Stress and Body Shape: Stress-Induced Cortisol Secretion Is Consistently Greater Among Women With Central Fat

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Objective: Excessive central fat puts one at greater risk of disease. In animal studies, stress-induced cortisol secretion has been shown to increase central fat. The objective of this study was to assess whether women with central fat distribution (as indicated by a high waist-to-hip ratio [WHR]), across a range of body mass indexes, display consistently heightened cortisol reactivity to repeated laboratory stressors. **Methods:** Fifty nine healthy premenopausal women, 30 with a high WHR and 29 with a low WHR, were exposed to consecutive laboratory sessions over 4 days (three stress sessions and one rest session). During these sessions, cortisol and psychological responses were assessed. **Results:** Women with a high WHR evaluated the laboratory challenges as more threatening, performed more poorly on them, and reported more chronic stress. These women secreted significantly more cortisol during the first stress session than women with a low WHR. Furthermore, lean women with a high WHR lacked habituation to stress in that they continued to secrete significantly more cortisol in response to now familiar challenges (days 2 and 3) than lean women with a low WHR. **Conclusions:** Central fat distribution is related to greater psychological vulnerability to stress and cortisol reactivity. This may be especially true among lean women, who did not habituate to repeated stress. The current cross-sectional findings support the hypothesis that stress-induced cortisol secretion may contribute to central fat and demonstrate a link between psychological stress and risk for disease. **Key words:** stress, cortisol, waist-to-hip ratio, body mass index.

ANCOVA = analysis of covariance; ANOVA = analysis of variance; AUC = area under the curve; BMI = body mass index; HPA = hypothalamic-pituitary-adrenal; WHR = waist-to-hip ratio.

INTRODUCTION

Obesity has reached epidemic levels in the United States (1). In addition to excess weight, body shape is a putative phenotypic marker of increased risk of disease. Central body fat distribution, as measured by the WHR, is a risk factor for hyperlipidemia, hypertension, coronary heart disease, stroke, and diabetes mellitus, *independent* of overall obesity (2, 3).

The disease–central fat link has a proposed physiological mechanism. Excessive central fat indicates greater visceral fat, which is morphologically different from peripheral fat. Visceral fat has greater blood flow and up to four times more glucocorticoid receptors than peripheral fat; thus, it is especially sensitive to the fat-accumulating effects of circulating cortisol and triglycerides (4). Visceral fat tissue responds to circulating cortisol by further increasing its size. Large central fat deposits may contribute to disease in part by releasing free fatty acids into the portal circulation, which can promote other risk factors, such as synthesis of cholesterol and insulin resistance (5).

Epidemiological studies have found that central fat distribution is related to adverse psychological states, such as depression and anxiety, and to social difficulties, such as unemployment and divorce (6–9). On the basis of these associations, Bjorntorp (10) and Rebuffe-Scrive (11) have hypothesized that greater vulnerability to stress increases exposure to stress-induced cortisol, which in turn fuels central fat deposition. The study reported here examined this hypothesis in a correlational manner. Although it would be ideal to examine whether exposure to chronic stress increases central fat over time, we selected women on the basis of fat distribution phenotypes and assessed their level of life stress and response to stress in a cross-sectional manner.

The clearest examples of the association between cortisol secretion and central fat in humans are seen in people with Cushing's syndrome and to a lesser extent in those with severe recurrent depression, both of which are characterized by hypersecretion of basal cortisol and increased central fat (12–14). It thus seems that excessive basal cortisol secretion, as found in these clinical syndromes, can affect the development of central fat deposits. It is less clear whether we might find a relationship between stress-induced cortisol and fat distribution among healthy, nondepressed people who have normal levels of basal cortisol. In other words, does exposure to stress-induced cortisol affect body fat distribution among the general public? If so, this would represent a common pathway for stress-

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Received for publication August 13, 1999; revision received February 15, 2000.

0033-3174/00/6205-0623

induced disease in people other than those with a recurrent depressive disorder or pathologic disorder of the HPA axis, such as Cushing's syndrome.

The primary goal of this study was to assess whether women with greater central fat (high WHR) adapt less effectively to repeated stress over time, both physiologically and psychologically, than women with relatively greater peripheral fat (low WHR). Two pilot studies of obese women found that those with greater central fat secreted more cortisol in response to a novel laboratory challenge (15, 16). However, these studies had methodological limitations that preclude conclusive interpretations and generalization of results. For example, in one of these studies, 32% of the sample had a history of smoking, which itself can increase both cortisol and abdominal obesity (17). Furthermore, they did not assess concurrent psychological responses to the stressors to determine whether there were differences in stress appraisal or performance that may have stimulated the greater cortisol secretion. It is important to determine whether greater physiological reactivity among women with central fat distribution is caused centrally (psychologically driven reactivity). Otherwise, we leave open the possibility that their physiological reactivity could be a mere peripheral epiphenomenon or a consequence of their increased central fat rather than a result of psychological differences.

Another limitation of the prior pilot studies is that they assessed exposure to a single episode of stress. Cortisol responses to a single laboratory challenge may not represent stable response patterns over time because the HPA axis is sensitive to novelty. Cortisol secretion to a novel challenge, as observed in these studies, may even represent a healthy response, whereas consistently high cortisol reactivity to repeated familiar challenges (or "nonhabituation") is an atypical response that may reflect chronic physiological stress (18). Kirschbaum et al. (18) found that the cortisol response does not habituate to repeated stress in one-third of healthy men. For cortisol reactivity to stress to affect the target tissue (visceral fat) enough to actually shape one's body, the reactivity would have to be consistent and exaggerated. Thus, we predicted that people with greater central fat would be "nonhabituators" in that they would reliably secrete cortisol in response to familiar stressful situations. We therefore measured cortisol responses to identical challenges over several days.

Lastly, both prior studies included only overweight women, so the question of whether fat distribution has similar correlates in lean women could not be addressed. Obesity itself affects fat distribution, contributing to greater central fat deposits. Although obesity and central fat tend to covary, that is, women tend to be lean with a low WHR (Figure 1, *A*) or overweight with high WHR (Figure 1, *D*), overall fatness and fat distribution can uncouple, creating the less frequently observed combinations of being lean but carrying greater central fat relative to peripheral fat (Figure 1, *B*) and, conversely, of being overweight but having less central fat relative to peripheral fat (Figure 1, *C*). Our secondary aim was to compare stress reactivity in lean women with central fat (Figure 1, *B*) with stress reactivity in lean women with peripheral fat (Figure 1, *A*), which has not been studied. This poses a more direct test of the association between stress and fat distribution because it is an assessment of fat distribution in the absence of *general* accumulation of fat, which can serve as a confounding factor. Whereas overweight women will inevitably have greater central fat as a result of their excess fat, lean women are less likely to have central fat. One possible contributor to central fat

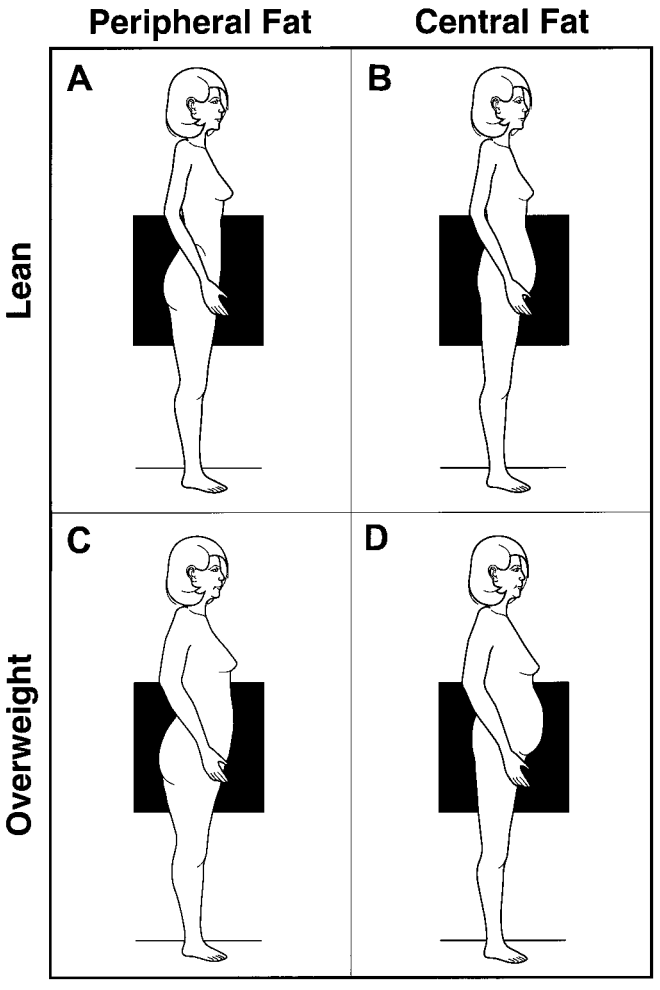

Fig. 1. Fat distribution phenotypes by level of obesity. *A*, Lean with peripheral fat. *B*, Lean with central fat. *C*, Overweight with peripheral fat. *D*, Overweight with central fat.

among lean women could be stress-induced endocrine dysregulation. Furthermore, there is evidence that being *lean* and having greater central fat is a particularly unhealthy profile because it predicts earlier death (19).

We used a stringent screening battery to obtain a sample of women without a history of behaviors, health conditions, or substance use that could affect either cortisol or central fat. We believed it was important to study the relationship between endogenous cortisol and central fat in the absence of confounding variables. For example, people reporting more stress may be more likely to have a history of alcohol, tobacco, or psychotropic medication use, all of which could potentially affect both HPA axis dysregulation and central fat.

We hypothesized that, compared with women with a low WHR, women with a high WHR would 1) respond to a novel laboratory stressor with greater cortisol reactivity, 2) fail to habituate to repeated stressors by showing high cortisol reactivity on subsequent exposures, and 3) report psychological traits and responses to the stressors indicative of ineffective coping. Lastly, we tested the novel and exploratory hypothesis that the above differences between WHR groups would be strongest among lean women.

METHODS

Study Participants

Participants were 59 regularly menstruating white women aged 30 to 46 years. Twenty-nine had a WHR ≤0.75 (low WHR), and 30 had a WHR ≥0.79 (high WHR), following the guidelines used by Moyer et al. (16). BMI ranged from very lean (BMI = 19.6) to obese (BMI = 39.8), with women selected so that the average BMI in the two WHR groups was equivalent. Exclusion criteria included factors that could influence fat distribution or cortisol reactivity: current smoking or past history of smoking, regular alcohol use (>7 drinks per week), current or past history of endocrine disorders, eating disorders, depression, hypertension, medication use (including oral contraceptives), irregular menstrual cycle, more than three pregnancies, recent weight changes, excessive exercise (>2 h/d), and past hospitalization for psychiatric or addictive disorders.

Participants were required to abstain from alcohol consumption during the week of study, from caffeine for 4 hours before cortisol sampling, and from food and drinks (excluding water) for 1 hour before laboratory sessions (all confirmed by daily questionnaires). These exclusion restrictions and the homogeneity of the sample eliminated many potentially confounding factors and thus allowed a robust test of the relationship between endogenous cortisol and body shape.

Recruitment and Procedure

Participants were recruited by flyers, newspaper advertisements, and radio announcements. Seven hundred women responded by telephone, and 157 were eligible after an initial telephone health screen. Of these, 72 women met the WHR criteria (ie, had either a high or low WHR). Eligible women were scheduled for four consecutive afternoon sessions during the follicular phase of their menstrual cycle (ie, women started the sessions within 5 days of beginning menstruation).

Twelve of the eligible women (three with a low WHR and nine with a high WHR) dropped out of the study after enrolling, reportedly because of a lack of time. One woman with a high WHR did not to return after the first session. Seventy-seven percent of dropouts were in the high WHR group. Among the high WHR dropouts, three were overweight and seven were lean. The group presumed to be most vulnerable (lean women with a high WHR, who tend to be less common in the general population because of their atypical (male) fat pattern) were overrepresented in the attrition rate.

To determine whether attrition may have led to sample bias, differences in chronic stress were tested between high WHR and low WHR dropouts. Despite the low statistical power, the 10 dropouts with a high WHR had significantly higher levels of chronic social stress than the 3 with a low WHR ($p < .03$). We also tested whether the dropouts in each WHR group were similar to those in the same group who completed the study. Dropouts with a high WHR had levels of chronic stress similar to those of women with a high WHR who completed the study. On the other hand, dropouts with a low WHR had marginally lower values on both measures of chronic stress than those with a low WHR who completed the study (p values $< .08$). These differences could potentially bias results against our hypothesis. Despite the differential attrition rate, we found that of the women who remained in the study, women with a high WHR were still different (eg, had higher levels of chronic stress) from women with a low WHR, as detailed below.

To identify women with disordered eating, we administered the Eating Attitudes Test (20). Seven women (two with a low WHR and five with a high WHR) scored in the potentially clinical range on this measure (>20) and thus were excluded from further analyses. The final sample consisted of 27 women with a low WHR and 25 with a high WHR.

The study included laboratory sessions on four consecutive days (three stress sessions followed by one control session). Each session lasted 3 hours and started at the same time each day (between 4:00 and 5:30 PM). This time period approaches the nadir of the cortisol diurnal rhythm, when basal cortisol is lowest and stress responsivity is highest (21). This helps ensure any cortisol elevations are due to the challenge manipulation.

During the three stress sessions, participants were exposed to 45 minutes of widely used psychosocial challenges, including serial arithmetic, visuospatial puzzle, and speech tasks, adapted from the Trier Social Stress Test (19, 22). The nature of the tasks, including the duration and level of difficulty, were identical each day, but the content was varied (in random order) so that participants never solved the same problem twice. On the counting task, they were given a different prime number to serially subtract from a large number each day. On the block design puzzles, they were given several different pictures to replicate with blocks each day. On the speech task, they tried to convince a committee that they were the best applicant for a job (using a different job each day) and answered questions from a research evaluator.

The original Trier Social Stress Test includes a live audience, which likely increases stress. Given the difficulty of gathering the same audience on 3 consecutive days, we used several other techniques to replace the audience. We made audiotapes and videotapes of the speeches, which were supposedly to be evaluated by a committee of researchers. The interviewer sat in the room and watched the participant closely. We also had each participant face a one-way mirror and told her that a trained research evaluator was behind the mirror and was rating her performance. After the speech, the interviewer left the room to confer with the research evaluator behind the

mirror to decide on the questions to be asked. A manipulation check showed that participants indeed believed there was a researcher behind the mirror. Participation in all procedures was completely voluntary and confidential.

Saliva samples (to assess free cortisol) were collected at matched time intervals throughout each session at the following times: while resting (15 and 30 minutes), before stress (45 minutes), during stress (60 and 70 minutes), at the cessation of stress (90 minutes), and during the recovery period (120 and 150 minutes, 30 and 60 minutes after stress, respectively). "Cortisol reactivity" refers to total cortisol output on the stress day, calculated as the AUC (in μg/dl $\times$ minutes).

Measures

Psychological/cognitive measures. All measures were internally consistent (Cronbach's α = 0.70–0.93) with established validity as cited.

Passive coping and responses to challenge. One's typical coping response was measured at baseline with use of the COPE (23). We focused on passive coping because it may prevent adaptation to stress and used summary subscales of problem avoidance and emotion avoidance coping (24). Immediately after completing the challenges on the first session, participants rated the extent to which they perceived the tasks as threatening (range = 1–4). After the challenges, participants rated how well they performed compared with when they are at their very best on a scale of 1 ("not at all my best effort") to 10 ("completely my best effort").

Mood. Mood was measured before and after challenge using different forms of a visual analog scale of 14 mood adjectives. Embedded in the list were the relevant adjectives of stress and control. Mood reactivity was calculated as the change in mood from baseline to during challenge. The Profile of Mood States scale was also used, but these data are not reported.

Psychological traits. The Rosenberg Self-Esteem Scale includes 10 items assessing feelings of self-worth (25). Pessimism was measured by summing the four items assessing negative expectations from the Optimism-Pessimism Scale (26). Negative affect was assessed using the Positive and Negative Affect Schedule (27). Chronic stress (work/financial and social stress) was assessed using the Social Stress Index (28).

Physical measures. Anthropomorphic measures. Body weight was assessed on a balance beam scale. Body height was measured to the nearest 0.25 inch. BMI was calculated as weight (kg) divided by height (m^2). BMI was categorized as lean to average ($\leq$24) or overweight (>24) on the basis of a median split. This created four groups (Figure 1): lean, low WHR (Figure 1, *A*); lean, high WHR (Figure 1, *B*); overweight, low WHR (Figure 1, *C*); and overweight, high WHR (Figure 1, *D*).

Waist circumference was measured twice at the midpoint between the upper iliac crest and lower costal margin in the midaxillary line. Hip circumference was measured twice at the maximum width of the buttocks or gluteofemoral fold (29). WHR was calculated as the mean waist circumference divided by the mean hip circumference. Percentage of body fat was assessed with the Futrex-5000 body fat computer (Gaithersburg, MD).

Salivary cortisol. Saliva samples were assayed with a commercial radioimmunoassay kit (Diagnostic Products Corporation, Los Angeles, CA). Intraassay coefficients of variation were 4.8% for low concentrations and 5.1% for high concentrations of salivary cortisol. The interassay coefficient of variation was 4%. Cortisol AUC, a summary measure of total cortisol secreted over time, was calculated for each laboratory session. Two women had out-of-range cortisol levels on more than half of the days; these women were excluded from all analyses of cortisol but included in all other analyses.

Data Analyses

The primary outcome assessed was salivary cortisol reactivity (AUC) to repeated challenge. To test for differences in cortisol habituation to stress (AUC of cortisol during the three stress sessions), we performed a repeated-measures ANCOVA using a 2 (WHR, high and low) $\times$ 2 (BMI, high and low) $\times$ 3 (time, session 1, 2, and 3) between-subjects design, controlling for rest-day cortisol AUC. Results are reported by WHR only unless there was a significant interaction between WHR and BMI.

To test for differences in psychological variables (response to challenge and baseline traits), we used a 2 (WHR, high and low) $\times$ 2 (BMI, high and low) ANOVA, again testing for the main effect of WHR and any interactions with BMI (to examine any differential effects of WHR across BMI groups).

Because of the a priori hypothesis that women with a high WHR would have worse psychological and cortisol profiles in general, one-tailed significance tests were used when appropriate (Tables 1-3). Two-tailed significance tests were used for all other statistics reported. Given the small size of our sample, we considered the primary criterion to be a main effect of WHR and the examination of subgroups by BMI to be exploratory.

RESULTS

Sample Description and Anthropometric Differences

On average, the women were 36 years old (SE = 0.70, range = 30–46 years), well educated (average years of education = 16, SE = 0.22, range = 12–17), and had an annual household income of $35,537 (SE = $3334). As expected, there were no differences between the two WHR groups on any sociodemographic variable.

Based on our recruitment criteria, the WHR groups were similar in BMI and percentage of body fat but different in WHR. Across the sample, the average BMI

TABLE 1. Mean Total Salivary Cortisol (AUC) Measured During Each Session by Lean and Overweight WHR

Group	Cortisol AUC (μg/dl $\times$ minutes)		*t* Test	*p* Values[a]
	Low WHR (*N* = 13)	High WHR (*N* = 12)		
	Mean (SE)	Mean (SE)		
Lean women				
Stress session 1	33.1 (3.3)	48.7 (6.4)	$t(23) = 2.2$, $p =$ **.02**	
Stress session 2	24.6 (2.8)	33.9 (3.2)	$t(23) = 2.2$, $p =$ **.02**	
Stress session 3	28.6 (2.9)	41.5 (6.2)	$t(23) = 1.9$, $p =$ **.04**	
Rest session (day 4)	33.4 (4.0)	31.84 (5.1)	$t(23) = 0.3$, $p = .75$	
Overweight women				
Stress session 1	33.0 (3.2)	41.8 (4.2)	$t(23) = 1.7$, $p =$ **.050**	
Stress session 2	32.5 (4.4)	27.4 (2.6)	$t(23) = 1.0$, $p = .330$	
Stress session 3	32.1 (3.3)	40.3 (5.7)	$t(23) = 1.3$, $p = .220$	
Rest session (day 4)	23.2 (2.3)	27.0 (3.5)	$t(23) = 0.9$, $p = .360$	

[a] Significance was determined by using one-tailed *t* tests.

was 25.4 (SE = 0.6, range = 19.8–39.6), and average percentage of body fat was 29.7% (SE = 1.1%). The high WHR group had an average WHR of 0.83 (SE = 0.01, range = 0.79–0.93), and the low WHR group had a significantly lower ($p < .0001$) average WHR of 0.72 (SE = 0.01, range = 0.67–0.75).

Cortisol Responses

Cortisol and WHR at stress and rest. First, we wanted to determine whether WHR was related to cortisol during stress but not during rest. We performed correlations between WHR and cortisol AUC each day. As expected, WHR was related to reactive cortisol (average AUC during stress sessions, $r = 0.29$, $p = .04$) but not to resting cortisol (AUC during rest session, $r = 0.02$, $p = .90$). We also tested whether there were differences in rest-day cortisol using a 2 × 2 ANOVA of WHR by BMI groups and, as expected, found no differences in resting cortisol ($F(3,45) = 1.4$, $p = .23$).

Cortisol and WHR by BMI. Next, we wanted to test whether WHR was related to higher cortisol during stress and whether this relationship was stronger among lean than overweight women. All four groups were examined: lean, high WHR women ($N = 12$); lean, low WHR women ($N = 13$); overweight, high WHR women ($N = 12$); and overweight, low WHR women ($N = 13$) (Figure 1). A repeated-measures ANCOVA was performed to test the interaction of cortisol over time (3 stress days) with WHR (high and low) and BMI groups (high and low), controlling for resting cortisol AUC from the rest day. There was a significant main effect of WHR ($F(1,45) = 6.4$, $p = .01$) and no main effect of BMI ($F = 0.38$, NS). As predicted, there was a significant three-way interaction between WHR, BMI, and average cortisol AUC across time ($F(1, 45) = 2.9$, $p = .05$). In addition, when we examined interactions over time, we found a quadratic interaction between WHR and time ($F(1,45) = 10.3$, $p = .001$). The high WHR group showed greater peaks of reactivity on days 1 and 3 but not day 2. As shown in Table 1, most groups showed partial habituation on day 2: They secreted less cortisol than on day 1 but reacted again on day 3 and returned to lower levels on the rest day. It is unclear why there was partial habituation on day 2, but we heard anecdotal reports from some participants that day 2 was easier than day 1 because they knew what to expect but that by day 3 they dreaded facing the same stressors yet again.

To examine differences in cortisol AUC on each day within the lean and overweight WHR groups, one-tailed *t* tests were performed. We found that lean women with a high WHR had significantly higher total cortisol levels than lean women with a low WHR on all 3 stress days (p values $< .05$) in response to both novel stress (Figure 2, *top*) and familiar stress (Figure 2, *middle* and *bottom*). There were much weaker differences in cortisol by WHR among the high BMI group (Table 1). Overweight women with a high WHR had significantly higher cortisol levels on day 1, but levels were similar on days 2 and 3.

Psychological Characteristics

To compare psychological traits across the four groups, 2 (WHR) × 2 (BMI) ANOVAs were performed. Across BMIs, women with a high WHR reported higher levels of chronic work/financial stress ($F(3,51) = 4.0$, $p < .025$) and had lower self-esteem scores ($F(3,49) = 1.8$, $p < .025$) (Table 2). Additionally, there were interactions between WHR with BMI for pessimism ($F(3,49) = 4.8$, $p < .025$), negative affectivity ($F(3,48) = 3.9$, $p < .025$), and problem avoidant coping ($F(3,49) = 3.9$, $p < .02$), all showing that the group presumed to be most vulnerable (lean, high WHR) reported a more negative profile (greater pessimism, negative affect, and avoidant coping) than lean women with a low

TABLE 2. Differences in Background Psychological Traits Between High WHR and Low WHR Groups

Trait	Low WHR ($N = 27$) Mean (SE)	High WHR ($N = 24$) Mean (SE)	*p* Values[a] for Main Effects of WHR *p*[a]	*p* Values[a] for Interactions Between WHR and BMI
Self-esteem	42.6 (1.2)	39.3 (1.3)	**.030**	.200
Pessimism	7.40 (0.51)	7.50 (0.53)	.910	**.020**
Chronic work/financial stress	1.37 (0.11)	1.65 (0.11)	**.025**	.700
Chronic social stress	0.68 (0.10)	0.66 (0.09)	.870	.420
Negative affect	1.81 (0.11)	2.03 (0.11)	.190	**.025**
Problem avoidant coping	1.37 (0.07)	1.44 (0.07)	.530	**.025**
Emotion avoidant coping	1.28 (0.08)	1.39 (0.08)	.250	.380

[a] Significance was determined by using one-tailed tests.

WHR, whereas women with a high BMI did not differ in this respect. Thus, there was consistency in findings in that women with a high WHR scored more poorly across five of the seven background psychological measures, although in some cases this was moderated by BMI (ie, only lean women with a high WHR were worse off).

Manipulation Check of Challenge Sessions

We then examined how the women responded to the laboratory stressors. The tasks were intended to produce perceptions of uncontrollable stress. To assess the effect of challenge on perceived stress and control, paired *t* tests were performed on pre- and post-stressor mood. Across groups, mood was averaged across the 3 stress days. There were significant increases in feelings of stress ($t = 7.2$, $p < .001$) and decreases in perceived control ($t = -3.4$, $p < .001$) on the stress days. On the recovery day, there were significant decreases in feelings of stress ($t = -5.5$, $p < .001$) and actually an increase in control ($t = 2.1$, $p < .05$). These results confirm that the challenge sessions, unlike the recovery session, were associated with uncontrollable stress. There were no differences in stress or control by WHR group.

Psychological Responses to Challenge

We predicted that women with a high WHR would have a more defeated response to challenge characterized by greater threat appraisals of the challenge, more passive coping with the tasks, less effort, and poorer performance. Indeed, we found that women with a high WHR made greater threat appraisals, exerted increasingly less effort over time, and made more errors than women with a low WHR (p values $< .05$) (Table 3). There were no interactions with BMI.

Lastly, we examined whether psychological response to challenge mediated the cortisol response of women with a high WHR. Threat could potentially serve as a mediator because it was correlated with both WHR ($r = 0.35$, $p < .05$) and cortisol AUC on day 1 ($r = 0.33$, $p < .05$). To test whether threat perceptions may have mediated the cortisol increases, an exploratory mediational analysis was tested with two regression models. All significance tests were two-tailed. In the first regression model, WHR significantly predicted cortisol AUC on day 1, controlling for rest-day cortisol ($\beta = 0.27$, $p < .05$). In the second model, we entered threat perceptions as well as WHR into the model. After entering threat into the model, the effect of WHR was reduced and no longer significant ($\beta = 0.19$, $p = .19$). This demonstrates at least partial mediation by threat appraisals.

TABLE 3. Differences in Psychological Response to Challenge Between Low WHR and High WHR Groups

Response to Challenge	Low WHR ($N = 27$) Mean (SE)	High WHR ($N = 25$) Mean (SE)	
Perceived threat	1.66 (0.18)	2.20 (0.19)	$F(3,42) = 3.8$, $p = .030$
Performance errors	3.25 (0.34)	4.72 (0.36)	$F(3,48) = 9.1$, $p = .002$
Effort by day 3	6.69 (0.45)	5.58 (0.47)	$F(3,46) = 2.9$, $p = .050$

[a] Significance was determined by using one-tailed *t* tests.

DISCUSSION

We predicted that women with a high WHR, especially lean women, would respond to repeated stressors with a more defeated psychological response and less resilient functioning of their HPA axes (ie, consistent and exaggerated cortisol reactivity). Indeed, lean women with a high WHR showed a lack of adaptation: They secreted more cortisol than women with a low WHR after the first stress exposure even though the two groups had similar cortisol levels at baseline. Furthermore, on the second and third days of challenge, after the stressor was familiar and predictable, the lean women with a high WHR continued to secrete more cortisol than lean women with a low WHR. The overweight women showed less exaggerated differences: Overweight women with a high WHR had higher cortisol levels only on exposure to novel stress but then seemed to habituate to stress and had levels similar to those of overweight women with a low WHR on subsequent days. The finding of greater cortisol reactivity to challenge among women with central fat replicates the findings of two prior studies (15, 16) but does so among a more selective sample with fewer confounding factors. Moreover, the results extend past findings by showing a consistent lack of adaptation over several days among lean women with a high WHR. This supports our prediction that stress-induced cortisol reactivity is more related to central fat among lean than among overweight women.

Because the greater cortisol reactivity of high WHR women could be a mere physical consequence or correlate of their greater central fat or, as we speculate, a result of chronic stress, it was important to identify whether there were psychological differences in tandem with physical evidence of greater stress. As predicted, the "on-line" psychological and cognitive responses of high WHR women to laboratory challenges

indicated defeat rather than adaptation. Women with a high WHR perceived greater threat, exerted less effort, and performed more poorly. Threat, in turn, was related to cortisol after challenge. At baseline, women with a high WHR reported greater chronic stress and negative affect. In addition, lean women with a high WHR scored higher in pessimism, negative affect, and passive coping.

The observed cortisol profile among *lean* women with a high WHR of greater initial reactivity to challenge and nonhabituation over time may add up to greater overall cortisol exposure under stressful conditions. If lean, high WHR women typically respond to familiar stressors as they did to the chronic laboratory stressor, it is likely that cumulative exposure to cortisol contributed to their increased central fat, given the known effect of cortisol on visceral fat tissue.

Historically, central fat has been related to stress-induced cortisol among overweight women (ie, BMI of 24–45) (15, 16). However, by examining women across a full range of weights, we found that BMI interacts with WHR. Although *overweight* women with a high WHR responded to the stressors in a defeated manner, they habituated to the stressors after one exposure. Thus, they showed some vulnerability to stress but were a more heterogeneous group than lean, high WHR women. Obesity itself can increase central fat; thus, the high WHR among obese and lean people may have resulted from different causes and may carry different levels of risk. For lean women, we speculate that central fat may indicate an underlying sensitivity to stress rather than being in part a result of obesity.

An alternative interpretation of our results is that the lean women with a high WHR may only seem more vulnerable relative to our "control group" of lean women with a low WHR. These lean, low WHR women may have actually been a particularly resilient group, because after exposure to a novel stressor designed to elicit cortisol responses, they had a barely detectable average increase in cortisol (Figure 2, *top*). It is possible that if we had used the original Trier stress test (with a live audience) we may have seen a greater cortisol response among this apparently hardy group. These women scored highest in self-esteem and lowest in negative affectivity of all the groups. We speculate that their healthy psychological outlook may have promoted greater release of growth hormone and female sex hormones, which are known to mobilize fat and store it peripherally (at the hips) rather than centrally (5).

Nevertheless, even if the lean, low WHR women were a particularly resilient group, the lean, high WHR women still showed signs of vulnerability, mainly consistent cortisol reactivity compared with their rest-day value. Lack of cortisol habituation is an uncommon atypical response to repeated stress and is related to lower self-esteem (18).

Other researchers (30, 31) have found abnormal HPA axis responsiveness (nonsuppression of cortisol after dexamethasone) among overweight men and women with greater central fat than peripheral fat, which confirms an association between HPA axis dysregulation and abdominal obesity in otherwise healthy humans. These studies leave us with the question of whether the HPA axis dysregulation is due to chronic stress or whether the dysregulation simply covaries with abdominal obesity. The current results suggest the dysregulation may be related to chronic stress.

Two recent studies have found that adults with central fat distribution have greater cardiovascular reactivity to stress, such as blood pressure reactivity, than those with peripherally distributed fat (32, 33). Davis et al. (32) tested for but did not find greater psychological vulnerability to stress among women with central obesity. Associations between central fat with dysregulated stress response systems (such as high blood pressure at baseline or in response to stress) seem consistent. On the other hand, associations between fat distribution and psychological factors may be less consistently found because of the multiple factors that can cause central fat accumulation.

The generalizability of our findings may be limited. To test our hypothesis about endogenous cortisol exposure, we had to identify a highly selective sample (eg, based on such factors as good health, no oral contraceptive use, body shape, and homogeneity of ethnicity) that is not representative of the population at large. Nevertheless, this restrictive sample allowed us to answer questions about body shape and stress that would be confounded by a sample with health behaviors such as smoking and alcohol use. In addition, relations between obesity, fat distribution, and related metabolic risk factors vary by ethnicity. One study found that WHR was strongly correlated with visceral fat ($r = 0.74$), and with fasting insulin and cholesterol, among white women but not African American women (34). It is unknown whether the current results would generalize to nonwhite samples.

We must also note that although the interactions of WHR with BMI are significant, we consider these findings preliminary because our sample was too small to reliably examine this secondary question of a moderating effect of BMI. Furthermore, WHR provides a less accurate measure of visceral fat than magnetic resonance imaging or computerized tomography, especially in overweight compared with lean women. We may have had stronger results, especially among over-

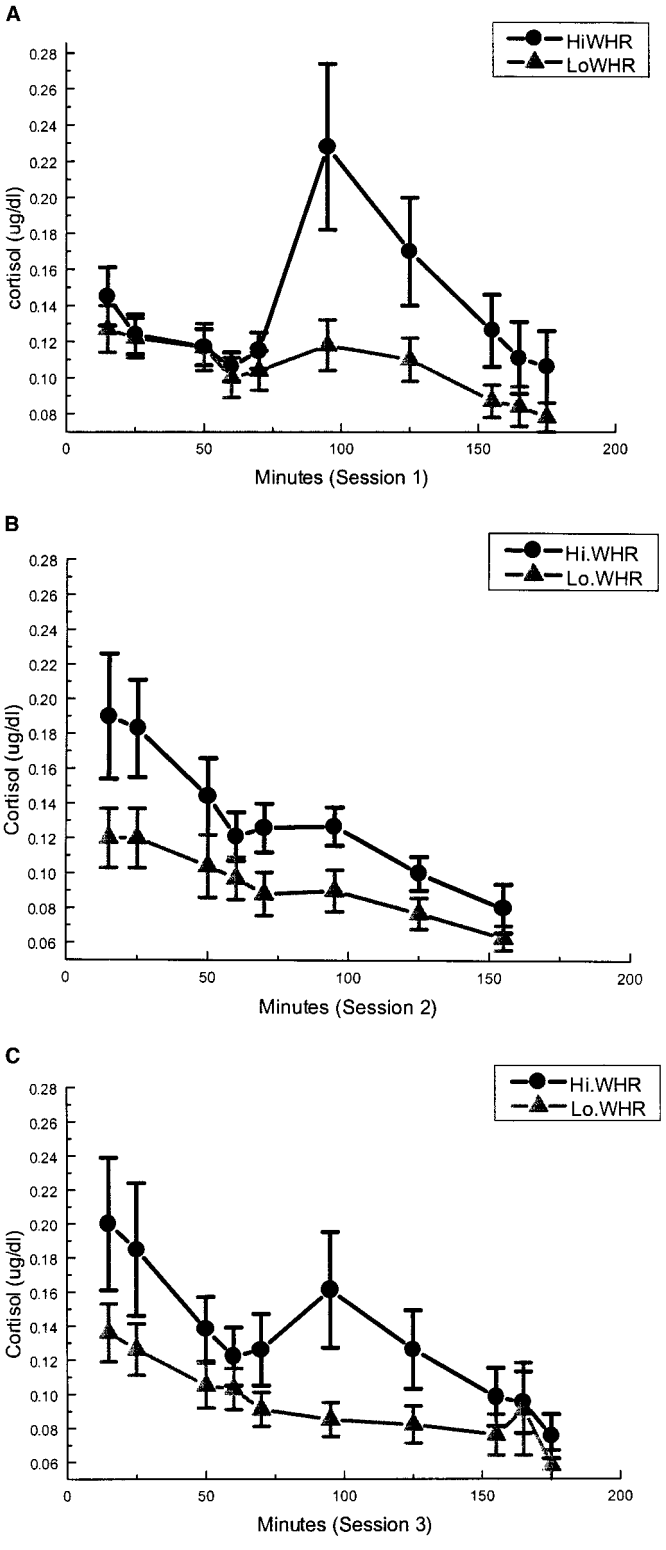

Fig. 2. Average cortisol response to stress sessions among lean women with a high or low WHR. *Top*, Mean cortisol response to first exposure to stressors (novel stress). *Middle*, Mean cortisol response to second exposure to stressors (familiar stress). Bottom, Mean cortisol response to third exposure to stressors (familiar stress).

weight women, had we been able to use a more accurate measure of visceral fat.

It is also important to note that genetics may play a role in the stress–central fat relationship, although we did not examine this in the current study. Genetics can account for up to 50% of the variance in fat distribution (36). That leaves another 50% of the variance to be shaped by environmental influences. There are also genetic influences on psychological coping with stress (37, 38) and cortisol reactivity (39), so it is possible that stress reactivity and central fat are genetically linked.

Nevertheless, experimental manipulations of stress show a causal relationship between stress and fat distribution in animal models, regardless of genetics. In vivo, visceral fat deposits increased in a dose-dependent manner in rats and primates randomly assigned to a chronic stress condition (40, 41). In vitro, cortisol increases lipoprotein lipase (a fat-storing enzyme) in fat tissue but has an especially exaggerated effect on visceral fat tissue (11).

CONCLUSIONS AND IMPLICATIONS

Although our findings are strictly correlational, the psychological and cortisol data are consistent with the hypothesis that greater life stress and stress reactivity contribute to central fat among lean women. The consistency of findings is striking: Vulnerability to stress was noted across both psychological and physiological measures among women with a high WHR. There is growing recognition that overexposure to cortisol can have pathophysiological consequences on many organ systems (42), stress-induced damage that has been labeled "allostatic load" (43). Central fat among lean women may serve as an indicator of one type of allostatic load, physical damage resulting from lack of adaptation to stress, that can eventually result in disease (43). Thus, lean women with a high WHR may be at higher risk of disease for two known and likely interrelated factors, greater exposure to cortisol and possible metabolic aberrations associated with central fat distribution, such as greater insulin resistance (2).

Only longitudinal and genetic studies will determine conclusively whether stress and central fat, with its related metabolic profile, are causally related or parallel phenomena. Future research needs to better define levels of risk and appropriate treatments based not only on one's girth but also on the multiple causes of central fat, such as genetics, behavior, general obesity, and chronic stress.

Funding for this study was provided by the John D. and Catherine T. MacArthur Foundation Research Network on Socioeconomic Status and Health. Addi-

tional support was provided by National Institutes of Health/National Center for Research Resources/General Clinical Research Center Program Grant RR00125, the Woodrow Wilson Grant in Women's Health, and the American Psychological Association, Division 38 (provided to E.S.E.). Acknowledgment is extended to Kris Morrow for creating Figure 1, to Mary Fran Sowers for her insightful analysis advice, and to anonymous reviewers for their helpful comments.

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