Journal of Traumatic Stress
October 2013, *26,* 621–625

ISTSS International Society for Traumatic Stress Studies

BRIEF REPORT

Cortisol and PTSD Symptoms Among Male and Female High-Exposure 9/11 Survivors

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Only a few studies have examined cortisol response to trauma-related stressors in relation to posttraumatic stress disorder (PTSD). We followed a sample of high-exposure survivors of the attacks on September 11, 2001 (9/11; 32 men and 29 women) and examined their cortisol response after recalling the escape from the attack, 7 and 18 months post-9/11. PTSD symptoms and saliva cortisol levels were assessed before and after trauma recollection. Hierarchical regression analyses revealed that PTSD symptoms and male sex predicted increased cortisol response following recollections. For men, elevated cortisol was associated with greater severity of reexperiencing symptoms ($p < .001$) and lower severity of avoidance symptoms ($p < .001$). For women, recall-induced cortisol was minimal and unrelated to PTSD symptoms ($p = .164$ and $p = .331$, respectively). These findings suggest that augmented cortisol response to trauma-related stressors may be evident in men reporting symptoms of PTSD. Thus, as cortisol abnormalities related to PTSD symptoms appear sex-specific, future research on mechanisms of sex differences in response to trauma is warranted.

Posttraumatic stress disorder (PTSD) symptoms develop in response to an extreme stressor. The hypothalamic–pituitary–adrenal (HPA) axis responds to stress with secretion of glucocorticoids (i.e., cortisol), which is vital in maintaining biological homeostasis and adaptation (allostasis) to chronic stress (Schulkin, 2003). Shortly after a traumatic event cortisol is generally enhanced (Kotozaki & Kawashima, 2012). Considerable research has also demonstrated that alterations in cortisol secretion are associated with PTSD. However, the relationship of cortisol levels with PTSD symptoms remains unresolved.

Diurnal basal-cortisol levels are typically, but not exclusively lower in participants with PTSD compared to those without PTSD (Yehuda, 2006); this was hypothesized to be due to an enhanced negative feedback loop in the HPA axis (Yehuda & Seckl, 2011). Although this hypothesis has gained support (Sriram, Rodriguez-Fernandez, & Doyle, 2012), it is possible that trauma exposure rather than PTSD may also account for these findings (Morris, Compas, & Garber, 2012).

Studies examining the cortisol response (i.e., stress-induced cortisol) following exposure to trauma-related reminders in individuals with current PTSD have shown inconclusive findings (Gola et al., 2012). However, trauma-memory-evoked cortisol alterations in PTSD might be moderated by a number of factors (Yehuda, 2006), including symptom clusters of PTSD, which differ in their involvement in consolidation of trauma-memory (Dekel, Solomon, & Ein-Dor, 2013), and gender. Sex differences were found in the cortisol response of healthy adults to stress (Kudielka, Buske-Kirschbaum, Helhammer, & Kirschbaum, 2004), but sex-specific cortisol profiles in PTSD are rare and more studies are warranted (Meewisse, Reitsma, de Vries, Gersons, & Olff, 2007). Thus, in the following study, we examined cortisol responses induced by trauma recollections at two time points in a mixed sex sample of high-exposure 9/11 survivors. We focused our analyses on the questions of whether cortisol elevation following trauma recollections are related to PTSD symptom clusters and moderated by gender.

Method

Participants

Data at 7 months (Time 1: March, 2001) and 18 months (Time 2: April, 2002) post- 9/11 were obtained from individuals who

Sharon Dekel was sponsored by Narsad (Dr. Dylan Tauber) and George A. Bonanno received grants BCS-0202772 and BCS-0337643 from the National Science Foundation.

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DOI: 10.1002/jts.21839

had been in or within four blocks of the World Trade Center (WTC) towers at the time of the 9/11 attacks (Bonanno, Rennicke, & Dekel, 2005). Following approval from Columbia University's Institutional Review Board, we enlisted participants through their companies in the WTC. All participants signed consent forms. Included were 29 men and 32 women; the average age was 39.30 years ($SD = 10.51$), average annual income was $70,000, ethnically 76.9% were White ($n = 48$), and 44.1% resided in Manhattan ($n = 28$). There were no gender differences in demographics.

Measures

Exposure during the event was measured by six items pertaining to feeling in physical danger and highly distressed (subjective), assessed on a 0 = *no* to 4 = *very much*; scale ($\alpha = .83$), and four items pertaining to witnessing deaths and injuries (objective), assessed on a 0 = *none* to 3 = *three or more*; scale (α between .70 and .80). Exploratory factor analysis supported 2-factor structures for the measure.

PTSD symptoms were measured using the PTSD Symptom Scale-Self Report (PSS-SR; Foa, Riggs, Dancu, & Rothbaum, 1993), a 17-item scale reflecting frequency and severity of PTSD symptoms according to the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., *DSM-IV*; American Psychiatric Association, 1994) in the past month using a 0 = *never/rarely* to 3 = *almost always* scale. We used symptom cluster severity scores (α per cluster between .77 and .87 and correlation between clusters between .56 and .72).

Procedure

Trauma recollections were obtained in a 30-minute open-ended standardized interview asking participants to freely recall their personal experiences escaping from the attacks prompted by the instruction: "I would like you to speak about what you went through on September 11; your experiences, thoughts and feelings on that day" (Dekel & Bonanno, 2013). Subsequently, participants were asked to report their level of distress during the interview from 1 = *none* to 7 = *very strong*.

Salivary cortisol was collected 2 minutes before and after the 30-minute interview using Salivette collection devices (Sarstedt, Newton, NC) and stored at -20°C. Salivary cortisol was analyzed by a high-sensitivity cortisol enzyme immunoassay (Salimetrics, State College, PA) as described in Dozier et al. (2006). Intra-assay (2.20%) and interassay (5.70%) variability and pH of the assays were within the range of precision expected by Salimetrics. Cortisol concentration was measured by optical density of duplicate samples using a Dynex spectrophotometer.

Data Analysis

Sex differences in study measures were analyzed using independent t test and χ^2 test for independence of measures. Cortisol responsivity (i.e., cortisol elevation) was examined using hierarchical regression analyses. Baseline (preinterview) cortisol level was entered on the first step to measure cortisol elevation. Next, we entered sex (female −1, male 1) and severity of PTSD symptom clusters. In a third step, we added the interactions between sex and the PTSD clusters. Finally, we added the interactions between baseline cortisol level and the clusters. Significant interactions were probed using Preacher, Curran, and Bauer's (2006) method.

Because Kolmogorov-Smirnov tests revealed that the distribution of cortisol concentration was skewed, analyses were conducted on the natural log of cortisol concentration scores.

Results

At Times 1 and 2, 16.0% ($n = 13$) and 13.5% ($n = 7$) of the sample, respectively, met PTSD symptoms criteria, (i.e., reported *often* or *always* of at least one reexperiencing, three avoidance, and two hyperarousal symptoms). Importantly, women had higher levels of PTSD symptoms than men 7 months after the attacks, and reported more distress during the attacks and following their recollections, although cortisol levels postinterview were lower than in men (Tables 1 and 2).

Baseline cortisol levels significantly predicted postinterview cortisol levels (Table 3). With baseline cortisol controlled, postinterview cortisol was greater in men than women and associated positively with PTSD reexperiencing symptoms and negatively with PTSD avoidance symptoms. These effects were qualified, however, by sex. For men, postinterview cortisol was greater at higher reexperiencing, $B = 0.75$, $p < .001$, and lower avoidance, $B = -0.98$, $p < .001$, whereas for women reexperiencing ($B = 0.16$, $p = .164$) and avoidance ($B = -0.11$, $p = .331$) were not significantly associated with postinterview cortisol. The same pattern of results was found when conducting an analysis with residual scores.

As in Time 1, the analyses revealed that baseline cortisol levels predicted Time 2 postinterview cortisol; men had higher elevation in their postinterview cortisol level than women; and reexperiencing symptoms severity was correlated with greater postinterview cortisol levels. These effects were again qualified by a significant interaction between sex and reexperiencing symptoms. For men, reexperiencing predicted greater postinterview cortisol, $B = 0.57$, $p < .001$; for women, reexperiencing symptoms were not significantly associated with postinterview cortisol ($B = 0.07$, $p = .721$).

Discussion

Our study demonstrated that among high-exposure WTC survivors, PTSD symptoms in men predicted cortisol response following recollections of their 9/11 experiences. At both 7 and 18 months post-9/11, men's postinterview cortisol levels were greater with more reexperiencing and fewer avoidance symptoms, whereas women's postinterview cortisol levels were relatively unchanged and unrelated to PTSD symptoms, even though they reported more PTSD at 7 months than men did.

Table 1
Sex Differences of Measures With Means and Standard Deviations

	7 Months				
	Men ($n = 32$)		Women ($n = 29$)		
Variable	*M*	*SD*	*M*	*SD*	*t*(59)
Baseline cortisol level (μg/dl)[a]	0.16	0.13	0.12	0.10	1.10
Postinterview cortisol level (μg/dl)[a]	0.24	0.24	0.09	0.06	3.15**
PTSD reexperiencing	0.90	1.21	1.81	1.69	−2.45*
PTSD avoidance	1.31	1.69	2.31	2.15	−2.01*
PTSD hyperarousal	1.17	1.36	2.44	1.64	−3.25**
Self-report distress	2.88	1.12	4.20	1.04	−4.30***
Self-report depression	10.16	7.04	14.17	7.36	−2.17*
Subjective exposure	1.97	0.83	2.66	0.96	−2.96**
Objective exposure	0.93	0.88	0.69	0.75	1.15
Time of assessment (hr:min)	15:17		14:32		0.89

Note. PTSD = posttraumatic stress disorder.
[a]Salivary cortisol levels in both men and women are within the range of those expected from the salimetric immunoassay.
*$p < .05$. **$p < .01$. ***$p < .001$.

Our findings suggesting reexperiencing symptoms contribute to enhancing cortisol levels (in men) are quite intuitive. Voluntary trauma recollection is expected to activate intrusive recollection, leading to an amplification of the stress response. Avoidance might buffer cortisol elevation in men. Horowitz (1986) postulated that avoidance serves to cognitively process and integrate trauma-related experiences during periods of intrusion. Trauma avoidance might operate as an adaptive coping mechanism in men by regulating cortisol secretion during active recall of the trauma performed in our study.

Women had flattened cortisol responsiveness to trauma recollection, but greater PTSD symptoms compared to men. Studies have generally found that low cortisol levels shortly after trauma are associated with increased risk for PTSD (Morris et al., 2012). However, cortisol responsiveness and PTSD symptoms were not correlated in women, suggesting a dysfunction in HPA regulation with PTSD symptomology in women, but not men. This idea is supported by studies that generally find low cortisol levels shortly after trauma are associated with increased risk for PTSD (Morris et al., 2012). Furthermore, women with PTSD

Table 2
Sex Differences of Measures With Means and Standard Deviations

	18 Months				
	Men ($n = 20$)		Women ($n = 29$)		
Variable	*M*	*SD*	*M*	*SD*	*t*(47)
Baseline cortisol level (μg/dl)[a]	0.15	0.11	0.20	0.16	−1.00
Postinterview cortisol level (μg/dl)[a]	0.16	0.11	0.16	0.14	0.03
PTSD reexperiencing	0.21	0.56	0.97	1.40	−2.83**
PTSD avoidance	0.77	1.64	1.72	2.16	−1.94
PTSD hyperarousal	0.90	1.50	2.09	1.65	−2.95**
Self-report distress	2.82	2.02	4.47	1.54	−2.84**
Self-report depression	10.66	6.93	13.96	6.25	−1.78
Subjective exposure	2.25	0.89	2.50	0.93	−0.96
Objective exposure	1.00	1.09	0.76	0.84	0.88
Time of assessment (hr:min)	14:34		13:44		0.74

Note. PTSD = posttraumatic stress disorder.
[a]Salivary cortisol levels in both men and women are within the range of those expected from the salimetric immunoassay.
*$p < .05$. **$p < .01$. ***$p < .001$.

Table 3
Standardized Regression Coefficients for Predicting WTC Survivors' Cortisol Elevation Following the Interview by Sex and PTSD Symptom Clusters

	7 Months				18 Months			
Variable	*B*	*SE*	β	R^2	*B*	*SE*	β	R^2
Baseline cortisol level	0.77	0.10	.67***	.57***	0.83	0.10	.83***	.73***
Sex	0.44	0.08	.47***	.16***	0.28	0.08	.31***	.08*
PTSD reexperiencing	0.46	0.13	.54***		0.34	0.11	.38***	
PTSD avoidance	−0.54	0.12	−.63***		−0.11	0.10	−.13	
PTSD hyperarousal	0.09	0.12	.11		0.02	0.10	.03	
Reexperiencing × sex	0.27	0.12	.31*	.08**	0.28	0.11	.30*	.05*
Avoidance × sex	−0.43	0.12	−.49**		−0.08	0.11	−.09	
Hyperarousal × sex	0.21	0.12	.22		−0.11	0.10	−.13	
Reexperiencing × baseline cortisol	−0.18	0.12	−.16	.02	0.01	0.14	.01	.01
Avoidance × baseline cortisol	0.02	0.12	.02		−0.11	0.14	−.12	
Hyperarousal × baseline cortisol	0.19	0.13	.20		0.11	0.13	.15	

Note. WTC = World Trade Center; PTSD = posttraumatic stress disorder.
*$p < .05$. **$p < .01$. ***$p < .001$.

have lower basal cortisol levels compared with non-PTSD female control groups, but men with PTSD do not differ from non-PTSD male controls (Meewisse et al., 2007).

The differential clustering of PTSD symptoms associated with the altered cortisol response among the sexes raises possible biological mechanisms underlining differential susceptibility to PTSD. This might be due to altered sympathetic and noradrenergic systems mediating the stress response between the sexes (Olff, Langeland, Draijer, & Gersons, 2007), but other biological mechanisms are possible. Open recollection of traumatic events and association to other biological markers, as done here for cortisol, could be utilized in future research to gain insight into basic biological mechanisms underling sex differences in susceptibility to PTSD.

Several limitations in this study include only a single postinterview measure of cortisol, and no information on menstrual cycle, oral contraceptive use, medications, smoking, eating, and physical exercise just before the interview. Although we measured PTSD symptoms, whether a participant had clinically diagnosed PTSD was not asked. The small sample size, although commonly used in studies like ours, raises the possibility of sample bias. No corrections for multiple testing might have overlooked significant statistical relationships. There is a risk of nonrandom attrition with measurements separated by 11 months. Nevertheless, the results were quite robust and consistent over Time 1 and Time 2.

In summary, this study demonstrates an HPA-axis response correlates with PTSD symptoms in men when confronted by trauma-reminders of the 9/11 WTC terrorist attacks. Importantly, trauma recollection, even 18 months posttrauma, might be an important protocol to assess biological mechanisms of prolonged effects of trauma. Our findings underscore the complexity of the cortisol response associated with PTSD symptoms with respect to sex and symptom clusters, which clearly warrant more research to identify additional factors and their interactions.

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