Published in final edited form as:

J Anxiety Disord. 2016 May ; 40: 37–43. doi:10.1016/j.janxdis.2016.04.003.

ELEVATED CORTISOL IN HEALTHY FEMALE ADOLESCENT OFFSPRING OF MOTHERS WITH POSTTRAUMATIC STRESS DISORDER

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Abstract

Offspring with maternal PTSD are at increased risk of developing PTSD themselves. Alterations in the hypothalamus-pituitary-adrenal (HPA) axis may play a role and have been noted in offspring, although evidence is mostly from adult offspring with PTSD symptoms themselves. The present study of adolescent girls ($N=472$) and their mothers ($n = 18$ with lifetime PTSD versus $n = 454$ with no PTSD) sought to determine whether healthy, non-affected offspring of mothers with PTSD would exhibit altered HPA axis function. Saliva samples were collected from the adolescent girls at waking, 30 minutes after waking, and 8 pm on 3 consecutive days. Offspring whose mothers were diagnosed with PTSD demonstrated higher cortisol awakening response (CAR; Cohen's $d = .58$) and greater total cortisol output (Cohen's $d = .62$). In this preliminary study, higher cortisol levels during adolescence among offspring of mothers with PTSD may index a vulnerability in these at-risk youth.

Keywords

Posttraumatic stress disorder; Maternal PTSD; Mother-daughter dyads; Cortisol; Adolescents; HPA axis

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Conflict of interest
None.

1. Introduction

Offspring of parents with posttraumatic stress disorder (PTSD), particularly maternal PTSD, are at increased risk of developing psychopathology in general and PTSD in particular (Chemtob & Carlson, 2004; Enlow et al., 2011; Leen-Feldner et al., 2013). For example, adolescent offspring of Cambodian refugees were approximately five times more likely to have PTSD when their mother had the disorder, whereas effects from paternal PTSD were not evident (Sack, Clarke, & Seeley, 1995).

Increased risk in offspring may be associated with alterations observed in the disorder. Notably, PTSD has been associated with altered hypothalamic-pituitary-adrenal (HPA) axis activity. In both adults and adolescents with PTSD, studies reported they had *lower* basal cortisol levels (e.g., Horn, Pietrzak, Corsi-travali, & Neumeister, 2014; Keeshin, Strawn, Out, Granger, & Putnam, 2014; King, Mandansky, King, Fletcher, & Brewer, 2001; Wessa, Rohleder, Kirschbaum, & Flor, 2006), exaggerated suppression of cortisol in response to dexamethasone (for review, see de Kloet et al., 2006; de Kloet et al., 2007), and greater density and sensitivity of glucocorticoid receptor (GR; Heim & Nemeroff, 2009; Labonte, Azoulay, Yerko, Turecki, & Brunet, 2014). However, not all studies have been consistent, with some finding *higher* basal cortisol levels associated with PTSD (Carrión et al., 2002; Cicchetti & Rogosch, 2001; Lindley, Carlson, & Benoit, 2004; Pfeffer, Altemus, Heo, & Jiang, 2007; Simsek, Uysal, Kaplan, Yuksel, & Aktas, 2015; Young & Breslau, 2004;) and *lower* GR density (e.g., Gotovac, K., Sabioncello, Berki, & Dekaris, 2003).

Some evidence suggests altered HPA axis activity may represent a pre-existing vulnerability to the disorder (for review, see van Zuiden, Kavelaars, Geuze, Olff, & Heijnen, 2013). A number of studies have investigated whether offspring of those with PTSD have evidence of altered HPA axis activity (Bader et al., 2014; Danielson, Hankin, & Badanes, 2015; Lehrner et al., 2014; Perroud et al., 2014; Yehuda et al., 2005; 2007a; 2007b; 2014). Similar to what is seen in PTSD, the majority of these studies found lower basal cortisol levels (Bader et al., 2014; Perroud et al., 2014; Yehuda et al., 2007b) and enhanced cortisol suppression following dexamethasone administration in the offspring (Lehrner et al., 2014; Yehuda et al., 2007a). However, most offspring studies were conducted in adults and most offspring had PTSD symptoms themselves, making it less clear whether the altered HPA activity axis existed earlier in developmental.

Two studies investigated the HPA axis activity in young, non-affected offspring with maternal PTSD (Danielson et al., 2015; Yehuda et al., 2005). The first study examined basal cortisol levels in infants of women who were pregnant during the World Trade Center attacks (Yehuda et al., 2005). Saliva samples from both mothers and their babies were collected by the mother at two times: wake-up time and bedtime. Infant offspring of mothers who developed PTSD symptoms had lower cortisol levels at both times in the first year of life compared to offspring of mothers who did not develop PTSD symptoms (Yehuda et al., 2005). Effects were only apparent for infants born to mothers exposed to the attack in the third trimester of pregnancy (Yehuda et al., 2005). The second study found attenuated

cortisol reactivity to acute stress in the laboratory among non-affected adolescents of mothers with PTSD (Danielson et al., 2015).

Thus, previous studies have not evaluated whether similar effects for adolescent offspring of maternal PTSD exist for cortisol awakening response (CAR; Pruessner et al., 1997). CAR is particularly important since it is distinct from other indices of circadian cortisol secretion (Wilhelm, Born, Kudielka, Schlotz, & Wüst, 2007; for review, see Stalder et al., 2016) and is less influenced by stressful events throughout the day (for review, see Chida & Steptoe, 2009). Moreover, CAR also differs from cortisol reactivity to an acute stress task, the index assessed in the only previous study of adolescent offspring of parents with PTSD (Danielson et al., 2015). A recent review has suggested cortisol measured through CAR is a better index of basal HPA axis activity compared to such laboratory-based paradigms (Stalder et al., 2016).

Given this background, the present study sought to compare basal cortisol activity, including CAR, in healthy (non-PTSD) female adolescent offspring with and without maternal PTSD. Offspring studies reviewed above are consistent with a hypothesis of lower basal HPA axis activity in the adolescent offspring of those with maternal PTSD. Exploratory analyses considered whether effects would differ across distinct indices of basal cortisol activity.

2. Methods

2.1 Participants

A total of 550 adolescent girls between the ages of 13.5 and 15.5 ($M_{\text{age}} = 14.39$, $SD = .63$) and one of their parents originally enrolled in an ongoing longitudinal study of adolescents, the Adolescent Development of Emotions and Personality Traits (ADEPT) project. In total, 78 participants were excluded because (1.) diagnostic history was not collected from the biological mother ($n = 40$), (2.) the biological mother's diagnostic history for PTSD was ambiguous (i.e., subsyndromal PTSD; $n = 16$), and (3.) the daughter's cortisol sample was deemed an outlier ($n = 22$; see below for details on outlier analysis). Of the remaining 472 participants in the present analysis, 18 mothers were diagnosed with lifetime PTSD; of those, eight of them were also diagnosed with current PTSD. The ethnic and racial composition of the adolescents was 81.6% non-Hispanic Caucasian, and 86% of the adolescents' mothers had a bachelor's degree or greater. Participants were recruited from the community through school events, online classifieds, word-of-mouth referral, and a commercial mailing list of homes in the area. Families were financially compensated for their participation. Inclusion criteria into the ADEPT project were ability to read and understand questionnaires and participation of at least one biological parent. To ensure a healthy sample, exclusion criteria were medication use (i.e., anti-inflammatory drugs) or disease that may impact HPA axis activities, lifetime history of major depressive disorder (MDD), dysthymia, or intellectual disabilities. Lifetime history of MDD or dysthymia was determined using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (KSADS; Kaufman et al., 1997). This clinical interview was administered by trained diagnostic interviewers who were under close supervision of clinical psychologists (R.K., G.P., and D.K.). None of the adolescents in the

final sample met criteria for a diagnosis of PTSD themselves based on KSADS. The study was approved by the Stony Brook University Institutional Review Board.

2.2 Clinical assessment

Parental trauma exposure and the history of psychopathology in mothers was assessed via the *Structured Clinical Interview for DSM-IV Disorders* (SCID; First, Spitzer, Gibbon, & Williams, 1997). All SCID interviews were recorded. PTSD diagnosis was operationalized as meeting the *DSM-IV* diagnostic criteria for PTSD. Inter-rater reliability of PTSD diagnosis from 25 SCID recordings was excellent ($\kappa = .87$).

Adolescent depression and anxiety symptoms were assessed with the *Inventory of Depression and Anxiety Symptoms* (IDAS-II; Watson et al., 2012). The IDAS-II is a 99-item self-report measure that yields scores on 19 symptom scales (Watson et al., 2012). The General Depression, Traumatic Intrusions, and Traumatic Avoidance subscales were the focus of the present study, as the latter two scales were designed to measure PTSD core symptoms dimensionally in diverse populations and were validated for adults and adolescents (Watson et al., 2007; 2012). The General Depression scale was designed to capture broad, non-specific psychological distress-related symptoms shared by depression and anxiety disorders (Watson et al., 2007). Participants were asked to rate their experience with each symptom in the last month on a 5-point Likert scale from 1 (*not at all*) to 5 (*extremely*). Scales had excellent internal consistency (α 's > .79).

2.3 Biological assessment

2.3.1 Saliva collection and cortisol assay—Saliva samples were collected with Salivette sampling devices (Salimetrics, Inc., the United States of America) from all adolescents. Samples were collected on three days at home. To capture peak cortisol values in the early morning in response to waking and total cortisol output, saliva samples were collected upon waking, 30 minutes after waking, and at 8 pm. Participants were asked to keep a diary of their waking time, the time of each cortisol sample collection, and any illness symptoms on a given sample collection day. Collection times were verified using a MEMSCap™ device that recorded when each saliva swab was taken from a storage container. Adolescents were instructed to store samples in the freezer before they delivered them to the lab. After their return to the lab, saliva samples were placed in a -80°C freezer. Experimenters followed standard laboratory safety procedures for handling saliva samples. Salivary cortisol levels were determined by a time-resolved immuno-assay with fluorescence detection (DELFI). An average coefficient of variation (CV) of duplicate assays of each sample was calculated. Any CV values greater than 12% for cortisol values greater than 5 nmol/L were reanalyzed, as were any values < 100 nmol/L. The average of the two assay values was used for analysis.

2.3.2 Adolescent body mass index (BMI) and pubertal stage—Adolescent BMI was calculated based on self-reported height and weight. Pubertal stage was assessed with two measures. The Pubertal Development Scale (PDS; Petersen et al., 1988) is a self-report measure that includes five indices of pubertal growth: growth in height, body hair, skin changes, and breast development on a 4-point Likert-type scale ranging from 1 (*not yet*

started) to 4 (*seems complete*), as well as menarche on a *yes* or *no* scale. Adolescents were also asked to complete a self-report version of Tanner Scale (Morris & Udry, 1980), which asks participants to rate pubic hair and breast development based on line drawings of the five puberty stages. In the present study, the pubertal stage was operationalized as a sum of two z-scores from the PDS and Tanner scale.

2.4 Procedure

Informed parental consent and adolescent assent were obtained during a lab visit. Adolescent participants completed the KSADS, IDAS-II, as well as the measurements of BMI and pubertal status. Parents provided demographic information and completed the SCID during this lab visit. Prior to the visit, participants received detailed instructions (verbal, written, and video) on how to collect three saliva samples a day for three consecutive days, keep a diary, and freeze samples prior to their first lab visit. Adherence to instructions was checked during the visit (diary, MEMS data) and generally was very high, but if significant problems or non-adherence were present, participants were given additional training and asked to retake samples in days after the visit. Both adolescents and their parents were compensated for participation in the study, including a bonus for documented adherence to cortisol collection instructions.

2.5 Analytic plan

Prior to testing hypotheses, cortisol data were prepared, scored and screened for outliers. Outliers for any given sample were defined as cortisol standardized scores > 3 standard deviations from the mean of the collected cortisol values. In such cases, the sample was removed, but the other samples for the given participant were retained. Other exclusion criteria were non-adherence to saliva sampling procedures. Non-adherence included any samples taken when participants were ill, when they failed to follow guidelines regarding eating or drinking around the time of sampling, or when samples were contaminated with blood (e.g., from cuts in the mouth). In addition, the saliva sample collection time recorded by participants were checked against MEMSCap™ times. Any saliva samples collected outside the instructed time were regarded as non-adherent and removed. In all cases, if a sample was deemed non-adherent, only the specific sample in question, not the entire 9 samples for that participant, was removed from analyses. However, there were 22 adolescents whose entire 9 samples were deemed non-adherent for one or many of the various reasons listed and their entire record was removed.

In order to capture cortisol changes over a day and summarize the information obtained from repeated measurements, each day's raw cortisol data were used to create four cortisol parameters: the area under the curve (AUC) for all three samples reflecting total volume of daily cortisol circulation (Pruessner et al., 2003), AUC ground for the two morning samples only, the cortisol diurnal slope (Adam & Kumari, 2009), and the CAR (Pruessner et al., 1997). The CAR is defined as the increase in cortisol that occurs during the period between waking and 30-45 minutes after awakening (Pruessner et al., 1997). Cortisol values at each of the three sampling collection times (waking, 30 minute after waking, and evening) were also analyzed. Thus, a total of seven cortisol parameters were included in analyses. Prior to analysis, all seven cortisol parameters were adjusted for any time difference between the

corresponding sample collection times and target times. We estimated a regression model of cortisol level at a given collection point as a function of collection time, and adjusted cortisol levels at the target time for each participant by entering their observed cortisol level and collection time in the model. Values for adjusted cortisol parameters were then averaged across three days to obtain more reliable indices (Hellhammer et al., 2007).

We first compared background characteristics of the mothers and daughter between the maternal PTSD group ($n = 18$) and non-PTSD comparison group ($n = 454$). Given the small sample size in the maternal PTSD group, non-parametric Fishers exact tests were used to compare categorical variables and Mann-Whitney U tests were used for continuous variables. Mann-Whitney U tests were used to assess hypotheses related to the association of maternal PTSD with cortisol parameters. Primary analyses were repeated using hierarchical multiple regression to first control for mothers' age and the history of depression, as well as adolescent's age, BMI, pubertal stage, and clinical symptoms of PTSD and depression; all above-mentioned potential covariates were entered in step 1 and maternal PTSD status (PTSD vs. non-PTSD) was entered in step 2. The latter additional analyses were run to ensure any group differences were not due to covariates known to affect cortisol.

3. Results

3.1 Descriptives

Sample characteristics and comparisons between the offspring with maternal PTSD ($n = 18$) and the offspring without maternal PTSD ($n = 454$) are presented in Table 1. Participating mothers' history of depression and offspring's race/ethnicity significantly differed between maternal PTSD and comparison group ($p < .05$). However, groups did not differ in participating mothers' age ($p = .42$), offspring's age ($p = .79$), BMI ($p = .73$), pubertal stage ($p = .79$), depressive symptoms ($p = .11$), traumatic intrusions symptoms ($p = .42$), traumatic avoidance symptoms ($p = .22$), or mothers' education levels ($p = .53$). Preliminary analysis showed that adolescents' age had a small association with CAR ($r = .12$, $p = .01$) and AUC ground of daily total cortisol secretion ($r = .10$, $p = .03$). However, adolescents' age was not related to other cortisol parameters ($p = .06 - .41$). Likewise, there was a small correlation between adolescents' pubertal stage and the cortisol evening sample ($r = .13$, $p = .01$), CAR ($r = .11$, $p = .02$), AUC ground of daily total cortisol secretion ($r = .09$, $p = .04$), and cortisol diurnal slope ($r = .11$, $p = .01$), but not other cortisol parameters ($p = .17 - .51$). There was no association between adolescents' BMI and any of the cortisol parameters ($p = .13 - .99$). Correlation analysis also showed that there was no association between adolescents' IDAS PTSD symptoms of intrusions and avoidance, and the cortisol parameters. ($p = .07 - .92$).

3.2 Association of maternal PTSD with cortisol of offspring

With respect to the primary hypothesis, Figure 1 depicts the mean salivary cortisol values of the two groups across the day, and Table 2 reports group differences for all cortisol parameters. There were significant group differences in four of the seven offspring cortisol parameters. Compared to offspring in the comparison group, adolescent offspring with maternal PTSD showed significantly higher CAR ($p = .01$) and other cortisol parameters in the morning as indicated by their 30-minute after waking cortisol values ($p < .01$), AUC

ground of morning cortisol secretion ($p = .01$), as well as greater cortisol circulation across the day as indexed by AUC ground of daily total cortisol secretion ($p = .01$). However, the other three cortisol parameters (i.e., waking cortisol values, evening cortisol values and diurnal slope) were not significantly different between the two groups ($p = .56$, $.71$, and $.73$, respectively). As shown in Table 3, all four of these cortisol markers remained associated with maternal PTSD after controlling for mothers' age, maternal history of depression, offspring's age, BMI, pubertal stage, offspring general depression, offspring PTSD symptoms, maternal PTSD status remained a significant predictor of CAR ($\beta = .13$, $p = .01$), 30-minute after waking cortisol values ($\beta = .14$, $p = .00$), AUC ground of morning cortisol secretion ($\beta = .13$, $p = .01$), and AUC ground of daily total cortisol secretion ($\beta = .13$, $p = .01$).

4. Discussion

To our knowledge, this is the first study to examine CAR in healthy female adolescent offspring of mothers who were diagnosed with lifetime PTSD. We found these high-risk offspring have *higher* CAR than offspring of mothers with no PTSD. This effect (higher CAR) may represent a pre-existing vulnerability for PTSD because the adolescents were not diagnosed with PTSD themselves. Although we could not test the predictive value of CAR (this requires a longitudinal follow-up), this interpretation is in the line with a previous study that reported higher urinary cortisol levels in youth who developed PTSD symptoms (Delahanty et al., 2005). Importantly, the effect in the present study was independent of several potential covariates (i.e., maternal diagnosis of MDD, clinical symptoms) and demographic or health variables (i.e., age, BMI, and pubertal stage).

Our findings diverge from studies that reported lower basal cortisol levels in adult offspring of mothers with PTSD, pattern similar to that reported in adults diagnosed with PTSD (for review, see Yehuda & Bierer, 2008). One explanation for this discrepancy is chronic PTSD may be associated with long-term alterations in the glucocorticoid system, especially in females, that are not yet present in adolescents. Speculatively, the present results may reflect a sensitive period of risk related to maternal PTSD: levels of cortisol may be higher during adolescence relative to controls, with higher cortisol levels contributing to what may later become glucocorticoid insensitivity and lower relative basal cortisol during adulthood. In this model, exposure to stress initially activates the HPA axis and leads to higher cortisol secretion in the vulnerable offspring, particularly during adolescence. As they move into adulthood, the effect of stress may persist and convert to lower cortisol secretion (Miller, Chen, & Zhou, 2007; Morris, Compas, & Garber, 2012).

Although speculative, higher basal HPA axis activity in the present study may be due to differences in stress exposure. Indeed, offspring of mothers with PTSD face increased and persistent stress during adolescence for several reasons (Brand et al., 2011). For instance, previously identified stressors associated with maternal PTSD include dysregulated mood (Leen-Feldner et al., 2013), problematic parenting behaviors (Leen-Feldner et al., 2011; Lehrner et al., 2014), and insecure attachment style (Yehuda et al., 2014), all of which may create conditions of chronic stress for offspring and contribute to alterations in glucocorticoid programming at early age (Kappeler & Meaney, 2010; Lehrner et al., 2014). Regardless of its source, persistently high cortisol secretions may eventually lead to an

imbalance in the numbers of mineralocorticoid receptor (MR) and GR, which further contribute to greater inhibitory activity of the HPA axis that may then be expressed as lower basal cortisol in adulthood (Kellner et al., 2009; Perroud et al., 2014). Previous findings have supported the alterations in these receptors showing adolescent offspring with maternal PTSD had higher MR levels and lower GR levels (Perroud et al., 2014).

Developmental animal models of chronic stress also provide support for this hypothesized trajectory of elevated cortisol in adolescence, but diminished cortisol in adulthood among those at highest risk for PTSD. Specifically, in adolescent rats exposed to chronic stress, corticosterone levels (total and free) were significantly higher than the levels in adult rats (Romeo et al., 2006; Romeo & McEwen, 2006). Once they reached adulthood, however, both male and female rats that were developmentally-exposed to chronic stressors exhibited blunted corticosterone responses to stress as adults (McCormick & Mathews, 2007). In humans, the developmental ramifications of early chronic stress are less understood, but subtle glucocorticoid dysregulation may not manifest until after the HPA axis is sufficiently developed (Spear, 2003).

The findings of the current study should be interpreted in light of limitations. First, the sample in this study consisted entirely of only mother-daughter dyads. Future studies of male adolescent offspring and offspring of paternal PTSD are needed. Second, only a small number of mothers in the current sample met full *DSM-IV* diagnostic criteria for PTSD. Despite this, the present study detected significant findings with moderate to large effects. In our study, we examined cortisol in a community-dwelling cohort, which enhances the generalizability of our results to the population at large. However, replication with a larger sample of high-risk offspring is important along with longitudinal research to evaluate how basal HPA axis activity changes in these at-risk youth over time. Third, the rate of maternal PTSD in the present study (i.e., 3.8%) is lower than that typically reported in epidemiological surveys (e.g., 11.7%, Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012), suggesting a healthier sample than would be representative of the general population, which is not surprising given that recruitment focused on healthy individuals. Fourth, participants in the maternal PTSD offspring group were less likely to be Caucasian, which may have contributed to effects. However, this possibility is unlikely given work showing lower basal cortisol levels in non-Caucasian youth (DeSantis et al., 2007). Fifth, maternal basal HPA axis activity was not assessed, which makes it difficult to confirm a direct link between PTSD and HPA axis alterations that have been observed in the literature (for review, see Yehuda & Bierer, 2008). Sixth, we lacked comprehensive data on history of trauma exposure in non-PTSD mothers and severity or type of offspring's own history of traumatic exposure. Thus, we could not examine whether either variable impacts cortisol (cf. Klaassens et al., 2012). Finally, the height and weight used to calculate BMI, as well as PTSD symptoms in adolescent offspring were measured through self-report, which may be prone to bias.

5. Conclusions

Despite limitations, the present study sheds light on the association between maternal PTSD and basal HPA axis activity in healthy adolescent offspring. Results underscore that even in

individuals at risk for PTSD, but who do not yet have the disorder, there is evidence of altered HPA axis activity. Such alterations may represent a vulnerability that predisposes these youth to increased risk for PTSD later in life.

Acknowledgement

This study was supported by National Institute of Mental Health grant MH093479 awarded to Roman Kotov. The funding source had no involvement in the production of this manuscript.

We gratefully thank all the adolescent participants and their parents for generously contributing their time and energy to the Adolescent Development of Emotions and Personality Traits (ADEPT) project. We also would like to thank all the research assistants and staff of the project for facilitating this study, especially Molly Gromatsky.

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Highlights

- Cortisol awakening response was measured in healthy adolescents with maternal PTSD
- Maternal PTSD is associated with higher cortisol in healthy adolescent offspring
- Altered cortisol may represent a vulnerability factor for PTSD in at-risk youth

Figure 1.

Adjusted mean salivary cortisol values for waking, 30-minutes after waking, and evening between offspring with maternal PTSD ($n = 18$) and the comparison group ($n = 454$). Error bars represent 95% confidence interval for the mean.

Table 1
Demographic and Clinical Characteristics for Maternal PTSD and Comparison Groups

	Maternal PTSD (<i>n</i> = 18)		Comparison group (<i>n</i> = 454)		Mann-Whitney <i>U</i> or Fisher's Exact Test	<i>p</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>		
Mothers' characteristics						
Age	44.28	6.84	46.63	4.32	<i>U</i> = 3633.50	.42
Bachelor degree or greater	78%		86%		$\chi^2(1) = 1.26$	.53
Lifetime MDD	67%		17%		<i>a</i>	.00
Adolescent characteristics						
Non-Hispanic Caucasian	61%		82%		<i>a</i>	.03
Age	14.36	.59	14.41	.62	<i>U</i> = 3937.50	.79
BMI	21.31	3.40	21.87	4.22	<i>U</i> = 3759.50	.73
Pubertal stage	.14	1.57	-.02	1.74	<i>U</i> = 3856.00	.79
General Depression	38.71	16.89	32.44	11.95	<i>U</i> = 3177.50	.11
Traumatic Intrusions	6.56	3.81	5.51	2.58	<i>U</i> = 3653.50	.42
Traumatic Avoidance	8.78	5.19	7.19	3.77	<i>U</i> = 3355.00	.22

Note. PTSD = Posttraumatic stress disorder; MDD = Major depressive disorder; BMI = Body mass index.

^a Fisher's Exact Test.

Table 2

Summary of Female Offspring Cortisol Parameters' Comparisons between Maternal PTSD Group and Comparison Group

Cortisol values (nmol/L)	Maternal PTSD (<i>n</i> = 18)		Comparison group (<i>n</i> = 454)		Mann-Whitney <i>U</i>	<i>p</i>	Cohen's <i>d</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>			
Waking Cortisol ^{ab}	7.91	3.54	7.34	3.54	<i>U</i> = 3752.00	.57	-
30-minute cortisol	19.06	4.84	15.25	6.07	<i>U</i> = 2401.00	.00	.63
Evening Cortisol	1.82	1.32	1.78	1.72	<i>U</i> = 3877.00	.71	-
CAR	11.15	4.57	7.91	5.59	<i>U</i> = 2572.00	.01	.58
AUC morning	6.94	1.88	5.71	2.09	<i>U</i> = 2655.00	.01	.59
Diurnal slope	-.45	.30	-.40	.28	<i>U</i> = 3892.00	.73	-
AUC daily	146.35	38.97	118.76	44.89	<i>U</i> = 2475.00	.01	.62

Note. PTSD = Posttraumatic stress disorder; CAR = Cortisol awakening response; AUC = Area under the curve.

^a All cortisol parameters are adjusted for the difference between the corresponding sample collection time and target times.

^b The skewness and kurtosis of all cortisol parameters are within reasonable ranges (cf. George & Mallery, 2010).

Hierarchical Multiple Regression on Cortisol Differences between Maternal PTSD and Comparison Group

Table 3

Predictor	30-minute cortisol		CAR		AUC morning		AUC daily	
	R ²	β	R ²	β	R ²	β	R ²	β
Step 1	.01		.02		.01		.02	
Mothers age		.07		.05		.07		.07
Mother's history of depression		-.07		-.07		-.05		-.06
Adolescents' age		.07		.08		.04		.08
Adolescents' BMI		-.01		.01		-.03		-.02
Adolescents' pubertal stage		.05		.09		.03		.09
Adolescents depression		.03		.07		-.00		.07
Adolescents intrusions		.01		.01		.01		-.03
Adolescents avoidance		-.01		.00		-.01		.02
Step 2	.02 ^{**}		.02 ^{**}		.01 ^{**}		.02 ^{**}	
Maternal PTSD		.14 ^{**}		.13 [*]		.13 [*]		.13 ^{**}

Note. PTSD = Posttraumatic stress disorder; CAR = Cortisol awakening response; AUC = Area under the curve.

*
p < .05

**
p < .01