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Physical Activity Moderates Effects of Stressor-Induced Rumination on Cortisol Reactivity

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Objective: Physically active individuals have lower rates of morbidity and mortality, and recent evidence indicates that physical activity may be particularly beneficial to those experiencing chronic stress. The tendency to ruminate increases and prolongs physiological stress responses, including hypothalamic-pituitary-adrenal (HPA) axis responses as indexed by cortisol reactivity to stressful experiences. We examined the association between ruminating in response to a laboratory stressor task and HPA axis reactivity and recovery and examined whether a physically active life-style moderates the associations between rumination and cortisol output trajectories. **Methods:** Forty-six postmenopausal women underwent the Trier Social Stress Test, whereas salivary cortisol was repeatedly measured. Twenty-five minutes after the end of the stressor, participants reported level of rumination in response to the stress. **Results:** Findings indicate that physical activity moderated the initial rate ($B = -0.10$, standard error = 0.04, $p < .05$) and curvature ($B = -0.03$, standard error = 0.01, $p = .06$) of the relationship between rumination and log-transformed cortisol trajectory. Among sedentary participants, those who responded to the stressor with higher levels of rumination had a more rapid initial increase in cortisol level (0.26 versus 0.21, $p < .001$), a later peak in cortisol reactivity (56 versus 39 minutes), and a delayed recovery from stress (curvature: −0.07 versus −0.08, $p < .001$) compared with those with lower levels of rumination. In active participants, cortisol trajectories were equivalent, regardless of the level of rumination. **Conclusions:** In sum, individuals who maintain a physically active life-style may be protected against the effects of rumination on HPA axis reactivity to and recovery from acute stress.
Key words: acute stress, rumination, physical activity, mixed modeling, cortisol reactivity.

HPA = hypothalamic-pituitary-adrenal; **TSST** = Trier Social Stress Task; **RRS** = Ruminative Responses Scale; **BMI** = body mass index; **REML** = restricted maximum likelihood; **HRT** = hormone replacement therapy.

INTRODUCTION

Numerous longitudinal and intervention studies have shown the direct benefits of exercise on health. For example, exercise and increased fitness reduce the risk for health problems, including depression (1–5), cognitive impairment and dementia (6–10), cardiovascular disease (11–13), diabetes (14,15), and mortality (16–18).

A growing body of evidence suggests that remaining physically active is particularly beneficial for those undergoing chronic stress (19–23). Sources of chronic stress, such as caregiving and low socioeconomic status, are associated with increased risk for cardiovascular disease, metabolic syndrome, and other markers of disease (24–27). These relationships are likely mediated at least partially through repeated and prolonged activation of the stress-responsive hypothalamic-pituitary-adrenal (HPA) axis. Exposure to even a brief stressor can stimulate the HPA axis and produce an elevated cortisol level that can persist for approximately 1 hour after exposure (28). Although adaptive in the short term, repeated and chronic stimulation of the HPA axis and release of cortisol can lead to allostatic load (i.e., the physiological effects of repeated or chronic exposure to stress that lead to pathophysiological state) and accelerated biologic aging (29–31).

Perseverative cognitions can prolong affective and physiological stress responses (32–36). A hallmark of perseverative cognition is rumination, the tendency to perseverate on self-relevant negative content and emotion often directed at one's past experiences (37–40). A disposition to ruminate, as measured by trait rumination measures, seems to be higher in women (41), predicts the severity and the number of major depressive episodes (37,42), and is also considered a feature of some psychiatric disorders (37,43). Trait rumination may unfold daily by increasing ruminative responses to daily stressors (44). Such responses may in turn lead to increases in daily negative affect (44–46) and related increases in daily cortisol output (47). There is also evidence that laboratory-induced rumination affects physiological systems, prolonging stress-related stimulation of the HPA axis as evidenced by increased cortisol reactivity to the stressor (48). Therefore, in this study, we examined the relationship between state rumination (i.e., rumination after a stressor) on concurrent cortisol responses.

Previous studies of exercise and fitness effects on stress response have compared fit individuals (i.e., trained athletes and physically fit individuals) and unfit individuals and how they respond physiologically to laboratory-induced acute mental stress. These have shown that fit versus unfit individuals have reduced HPA axis (49–51), inflammatory (52), and cardiovascular reactivity and faster recovery (49,53–56). For example, Rimmele and colleagues (50) demonstrated that elite young adult male athletes had significantly lower cortisol and autonomic responses to the Trier Social Stress Task (TSST) compared with untrained men, and they additionally maintained positive mood and calmness in the face of stress. In another study, Traustadóttir and colleagues (51) examined physiological stress reactivity in response to a laboratory stressor in unfit young women and fit and unfit postmenopausal women. Fit postmenopausal women had similar cortisol responses to a

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laboratory stressor as the unfit younger women. On the other hand, unfit postmenopausal women had significantly greater output compared with their age-matched cohort and younger unfit equivalents. The findings from these studies suggest that being physically active seems to promote a healthier physiological response to stress in postmenopausal women.

In the present study, we examined the association between laboratory-induced rumination and cortisol reactivity and recovery in postmenopausal women. We additionally examined whether the relations between stress-induced rumination and cortisol varied as a function of activity level. We hypothesized that higher levels of rumination would be associated with faster initial cortisol reactivity and slower rate of recovery in response to the laboratory challenge tasks. In addition, we examined whether these associations would be more pronounced in sedentary participants compared with physically active participants.

Growth curve modeling was used to capture reactivity to and recovery from stress (57). Measuring cortisol output repeatedly permits the examination of the trajectory of cortisol in response to stress across time. Growth curve modeling can successfully attend to our outcomes of interest, such as whether rumination is related to participants' baseline cortisol levels, initial rate of cortisol increase (i.e., reactivity) in response to stress induction, and recovery over time. From these models, we can then extrapolate the number of minutes the average person takes to peak in cortisol levels and to return to baseline. Modeling the overall pattern of HPA axis responses to stress, including initial rise, time to peak, and time to recovery from stress to basal state, addresses increasing calls in the literature for a more nuanced understanding of HPA axis response to stress (58,59).

METHODS

Postmenopausal women aged between 54 and 82 years were recruited through flyers and posters in the community and from service providers serving the elderly in the San Francisco Bay Area. Participants were part of a prospective study on caregiving and its effects on physical and psychological well-being that began in May 2005. All data presented are from participants' baseline visit. Women included both healthy women who were providing at least 4 hours of care to a relative with dementia per day and who reported high levels of perceived stress and age-matched noncaregiver controls reporting low levels of daily stress. Exclusion criteria included the presence of major medical conditions such as heart disease, cancer, or diabetes; use of medications containing agents known to affect stress hormone levels; and regular smoking. The study protocol was approved by the institutional review board of the University of California, San Francisco. Written informed consent was obtained from all participants.

Procedures

Women who called or e-mailed indicating interest were screened for eligibility criteria by telephone. They underwent a physical examination, had fasting blood drawn, and provided written informed consent at the University of California, San Francisco, Clinical and Translational Science Institute's Clinical Research Center. They were scheduled to return on a separate afternoon 1 week later to undergo the TSST. During the week, between visits, participants completed three consecutive days of daily diary assessment on mood, daily events, coping, and physical activity. On their return to the laboratory, they ate a standardized lunch provided by the Clinical Research Center metabolic kitchen and had an intravenous forearm catheter inserted around 1 PM. Participants had a 1-hour resting baseline period while listening to relaxing music using headphones after catheter insertion. At the end of this baseline period (Time 0), the first saliva sample was collected. A modified form of the TSST (60) including the performance of a speech and math task was administered. Phases of the stressor included four 5-minute stressful periods (a total of 20 minutes), including introduction to two trained evaluators who described the task; a preparatory period for the speech; a speech (about strengths and weaknesses, instead of a job interview, to fit the age group, which includes many retirees); and lastly, a math task (serial subtraction of consecutive prime numbers). In line with the TSST, evaluators maintained neutral expressions throughout the tasks and followed a script to provide neutral feedback throughout the tasks.

MATERIALS

Sociodemographics

Participants' *age* was calculated from date of birth. *Ethnicity* was assessed with a list from which participants selected one option (i.e., white, black, Hispanic, Asian, Pacific Islander, Native American). Participants selected from the following choices for *education*: "less than 12 years," "high school graduate," "some college or technical degree," "associate in arts degree," "bachelor's degree," and "advanced degree." *Income* was assessed by providing 22 categories of income ranges (lowest category, from $0 to $3000, to highest category, $250,000 and more).

Saliva Sample Collections

Saliva samples were collected via passive drool method, using polypropylene saliva tubes at six time points throughout for the assessment of cortisol. Samples were collected at the following times in minutes: 0 (baseline), 15 (after the speech task), 20 (after the stressor ended), 30 (to capture cortisol peak), 50 (short-term recovery), and 90 minutes (long-term recovery, which is 70 minutes after the stressor ended, when cortisol is typically back to baseline levels) (61). Saliva samples were kept on ice and frozen at the end of each session, and they were sent for batch assay to Dresden, Germany (laboratory of Clemens Kirschbaum). Salivary cortisol was assayed using a chemiluminescence immunoassay. Intra-assay coefficient of variation was 2.9% for high levels and 7.7% for low levels. The inter-assay coefficient of variation was 5.7% for high levels and 9.1% for low levels. The lower limit of sensitivity was 0.16 ng/mL. Cortisol values ranged from 0.58 to 33.75 ng/mL, well within the range of detection of the assays. Slight skewness (skewness statistic = 2.15) existed in the data; therefore, all values were log transformed for correction. Log-transformed values were normally distributed, and no outliers existed in the data.

Psychological Measures

Stress-Induced Rumination

Rumination items were adapted from the Ruminative Responses Scale (RRS) (37,61). Twenty-five minutes after completion of the TSST, when we sampled their 50-minute cortisol, participants completed the following rumination items based on the RRS and in response to completing the tasks: "I thought 'Why do I always react this way?'" "I thought about the tasks, wishing they would have gone better," and "I thought 'Why can't I handle things better?'" Participants responded on a four-point Likert scale from 1 (never) to 4 (always). Average scores were calculated for the three questions for each participant. Because of concerns about item overlap between rumination and depression (62), we used items from the brooding

subscale of the RRS without the items that included references to depressive symptoms. Examples of excluded statements are "I thought about how hard it is to concentrate" and "I thought about all my shortcomings, failings, faults, mistakes." The TSST-induced rumination subscale had good internal consistency (Cronbach $\alpha = 0.75$).

Physical Activity

Participants reported at the end of each day, on three consecutive days, the number of minutes they engaged in vigorous exercise. They were asked, "Did you exercise today?" and they were given the definition of vigorous activity that produced "increased heart rate and/or sweating." If participants reported exercising then they were asked, "How long did you exercise today?" For those participants who did not exercise on a particular day, minutes of exercise for that day were recoded to 0. All participants who participated in the daily component of the study answered these questions on all 3 days. Higher levels of self-reported physical activity are associated with greater fitness (62). Retrospective reporting is plagued by recall bias (63); therefore, daily reporting of behaviors is considered a stronger measure of behavior (64,65). Daily reports of physical activity were extremely skewed (range, 0–300 minutes; 24 participants reported no exercise throughout the 3-day period); therefore, we split participants based on reported required amounts of physical activity for good health per week. The Centers for Disease Control and Prevention (66), based on previous work (67), recommends an average of 75 minutes of vigorous activity per week (an average of 33 minutes for a 3-day period, which is the number of days participants recorded their activities). We have previously split participants based on meeting these recommended guidelines (<33 minutes for a 3-day period = 0, ≥33 minutes = 1), labeled here, for brevity, as "sedentary" versus "active" (22).

Covariates

Body mass index (BMI [kg/m^2]) was included based on associations between BMI and cortisol in previous work (68). Depressive symptoms were measured with the Inventory of Depressive Symptoms and were included as a covariate given its strong associations with rumination (69), physical activity (70), and cortisol reactivity to stress (71).

STATISTICAL APPROACH

Descriptive statistics and Figure 1 for cortisol trajectories are presented with raw values. Log-transformed values of cortisol were included in all analyses. Successive measurement of cortisol during and after a stressor permits the examination of cortisol trajectory over time with multilevel growth curve modeling (57). Multilevel growth curve modeling requires the use of mixed-modeling statistical designs. Given our small sample size and skewed data, we fitted a restricted maximum likelihood (REML) to our mixed models. We also fitted an unstructured covariance structure. Two strengths of mixed modeling with REML are that it can accommodate missing and skewed data and that it computes unbiased estimators (57,72).

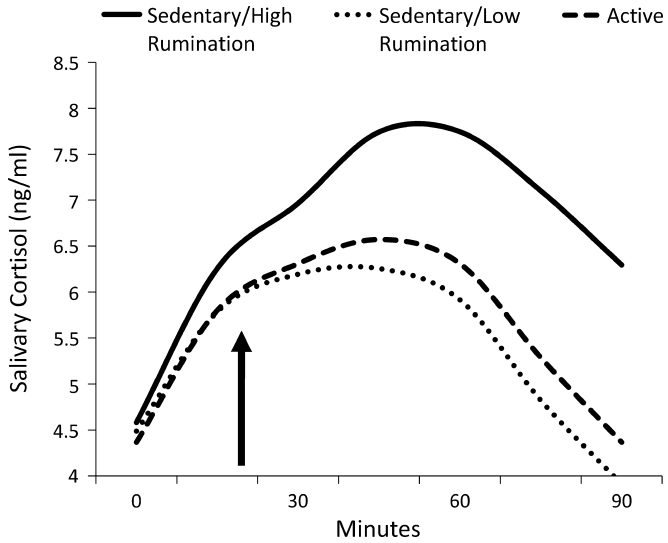

Figure 1. Cortisol trajectory over the course of the Trier Social Stress Task (90 minutes) as a function rumination and activity level. Values on the *y* axis are solved *y* values for salivary cortisol (in nanograms per milliliter) from the quadratic equations for sedentary participants at low and high rumination and for all active participants. The *x* axis corresponds to the time elapsed 90 minutes from the beginning to the end of the Trier Social Stress Task. The vertical black arrow corresponds to the approximate time the stressor ended. All active participants had similar trajectories, regardless of the level of rumination, and are thus graphed as one group.

Analyses were conducted with SPSS 18.0 (IBM, Armonk, NY), using the MIXED syntax as recommended by Singer and Willett (57). All analyses were replicated with BMI, age, depressive symptoms, and control versus caregiver group as covariates; and the findings were consistent with reported results. In addition, the results did not vary as a function of hormone replacement therapy (HRT) (either when the three on HRT were excluded or when HRT was included as a covariate).

We first examined the unconditional means model (i.e., with no predictors) to determine the amount of variation occurring at the within-person level. Next, we examined the unconditional multilevel growth curve model to determine the cortisol reactivity and recovery trajectory across the whole sample. Multilevel growth curve modeling of cortisol over time (set at 30-minute intervals) permits the delineation of a series of parameters that increase our understanding of reactivity to and recovery from laboratory stressors. Growth curve modeling estimates the intercept (B_0), initial rate of change (i.e., time at each sampling of cortisol [B_{rise}]), and curvature of the cortisol trajectory (i.e., time squared [$B_{\text{curvature}}$]). Stressor reactivity is captured by the intercept, initial rate of change, and the number of minutes to peak, all of which is estimated by the growth curve model. The number of minutes for cortisol to peak is calculated with the equation: peak = ($-B_{\text{rise}}$ / [$2 \times B_{\text{curvature}}$]) (57). Recovery was captured by the curvature in the trajectory and the minutes estimated to return to baseline.

Next, we conducted two analyses: the first examined the interaction between rumination and time and the second examined the interaction between physical activity and time. We used the approach of Cohen et al. (73) to regression analyses to analyze a three-way interaction between two continuous

variables (time and rumination) and a dichotomous variable (activity level). In line with the recommendations of Cohen and colleagues (73), significant three-way interactions would suggest that cortisol trajectory varies differentially as a function of rumination at the two different activity levels. To follow up on a significant three-way interaction, we examined simple interactions between rumination and time at activity = 0 and activity = 1. Significant simple interactions suggest that cortisol trajectories are significantly different at varying levels of rumination. As a result, simple slopes are examined at 1 standard deviation (SD) above and below the mean rumination score to determine the intercept, rise, and curvature at these two levels of rumination. If the simple interactions are not significant at a particular activity level, simple slopes are not examined because this suggests that rumination does not predict trajectory at that activity level.

RESULTS

Univariate and Bivariate Results

Forty-six postmenopausal women completed cortisol measurement during the TSST. Table 1 presents means (SDs) of age, BMI, rumination, depression, and raw cortisol values (in nanograms per milliliter) at each time point during the TSST for the entire sample of participants and for active versus sedentary participants. The range of time spent exercising ranged from 0 to 300 minutes during the 3 days of reporting, with a mean of 43 (SD = 66.23) minutes. When categorized by activity level, 18 participants were in the active group and 28 were in the sedentary group. Of those categorized as sedentary, the majority (n = 24, 86%) reported no activity for 3 days, and the remaining four participants reported less than 20 minutes total time spent exercising for 3 days. Although there were no significant differences between caregivers and controls in activity levels (p = .23), most controls (61%) were active and most caregivers (61%) were sedentary. Furthermore, caregivers and controls did not significantly differ in rumination (p = .72). Bivariate analyses indicated that only depression scores were different between the groups, such that those who were more active had fewer depressive symptoms than those who were sedentary (p = .05). All cortisol measures (log transformed) were moderately to strongly significantly correlated with one another (correlations range, 0.42–0.85) with the exception of baseline cortisol to 50 and 90 minutes after baseline (p = .09).

TABLE 1. Means (Standard Deviations) for the Overall Sample and the Active and Sedentary Subgroups of Participants

	Total (n = 46)	Sedentary (n = 28)	Active (n = 18)
Group (control), n (%)	24 (51)	11 (39)	11 (60)
BMI, kg/m^2	26.40 (5.82)	27.16 (6.16)	25.22 (5.18)
Age, y	65.33 (5.81)	65.04 (5.98)	65.78 (5.67)
Depressive symptoms	14.31 (10.73)	16.62 (11.99)	10.83 (7.54)
Rumination	1.81 (0.70)	1.89 (0.81)	1.72 (0.50)
Cortisol level, ng/mL			
0 min	5.04 (2.49)	5.08 (2.84)	4.98 (1.92)
15 min	5.88 (3.23)	6.32 (3.70)	5.14 (2.15)
20 min	8.04 (5.90)	8.88 (7.12)	6.72 (2.86)
30 min	7.90 (4.34)	7.61 (4.78)	8.32 (3.74)
50 min	7.36 (4.50)	7.49 (4.71)	7.16 (4.29)
90 min	5.06 (2.36)	5.33 (2.66)	4.62 (1.78)

BMI = body mass index.

Unconditional Means Model

We partitioned the between-person and within-person variations in cortisol output in response to the TSST among our participants. The estimates of the residual and intercept covariance parameters were 10.07 (standard error [SE] = 0.96) and 7.61 (SE = 2.01), respectively. The intraclass correlation was 0.43—in other words, 57% of the variation in cortisol response occurred at the within-person level.

Growth Models

We examined model fit for time in log-transformed cortisol, and results indicated that, across all participants, log-transformed cortisol output followed a curvilinear relationship where the intercept was 0.65 (SE = 0.04, $p < .01$) and the initial rate (time) of increase was 0.23 (SE = 0.04, $p < .01$) with a curvature (time squared) of −0.08 (SE = 0.01, $p < .01$). The moment when the quadratic trajectory curve reached its peak and turned downward was at 44 minutes after the onset of stressor for the entire sample.

Next, we examined cortisol trajectory as a function of rumination alone, activity level alone, and the interaction between activity and rumination. In analyses with rumination alone, rumination did not significantly predict the trajectory of cortisol in response to stress (interaction B_{slope} = 0.04, SE = 0.05, p = .48; interaction $B_{curvature}$ = −0.01, SE = 0.01, p = .68). Similarly, in analyses with activity level alone, activity did not significantly predict the trajectory of cortisol in response to stress (interaction B_{slope} = −0.01, SE = 0.11, p = .95; interaction $B_{curvature}$ = −0.00, SE = 0.03, p = .98). However, as hypothesized, the interaction term between rumination and exercise was significant in relation to the initial rate of cortisol increase (interaction B_{slope} = −0.10, SE = 0.04, p = .01) and was marginally significant in relation to curvature (interaction $B_{curvature}$ = −0.03, SE = 0.01, p = .06). The nature of the three-way interaction (i.e., rumination, exercise, time) was further examined for sedentary versus active participants. Results indicated that the association between rumination and cortisol trajectory (slope and curvature), but not baseline levels, significantly varied as a function of activity.

Rumination and Cortisol Trajectory in Sedentary Participants

For sedentary participants, initial increase and curvature in cortisol trajectory varied significantly as a function of levels of rumination (B_{slope} = 0.23, SE = 0.04, $p < .001$ and $B_{curvature}$ = −0.08, SE = 0.01, $p < .001$, respectively). For sedentary

participants at 1 SD below the mean of rumination, baseline levels of log-transformed cortisol were 0.70 (SE = 0.06, $p < .001$), and cortisol level initially increased at a rate of 0.21 (SE = 0.04, $p < .01$) and had a significant curvature of −0.08 (SE = 0.01, $p < .001$), corresponding to a peak in cortisol reactivity at 39 minutes. At 1 SD above the mean of rumination, baseline levels of log-transformed cortisol were 0.63 (SE = 0.05, $p < .001$), and cortisol initially increased at a rate of 0.26 (SE = 0.04, $p < .001$) and had a significant curvature of −0.07 (SE = 0.01, $p < .001$), corresponding to a peak in cortisol reactivity at 56 minutes, 17 minutes after the peak of sedentary low ruminators. In relation, although sedentary low ruminators were, on average, likely to have returned to their baseline levels by the end of the study (extrapolated time from the graph was 49 minutes after the end of the stressor), the high ruminators who were sedentary had, on average, not yet returned to their own baseline. Recovery to baseline did not occur during our measurement period in sedentary high ruminators, and extrapolation showed average recovery to baseline at approximately 115 minutes—nearly 90 minutes after the end of the TSST and 36 minutes after the sedentary low ruminators. In summary, compared with sedentary low ruminators, sedentary high ruminators had a more pronounced initial rate of cortisol increase, a later cortisol peak, and a slower return to baseline cortisol levels.

Rumination and Cortisol Trajectory in Active Participants

For all active participants, there was a significant cortisol intercept ($B = 0.64$, SE = 0.05, $p < .001$), significant rise ($B_{slope} = 0.24$, SE = 0.06, $p < .001$), and significant curvature ($B_{curvature} = -0.08$, SE = 0.02, $p < .001$) to the stressor corresponding to a peak of 41 minutes and return to baseline 60 minutes after the stressor. However, rumination was unrelated to cortisol intercept ($p = .53$), initial rate of change ($p = .10$), or curvature ($p = .18$). In other words, all active participants had similar trajectories, regardless of the level of rumination.

Figure 1 summarizes these interaction effects. As illustrated, sedentary high ruminators had a more marked stress response and slower recovery than both sedentary low ruminators and all active participants. Furthermore, it seems that sedentary, low-ruminating participants had, on average, similar trajectories to those who were active.[1]

DISCUSSION

The present study examined whether being physically active moderates the effects of rumination on the trajectory of cortisol responses to acute stress. We hypothesized that one pathway through which physical activity could lower the stress response is by mitigating the effects of stress-related cognitions on the body's stress arousal systems. Our findings support this notion by demonstrating that the cortisol trajectory was a function of stress-induced rumination only in those who were sedentary and unrelated to rumination in those who were active. Specifically, sedentary participants who had higher self-reported levels of rumination in response to the stressor had faster and prolonged reactivity to and delayed recovery from stress, evidenced by a more rapid initial increase, a later peak, and a delayed return to baseline cortisol level compared with the sedentary lower ruminating participants. For active participants, cortisol trajectory was not a function of rumination, regardless of the level of stressor-induced rumination.

It is interesting to note that we may be detecting a trait-like effect rather than just the immediate effect of state rumination on cortisol. Rumination was determined after the acute stressor had terminated. Cortisol levels of sedentary ruminators were high not only during the recovery phase when we measured their levels of rumination but also during the initial onset of the stressor. Therefore, our measure of state rumination may be differentiating people who are different in their initial acute stress reactivity, possibly because of differential appraisal of the stressor. Furthermore, activity alone may not shape cortisol responses. Rather, activity may be especially beneficial to those responding to stress with rumination, given the findings that activity moderates the relationship between rumination and cortisol reactivity and recovery but does not directly predict cortisol reactivity to and recovery from stress.

We have recently demonstrated that being physically active, as defined here, moderates the relationship between chronic stress and short leukocyte telomere length, a marker increasingly understood to capture the accumulated burden of genetics, life stressors, and health behaviors (22). Understanding the psychological and physiological mechanisms through which physical activity confers such effects to those most vulnerable to stress is critical for the development of interventions to enhance health and for identifying those individuals for whom new interventions would be beneficial. The present findings address these issues and suggest that the one pathway that may explain the physiological benefits of physical activity is reduced activation and enhanced recovery of stress arousal systems tied to psychological responses to stress. Overall, these findings lend support to the idea that being physically active may confer stress resistance, at least in postmenopausal women. Importantly, these findings seem to extend to elderly women.

Chronic stress is documented to produce different profiles of HPA axis dysregulation, including either hyperactive or blunted cortisol responses to stressors (29,72). In this study, we examined HPA axis reactions to acute stress in the context of rumination, a potential psychological mechanism of chronic stress. A recent meta-analysis by Denson and colleagues (36) provides evidence that rumination may induce increased cortisol levels to maintain vigilance toward unresolved stressors. Repeatedly ruminating in response to stress in the real world

[1]We examined interactive effects of rumination and activity on the trajectories of HR, diastolic blood pressure (BP), and systolic BP. Our data suggest no direct or interaction effects on BP and diastolic or systolic BP trajectory. However, for diastolic BP, physical activity and rumination significantly interacted to predict diastolic BP across all sampling times (matched to times of cortisol sampling). For sedentary participants, higher rumination was significantly related to increased diastolic BP across the entire recording during and after the TSST. However, in active participants, rumination was unrelated to diastolic BP.

may repeatedly stimulate the HPA axis resulting in chronically elevated cortisol level. Chronic exposure to elevated cortisol level is in turn linked with insulin resistance, accumulation of abdominal fat, and increased risk for cardiovascular disease (29,31). Healthy levels of physical activity may differentially affect high ruminating individuals by creating a physiological eustress state (74) and attenuating biologic stress responses including cortisol responses (49–51). A caveat of our study is that the heightened cortisol reactivity and delayed recovery observed in high ruminators was defined as such based on comparisons with low ruminators. At present, to our knowledge, there are no standard trajectories that are understood to represent excessively high cortisol reactivity or delayed cortisol recovery.

Our study adds to the current literature on the benefits of physical activity in that it tests whether being physically active moderates the physiological effects of commonly experienced stress-related cognitions. There are a number of neurobiological and physiological mechanisms by which exercise may confer benefits, including increases in the expression of genes that encode brain-derived neurotrophic factor leading to an increased cognitive functioning and neural plasticity (75–77), a heightened anti-inflammatory environment in the body (78–80), an enhanced insulin sensitivity (81–83), and an enhanced oxidative buffering capacity (74,84). Physical activity reduces depressive symptoms among those genetically predisposed to lower levels of brain-derived neurotrophic factor (20) and reduces symptom reporting and physician visits in those with increased numbers of stressful life events (19,21). We demonstrate that physical activity may attenuate the acute physiological response to stress, as indexed by HPA axis reactivity, in those particularly vulnerable to stress—ruminators.

Limitations of the study included our short-term and self-reported measure of physical activity. Physical activity was reported on a daily basis across 3 days, and participants reported the number of minutes they engaged in activities in which their heart rate was increased and/or they perspired. We assume that these 3 days of reporting represent typical exercise behaviors and thus a long-term life-style factor. However, we do not know whether the short-term activity specifically occurring in the days before the TSST was important in the results here or whether this was a proxy measure for general fitness. Although our measure represents an important advance over the usual retrospective report of physical activity, future studies should measure participants' baseline fitness levels and objectively capture daily physical activity with the use of accelerometers or assessments of current physical fitness. Our measurement across 3 days may be an overrepresentation or underrepresentation of actual engagement in physical activity per week; therefore, extending measurement longer than 3 days to a week or 2 weeks would benefit future studies that aim to use daily measurement of vigorous activity as a measure of high activity level. These limitations of our measure of physical activity may explain why we did not detect a main effect of physical activity on cortisol trajectory, in contrast with other studies on fitness and cortisol output (51–53). Self-report of physical activity is not as strong a predictor of health as measurements of actual fitness levels (80). Finally, only a randomized controlled aerobic exercise intervention study can truly test the buffering effects of physical activity on HPA axis activation because of stress induction. Our results are thus limited to between-group differences that can also be a function of personality and other between-group differences.

Findings of the present study are also limited to postmenopausal women and should be replicated in larger samples, including men and individuals with diverse ages and ethnic backgrounds. Of particular importance, our sample size is limited to 18 participants in the active group and 28 in the sedentary group. Although mixed modeling with REML estimation is considered unbiased and robust, it may be possible that our findings are limited to our specific sample. We thus consider these findings preliminary and suggest that follow-up studies with larger sample sizes and more diverse groups and ages may be worthwhile. Given the sample size, we were unable to stratify our results by caregiver group, age, and BMI. Exposure to ongoing chronic stress may change psychological responses including ruminative responses to acute stressors. However, in our sample, caregivers and controls showed similar levels of rumination in response to the acute laboratory stress, and our findings were significant over and above the effects of caregiver status. Exposure to chronic stress may also influence physical activity levels. Although not statistically significant, the caregivers in our study were disproportionately sedentary compared with controls. Although significant differences between caregivers and controls in our study were not apparent, possibly due to sample size limitations, the current findings may be particularly relevant to caregivers, given their lower rates of physical activity. Caregivers who ruminate about everyday stressors may benefit from physical exercise interventions.

Furthermore, there may be sex differences, which we could not test in this all-female sample. It may be that rumination not only is more common in women but also has different physiological effects in women. Thus, including men in future studies is important to further our understanding of the moderating potential of being active on physiological consequences of rumination. Comparing these trajectories to younger, fit and unfit women who are high and low on rumination level will also deepen our understanding of the interplay of age with psychological and physiological responses to stress.

In summary, the findings reported in the present study are the first, to our knowledge, that demonstrate the moderating effects of being physically active on the physiological responses associated with rumination after acute laboratory stressors. We applied a statistical model, namely, growth curve modeling, which better captures the nature of physiological responses by modeling initial increases, the number of minutes to peak responses, and speed of recovery. The effects found in the present study were apparent, even after covarying for age, BMI, caregiving group, and depressive symptoms. Heightened increases in cortisol responses and delayed recoveries to repeated stressors across the day would possibly lead to sustained exposure to elevated cortisol levels, ultimately affecting physical health

outcomes (32). Our study demonstrates the potential for physical activity to allow rapid recovery of the HPA axis after the induction of stress, especially in those who are ruminating, thus reducing the heightened cortisol response earlier and potentially protecting individuals from continued, prolonged exposure. It has been increasingly clear that it is important to understand factors that enhance physiological recovery from stressors in the service of promoting health. Exercise seems to be one promising way to promote physiological stress resistance, particularly in stressed ruminators who are prone to affective and physiological disorders.

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REFERENCES

1. Babyak M, Blumenthal JA, Herman S, Khatri P, Doraiswamy M, Moore K, Craighead WE, Baldewicz TT, Krishnan KR. Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months. Psychosom Med 2000;62:633.
2. Blumenthal JA, Babyak MA, Doraiswamy PM, Watkins L, Hoffman BM, Barbour KA, Herman S, Craighead WE, Brosse AL, Waugh R, Hinderliter A, Sherwood A. Exercise and pharmacotherapy in the treatment of major depressive disorder. Psychosom Med 2007;69:587.
3. Blumenthal J, Babyak M, Moore K, Craighead W, Herman S, Khatri P, Waugh R, Napolitano M, Forman L, Appelbaum M, Doraiswamy P, Krishnan K. Effects of exercise training on older patients with major depression. Arch Intern Med 1999;159:2349–56.
4. Dunn AL, Trivedi MH, Kampert JB, Clark CG, Chambliss HO. Exercise treatment for depression: efficacy and dose response. Am J Prev Med 2005;28:1–8.
5. Hamer M, Molloy GJ, de Oliveira C, Demakakos P. Leisure time physical activity, risk of depressive symptoms, and inflammatory mediators: the English Longitudinal Study of Ageing. Psychoneuroendocrinology 2009; 34:1050–5.
6. Etgen T, Sander D, Huntgeburth U, Poppert H, Forstl H, Bickel H. Physical activity and incident cognitive impairment in elderly persons: the INVADE study. Arch Intern Med 2010;170:186.
7. Larson EB, Wang L, Bowen JD, McCormick WC, Teri L, Crane P, Kukull W. Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. Ann Intern Med 2006;144:73.
8. Rolland Y, Pillard F, Klapouszczak A, Reynish E, Thomas D, Andrieu S, Rivière D, Vellas B. Exercise program for nursing home residents with Alzheimer's disease: a 1-year randomized, controlled trial. J Am Geriatr Soc 2007;55:158–65.
9. Rovio S, Kåreholt I, Helkala EL, Viitanen M, Winblad B, Tuomilehto J, Soininen H, Nissinen A, Kivipelto M. Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. Lancet Neurol 2005;4:705–11.
10. Teri L, Gibbons LE, McCurry SM, Logsdon RG, Buchner DM, Barlow WE, Kukull WA, LaCroix AZ, McCormick W, Larson EB. Exercise plus behavioral management in patients with Alzheimer disease: a randomized controlled trial. JAMA 2003;290:2015–22.
11. Smith GD, Shipley M, Batty G, Morris J, Marmot M. Physical activity and cause-specific mortality in the Whitehall study. Public Health 2000;114: 308–15.
12. Thompson PD, Buchner D, Piña IL, Balady GJ, Williams MA, Marcus BH, Bera K, Blair SN, Costa F, Franklin B, Fletcher GF, Gordon NF, Pate RR, Rodriguez BL, Yancey AK, Wenger NK. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). Circulation 2003;107:3109–3116.
13. Twisk JWR, Kemper HC, van Mechelen W. Tracking of activity and fitness and the relationship with cardiovascular disease risk factors. Med Sci Sports Exerc 2000;32:1455–61.
14. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Aunola S, Cepaitis Z, Moltchanov V, Hakumaki M, Mannelin M, Martikkala V, Sundvall J, Uusitupa M; the Finnish Diabetes Prevention Study Group. Prevention of Type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001; 344:1343–50.
15. Manson JE, Nathan DM, Krolewski AS, Stampfer MJ, Willett WC, Hennekens CH. A prospective study of exercise and incidence of diabetes among US male physicians. JAMA 1992;268:63–7.
16. Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality. JAMA 1995;273: 1093–8.
17. Blair SN, Kampert JB, Kohl HW, Barlow CE, Macera CA, Paffenbarger RS, Gibbons LW. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. JAMA 1996;276:205–10.
18. Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. N Engl J Med 1999;341:1351–7.
19. Kobasa SC, Maddi SR, Puccetti MC. Personality and exercise as buffers in the stress-illness relationship. J Behav Med 1982;5:391–404.
20. Mata J, Thompson RJ, Gotlib IH. *BDNF* genotype moderates the relation between physical activity and depressive symptoms. Health Psychol 2010; 29:130.
21. Ouellette Kobasa SC, Maddi SR, Puccetti MC, Zola MA. Effectiveness of hardiness, exercise and social support as resources against illness. J Psychosom Res 1985;29:525–33.
22. Puterman E, Lin J, Blackburn E, O'Donovan A, Adler N, Epel E. The power of exercise: buffering the effect of chronic stress on telomere length. PLoS One 2010;5:e10837.
23. Roth D, Holmes D. Influence of physical fitness in determining the impact of stressful life events on physical and psychologic health. Psychosom Med 1985;47:164–73.
24. Janicki-Deverts D, Cohen S, Matthews KA, Cullen MR. History of unemployment predicts future elevations in C-reactive protein among male participants in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Ann Behav Med 2008;36:176–85.
25. Kiecolt-Glaser JK, Glaser R, Shuttleworth EC, Dyer CS, Ogrocki P, Speicher CE. Chronic stress and immunity in family caregivers of Alzheimer's disease victims. Psychosom Med 1987;49:523.
26. Mooy JM, De Vries H, Grootenhuis PA, Bouter LM, Heine RJ. Major stressful life events in relation to prevalence of undetected Type 2 diabetes. Diabetes Care 2000;23:197–201.
27. Steptoe A, Brydon L, Kunz-Ebrecht S. Changes in financial strain over three years, ambulatory blood pressure, and cortisol responses to awakening. Psychosom Med 2005;67:281–7.
28. Kirschbaum C, Hellhammer DH. Salivary cortisol in psychoneuroendocrine research: recent developments and applications. Psychoneuroendocrinology 1994;19:313–33.
29. McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med 1998;338:171.
30. McEwen BS. Protection and damage from acute and chronic stress. Ann N Y Acad Sci 2004;1032:1–7.
31. McEwen BS. Stress, adaptation, and disease: allostasis and allostatic load. Ann N Y Acad Sci 1998;840:33–44.
32. Brosschot JF, Pieper S, Thayer JF. Expanding stress theory: prolonged activation and perseverative cognition. Psychoneuroendocrinology 2005; 30:1043–9.
33. Brosschot JF, Gerin W, Thayer JF. The perseverative cognition hypothesis: a review of worry, prolonged stress-related physiological activation, and health. J Psychosom Res 2006;60:113–24.
34. Kubzansky LD, Davidson KW, Rozanski A. The clinical impact of negative psychological states: expanding the spectrum of risk for coronary artery disease. Psychosom Med 2005;67(Suppl 1):S10–4.
35. Thayer JF, Lane RD. Perseverative thinking and health: neurovisceral concomitants. Psychol Health 2002;17:685.
36. Denson TF, Spanovic M, Miller N. Cognitive appraisals and emotions predict cortisol and immune responses: a meta-analysis of acute laboratory social stressors and emotion inductions. Psychol Bull 2009;135:823–53.
37. Nolen-Hoeksema S, Morrow J. A prospective study of depression and posttraumatic stress symptoms after a natural disaster: the 1989 Loma Prieta earthquake. J Pers Soc Psychol 1991;61:115–21.

38. Nolen-Hoeksema S, Wisco BE, Lyubomirsky S. Rethinking rumination. Perspect Psychol Sci 2008;3:400–24.
39. Trapnell PD, Campbell JD. Private self-consciousness and the five-factor model of personality: distinguishing rumination from reflection. J Pers Soc Psychol 1999;76:284–304.
40. Wyer RS, Martin LL, Tesser A. Ruminative Thoughts: Advances in Social Cognition. Vol. 9. Mahwah, NJ: Lawrence Erlbaum Associates; 1996.
41. Nolen-Hoeksema S. Sex differences in unipolar depression: evidence and theory. Psychol Bull 1987;101:259–82.
42. Nolen-Hoeksema S, Morrow J, Fredrickson BL. Response styles and the duration of episodes of depressed mood. J Abnorm Psychol 1993;102: 20–8.
43. Muris P, Roelofs J, Rassin E, Franken I, Mayer B. Mediating effects of rumination and worry on the links between neuroticism, anxiety and depression. Pers Individ Differ 2005;39:1105–11.
44. Puterman E, DeLongis A, Pomaki G. Protecting us from ourselves: social support as a buffer of trait and state rumination. J Soc Clin Psychol 2010; 29:797–820.
45. Wood JV, Saltzberg JA, Neale JM, Stone AA, Rachmiel TB. Self-focused attention, coping responses, and distressed mood in everyday life. J Pers Soc Psychol 1990;58:1027–36.
46. Lavallee LF, Campbell JD. Impact of personal goals on self-regulation processes elicited by daily negative events. J Pers Soc Psychol 1995; 69:341–52.
47. McCullough ME, Orsulak P, Brandon A, Akers L. Rumination, fear, and cortisol: an in vivo study of interpersonal transgressions. Health Psychol 2007;26:126–32.
48. Zoccola PM, Dickerson SS, Zaldivar FP. Rumination and cortisol responses to laboratory stressors. Psychosom Med 2008;70:661.
49. Rimmele U, Seiler R, Marti B, Wirtz PH, Ehlert U, Heinrichs M. The level of physical activity affects adrenal and cardiovascular reactivity to psychosocial stress. Psychoneuroendocrinology 2009;34:190–8.
50. Rimmele U, Zellweger BC, Marti B, Seiler R, Mohiyeddini C, Ehlert U, Heinrichs M. Trained men show lower cortisol, heart rate and psychological responses to psychosocial stress compared with untrained men. Psychoneuroendocrinology 2007;32:627–35.
51. Traustadóttir T, Bosch PR, Matt KS. The HPA axis response to stress in women: effects of aging and fitness. Psychoneuroendocrinology 2005;30: 392–402.
52. Ford ES. Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. adults. Epidemiology 2002;13:561–8.
53. Blumenthal JA, Fredrikson M, Kuhn CM, Ulmer RL, Walsh-Riddle M, Appelbaum M. Aerobic exercise reduces levels of cardiovascular and sympathoadrenal responses to mental stress in subjects without prior evidence of myocardial ischemia. Am J Cardiol 1990;65:93–8.
54. Crews DJ, Landers DM. A meta-analytic review of aerobic fitness and reactivity to psychosocial stressors. Med Sci Sports Exerc 1987;19:S121.
55. Dishman RK, Jackson EM, Nakamura Y. Influence of fitness and gender on blood pressure responses during active or passive stress. Psychophysiology 2002;39:568–76.
56. Jackson EM, Dishman RK. Cardiorespiratory fitness and laboratory stress: a meta-regression analysis. Psychophysiology 2006;43:57–72.
57. Singer JD, Willett JB. Applied Longitudinal Data Analysis: Modeling Change and Event Occurrence. New York City, NY: Oxford University Press; 2003.
58. Dienstbier RA. Behavioral correlates of sympathoadrenal reactivity: the toughness model. Med Sci Sports Exerc 1991;23:846.
59. Linden W, Earle TL, Gerin W, Christenfeld N. Physiological stress reactivity and recovery: conceptual siblings separated at birth? J Psychosom Res 1997;42:117–35.
60. Kirschbaum C, Pirke KM, Hellhammer DH. The 'Trier Social Stress Test'—a tool for investigating psychobiological stress responses in a laboratory setting. Neuropsychobiology 1993;28:76–81.
61. Treynor W, Gonzalez R, Nolen-Hoeksema S. Rumination reconsidered: a psychometric analysis. Cognit Ther Res 2003;27:247–59.
62. Church TS, Cheng YJ, Earnest CP, Barlow CE, Gibbons LW, Priest EL, Blair SN. Exercise capacity and body composition as predictors of mortality among men with diabetes. Diabetes Care 2004;27:83–8.
63. Fransson E, Knutsson A, Westerholm P, Alfredsson L. Indications of recall bias found in a retrospective study of physical activity and myocardial infarction. J Clin Epidemiol 2008;61:840–7.
64. Verbrugge LM. Health diaries. Med Care 1980;18:73–95.
65. Gillmore MR, Gaylord J, Hartway J, Hoppe MJ, Morrison DM, Leigh BC, Rainey DT. Daily data collection of sexual and other health-related behaviors. J Sex Res 2001;38:35–42.
66. Centers for Disease Control and Prevention. Physical activity for everyone: guidelines: adults. Available at: http://www.cdc.gov/physicalactivity/everyone/guidelines/adults.html. Accessed October 26, 2009.
67. Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, Macera CA, Castaneda-Sceppa C. Physical activity and public health in older adults. Recommendation from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc. 2007;39:1435–45.
68. Epel E, Lapidus R, McEwen B, Brownell K. Stress may add bite to appetite in women: a laboratory study of stress-induced cortisol and eating behavior. Psychoneuroendocrinology 2001;26:37–50.
69. Nolen-Hoeksema S. The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. J Abnorm Psychol 2000;109:504–11.
70. Camacho TC, Roberts RE, Lazarus NB, Kaplan GA, Cohen RD. Physical activity and depression: evidence from the Alameda County Study. Am J Epidemiol 1991;134:220–231.
71. Burke HM, Davis MC, Otte C, Mohr DC. Depression and cortisol responses to psychological stress: a meta-analysis. Psychoneuroendocrinology 2005;30:846–56.
72. Raudenbush SW, Bryk AS. Hierarchical Linear Models: Applications and Data Analysis Methods. Thousand Oaks, CA: Sage Publications Inc; 2002.
73. Cohen P, Cohen J, West SG, Aiken LS. Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences. 3rd ed. Mahwah, NJ: Lawrence Erlbaum Associates; 2002.
74. Li G, He H. Hormesis, allostatic buffering capacity and physiological mechanism of physical activity: a new theoretic framework. Med Hypotheses 2009;72:527–32.
75. Dishman RK, Berthoud HR, Booth FW, Cotman CW, Edgerton VR, Fleshner MR, Gandevia SC, Gomez-Pinilla F, Greenwood BN, Hillman CH, Kramer AF, Levin BE, Moran TH, Russo-Neustadt AA, Salamone JD, Van Hoomissen JD, Wade CE, York DA, Zigmond MJ. Neurobiology of exercise. Obes Res 2006;14:345–56.
76. Vaynman S, Ying Z, Gomez-Pinilla F. Interplay between brain-derived neurotrophic factor and signal transduction modulators in the regulation of the effects of exercise on synaptic-plasticity. Neuroscience 2003;122: 647–57.
77. Vaynman S, Ying Z, Gomez-Pinilla F. Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. Eur J Neurosci 2004;20:2580–90.
78. Gielen S, Adams V, Mobius-Winkler S, Linke A, Erbs S, Yu J, Kempf W, Schubert A, Schuler G, Hambrecht R. Anti-inflammatory effects of exercise training in the skeletal muscle of patients with chronic heart failure. J Am Coll Cardiol 2003;42:861.
79. Goldhammer E, Tanchilevitch A, Maor I, Beniamini Y, Rosenschein U, Sagiv M. Exercise training modulates cytokines activity in coronary heart disease patients. Int J Cardiol 2005;100:93–9.
80. Petersen AM, Pedersen BK. The anti-inflammatory effect of exercise. J Appl Physiol 2005;98:1154.
81. Perseghin G, Price TB, Petersen KF, Roden M, Cline GW, Gerow K, Rothman DL, Shulman GI. Increased glucose transport-phosphorylation and muscle glycogen synthesis after exercise training in insulin-resistant subjects. N Engl J Med 1996;335:1357–62.
82. Koivisto VA, Yki-Järvinen H, DeFronzo RA. Physical training and insulin sensitivity. Diabetes Metab Rev 1986;1:445–81.
83. Kang J, Robertson RJ, Hagberg JM, Kelley DE, Goss FL, DaSilva SG, Suminski RR, Utter AC. Effect of exercise intensity on glucose and insulin metabolism in obese individuals and obese NIDDM patients. Diabetes Care 1996;19:341.
84. Jackson MJ. Reactive oxygen species and redox-regulation of skeletal muscle adaptations to exercise. Philos Trans R Soc Lond B Biol Sci 2005; 360:2285.