemic inflammation.

Mounting evidence suggests that feelings of loneliness increase individuals' vulnerability to a variety of physical health problems (1,7–10). Moreover, the processes that underlie the loneliness-health link could be related to individuals' increased vulnerability to biologic dysregulation (11). In this regard, lonely individuals may accumulate health-related problems because they construe their world as threatening (12), and these views trigger stress-related disturbances in endocrine functioning and disrupt the regulation of inflammation (7,13,14).

In support of such a process, studies have documented that feelings of loneliness are associated with poor health behaviors, greater diurnal cortisol secretion (7,13,15,16), and higher levels of the inflammatory biomarker C-reactive protein (CRP) (17). A recent study that used a functional genomic methodology found evidence suggesting that loneliness was associated with an underlying resistance to glucocorticoid signaling (18). This tendency could explain why lonely individuals simultaneously have both high levels of cortisol and inflammatory biomarkers.

Empirical evidence further suggests that associations between loneliness and patterns of morbidity and mortality can be particularly strong in older adulthood (3). This effect may be related to the previously discussed biologic consequences of loneliness, given that inflammation can play a key role in the development of a wide range of physical health problems associated with aging (e.g., cardiovascular disease, functional disability, or mortality) (19–23). Furthermore, the stress-related biologic disturbances associated with loneliness could accrue from normative health threats that are experienced by most individuals in older adulthood (e.g., physical symptoms, functional declines, or chronic illness) (24). Such adverse effects of common age-related challenges may be exacerbated among lonely older adults because they lack emotionally satisfying social networks that are useful for regulating the distress generated by normative health threats. By contrast, older adults who perceive themselves as socially embedded should be less likely to accumulate stress-related problems because their relationships may facilitate the management of normative health challenges. This argument is consistent with research documenting that the adaptive value of satisfying personal relationships and emotional closeness becomes increasingly important for older adults' emotion regulation and the resulting benefits for mental and physical health (25,26).

Although the discussed literature suggests that lonely older adults' could display inflammation due to age-normative challenges and associated cortisol dysregulation, some studies did not find any relations between loneliness and cortisol patterns

From the Department of Psychology (R.R., C.W.), Concordia University, Montreal, Canada; Department of Psychology (G.E.M.), University of British Columbia, Vancouver, Canada; and Department of Anthropology (T.W.M.), Northwestern University, Evanston, Illinois.

Address correspondence and reprint requests to Carsten Wrosch, PhD, Department of Psychology and Centre for Research in Human Development, Concordia University, 7141 Sherbrooke Street West, Montreal, Quebec, Canada H4B 1R6. E-mail: carsten.wrosch@concordia.ca

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in either younger or older adults (1). In addition, there is evidence suggesting that feelings of loneliness do not always explain large portions of variance in health-related outcomes (27,28). To reconcile these mixed findings, we reason that there may be certain psychological factors that could counteract downstream biologic consequences of feelings of loneliness. In this regard, the *Motivational Theory of Life-Span Development* postulates that older adults who engage in self-protective control strategies can forestall the mental and physical health declines associated with age-related challenges (5). These control strategies involve making positive reappraisals or external attributions for health threats (e.g., seeing the silver lining or avoiding self-blame for problems) and have been shown to benefit older adults' mental and physical health (6,29,30). Such adaptive effects are likely to be observed if self-protective strategies foster acceptance of, and disengagement from, problems that cannot be overcome through a person's active coping behaviors (5,31).

The documented benefits of health-related self-protection imply that these strategies could act as something akin to a stress buffer among older adults who are lonely (for a review on stress-buffering functions of coping resources, see Ref. 32). Given that lonely older adults often lack satisfying social networks that could provide emotional and/or tangible support, internal self-protection processes could facilitate the management of normative health threats and thereby prevent downward spirals in mental and physical health. By contrast, the use of health-related self-protection may generally be less necessary among older adults who do not feel lonely because they can rely on emotionally satisfying networks that help them to adjust to age-related challenges. In sum, we propose that health-related self-protection can become paramount among lonely older adults because the emotional benefits of these strategies are likely to counteract some of the psychological and biologic processes through which feelings of loneliness contribute to physical health problems.

To test this hypothesis, we analyzed data from a 6-year longitudinal study of older adults and compared biologic outcomes among relatively lonely versus nonlonely participants. Given that loneliness can produce adverse biologic effects in the context of widespread and normative health threats in older adulthood, we expected that relatively lonely participants would experience increases in diurnal cortisol output over a 2-year follow-up period and heightened levels of the inflammatory biomarker CRP at 6-year follow-up. In addition, we predicted that higher baseline levels of health-related self-protection would enable participants to cope with normative health threats and prevent these biologic problems from occurring among lonely participants. Finally, we tested whether the inflammatory benefits associated with lonely participants' self-protection would be mediated by prospective reductions in cortisol output.

METHODS

Participants

The data stem from a longitudinal study of community-dwelling older adults known as the *Montreal Aging and Health Study* (33). Participants were recruited through newspaper advertisements. The only inclusion criterion was that participants had to be older than 60 years because we were interested in examining a normative sample of older adults. After contacting the laboratory, participants were invited for an initial appointment. Participants who were unable to visit the laboratory were assessed in their homes. This project was approved by the university research ethics board, and informed consent was obtained from all participants.

In 2004, we enrolled the first wave of a heterogeneous sample of 215 older adults from the Montreal area. The 2- and 4-year follow-ups included 184 and 164 participants, respectively. One hundred thirty-seven participants were included in the 6-year follow-up. Study attrition from baseline to 6-year follow-up was attributable to being deceased (n = 23), refusing to participate further (n = 9), being unable to locate participants (n = 19), or having other personal problems that precluded participation (n = 27). Study attrition was not significantly associated with baseline measures of the study variables, except for participants' age. Older, as compared with younger, participants were more likely to discontinue their study participation over time ($t_{128.91} = -2.46$, $p = .02$). The analyses for testing our hypotheses are based on 122 participants because we excluded 15 participants who did not provide any data on CRP or cortisol.[1]

Materials

The main study variables incorporated measures of participants' health-related self-protection, loneliness, diurnal cortisol rhythms, and CRP. In addition, the study included a number of sociodemographic (i.e., age, sex, and socioeconomic status [SES]) and health-related (i.e., chronic illness, smoking, body mass index (BMI), and cortisol-related medication usage) covariates.

Health-related self-protection was measured at baseline by administering three items from a previously validated self-report questionnaire (6). These items were developed based on the "Motivational Theory of Life-Span Development" (5) and represent core aspects of self-protective secondary control (i.e., external attributions and positive reappraisals) (29,34). The specific items were "Even if my health is in very difficult condition, I can find something positive in life," "When I am faced with a bad health problem, I try to look at the bright side of things," or "When I find it impossible to overcome a health problem, I try not to blame myself." The items were answered with 5-point Likert-type scales (0 = *almost never true* to 4 = *almost always true*), and an indicator of participants' health-related self-protection was obtained by computing a mean score of the three items (α = .73).

Loneliness was measured at baseline by asking the participants at the end of three nonconsecutive typical days to what extent they felt "lonely" or "isolated" during the day. These two items have been used for assessing loneliness in previous research (35). The participants responded to the items by using 5-point Likert-type scales, ranging from 0 (*very slightly or not at all*) to 4 (*extremely*). For each day, the two items were correlated (r values = 0.36–0.59, p values < .001), and we computed the sum scores of the two items (M_{D1} [SD_{D1}] = 0.40 [1.01], M_{D2} [SD_{D2}] = 0.36 [1.05], M_{D3} [SD_{D3}] = 0.39 [0.96]). This loneliness composite was relatively stable across the 3 days of assessment (r values = 0.55–0.67, p values < .001), so we formed a global indicator by summing the daily values (α = .82). The range of loneliness in our sample was comparable with other studies with older community-dwelling adults (36,37). Specifically, 30.3% (n = 37) of our participants reported some feelings of loneliness across the three measurement days. In addition, the validity of the loneliness measure was indicated by associations between loneliness and less satisfactory ($r = -0.30$, p = .001) and smaller ($r = -0.16$, p = .08) social support networks (38).

Diurnal cortisol rhythms were measured across three nonconsecutive typical days, at both baseline and 2-year follow-up. We asked the participants to

[1]The 15 excluded individuals did not differ statistically from the remaining 122 participants with regards to age, sex, chronic illness, smoking, BMI, cortisol-related medication, self-protective coping or loneliness (all p values > .18). In cases in which single values of variables were missing, we replaced them with the sample mean. Missing replacement related to participants who did not provide cortisol values at 2-year follow-up (n = 7), baseline covariates, and main predictors (range of missing values = 0 [chronic illness] to 2 [BMI]).

collect saliva samples as they engaged in their normal daily activities. On each of the 3 days, participants collected five saliva samples (by using salivettes) at specific times of the day: awakening, 30 minutes after awakening, 2 PM, 4 PM, and bedtime. Participants were asked not to eat or brush their teeth immediately before saliva collection to prevent contamination with food or blood. They were provided with a timer that they had to set at 30 minutes at the time they collected their first saliva sample after awakening. To ensure compliance concerning the collection of the afternoon and evening samples, participants were called at 2 PM and 4 PM. They were further instructed to collect the last sample of the day by themselves at the time they went to bed. The actual time of day was recorded by the participants for all of the collected saliva samples. The saliva samples were stored in participants' home refrigerators until they were returned to the laboratory 2 to 3 days after the collection was completed (39). After the saliva containers were returned to the laboratory, they were frozen until the completion of the study. Cortisol analysis was performed at the University of Trier, in duplicate, using a time-resolved fluorescence immunoassay with a cortisol-biotin conjugate as a tracer (40). The intra-assay coefficient of variation was less than 5%; the interassay variability has been found to be routinely 10%.

Across both assessments, we obtained typical patterns of cortisol secretion over the 3 days, demonstrating high levels at awakening (Ms [SDs] = 12.45–13.91 [6.33–8.58]), peaking 30 minutes after awakening (Ms [SDs] = 16.76–19.90 [9.96–12.27]), and continuously decreasing over the later part of the day (2 PM: Ms [SD] = 5.38–6.68 [2.99–4.06]; 4 PM: Ms [SDs] = 4.88–5.39 [3.06–4.11]; and bedtime: Ms [SDs] = 3.18–3.70 [3.06–4.77]). All raw cortisol values were log transformed to stabilize variance, and total diurnal cortisol secretion was indexed by calculating the area under the curve (AUC) for each collection day using trapezoidal estimation (based on hours after awakening). AUC was chosen because it captures individual differences in cumulative tissue exposure to cortisol, which could, in turn, affect the immune system's capacity to regulate systemic inflammation. AUC was calculated for days on which participants provided five saliva samples (on average, 5.52 of the 6 days). For each wave, AUC was averaged across collection days to obtain a stable indicator of individual differences in diurnal cortisol secretion. At wave 1, 95.9% of our sample had either complete cortisol data or missing data on only one of the three measurement days (93.4% at wave 2). We computed a measure of changes in cortisol secretion over time by predicting 2-year follow-up levels from baseline levels of cortisol (AUC) and saving the standardized residuals. Participants' diurnal cortisol levels were significantly correlated with each other across waves (see Table 2) and did not significantly increase from baseline to 2-year follow-up ($t_{121} = 0.59$, $p = .55$).

CRP was measured as an indicator of systemic inflammation at 6-year follow-up. CRP was not measured during earlier waves of the study. We collected capillary whole blood from participants on filter paper by using a finger prick. A disposable, single-use lancet was used to deliver a controlled, uniform puncture to the finger, and up to five drops of blood was collected on a filter paper designed for this purpose (Whatman 903; GE Healthcare, Piscataway, NJ). Samples were allowed to dry and subsequently stored in a freezer with desiccant in resealable plastic bags until completion of the study. CRP was analyzed in the Laboratory for Human Biology Research at Northwestern University using a high-sensitivity enzyme immunoassay protocol (41,42). Prior validation of the blood-spot CRP method has shown good sensitivity and reliability, as well as high correlations between CRP levels obtained from matched plasma and blood-spot samples (41). The median CRP concentration at 6-year follow-up was 0.98 mg/l (25th percentile: 0.51 and 75th percentile: 2.13).

Covariates. To minimize the likelihood of spurious associations, we included a number of covariates into our analyses that could influence cortisol or CRP. These variables included baseline levels of participants' age, sex, SES, chronic illness, smoking, and BMI and cortisol-related medication use. SES was assessed by averaging the standardized scores of participants' highest level of education, yearly family income, and perceived SES ($\alpha = .69$) (43). Baseline levels of chronic illness were measured by counting the presence of 17 different health problems (e.g., coronary heart disease, cancer, osteoarthritis, or diabetes). Smoking was indexed as whether cigarettes were used daily. BMI was defined as the individuals' self-reported body weight (in kilograms) divided by the square of their self-reported height (in meters). Finally, use of medications that could be associated with cortisol secretion was indexed as whether participants took any medications that either contained glucocorticoids or have known influences on hypothalamic-pituitary-adrenal axis activity (e.g., antidepressants, β-blockers, or anti-inflammatory drugs).

DATA ANALYSES

We tested our hypotheses in two sets of regression analyses. In the first set, we examined whether health-related self-protection would be associated with lower levels of CRP at 6-year follow-up in lonely (but not in nonlonely) participants. To this end, we tested the interaction effect between health-related self-protection and loneliness on levels of CRP at 6-year follow-up for significance. In a second set, we investigated whether the interaction effect between health-related self-protection and loneliness on CRP levels at 6-year follow-up would be statistically mediated by 2-year reductions of diurnal cortisol secretion. Mediation was examined by conducting bootstrap analyses (44), which examined whether 2-year changes in cortisol secretion would exert an indirect effect on the interaction between health-related self-protection and loneliness on CRP at 6-year follow-up. The mediation analysis was based on 5000 bootstraps, and the indirect effect was evaluated as significant if the 95% bias-corrected confidence interval of the indirect effect did not cross zero (44). All analyses controlled for sociodemographic (i.e., age, sex, and SES) and health-relevant (i.e., chronic illness, smoking, BMI, and cortisol-related medication use) covariates, and predictor variables were standardized before conducting the analyses.

RESULTS

Sample

Table 1 provides a description of the sample, and Table 2 reports the zero-order correlations between the main constructs. Participants used in the analyses were, on average, 72 years old, and approximately half of the sample were women. They reported an average of two to three chronic health problems, and their mean BMI was between normal and overweight. Thirty-four percent obtained an undergraduate degree or a higher education, and the minority of the sample smoked. Most of the sample took medication that either contained glucocorticoids or can influence hypothalamic-pituitary-adrenal axis activity. The participants' sociodemographic characteristics and health status were within the normative range for older adults residing at home (45).

Main Analyses

We examined whether health-related self-protection was associated with CRP among lonely participants by conducting a hierarchical regression analysis. The analysis predicted CRP at 6-year follow-up by baseline levels of loneliness and self-protection and the covariates (step 1), followed by the interaction between loneliness and self-protection (step 2). The results of the analyses are reported in Table 3. None of the incorporated covariates or main effects were significantly associated with levels of CRP at 6-year follow-up (F values$(1,112) < 2.15$, R^2 values < 0.02, p values $> .15$), except for smoking ($F(1,112) = 11.01$, $R^2 = 0.08$, $p = .001$). Participants who smoked at baseline exhibited higher levels of CRP 6 years later than did their

TABLE 1. Means, Standard Deviations, and Frequencies of Main Study Variables (n = 122)

Constructs	M (SD) or Percentage[a]	Range
C-reactive protein (mg/l)		
6 y	1.58 (1.69)	0.09–10.76
Diurnal cortisol (AUC) (log nmol/l h)		
2 y	13.04 (2.32)	6.64–19.14
Baseline	12.87 (2.70)	5.04–20.53
Self-protection (T1)	3.06 (0.78)	0.33–4.0
Loneliness (T1)	1.13 (2.58)	0–15
No. chronic health problems (T1)	2.24 (1.61)	0–8
Age, y	71.61 (5.00)	64–85
Male, %	49.2	
Socioeconomic status	3.30 (1.07)	0.33–6.33
Education (T1)[b]	2.09 (1.09)	0–4
Yearly family income (T1)[c]	1.57 (1.23)	0–5
Perceived socioeconomic status (T1)	6.25 (1.71)	0–10
Smoking (T1), %	8.2	
Body mass index (T1)	25.54 (3.69)	16.49–40.79
Cortisol-related medication, %	78.7	

M = mean; SD = standard deviation; AUC = area under the curve.
[a] M and SD are presented for continuous variables.
[b] Education was indexed as 0 = no education, 1 = high school, 2 = trade, and 3 = masters or doctorate.
[c] Income was indexed as 0 = less than $17,000, 1 = up to $34,000, 2 = up to $51,000, 3 = up to $68,000, 4 = up to $85,000, and 5 = more than $85,000.

nonsmoking counterparts (β = .30, $p < .01$). In fact, the inclusion of smoking as a covariate into the multivariate model rendered the zero-order correlation between self-protective strategies and CRP nonsignificant. This finding appeared because smokers, as compared with nonsmokers, also engaged in lower levels of self-protection (see Table 2).

TABLE 3. Hierarchical Regression Analyses Predicting Levels of C-Reactive Protein at 6-Year Follow-Up by Baseline Levels of Loneliness and Health-Related Self-Protection

Baseline predictors	C-Reactive Protein at 6-y Follow-Up	
	R^2	β
Main effects		
Age	0.00	−.00
Sex	0.00	.03
Socioeconomic status	0.00	−.04
Chronic health problems	0.01	.10
Smoking	0.08	.30**
Body mass index	0.00	.07
Cortisol-related medication	0.01	−.12
Loneliness	0.00	.01
Self-protection	0.02	−.13
Interaction		
Loneliness × self-protection	0.04*	−.21*

R^2 values represent the unique proportion of variance explained in each step of analyses. β represents standardized regression coefficient in each step of analyses.
* $p < .05$.
** $p < .01$.

Of importance, the second step of the analysis demonstrated a significant two-way interaction effect between loneliness and self-protection on CRP at 6-year follow-up ($F(1,111) = 5.64$, $p = .02$). To illustrate the significant interaction effect, we plotted in Figure 1 the association between health-related self-protection (1 SD above and below the sample mean) and levels of CRP at 6-year follow-up, separately for participants who experienced relatively high (+1 SD) and no loneliness (46). In support of our hypotheses, Figure 1 shows that baseline levels of self-protection were significantly associated with lower levels of CRP at 6-year follow-up among relatively lonely

TABLE 2. Zero-Order Correlations Between Covariates and Main Constructs

	1	2	3	4	5	6	7	8	9	10	11
1. Age											
2. Sex (female)	.09										
3. Socioeconomic status	−.01	−.26**									
4. Chronic health problems	.00	−.16	−.12								
5. Smoking	−.12	−.13	−.10	.12							
6. Body mass index	−.19*	−.04	−.19*	.23**	.08						
7. Cortisol-related medication	−.00	.09	−.14	.45**	.08	.20*					
8. C-reactive protein (6 y)	−.05	−.03	−.16	.09	.34**	.12	−.03				
9. Cortisol volume (2 y)	−.05	−.12	.24**	−.13	−.02	.13	−.08	.29**			
10. Cortisol volume (baseline)	−.02	−.24**	−.04	−.10	.24**	.05	−.06	.23**	.31**		
11. Loneliness (baseline)	.16	.09	−.31*	−.01	−.00	−.01	−.01	.04	−.02	−.05	
12. Self-protection (baseline)	.05	.03	.07	.06	−.22**	−.16	.01	−.21*	−.11	−.07	−.12

* $p < .05$.
** $p < .01$.

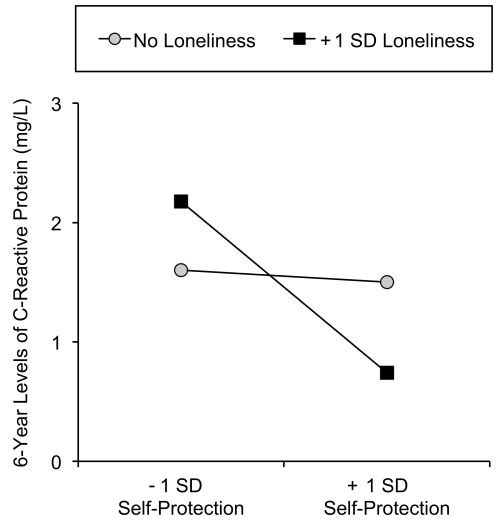

Figure 1. Associations between baseline levels of health-related self-protection (1 SD above and below the sample mean) and CRP at 6-year follow-up, separately for participants who experienced no loneliness (n = 85) and loneliness levels 1 SD above sample mean. SD = standard deviation; CRP = C-reactive protein.

participants ($\beta = -.42$, $p = .006$) but not among their nonlonely counterparts ($\beta = .13$, $p = .37$).[2]

Next, we examined whether 2-year changes in cortisol secretion would mediate the observed interaction effect between health-related self-protection and loneliness on levels of CRP at 6-year follow-up. To this end, we repeated the previously reported analyses for predicting CRP by additionally incorporating 2-year changes in cortisol secretion as a potential mediator (using the "indirect SPSS macro") (44).[3]

The results of the mediation analyses are illustrated in Figure 2 and demonstrated that the interaction effect between health-related self-protection and loneliness was also a significant predictor of 2-year changes in diurnal cortisol secretion ($F(1,111) = 4.00$, $p = .048$). In addition, Figure 2 shows that 2-year increases in diurnal cortisol secretion were significantly associated with higher levels of CRP at 6-year follow-up ($F(1,111) = 10.39$, $\beta = .29$, $R^2 = 0.07$, $p = .002$). Finally, the previously reported interaction effect between self-protection and loneliness on CRP was rendered nonsignificant ($F(1,110) = 3.52$, $\beta = -.16$, $R^2 = 0.02$, $p = .06$) if 2-year changes in cortisol secretion were included as a mediator into the analysis. Bootstrap analysis confirmed that 2-year changes in cortisol secretion exerted a significant indirect effect on the interaction effect between self-protection and loneliness on levels of CRP at 6-year follow-up (95% bias-corrected confidence interval = −0.378 to −0.001).

[2]Follow-up analyses estimating the regions of significance indicated that the effect of self-protection on lower levels of CRP at 6-year follow up was significant for participants who scored greater than 0.20 SDs above the sample mean of loneliness.

[3]The reported pattern of results of the regression and mediation remained identical if we predicted, or controlled for, 2-year levels of cortisol secretion (instead of 2-year changes in cortisol secretion) and additionally included baseline levels of cortisol secretion, the interaction between self-protection and loneliness, and the reported covariates into the analyses.

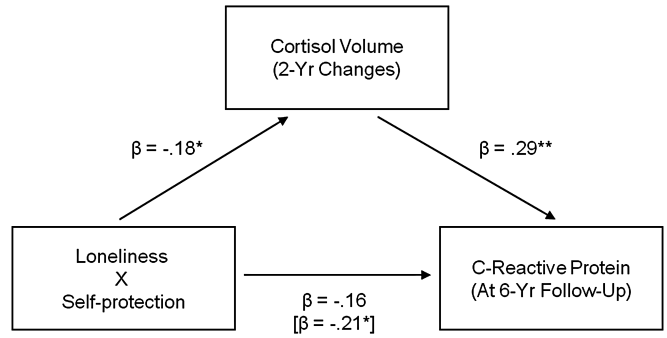

Figure 2. Mediation model examining whether 2-year changes in cortisol volume mediate the interaction effect between health-related self-protection and loneliness on C-reactive protein (CRP) at 6-year follow-up. Note. Values represent standardized regression coefficients. The coefficient in parentheses represents the unique effect, not controlling for the mediator. Bootstrap analyses showed that 2-year changes in diurnal cortisol volume exerted a significant indirect effect on the association between the interaction of loneliness and health-related self-protection with CRP at 6-year follow-up.

To interpret the obtained mediation effect, we plotted in Figure 3 the association between health-related self-protection (1 SD above and below the sample mean) and 2-year changes in diurnal cortisol secretion, separately for participants who experienced relatively high (+1 SD) and no loneliness. The obtained pattern of interaction closely resembled the results found for predicting CRP at 6-year follow-up. In particular, self-protection significantly predicted 2-year decreases in cortisol secretion among lonely participants ($\beta = -.34$, $p = .03$) but not among participants who did not feel lonely ($\beta = .14$, $p = .33$). This pattern of results lends support to a scenario in which health-related self-protection contributed to a decline of lonely participants' diurnal cortisol section for 2 years, which, in turn, was associated with lower levels of CRP at 6-year follow-up.

DISCUSSION

The results from this study suggest that self-protective strategies may ameliorate some of the adverse biologic consequences

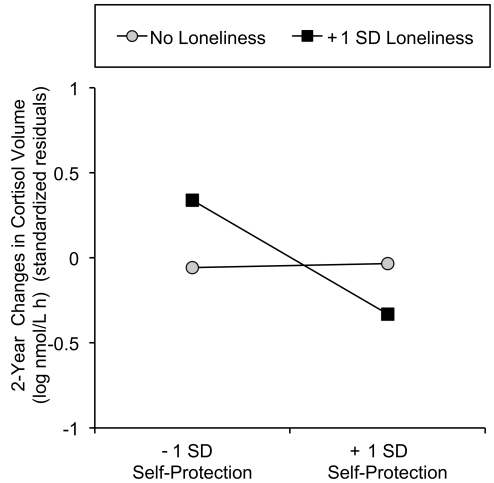

Figure 3. Associations between baseline levels of health-related self-protection (1 SD above and below the sample mean) and 2-year changes in cortisol volume, separately for participants who experienced no loneliness (n = 85) and loneliness levels 1 SD above sample mean. SD = standard deviation.

of loneliness in older adulthood. More specifically, the findings showed that, among lonely older adults, the use of health-related self-protection buffered against 2-year increases in cortisol secretion and was associated with lower levels of CRP at 6-year follow-up. In addition, mediation analyses showed that the obtained differences in CRP were partly attributable to self-protection's association with cortisol output during the initial 2 years of the study. No effects of self-protection were observed among older adults who did not feel lonely.

This pattern of findings suggests that among lonely older adults, the capacity to cope internally with common health threats is a contributor to later biologic outcomes. Those lonely older adults who reframe problematic health circumstances positively and do not blame themselves for health-related threats can prevent increases in diurnal cortisol secretion over time. Furthermore, by reducing cortisol output, self-protective strategies seem to be able to forecast lower CRP 4 years later. By contrast, lonely older adults who do not use self-protective strategies to manage their health threats are at risk for showing higher levels of biomarkers associated with disease and disability. In fact, our analyses of the regions of significance suggest that self-protection starts having a significant influence on CRP among participants who experienced levels of loneliness that were only a fifth of an SD above the sample mean. Although only 30% ($n = 37$) of our sample reported any feelings of loneliness, this finding may mean that relatively small increases in loneliness can have measurable implications for older adults' health-related processes, unless they engage in self-protective processes.

The results further imply that using health-related self-protection is less influential among older adults who do not feel lonely, presumably because they can rely on social relationships to facilitate the management of age-normative health threats. These conclusions are consistent with life-span developmental theories of socioemotional and motivational functioning, which postulate that adaptive control striving (5) and emotionally gratifying social relationships (47) can foster pathways to successful aging.

We think that the observed benefits of health-related self-protection may occur because most older adults are confronted with managing a loss of resources and the occurrence of physical health threats (4,5). Nonetheless, it is also possible that variability in the experience of health threats could additionally contribute to the observed process. Post hoc analyses, examining this possibility revealed a significant two-way interaction between baseline self-protection and chronic illness in predicting CRP at 6-year follow-up ($F(1,111) = 5.44$, $p = .02$; but not 2-year changes in cortisol secretion), indicating that among individuals who reported many (but not few) chronic health problems, self-protective strategies were associated with lower levels of CRP at 6-year follow-up ($\beta = -.31$, $p = .009$).[5] However, there was no significant three-way-interaction between loneliness, self-protection, and chronic illness in predicting cortisol or CRP, which implies that health-related self-protection becomes increasingly adaptive if both lonely and nonlonely older adults confront a higher level of health threats. Supposedly, this process may have been observed not only among lonely but also among nonlonely, older adults because supportive social networks could become less sufficient in the context of particularly high levels of health threats, and even socially embedded older adults may need to engage in self-protection in these circumstances.

Finally, our findings contribute to knowledge about how psychosocial factors modulate cross talk between glucocorticoids and inflammation (18,48,49). We found that self-protective strategies forecasted a reduction in cortisol secretion 2 years later. This reduced cortisol output was, in turn, associated with lower CRP 4 years later. At first blush, these findings may seem difficult to reconcile because cortisol generally has anti-inflammatory properties. However, sustained exposure to high levels of cortisol may render innate immune cells partially resistant to glucocorticoid inhibition, allowing inflammation to escape normal regulatory controls (49,50). Indeed, evidence of glucocorticoid resistance has emerged in functional genomic studies of lonely individuals (18).

Overall, the study's findings have important implications for understanding pathways to successful aging. Given that they can accentuate the impact of normatively occurring age-related challenges, feelings of loneliness are likely to aggravate biologic dysregulation in older adulthood (3). In such circumstances, the psychological benefits derived from the use of self-protective strategies can protect emotional resources and free up time and energy for the pursuit of other important (health-related) activities (5). Through this mechanism, self-protective processes could buffer against some downstream consequences of loneliness, like inflammation. Given the role of inflammation in the pathophysiology of several major diseases (51,52), this mechanism could have generalized benefits for older adults' long-term health.

In addition, the findings contribute to the literature on socioemotional functioning. Although there is evidence that loneliness can affect mental and physical health, and the biologic processes that underlie them, such effects have not been found consistently across studies (1,27,28,53). Our research provides an explanation for these inconsistent findings by suggesting that variability in the effects of loneliness can be associated with individual differences in self-protective coping. This implies that socioemotional problems can interact with self-regulation processes in predicting health-related outcomes, and adaptive self-regulation becomes particularly important for promoting successful aging among individuals who feel lonely.

Finally, the present research may have some implications for clinical treatment. Given that the use of adaptive control strategies can be improved in therapy (54), interventions should aim at teaching lonely older adults how to engage in

[4]Follow-up analyses estimating the regions of significance showed that the effect of self-protection on 2-year reduction in cortisol secretion was significant for participants who scored 0.88 SDs above the sample mean of loneliness.

[5]This interaction, however, did not statistically explain the previously reported interaction effect of loneliness and self-protection on CRP, or vice versa.

self-protective control strategies. The implementation of such programs could reduce stress-related biologic problems among lonely older adults and perhaps, as a result, dampen their systemic inflammation.

There are limitations to this study. First, we measured levels of CRP only at 6-year follow-up and did not include earlier assessments of CRP. This implies that the results reporting effects on levels of CRP need to be interpreted cautiously because they are based on longitudinal but not prospective analyses. As a consequence, it is possible that individual differences in CRP levels were already present at baseline and could have contributed to participants' coping responses, feelings of loneliness, and cortisol secretion. In turn, given that our results could equally be due to baseline differences in CRP levels rather than change in CRP over time, we cannot draw conclusions about the direction of effects. However, there are several reasons to believe that this limitation does not seriously compromise the overall interpretation of findings. First, baseline measures of psychological variables predicted reliable 2-year changes in diurnal cortisol secretion, which were associated with CRP at 6-year follow-up. Second, we note that our study also included cortisol levels at 6-year follow-up. In this regard, supplemental analyses showed that, unlike earlier measured cortisol output, concurrent (6-year follow-up) levels of cortisol were unrelated to levels of CRP ($r = 0.01$, $p = .95$), which provides additional evidence for a potential directional effect of cortisol on CRP. Third, CRP levels were unrelated to baseline levels of chronic illness, which makes it unlikely that CRP levels influenced coping responses among lonely individuals because they reflected underlying chronic illness. Finally, our empirical results are consistent with general models of health, suggesting that the association between psychological risk factors and immune function can be conferred through stress hormones such as cortisol (55,56). Nonetheless, we recommend that future studies should assess psychological, endocrine, and immune variables over multiple time points to substantiate our findings.

Second, although the reported results generally support our hypotheses, cortisol changes and levels of CRP among nonlonely individuals were somewhat higher than those of lonely individuals who used self-protective strategies. Although these differences were neither expected nor statistically significant, they could result from the experience of additional stressors that are not experienced by lonely individuals. For example, even satisfying social support networks may sometimes produce challenges (e.g., having arguments). In this regard, we suggest that future research should include more fine-grained measures about specific social interactions to address this possibility empirically.

Third, we focused in our analysis on the overall volume of cortisol secretion because we reasoned that such cumulative concentrations of cortisol output across day are particularly likely to show reliable associations with psychological and inflammatory variables. However, other research has demonstrated that loneliness is also associated with a flattened diurnal cortisol slope and an increased cortisol awakening response (27). Follow-up analyses of our data showed that this was not the case for our sample because changes in these alternative cortisol indices were associated neither with the interaction between loneliness and self-protection nor with levels of CRP at 6-year follow-up.

Fourth, although our analysis included a number of covariates, there may be underlying personality constructs that could have influenced older adults' feelings of loneliness and coping responses and, through this process, caused the observed effects on participants' biologic disturbances. A trait that could produce such effects is neuroticism (57,58). We note that our study included a baseline measure of neuroticism (59), and subsequently conducted follow-up analyses revealed that all reported effects remained significant if individual differences in neuroticism were taken into account.

Finally, the present research did not capture the complexity associated with the management of age-related challenges. For example, our theoretical model (24,30) would suggest that the observed effects of psychological predictors on inflammation could contribute to a higher likelihood of developing subsequent physical disease (56). Addressing these possibilities more comprehensively would have been beyond the scope of the present study because we did not have the data to examine links between CRP and changes in physical health outcomes. However, given the complex and often reciprocal processes involved in older adults' psychological, biologic, and physical health, research along these lines is warranted and has the potential to contribute to maintaining older adults' quality of life.

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