Published in final edited form as:

Psychosom Med. 2009 November ; 71(9): 996–1003. doi:10.1097/PSY.0b013e3181ba6cd1.

Cortisol Secretion and Functional Disabilities in Old Age: Importance of Using Adaptive Control Strategies

Carsten Wrosch, PhD,

Department of Psychology, Concordia University, Montreal, QC, Canada

Gregory E. Miller, PhD, and

Department of Psychology, University of British Columbia, Vancouver, BC, Canada

Richard Schulz, PhD

University Center for Social and Urban Research, University of Pittsburgh, Pittsburgh, Pennsylvania

Abstract

Objectives—To examine whether the use of health-related control strategies moderates the association between elevated diurnal cortisol secretion and increases in older adults' functional disabilities.

Methods—Functional disabilities of 164 older adults were assessed over 4 years by measuring participants' problems with performing activities of daily living. The main predictors included baseline levels of diurnal cortisol secretion and control strategies used to manage physical health threats.

Results—A large increase in functional disabilities was observed among participants who secreted elevated baseline levels of cortisol and did not use health-related control strategies. By contrast, high cortisol level was not associated with increases in functional disabilities among participants who reported using these control strategies. Among participants with low cortisol level, there was a relatively smaller increase in functional disabilities over time, and the use of control strategies was not significantly associated with changes in functional disabilities.

Conclusions—The findings suggest that high cortisol level is associated with an increase in older adults' functional disabilities, but only if older adults do not engage in adaptive control strategies.

Keywords

cortisol; control strategies; functional disabilities; successful aging

INTRODUCTION

Cortisol is a hormone that influences a variety of biological processes and health-related outcomes (1–3). Moreover, although research has found much variability in the age-related trajectories of cortisol secretion (4,5), there is accumulating evidence that advancing age can be associated with a higher level of diurnal cortisol secretion (6,7) and an increased cortisol response to challenge (8). In this regard, the neuroendocrine system that coordinates the release of cortisol, the hypothalamic-pituitary-adrenocortical (HPA) axis, is known to be activated by the experience of common psychological challenges. These effects have been documented in

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

Disclosure: None of the authors has a biomedical financial interest or a conflict of interest to declare related to this project.

samples across the life span including old age (1,9–15). Because cortisol has important regulatory influences in the metabolic, immune, skeletal, nervous, and circulatory systems (3,12,14,16–18), there has been much speculation that stress-related disturbances in its output could increase a person's likelihood of developing a variety of health problems (19).

However, studies examining the association between cortisol and physical health show a mixed pattern of findings. Although some studies indicate that individuals with dysregulated patterns of cortisol secretion are more prone to morbidity and mortality (20–23), other studies find no such effects (13,24), and even fail to document associations with presumptive downstream mediators like immune functions (15,25,26). To address these inconsistencies, we have suggested that individual differences in adaptive personality and behavioral processes can ameliorate an adverse effect of cortisol disturbance on a person's physical health (7). Consistent with this assumption, elevated cortisol levels were shown to be associated with increases in older adults' physical symptoms over 2 years, but only in the context of trait negative affect and inefficient sleep behaviors, and not among individuals who were emotionally well or exhibited efficient sleep (7).

Taking a motivational perspective, we argue that the use of control strategies may represent another factor that could influence the association between cortisol secretion and older adults' physical health. Control strategies are behavioral and cognitive processes that facilitate adaptation to common life challenges and enable individuals to cope effectively with these challenges and secure desired developmental outcomes (27–29). In the context of physical health, people can employ several different types of control strategies. First, health-engagement control strategies can be used to counteract a health threat by investing time and effort, seeking help and advice, or increasing the commitment to overcoming the problem (30). Second, individuals can use compensatory secondary control strategies to manage the emotional turmoil resulting from threats to physical health (27). Such secondary control strategies involve, for example, positive reappraisals or external attributions (31,32), which help maintain an older person's emotional and motivational resources and thereby facilitate the use of time and energy for the pursuit of important activities (27,33,34). In support of these assumptions, research has shown that health-engagement and compensatory secondary control strategies predict better well-being and physical health in older adulthood (31,32,35–40).

These adaptive effects of control strategies suggest that they may also play an important role in the cortisol-health link. This is a plausible hypothesis as associations between cortisol secretion and control strategies (or related constructs, such as coping or mastery) are typically small (36,37,41,42), which implies that there is considerable variability in the use of control strategies among people with high cortisol level. Furthermore, individual differences in health-engagement control strategies may contribute to obtaining critical information about illness, receiving adequate professional advice and help, and adhering to difficult treatment regimes, medication, or beneficial health behaviors. In a similar vein, the emotional benefits derived from the use of secondary control strategies may attenuate the downstream biological consequences of a persistently high cortisol level, and the motivational advantages of these strategies may foster investments in overcoming emerging threats to a person's well-being and physical health. These consequences of using adaptive control strategies could counteract potential adverse effects of high cortisol level on the development of older adults' physical health problems.

To test the hypothesis that control strategies can be associated with an effect of high cortisol level on physical health problems, we predicted 4-year trajectories of older adults' functional disabilities (e.g., difficulty bathing or doing housework). We examined functional disabilities because they are common and severe challenges in older adulthood, associated with depression and mortality (43,44), which typically increase over time (45,46). Although there is no direct

evidence linking functional disability and cortisol secretion, functional disabilities can develop from other health problems (e.g., symptoms of disease or chronic illness) (47) that have been linked with cortisol disturbance (7,37). Moreover, given that cortisol regulates a wide variety of biological processes in the nervous, metabolic, skeletal, and immune systems (3,16–18), persistent exposure to higher cortisol levels could plausibly contribute to the accumulation of visceral fat, to the softening of bone, and to the dysregulation of inflammation. Over time, these changes could impair individuals' capacities to carry out activities of daily living, particularly if they do not engage in adaptive control behaviors. Thus, we predicted that older adults who secrete high baseline levels of cortisol and report low levels of health-related control strategies would show a steep increase in their functional disabilities over time. By contrast, older adults who secrete high levels of cortisol and engage in high levels of control strategies, and older adults with generally low cortisol level, were expected to show considerably smaller increases in their functional disabilities.

To help preclude spurious associations, this analysis incorporated two classes of covariates that were selected on the basis of previous research. The first class of covariates included factors that have been shown to moderate the cortisol-health link (i.e., negative affectivity and sleep efficiency) (7). The second class of covariates included variables that could be associated with cortisol, control strategies, or functional disabilities (i.e., mortality risk index, education, physical symptoms, daytime dysfunction, depressive symptoms, and medication use) (48–50) and therefore could statistically explain the hypothesized effects.

METHODS

Participants

This study is based on a heterogeneous sample of older adults who participated in the Montreal Aging and Health Study (36). A total of 215 participants were recruited in 2003 (T1) through newspaper advertisement. The only inclusion criterion was that participants had to be >60 years of age because we were interested in examining a normative sample of older adults. Participants were invited to the laboratory for an initial appointment. If they were unable to visit the laboratory, they were assessed in their homes. During the initial appointment, they were instructed to complete a questionnaire and to collect saliva samples over the course of 3 nonconsecutive days. All study materials were collected after participants finished the daily assessment, and participants received \$50 for their participation. The study was approved by the Human Research Ethics Committee of Concordia University.

A second wave (T2) and a third wave (T3) of the study were conducted approximately 2 years (mean = 1.89, standard deviation [SD] = 0.08; range = 1.72–2.13 years) and 4 years (mean = 3.78, SD = 0.24; range = 3.28–4.77 years) after the baseline assessment. A total of 184 subjects (85.6%) participated at T2 and 164 (76.3%) participated at T3. Reasons for attrition from T1 to T3 were being deceased ($n = 13$), having problems that prevented participation ($n = 17$), refusing further participation ($n = 8$), and being unable to locate participants ($n = 13$). Study attrition was not significantly associated with baseline measures of the main constructs, except for participants' age. Older participants were more likely than younger participants to discontinue their participation from T1 to T3, $t = 2.06$, $p < .05$. Five subjects were further excluded from the analyses because they did not provide sufficient cortisol data, and the final sample thus included 159 participants. At baseline, subjects who were included into the study were on average 71.85 years old (SD = 5.63; range = 64–94 years), 81 were female, and 53 participants had attained an undergraduate university degree or a higher education.

Materials

The study variables included three assessments of participants' functional disabilities over 4 years of study. In addition, baseline levels of diurnal cortisol secretion, health-related control strategies, and a number of covariates (i.e., mortality risk index, education, physical symptoms, medication usage, depressive symptoms, daytime dysfunction, negative affectivity, and sleep efficiency) were incorporated into the study. Table 1 documents the mean and SD values, or frequencies of these variables.

Functional disabilities were assessed at T1, T2, and T3. Participants were asked by the research assistant to report whether or not they had difficulty or were unable to perform each of six instrumental activities of daily living (ADLs) (heavy housework; light housework; shopping; preparing meals; managing money; and using the phone) and six basic ADLs (eating; dressing; showering; using the toilet; walking around at home; and getting in and out of a bed or chair). At baseline, 23.9% of participants reported having difficulty with performing one or more ADLs (T2 = 28.9%; T3 = 37.7%), which indicates that our sample was relatively healthy at baseline, but resembled in later waves the prevalence of functional disability documented in population-based Canadian data (51). Instrumental and basic ADLs were correlated, $r = .48-.54$, $p < .01$, and we computed variables at each assessment, representing the total number of instrumental and basic ADLs participants had difficulty performing.

Diurnal cortisol secretion was measured at baseline as participants engaged in their normal daily activities. To minimize the influence of singular stressors on participants' cortisol scores, the assessment took place on each of 3 nonconsecutive days that did not involve unusual events (e.g., physician appointment). The assessment involved weekdays (70.33%) and weekends (29.67%), which was not associated with differences in cortisol level, $t(128) = -0.04$, $p = .97$. Ninety-seven percent of cortisol assessments were completed within 5 days and the remaining cortisol samples were collected within 1 week. On each assessment day, participants collected five saliva samples, by using salivettes, at: awakening, 30 minutes after awakening, 2 PM, 4 PM, and bedtime. Participants set a timer to 30 minutes at the time they collected their first saliva sample after awakening. For the collection of the afternoon and evening samples, participants were called at 2 PM and 4 PM. The last sample of the day was collected at the time participants 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 collection was completed, and they were subsequently frozen until the completion of the study. At the University of Trier, cortisol analysis was performed in duplicate, using a time-resolved fluorescence immunoassay with a cortisol-biotin conjugate as a tracer (52). The intra-assay coefficient of variation was $<5\%$; the interassay variability has been found to be routinely $<10\%$. Values are expressed in nmol/L.

We obtained typical patterns of cortisol secretion. The sample means over the 3 assessment days were relatively high at awakening (mean = 12.60–13.39, SD = 8.41–9.21), peaking 30 minutes after awakening (mean = 16.51–17.60, SD = 10.70–11.38), and continuously decreasing over the later part of the day (2 PM: mean = 5.32–6.26, SD = 3.29–4.42; 4 PM: mean = 4.87–5.09, SD = 3.19–3.99; and bedtime: mean = 3.03–3.88 SD = 2.59–5.52). To compute a measure of participants' level of diurnal cortisol secretion, we calculated the area under the curve (AUC) of cortisol secretion for each day separately, using the trapezoidal method (based on hours after awakening). AUC of cortisol secretion was chosen as predictor variable because we reasoned that a reliable measure of cumulative concentration of cortisol is most likely to influence physical health outcomes. Given that some saliva samples may have been contaminated with blood or food, we excluded all samples that deviated >3 SDs from the mean cortisol secretion for the time of day. In addition, we calculated AUC only if the

participants provided five complete saliva samples for a specific day. Single-day measures of AUC were significantly correlated, $r = .51-.72$, all $p < .01$, and were averaged to obtain a stable indicator of diurnal cortisol secretion.

Health-related control strategies were assessed at baseline by administering a 12-item self-report questionnaire. All items were answered by using 5-point Likert-type scales (0 = almost never true to 4 = almost always true). Nine items measured health-engagement control strategies, which have been validated in previous research (35–37). Of these nine items, three items measured investments of time and effort (e.g., “If I have a health problem that gets worse, I put in even more effort to get better”), three items measured recruitment of external resources (e.g., “If I develop a new health problem, I immediately get help from a health professional” [e.g., doctor, nurse]), and three items measured commitment to health goals (e.g., “When I decide to do something about a health problem, I am confident that I will achieve it”). In addition, the instrument included three items measuring compensatory secondary control strategies. These items represented core aspects of secondary control, such as attributions or positive reappraisals (31,32). The specific items were: “When I find it impossible to overcome a health problem, I try not to blame myself”; “Even if my health is in very difficult condition, I can find something positive in life”; and “When I am faced with a bad health problem, I try to look at the bright side of things.”

To examine whether the control strategy scale consisted of different factors, we subjected the 12 items to a principal component factor analysis. The scree test of the factor analysis suggested one single factor with an Eigenvalue of 5.99. The factor loadings of the 12 items ranged between 0.59 and 0.82. As a consequence, we computed a mean score of all 12 items ($\alpha = 0.90$). We note that the obtained control strategies scores were associated with specific health behaviors at baseline (e.g., more weekly physical activity: $r = .25$, $p < .01$; less smoking: $r = -.16$, $p = .05$), thereby lending further support to the validity of the scale.

Additional Measures—The study also included a number of additional sociodemographic, health-related, and psychological variables that were assessed at baseline (Table 1). First, a mortality risk index was obtained, containing the weighted information of the following risk factors: age, being male, presence of diabetes, cancer, lung or other respiratory disease, heart condition, body mass index of <25 , and smoking. The original index, developed by Lee and colleagues (48), also included functional aspects of aging, which were excluded from our index because they overlapped conceptually with the study’s outcome variables. Second, education was measured by asking participants to report their highest educational degree completed (0 = none, 1 = high school, 2 = trade, 3 = undergraduate degree, 4 = graduate degree). Third, a measure of physical symptoms was derived by counting the number out of 12 symptoms (e.g., chest pain, joint pain, or shortness of breath) participants reported having experienced often during the past month (53). Fourth, usage of medication was assessed by counting the number of different medications participants were taking. Fifth, daytime dysfunction associated with fatigue was assessed by asking participants to report how often they have trouble staying awake while driving, eating meals, or in social activity (0 = not during the past month; 1 = less than once per week; 2 = once or twice per week; 3 = three or more times per week) (54). Sixth, depressive symptomatology during the past week was operationalized as a sum score, using a 10-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) (e.g., “I felt that everything I did was an effort”; 0 = rarely or none of the time to 3 = most or almost all of the time; $\alpha = 0.72$) (55). Seventh, negative affectivity was assessed by computing the mean of ten negative emotions, participants rated with respect to the extent they had experienced them over the past year (e.g., distressed, guilty, or afraid; 1 = very slightly or not at all to 5 = extremely; $\alpha = 0.88$) (56). Finally, sleep efficiency was operationalized by computing an index, representing the time participants spent in bed during the night sleeping, relative to the overall time they spent in bed (54). To this end, participants reported for the

majority of recent nights during the past month the time they usually went to bed and got out of bed, and the time related to falling to sleep, being awake in the middle of the night, and waking up earlier than their usual time to get up.

Data Analyses

The hypothesis that control strategies could predict whether high cortisol level is associated with an increase in older adults' functional disabilities was tested by conducting a set of growth-curve models, utilizing HLM 6.0 (57). In the Level 1 model, we estimated within-person variability in participants' functional disabilities (using data from T1, T2, and T3) as a function of years from the time of study entry and a residual term. In the Level 2 model, we subsequently estimated between-person variation in the within-person slopes of functional disabilities as a function of the centered baseline scores of cortisol level, health-related control strategies, and a random residual term. The Level 2 model also incorporated a number of covariates (i.e., mortality risk index, physical symptoms, medication usage, daytime dysfunction, depressive symptoms, education, sleep efficiency, and negative affectivity). Table 2 shows zero-order associations between predictor variables. To test our hypothesis, we included in the last step of the analysis the interaction term between cortisol level and control strategies into the Level 2 model. In addition, the Level 1 and Level 2 models were estimated to predict simultaneously the intercept, which represented participants' levels of functional disability at study entry. The interaction effect was followed up by recalculating the growth-curve model separately for participants who scored in the upper and lower quartile of the cortisol distribution, and examining the effect of control strategies on changes in functional disability at the same time controlling for those predictor variables that were significant in the main analysis.

RESULTS

The results of the analysis are summarized in Table 3. The Level 1 model showed a significant effect for the intercept, indicating that participants' baseline levels of functional disabilities were significantly different from zero. In addition, there was significant variability around the average intercept, $\chi^2 > 255$, $df = 158$, $p < .01$, which we predicted in the subsequent Level 2 model. This Level 2 model revealed significant effects for baseline levels of control strategies and physical symptoms on the intercept of functional disabilities. These findings indicate that, at baseline, lower levels of health-related control strategies and higher levels of physical symptoms were significantly associated with higher levels of functional disabilities. The main effects of the other predictor variables did not significantly predict the intercept, and there was no significant interaction effect between cortisol level and control strategies on the intercept of participants' functional disabilities.

Table 3 also indicates that the analysis confirmed a significant slope effect for the Level 1 model, demonstrating that levels of functional disabilities exhibited a linear increase over the course of 4 years. In addition, there was significant variability around the average within-person slope of functional disabilities, $\chi^2 > 202$, $df = 158$, $p < .01$, suggesting the presence of reliable between-person differences in this slope. The subsequent Level 2 model, predicting the observed variability in the slopes of participants' functional disabilities, showed that only medication usage significantly predicted the slope of functional disabilities. This finding suggests that participants who took more medication at baseline experienced a steeper increase in their functional disabilities over time (upper quartile: $\beta = 0.15$, standard error [SE] = 0.04, $t = 3.63$, $p < .01$), as compared with their counterparts who took less medication, (lower quartile: $\beta = 0.05$, SE = 0.03, $t = 1.50$, $p > .10$). None of the other predictor variables showed a significant main effect on participants' functional disability slopes.

The inclusion of the interaction term between cortisol level and control strategies into the Level 2 model demonstrated a significant effect on the slope of functional disabilities (Table 3). To

illustrate this interaction, we applied recommended growth-curve techniques (58), and plotted in Figure 1 the trajectories of functional disabilities over 4 years of study for the averaged upper and lower quartiles of the distribution of the predictor variables. The upper panel of Figure 1 represents the association between levels of control strategies and changes in functional disabilities among participants with high baseline levels of cortisol; the lower panel of Figure 1 illustrates the same association for participants with low cortisol level.

The shape of the obtained interaction effect suggests two conclusions. First, control strategies were related more strongly to changes in functional disabilities among participants with high levels of cortisol, as compared with participants who secreted low levels of cortisol. Second, among participants with relatively high cortisol level, only those who reported low levels of health-related control strategies experienced an increase in their functional disabilities.

Follow-up analyses of the previously reported growth-curve model, conducted separately for participants who scored in the upper and lower quartile of the cortisol distribution, supported this interpretation of the data. The Level 1 models of these analyses suggested an increase in functional disabilities in both groups of subjects (upper quartile of the cortisol distribution: coefficient = 0.149, SE = 0.065, T ratio = 2.30, $df = 39$, $p < .05$; lower cortisol quartile: coefficient = 0.150, SE = 0.068, T ratio = 2.20, $df = 39$, $p < .05$).

The subsequent Level 2 models, incorporating baseline levels of those variables as predictors of the intercept and slope of functional disability that were significant in the previous analysis (i.e., control strategies, physical symptoms, and medication usage), showed that control strategies were not significantly associated with changes in functional disabilities among participants in the lower quartile of the cortisol distribution, coefficient = 0.150, SE = 0.100, T ratio = 1.50, $df = 36$, $p > .10$. However, there was a significant effect of control strategies on changes in functional disabilities among participants in the upper quartile of the cortisol distribution, coefficient = -0.235, SE = 0.098, T ratio = -2.39, $df = 36$, $p < .05$. This effect is consistent with the trajectories obtained from the original growth-curve model (Fig. 1, upper panel), which showed that functional disabilities increased significantly over time among participants with high cortisol level, if they reported low levels of health-related control strategies, $\beta = 0.34$, SE = 0.12, $t = 2.85$, $p < .01$, but remained stable among their counterparts who reported high levels of these control strategies, $\beta = -0.05$, SE = 0.08, $t = -0.64$, $p > .10$.

DISCUSSION

The results of this study showed that older adults who secreted relatively high levels of diurnal cortisol experienced an increase in their functional disabilities, but only if they endorsed low levels of health-related control strategies. By contrast, high cortisol level was not associated with an increase in functional disabilities among older adults who reported using high levels of these control strategies. In addition, the findings showed that there was a relatively smaller increase in functional disabilities among older adults who secreted low cortisol level, and the use of control strategies was not significantly associated with changes in functional disabilities among these individuals.

These findings are consistent with the hypothesis that engagement in health-related control strategies may ameliorate an effect of elevated cortisol level on increases in older adults' functional disabilities. The size of this association was substantial. After 4 years of study, a difference of almost two ADLs emerged as a function of control strategy use among participants who secreted high levels of cortisol. For an average older adult, this might mean, for example, losing the ability to get in and out of a chair and shop for personal items.

The reported analysis also points to the unique role played by control strategies in the cortisol-health link, given that it controlled for associations between predictors and outcome at baseline

as well as variables that could influence older adults' functional disabilities. In addition, the results provided further support for the validity of both our control measure and other indicators of health and functioning. First, lower baseline levels of functional disabilities were associated with higher baseline levels of health-related control strategies. Second, and consistent with previous research, higher baseline levels of physical symptoms were associated with higher baseline levels of functional disabilities, and the use of more medication at study entry predicted a steeper increase in older adults' functional disabilities over time (43,49).

Overall, the study's results link for the first time elevated levels of cortisol secretion with changes in older adults' functional disability. These elevated levels of cortisol may indicate a dysregulation of the HPA axis, which could affect a variety of biological processes in the nervous, metabolic, skeletal, or immune systems (3,16–18). As a consequence, it is plausible that persistent exposure to higher cortisol levels could contribute to the accumulation of visceral fat, to the softening of bone, and to the dysregulation of inflammation, and by doing so over time impair a person's capacity to carry out activities of daily living. In such circumstances, the motivational, emotional, and behavioral benefits derived from the use of adaptive control strategies may contribute to an earlier diagnosis and timely treatment of emerging health declines, beneficial health behaviors, or adherence to difficult treatment regimes, thereby attenuating the downstream biological consequences of a persistently high cortisol level and preventing the development of functional disabilities.

These findings have important implications for psychological theories of physical health. Although it has been suggested that cortisol dysregulation plays a role in the association between challenge and physical health (19), extant research has not consistently demonstrated that cortisol disturbance influences biological intermediaries or physical health outcomes (13,15,24–26). In this regard, our previous work has shown that these inconsistencies may, in part, be explained by low negative affectivity and efficient sleep behaviors, which significantly reduced the effect of elevated cortisol level on 2-year increases in physical symptoms (7). The present research extends these findings by suggesting that control strategies can play a similar and unique role in the development of even more severe physical health problems over a longer period of time. This implies that theory and research should take into account the interaction of different personality factors with biological mediators to improve our understanding of the pathways linking cortisol response with physical health outcomes.

The reported study also informs theories of successful aging. There is much variability in older adults' physical health, and the emergence of functional disabilities represents a serious challenge, associated with depression and mortality (43,44). However, there is little in the way of empirically informed evidence that can be used to assist people in managing these challenges as they approach the end of their lives (33,59). In this regard, the results of our study suggest that the use of adaptive control strategies may represent a mechanism that could explain some of the health-related variability, and prevent or delay the development of functional disability among older adults with elevated cortisol output. Given that cortisol secretion may increase in old age (6,7), and the substantial size of the observed effect, it seems important to translate these findings into interventions that teach older adults how to use adaptive control strategies (60). Alternatively, it would be plausible that a pharmacological intervention that successfully reduces tissue exposure to cortisol could ameliorate the development of functional disability, particularly among older adults who have difficulty engaging in adaptive control strategies.

There are limitations to this study. First, above and beyond the covariates used in our analysis, there may be other preexisting or subclinical conditions, such as certain aspects of frailty or undiagnosed illness (61) that could have contributed to the study's findings. Although the existence of such conditions may be related to some of our covariates, such as physical symptoms or daytime dysfunction associated with fatigue, they were not directly measured in

this study and therefore could represent an alternative explanation for the findings. In addition, our analysis did not address whether participants' cortisol levels were directly associated with the use of certain drugs that could influence cortisol secretion (e.g., antidepressants, β blockers, or anti-inflammatory drugs). However, follow-up analyses controlling for the presence and number of drugs that may influence cortisol showed that the use of these drugs did not explain variance in functional disability or the reported interaction effect involving cortisol and control strategies.

Second, we focused in our analysis on the overall volume of cortisol secretion because we reasoned that such cumulative concentrations of cortisol output across the day might have a high likelihood of predicting physical health outcomes. However, other research has shown that cortisol slope can also predict physical health outcomes (20,22). In addition, it may be that individual differences in the awakening level of cortisol, in the early morning rise of cortisol, or in the variability of cortisol level across days contributed to the reported results. Follow-up analyses of our data showed that this was not the case for our sample, as neither of these alternative cortisol indices was significantly associated with levels or changes in functional disabilities, or interacted with participants' control strategies.

Third, as research from nonhealth-related areas of life has documented distinct effects of goal engagement and compensatory secondary control strategies on outcome variables (62,38), our analyses showed that these types of control strategies were highly correlated in the health domain. Both types of control strategies would have interacted with cortisol level for predicting changes in functional disability, $t < 2.21$, $p < .05$, if they were analyzed separately. Future research should identify potential reasons for the high association between health-related control strategies in old age, which may be due to the possibility that successful management of health problems requires simultaneous investment in different types of control strategies. Alternatively, there may be underlying neuropsychological problems, such as declines in frontal lobe function and associated executive abilities, that undermine high levels of control strategy use (63,64).

Finally, future research should examine other biological variables because cortisol disturbance is thought to influence physical health through its effects on other body systems (e.g., immune, metabolic, or skeletal systems) (3,16–18). Thus, similar interaction effects may be found with regard to other biological processes that could be influenced by cortisol secretion. Given these considerations, we feel that future research on the roles played by control strategies and other personality factors may improve our understanding of the psychological and biological pathways leading to a person's long-term physical health.

Acknowledgments

This research was funded, in part, by a grant from Canadian Institutes of Health Research (C.W.). Preparation of this manuscript was further supported by other grants and awards from the Canadian Institutes of Health Research, the Heart and Stroke Foundation of Canada, and Grants NR08272 and NR09573 from the National Institutes of Health, Grants AG15321 and AG026010 from NIA, Grant MH071944 from the National Institute of Mental Health, Grants HL076852 and HL076858 from National Heart, Lung and Blood Institute, Grant HD058502 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and Grant EEEC-0540856 from the National Science Foundation.

Glossary

AUC	area under the curve
ADLs	activities of daily living

References

1. Heim C, Ehlert U, Hellhammer DH. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology* 2000;25:1–35. [PubMed: 10633533]
2. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. *JAMA* 2007;298:1685–7. [PubMed: 17925521]
3. McEwen BS. Seminars in medicine of the Beth Israel Deaconess Medical Center: protective and damaging effects of stress mediators. *N Engl J Med* 1998;338:171–9. [PubMed: 9428819]
4. Lupien S, Schwartz G, Ng Y, Fiocco A, Wan N, Pruessner J, Meaney M, Nair N. The Douglas Hospital longitudinal study of normal and pathological aging: summary of findings. *J Psychiatry Neurosci* 2005;30:328. [PubMed: 16151537]
5. Seeman TE, McEwen BS, Singer BH, Albert MS, Rowe JW. Increase in urinary cortisol excretion and memory declines: MacArthur studies of successful aging. *J Clin Endocrinol Metab* 1997;82:2458–65. [PubMed: 9253318]
6. Van Cauter E, Leproult R, Plat L. Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA* 2000;284:861–8. [PubMed: 10938176]
7. Wrosch C, Miller GE, Lupien S, Pruessner JC. Diurnal cortisol secretion and 2-year changes in older adults' acute physical symptoms: the moderating roles of negative affect and sleep. *Health Psychol* 2008;27:685–93. [PubMed: 19025263]
8. Otte C, Hart S, Neylan TC, Marmar CR, Yaffe K, Mohr DC. A meta-analysis of cortisol response to challenge in human aging: importance of gender. *Psychoneuroendocrinology* 2005;30:80–91. [PubMed: 15358445]
9. Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. *Psychol Bull* 2004;130:355–91. [PubMed: 15122924]
10. Jacobs N, Myin-Germeys I, Derom C, Delespaul P, van Os J, Nicolson NA. A momentary assessment study of the relationship between affective and adrenocortical stress responses in daily life. *Biol Psychol* 2007;74:60–6. [PubMed: 16942831]
11. Schaeffer MA, Baum A. Adrenal cortical response to stress at Three Mile Island. *Psychosom Med* 1984;46:227–37. [PubMed: 6739683]
12. Weiner, H. *Perturbing the Organism: The Biology of Stressful Experience*. Chicago: University of Chicago Press; 1992.
13. Wrosch C, Bauer I, Miller G, Lupien S. Regret intensity, diurnal cortisol secretion, and physical health in older individuals: evidence for directional effects and protective factors. *Psychol Aging* 2007;22:319–30. [PubMed: 17563187]
14. Lupien SJ, de Leon M, De Santi S, Convit A, Tarshish C, Nair NP, Thakur M, McEwen BS, Hauger RL, Meaney MJ. Cortisol levels during human aging predict hippocampal atrophy and memory deficits. *Nature Neurosci* 1998;1:69–73. [PubMed: 10195112]
15. Miller GE, Chen E, Zhou ES. If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychol Bull* 2007;133:25–45. [PubMed: 17201569]
16. Sapolsky R, Romero L, Munck A. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions 1. *Endocr Rev* 2000;21:55–89. [PubMed: 10696570]
17. Angeli A, Dovio A, Sartori M, Masera R, Ceoloni B, Prolo P, Racca S, Chiappelli F. Interactions between glucocorticoids and cytokines in the bone microenvironment. *Ann N Y Acad Sci* 2002;966:97–107. [PubMed: 12114264]
18. Bjorntorp P, Rosmond R. Hypothalamic origin of the metabolic syndrome X. *Ann N Y Acad Sci* 1999;892:297–307. [PubMed: 10842670]
19. Cohen, S.; Kessler, RC.; Gordon, LU.; Cohen, S.; Kessler, RC.; Gordon, LU. *Measuring Stress: A Guide for Health and Social Scientists*. New York: Oxford University Press; 1995. Strategies for measuring stress in studies of psychiatric and physical disorders.
20. Sephton SE, Sapolsky RM, Kraemer HC, Spiegel D. Diurnal cortisol rhythm as a predictor of breast cancer survival. *J Natl Cancer Inst* 2000;92:994–1000. [PubMed: 10861311]

21. Smith GD, Ben-Shlomo Y, Beswick A, Yarnell J, Lightman S, Elwood P. Cortisol, testosterone, and coronary heart disease: prospective evidence from the Caerphilly study. *Circulation* 2005;112:332–40. [PubMed: 16009799]
22. Matthews K, Schwartz J, Cohen S, Seeman T. Diurnal cortisol decline is related to coronary calcification: CARDIA study. *Psychosom Med* 2006;68:657–61. [PubMed: 17012518]
23. Parker K, Schatzberg A, Lyons D. Neuroendocrine aspects of hypercortisolism in major depression. *Horm Behav* 2003;43:60–6. [PubMed: 12614635]
24. Cohen S, Frank E, Doyle WJ, Skoner DP, Rabin BS, Gwaltney JM Jr. Types of stressors that increase susceptibility to the common cold in healthy adults. *Health Psychol* 1998;17:214–23. [PubMed: 9619470]
25. Miller GE, Cohen S, Pressman S, Barkin A, Rabin BS, Treanor JJ. Psychological stress and antibody response to influenza vaccination: when is the critical period for stress, and how does it get inside the body? *Psychosom Med* 2004;66:215–23. [PubMed: 15039506]
26. Segerstrom SC, Miller GE. Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychol Bull* 2004;130:601–30. [PubMed: 15250815]
27. Heckhausen J, Schulz R. A life-span theory of control. *Psychol Rev* 1995;102:284–304. [PubMed: 7740091]
28. Schulz R, Heckhausen J. A life span model of successful aging. *Am Psychol* 1996;51:702–14. [PubMed: 8694390]
29. Heckhausen J, Wrosch C, Schulz R. A motivational theory of lifespan development. *Psychological Review*. 2008in press
30. Wrosch C, Schulz R, Heckhausen J. Health stresses and depressive symptomatology in the elderly: a control-process approach. *Curr Dir Psychol Sci* 2004;13:17–20.
31. Wrosch C, Heckhausen J, Lachman ME. Primary and secondary control strategies for managing health and financial stress across adulthood. *Psychol Aging* 2000;15:387–99. [PubMed: 11014704]
32. Wrosch C, Heckhausen J. Perceived control of life regrets: good for young and bad for old adults. *Psychol Aging* 2002;17:340–50. [PubMed: 12061416]
33. Wrosch C, Dunne E, Scheier MF, Schulz R. Self-regulation of common age-related challenges: benefits for older adults' psychological and physical health. *J Behav Med* 2006;29:299–306. [PubMed: 16724284]
34. Wrosch C, Scheier MF, Carver CS, Schulz R. The importance of goal disengagement in adaptive self-regulation: when giving up is beneficial. *Self and Identity* 2003;2:1–20.
35. Wrosch C, Schulz R, Heckhausen J. Health stresses and depressive symptomatology in the elderly: the importance of health engagement control strategies. *Health Psychol* 2002;21:340–8. [PubMed: 12090676]
36. Wrosch C, Schulz R, Miller GE, Lupien S, Dunne E. Physical health problems, depressive mood, and cortisol secretion in old age: buffer effects of health engagement control strategies. *Health Psychol* 2007;26:341–9. [PubMed: 17500621]
37. Wrosch C, Schulz R. Health-engagement control strategies and 2-year changes in older adults' physical health. *Psychol Sci* 2008;19:537–41. [PubMed: 18578842]
38. Wrosch C, Heckhausen J. Control processes before and after passing a developmental deadline activation and deactivation of intimate relationship goals. *J Pers Soc Psychol* 1999;77:415–27.
39. Bauer I, Wrosch C, Jobin J. I'm better off than most other people: the role of social comparisons for coping with regret in young adulthood and old age. *Psychol Aging* 2008;23:800–11. [PubMed: 19140651]
40. Bailis DS, Chipperfield JG, Perry RP. Optimistic social comparisons of older adults low in primary control: a prospective analysis of hospitalization and mortality. *Health Psychol* 2005;24:393–401. [PubMed: 16045375]
41. Vedhara K, Tuinstra J, Miles J, Sanderman R, Ranchor A. Psychosocial factors associated with indices of cortisol production in women with breast cancer and controls. *Psychoneuroendocrinology* 2006;31:299–311. [PubMed: 16183206]
42. O'Donnell K, Badrick E, Kumari M, Steptoe A. Psychological coping styles and cortisol over the day in healthy older adults. *Psychoneuroendocrinology* 2008;33:601–11. [PubMed: 18329182]Epub 2008 Mar 7

43. Williamson G, Schulz R. Activity restriction mediates the association between pain and depressed affect: a study of younger and older adult cancer patients. *Psychol Aging* 1995;10:369–78. [PubMed: 8527058]
44. Gill T, Kurland B. The burden and patterns of disability in activities of daily living among community-living older persons. *J Gerontol A Biol Sci Med Sci* 2003;58:70–5. [PubMed: 12560415]
45. Herbert R. Functional decline in old age. *Can Med Assoc J* 1997;157:1037–45. [PubMed: 9347774]
46. Manton KG, Gu X, Lamb VL. Change in chronic disability from 1982 to 2004/2005 as measured by long-term changes in function and health in the U.S. elderly population. *Proc Natl Acad Sci U S A* 2006;103:18374–9. [PubMed: 17101963]
47. Kelley-Moore JA, Ferraro KF. A 3-D model of health decline: disease, disability, and depression among black and white older adults. *J Health Soc Behav* 2005;46:376–91. [PubMed: 16433282]
48. Lee S, Lindquist K, Segal M, Covinsky K. Development and validation of a prognostic index for 4-year mortality in older adults. *JAMA* 2006;295:801–8. [PubMed: 16478903]
49. Stuck AE, Walthert JM, Nikolaus T, Büla CJ, Hohmann C, Beck JC. Risk factors for functional status decline in community-living elderly people: a systematic literature review. *Soc Sci Med* 1999;48:445–69. [PubMed: 10075171]
50. Newman AB, Enright PL, Manolio TA, Haponik EF, Wahl PW. Sleep disturbance, psychosocial correlates, and cardiovascular disease in 5201 older adults: the cardiovascular health study. *J Am Geriatr Soc* 1997;45:1–7. [PubMed: 8994480]
51. Hogan DB, Ebly EM, Fung TS. Disease, disability, and age in cognitively intact seniors: results from the Canadian study of health and aging. *J Gerontol A Biol Sci Med Sci* 1999;54:M77–82. [PubMed: 10051859]
52. Dressendörfer R, Kirschbaum C, Rohde W, Stahl F, Strasburger C. Synthesis of a cortisol-biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. *J Steroid Biochem Mol Biol* 1992;43:683–92. [PubMed: 1472460]
53. Spitzer RL, Williams JBW, Kroenke K, Linzer M. Utility of a new procedure for diagnosing mental disorders in primary care: the PRIME-MD 1000 study. *JAMA* 1994;272:1749–56. [PubMed: 7966923]
54. Buysse DJ, Reynolds CF, Monk TH, Berman SR. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989;28:193–213. [PubMed: 2748771]
55. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D. *Am J Prev Med* 1994;10:77–84. [PubMed: 8037935]
56. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol* 1988;54:1063–70. [PubMed: 3397865]
57. Raudenbush, SW. HLM 6: Hierarchical Linear and Nonlinear Modeling. Lincolnwood, IL: Scientific Software International; 2004.
58. Preacher KJ, Curran PJ, Bauer DJ. Computational tools for probing interaction effects in multiple linear regression, multilevel modeling, and latent curve analysis. *J Edu Behav Stat* 2006;31:437–48.
59. Gitlin L, Hauck W, Winter L, Dennis M, Schulz R. Effect of an in-home occupational and physical therapy intervention on reducing mortality in functionally vulnerable older people: preliminary findings. *J Am Geriatr Soc* 2006;54:950–5. [PubMed: 16776791]
60. Nathan, P.; Gorman, J. *A Guide to Treatments That Work*. New York: Oxford University Press; 2007.
61. Bergman H, Ferrucci L, Guralnik J, Hogan DB, Hummel S, Karunanathan S, Wolfson C. Frailty: an emerging research and clinical paradigm issues and controversies. *J Gerontol A Biol Sci Med Sci* 2007;62:731. [PubMed: 17634320]
62. Heckhausen J, Wrosch C, Fleeson W. Developmental regulation before and after a developmental deadline: the sample case of “biological clock” for childbearing. *Psychol Aging* 2001;16:400–13. [PubMed: 11554519]
63. Salthouse TA, Atkinson TM, Berish DE. Executive functioning as a potential mediator of age-related cognitive decline in normal adults. *J Exp Psychol Gen* 2003;132:566–94. [PubMed: 14640849]
64. West RL. An application of prefrontal cortex function theory to cognitive aging. *Psychol Bull* 1996;120:272–92. [PubMed: 8831298]

Figure 1.

Changes in functional disabilities across 4 years of study as a function of baseline levels of health-related control strategies, separately for participants who secreted high (*upper panel*) versus low (*lower panel*) baseline levels of diurnal cortisol. Trajectories were estimated from HLM coefficients for the averaged upper and lower quartiles of the cortisol (upper quartile = 199.61; lower quartile = 59.88) and control strategy (upper quartile = 3.89; lower quartile = 2.15) distributions.

TABLE 1Means, Standard Deviations, and Frequencies of Main Study Variables ($n = 159$)^a

Functional disabilities (T1)	0.42 (1.05)
Functional disabilities (T2)	0.51 (1.07)
Functional disabilities (T3)	0.88 (1.56)
Cortisol (AUC) (T1)	121.08 (55.55)
Control strategies scale (T1)	3.13 (0.66)
Mortality risk index (T1)	5.76 (2.34)
Age (y)	71.85 (5.63)
Male (%)	49.01
Diabetes (%)	13.80
Cancer (%)	3.10
Lung or other respiratory disease (%)	10.70
Heart condition (%)	17.60
BMI <25 (%)	42.10
Current smoker (%)	10.10
Physical symptoms scale (T1)	2.02 (1.98)
Daytime dysfunction scale (T1)	0.41 (0.80)
Medication usage (T1)	5.40 (3.57)
Depressive symptoms scale (T1)	5.80 (4.35)
Negative affectivity scale (T1)	1.91 (0.66)
Sleep efficiency scale (T1)	0.82 (0.13)
Education	2.07 (1.07)
None (%)	3.9
High school (%)	32.9
Trade (%)	28.3
Bachelor's degree (%)	22.4
Master's degree or doctorate (%)	12.5

^aMean (SD) are presented for continuous variables.

AUC = area under the curve; BMI = body mass index.

TABLE 2

Zero-Order Correlations Between Baseline Levels of Main Predictor Variables

	1	2	3	4	5	6	7	8	9
1. Cortisol (AUC)									
2. Control strategies scale	-0.05								
3. Mortality risk index	0.17*	0.12							
4. Physical symptoms scale	-0.11	-0.06							
5. Daytime dysfunction scale	-0.03	0.04	-0.09						
6. Medication usage	-0.02	0.08	-0.05	0.31**					
7. Depressive symptoms scale	-0.06	0.33**	-0.01	0.30**	-0.02				
8. Negative affectivity scale	0.00	-0.23**	-0.11	0.35**	0.13	0.18*			
9. Sleep efficiency scale	0.03	0.34**	-0.21**	0.29**	0.08	0.17*	0.55**		
10. Education	0.04	-0.01	0.14	-0.24**	0.06	0.03	-0.25**	-0.26**	
			0.06	-0.09	0.14	-0.06	-0.32**	-0.13	0.20**

* $p \leq .05$;

** $p \leq .01$.

AUC = area under the curve.

TABLE 3

Results of Growth-Curve Analysis Predicting 4-Year Changes in Functional Disabilities

	Functional Disabilities			
	Intercept		Slope	
	Coefficient (SE)	T Ratio	Coefficient (SE)	T Ratio
Level 1 (β_0, β_1) ^a	0.376 (0.078)	4.79**	0.121 (0.029)	4.21**
Level 2: Main effects				
Cortisol (AUC) ($\gamma_{01}; \gamma_{11}$)	0.000 (0.001)	0.22	-0.000 (0.000)	0.01
Control strategies ($\gamma_{02}; \gamma_{12}$)	-0.194 (0.099)	-1.97*	-0.040 (0.052)	-0.77
Education ($\gamma_{03}; \gamma_{13}$)	-0.102 (0.061)	-1.66	0.033 (0.024)	1.39
Mortality risk index ($\gamma_{04}; \gamma_{14}$)	0.042 (0.027)	1.52	-0.006 (0.010)	-0.61
Physical symptoms ($\gamma_{05}; \gamma_{15}$)	0.097 (0.047)	2.06*	-0.009 (0.017)	-0.56
Daytime dysfunction ($\gamma_{06}; \gamma_{16}$)	-0.048 (0.111)	-0.44	0.024 (0.035)	0.70
Medication usage ($\gamma_{07}; \gamma_{17}$)	0.046 (0.031)	1.49	0.026 (0.010)	2.68**
Depressive symptoms ($\gamma_{08}; \gamma_{18}$)	0.009 (0.025)	0.34	0.009 (0.009)	0.98
Negative affectivity ($\gamma_{09}; \gamma_{19}$)	0.050 (0.173)	0.29	0.023 (0.062)	0.37
Sleep efficiency ($\gamma_{010}; \gamma_{110}$)	0.735 (0.572)	1.28	0.139 (0.180)	0.77
Level 2: Interaction				
Cortisol $\times$ Control strategies ($\gamma_{011}; \gamma_{111}$)	0.001 (0.002)	0.31	-0.002 (0.001)	-2.44*

*
 $p \leq .05$;**
 $p \leq .01$.

^aThe first parameter (e.g., β_0) estimated the intercept, which represents participants' levels of functional health problems at study entry, and the second parameter (e.g., β_1) estimated the slope, which represents the within-person associations between years from the time of study entry and participants' functional health problems.

Level 1 model had 158 *df*; Level 2 results had 148 *df* (main effects) and 147 *df* (interaction).

SE = standard error.