Stress, Cortisol, and Externalizing Behavior in Adolescent Males: An Examination in the Context of Multisystemic Therapy

Julia C. Schechter · Patricia A. Brennan ·
Phillippe B. Cunningham · Sharon L. Foster ·
Elizabeth Whitmore

Published online: 16 February 2012
© Springer Science+Business Media, LLC 2012

Abstract Stress and hypothalamic–pituitary–adrenal (HPA) axis dysregulation have been associated with externalizing behavior in adolescence, but few studies have examined these factors in a treatment context. This study investigated the relationship between stress, cortisol, and externalizing behavior among 120 adolescent males (mean age=15) receiving Multisystemic Therapy (MST). To examine the differential relationship of cortisol with various types of stressors, self-report measures assessed lifetime stress, current episodic stress, and daily hassles. Morning and afternoon cortisol samples were collected to examine whether the relationship between stress and treatment outcome depended on the youth's biological stress levels. Regression analyses indicated that awakening cortisol levels moderated the relationship between daily hassles and externalizing behaviors at post-treatment.

More specifically, higher levels of daily hassles predicted worse outcomes only among adolescents with high levels of morning cortisol. In addition, lifetime stressors and afternoon measures of cortisol interacted to predict changes in caretaker reports of externalizing problems and youth arrests following treatment; lifetime stressors were positively associated with externalizing behavior when adolescents had low levels of afternoon cortisol. Implications for theory and future directions for evidence-based treatment are discussed.

Keywords Externalizing behaviors · Stress · Cortisol · Treatment · Adolescence

J. C. Schechter · P. A. Brennan
Department of Psychology, Emory University,
Atlanta, GA, USA

P. B. Cunningham
Department of Psychiatry and Behavioral Sciences,
Medical University of South Carolina,
Charleston, SC, USA

S. L. Foster
Alliant International University,
San Diego, CA, USA

E. Whitmore
Department of Psychiatry,
University of Colorado Denver School of Medicine,
Denver, CO, USA

J. C. Schechter (✉)
Emory Psychology Department,
36 Eagle Row,
Atlanta, GA 30322, USA
e-mail: jcschec@emory.edu

Serious externalizing behavior (e.g., aggression, substance abuse, delinquency) in adolescence is associated with significant deleterious short-term outcomes and long-term costs for the adolescents, their families and communities, and society overall (Cohen et al. 2010). Although certain types of interventions, particularly family-based interventions, have been well-established for treating externalizing behavior (Eyberg et al. 2008; Nock 2003; Williams and Chang 2000), even the most promising evidence-supported treatments have been shown to be effective for only about two-thirds of treated youth (Webster-Stratton and Hammond 1997). Clearly more research is needed to identify and address factors that may be associated with the differential effectiveness of evidence-based treatments. The goal of the current study was to address this issue by providing a better understanding of the role that stress-related risk factors play in treatment outcomes for youth receiving Multisystemic Therapy (MST), an intensive, evidence-based intervention for externalizing and antisocial behavior (Henggeler et al. 2009). Specifically, the aims of the current study were to

investigate how certain types of stress (i.e., lifetime stress, recent negative life stress, and daily hassles) and related biological factors (i.e., basal cortisol levels) are associated with treatment outcomes in evidence-based family treatment for adolescent males referred to treatment for externalizing behavior problems.

Multisystemic Therapy (MST) is based on the concept that behavior develops in the context of multiple environments, and that it is necessary to address the interaction between the child and these ecologies to change behavior (Henggeler et al. 2009). Therapists provide treatment according to an MST manual, and use a variety of evidence-based therapies (e.g., cognitive-behavioral therapy) and procedures (e.g., parent-training techniques) in an effort to reduce externalizing behavior (Eyberg et al. 2008; Henggeler et al. 2009). MST has been shown to be an efficacious treatment, reducing rearrest rates up to 70% in some studies (see Henggeler et al. 2009, for review), and has been deemed as either demonstrating effectiveness or showing great promise in curbing antisocial behavior by the United States Surgeon General (1999). However, relatively few studies to date have explored individual level factors that might predict outcome in the context of MST.

Stress is one such factor that warrants increased examination with regard to treatment outcome for youth with externalizing behavior problems. Multiple models address the relationship between stress and persistent externalizing behavior. The diathesis-stress model (Ingram and Luxton 2005) suggests that psychological disorders result from an interaction between individuals' biological or genetic predispositions and their environments. Thus, youth with biologically or genetically based vulnerability, such as HPA axis dysregulation, who are also exposed to chronic or acute environmental stressors, may present with more persistent psychopathology. In addition, some have suggested that early life stressors might program or sensitize the stress response system (Post 1992), leaving the individual more vulnerable to increases in behavioral and emotional problems in the face of later stressors (Cicchetti and Rogosch 2001; Gunnar et al. 2001; Willemen et al. 2008).

Indeed, research suggests that higher levels of stress are associated with protracted psychopathology that may be harder to modify with treatment. For example, Willemen and colleagues (2008) found that stressors occurring after referral and through their four-year longitudinal study were associated with slower recovery of internalizing problems. Similarly, Mathijssen et al. (1999) found that greater parent reports of their child's stressful life events in the past year predicted a lack of change in externalizing behavior post-treatment.

What is less clear is whether particular types of stressors differentially predict treatment response. To address this gap in the literature we examined associations between MST

treatment outcome (i.e., changes in externalizing behavior) and lifetime exposure to stress, recent episodic events, and daily hassles. Notably, the focus of MST is to reduce externalizing behaviors rather than to reduce stress. However, the intervention may target stress reduction in certain cases. For example, therapists may decide to employ empirically supported therapies that reduce stress (e.g., cognitive behavioral therapy) with certain individuals and their families when warranted.

In the current study, lifetime stress was defined as exposure to major life events (e.g., death of an immediate family member, physical or sexual abuse, etc.) from childhood through adolescence. In contrast, episodic, current life stress was defined as recent stressful events (e.g., family move, parent change in employment, etc.) that occurred within the past 30 days, and that the youth perceived as negatively impacting his life. Finally, daily hassles were defined as frustrating demands and stressors that occur during everyday interactions between individuals and their environment (e.g., noisy neighborhoods, peer pressure, etc.). As compared to other stressors, daily hassles occur more regularly and have less readily identifiable beginnings or endings.

We also examined a physiological measure of stress—cortisol, a hormone produced by the hypothalamic–pituitary–adrenal (HPA) axis, which is a central component in the body's stress response system. Under non-stressful conditions, the HPA axis follows a normal circadian rhythm with highest levels reached in the morning and a slow decline throughout the day. When stressed, cortisol levels increase in order to best prepare the organism to deal with the impending stressor (Sapolsky 1994).

Lower levels of basal cortisol have often been found among individuals who engage in externalizing behavior (Alink et al. 2008; McBurnett et al. 2000; Oosterlaan et al. 2005; Shoal et al. 2003). For example, Oosterlaan et al. (2005) found that lower levels of basal cortisol (collected between 10:00 AM and 2:25 PM) were related to higher rates of conduct disorder symptoms in youth. Similarly, Popma et al. (2007) found lower levels of cortisol during the awakening response (the peak occurring within an hour of awakening) in minors with disruptive behavior disorders.

However, a recent review suggests that the association between cortisol and aggressive behavior is less clear than previously thought (Hawes et al. 2009). For example, Van Bokhoven et al. (2005) found a positive relationship between morning basal cortisol levels and aggressive behavior in longitudinal studies with adolescent boys, whereas several other studies have found no link between basal cortisol and disruptive behaviors (Alink et al. 2008; Scerbo and Kolko 1994; Van Goozen et al. 2000b).

These mixed results could be explained by examining possible moderating influences on the relationship between cortisol and externalizing behaviors. For example, time of

day (as it impacts the diurnal rhythm of cortisol) or psychosocial context might moderate the relationship between basal cortisol and externalizing behavior. Murray-Close et al. (2008) found that higher levels of cortisol in the morning and lower levels of cortisol in the afternoon were associated with physical aggression, while lower cortisol levels in the morning and little change in cortisol levels throughout the day were associated with relational aggression. Cicchetti and Rogosch (2001) also found differential relationships between morning and afternoon basal cortisol levels and child behavior, such that lower morning cortisol and a flat diurnal pattern were related to increased externalizing behaviors, whereas a rise in cortisol levels throughout the day was related to comorbid internalizing and externalizing behaviors. In addition, Murray-Close et al. (2008) found that the association between cortisol dysregulation and externalizing behavior was moderated by a history of maltreatment, such that antisocial youth who had not experienced lifetime stress in the form of maltreatment had greater levels of cortisol dysregulation than their maltreated counterparts.

Only one study to date has looked at cortisol and externalizing behavior changes in treatment. Van de Wiel et al. (2004) examined boys, ages 8–13, in treatment for disruptive behavior disorders and found that lower cortisol in response to an experimentally-induced stressor was related to increased levels of aggression post-treatment. These results and the divergent findings in the literature suggest that further investigation of cortisol as a predictor of treatment response for externalizing boys is warranted.

Like Van de Wiel et al.'s (2004) investigation, the current study focused on males. Our study focused on males because cortisol-behavior and cortisol-stress associations have been found to differ by gender (Kirschbaum et al. 1992; Tout et al. 1998). Some research has indicated that boys have lower basal cortisol levels and exhibit a greater cortisol response than girls (Jessop and Turner-Cobb 2008; Kudielka and Kirschbaum 2005). For example, Kirschbaum and colleagues (1992) observed that men's cortisol levels were twice that of women's when undergoing a laboratory stressor task, and also increased in anticipation of a stressor, while cortisol concentrations in women decreased or were unchanged. In addition, gender has been shown to be a moderator in treatment outcome for behavior problems, such that girls may respond better to parent-training interventions than boys (Lavigne et al. 2007). Given these variations as well as our limited female sample size ($n=64$), the current study only examined treatment outcomes in a sample of males.

Because stress occurring during treatment has been found to predict poor treatment outcome (Mathijssen et al. 1999; Willemen et al. 2008), we hypothesized that stress and HPA axis dysregulation (both at awakening and in the afternoon) would predict treatment response, such that increased levels

of stress and HPA axis dysregulation early in treatment would predict fewer reductions in externalizing behavior in response to MST treatment. In light of past studies suggesting that cortisol measured at different times of the day may be differentially related to both stressful life events (Bevans et al. 2008) and externalizing behaviors (Cicchetti and Rogosch 2001; Shirtcliff et al. 2005; Sondejker et al. 2007), we examined cortisol levels assessed at two different times of the day, and explored different types of psychosocial stress as a potential moderator of the cortisol and externalizing behavior relationship.

Method

Participants

Data for this study were collected as part of a larger longitudinal evaluation of MST in an effectiveness context using "real-world" MST providers. The current sample included 120 males ages 12 to 18 with a mean age of 15.47 ($SD=1.30$) years. The sample was 46% European American, 26% Latino American, 23% African American, and 5% Asian, Native American, or Pacific Islander. Participants were recruited from four licensed MST provider agencies in Denver, Colorado. Socioeconomic status (SES) was calculated using the widely used Hollingshead SES scale (Hollingshead 1975), which takes into account parental education and occupation. The mean Hollingshead score was 30.05 ($SD=11.13$), indicating that most of the sample fell into the lower middle class category.

Inclusion criteria included: (a) male youth, aged 12 to 18 years; (b) referral for MST by social service agencies, juvenile justice agencies, or juvenile and family courts, due to crimes against another person, property offenses, substance abuse, or other externalizing behavior problems; (c) availability to participate in current MST treatment; and (d) living within the caregiver's home for at least one month prior to treatment, with no immediate plan for the youth to live elsewhere. Informed consent was obtained from the caregiver, and consent or assent was obtained from the youth participant using procedures approved by the Institutional Review Boards at the University of Colorado Denver, the Medical University of South Carolina, Alliant International University, and Emory University.

Design and Procedures

Youth, family, and therapist variables were examined at four assessment points during the course of treatment: early in treatment (T1), two mid-treatment assessments, and immediate post-treatment (T4). For purposes of this study, only T1 and T4 time periods were examined: stress, HPA axis

dysregulation, and externalizing behavior at pretreatment were measured at T1 as predictors of immediate treatment outcome at T4.

Families were referred to the study at the outset of MST treatment. An initial family interview was then scheduled in the home at the family's earliest convenience. At this interview, caregivers completed measures of behavior problems exhibited by their child during the 30 days prior to beginning treatment. Youth participants completed a questionnaire concerning lifetime stress and provided a saliva sample for the assessment of afternoon basal cortisol. On a separate day early in treatment, a research assistant returned to the home to collect an awakening cortisol sample and youth participants completed self-report questionnaires to measure current episodic stressors and daily hassles. Both of these meetings (i.e., the family interview and the morning cortisol collection) were completed early in treatment and represent T1.

All families were treated with MST. Because the purpose of the research was to examine factors related to the course of treatment within a well-established evidence-based therapy as delivered in community settings, and because the superiority of MST to treatment-as-usual has been indicated in numerous randomized controlled trials (see Henggeler et al. 2009, for review), a control group was not included. The duration of treatment was consistent with MST program practices and recommendations. Therapists carried low caseloads and received supervision and consultation following standard MST protocols, consistent with requirements for treatment sites to be licensed MST providers. Following treatment termination, caregivers completed questionnaires of current levels of externalizing problems in the youth. Official arrest records were also gathered from the criminal justice system in Colorado to assess pre- and post-treatment arrests.

Cortisol Collection Levels of cortisol secretion were measured on two separate days, once during the afternoon hours (between 12:00 PM and 5:00 P.M.) during the initial family assessment interview, and once (approximately 1 to 2 weeks later) at awakening on a non-school day (typically Saturday morning). Morning saliva samples were collected by a research assistant who visited each youth at home and personally woke the youth to collect the sample (with caretaker oversight), thereby confirming the time and conditions under which each sample was obtained. Research assistants administered a health questionnaire at both the morning and afternoon cortisol collections to assess time of awakening (for the afternoon samples), number of hours slept the previous night, and the youth's average number of hours of sleep. The health questionnaire also asked youths to indicate the last time they had consumed caffeine, eaten, and/or exercised (in the preceding 2 hours). It also asked

whether and when, on the day of sample collection, they had used cigarettes, chewing tobacco, prescription medications, recreational drugs, antihistamines, steroids, or over-the-counter medications (sleep, cold/flu, allergy). Youth also completed the Petersen Pubertal Development Scale (Petersen et al. 1988) as part of the initial interview assessment.

Cortisol samples were obtained by having the participants spit directly into a plastic tube. Thirteen of the 120 samples were not obtained for the morning collection due to scheduling difficulties, and one afternoon sample could not be assayed due to an insufficient quantity of saliva. Once collected, saliva samples were stored in an adult size lunch box with an ice pack until they were frozen and stored at -20°C at the research lab immediately following the home visit for an average of 3 months before being sent overnight for assay at the Yerkes National Primate Research Lab at Emory University. Upon arrival to Yerkes, saliva samples were stored at -20°C until the day of assay. On the day of assay, samples were thawed, vortexed, and centrifuged to remove particulate matter. Salivary cortisol was assayed using an enzyme immunoassay kit (DSL, Webster, TX), catalogue number DSL-10-67100. This assay procedure has an analytical sensitivity of 0.10 mg/dl, using 25 ml of saliva. The intra- and inter-assay coefficient of variation is 4.1 and 7.2%, respectively. Each sample was assayed in duplicate. Duplicate test results were averaged, and duplicates with an error of more than 20% were re-assayed.

Measures

Treatment Outcome Treatment outcome was operationalized in two ways. First, we examined Child Behavior Checklist (CBCL; Achenbach 1991) Externalizing Behavior scores as reported by the caregiver at treatment completion, controlling for caregiver reported CBCL Externalizing Behavior scores early in treatment. The CBCL includes 113 behavioral items, and is used to measure an array of behavior problems in youth ages 2 to 18. This study looked specifically at the CBCL Externalizing raw scores (see Table 1), which have strong evidence of their reliability and validity (Achenbach 1991). Caregivers reported on the youth's behavior for the last 30 days at T4 and for the 30 days prior to the T1 assessment (i.e., retrospectively). Cronbach's alpha for the externalizing scales was 0.94 at both the T1 and T4 administrations.

The second measure of treatment outcome was youth arrest following the post-treatment family interview, statistically controlling for number of youth pretreatment arrests and the time window between conclusion of treatment and collection of follow-up arrest information (approximately 1 1/2 years post-treatment, range 5–30 months). Criminal

Table 1 Descriptive statistics

	<i>M (%)</i>	<i>SD</i>	Minimum	Maximum
Morning Cortisol	0.59	0.29	0.10	1.43
Afternoon Cortisol	0.39	0.23	0.10	1.35
Lifetime Stress	3.72	2.22	0	9.00
Negative Recent Events	1.43	2.02	0	11.00
Daily Hassles	8.80	8.66	0	55.00
Externalizing Scores at Pretreatment	21.18	13.37	1.00	51.00
Externalizing Scores at Post-Treatment	15.36	12.46	0	58.00
Number of Arrests at Pretreatment	2.51	2.91	0	16
Percent arrested at Post-Treatment	31%	n.a.	n.a.	n.a.

Arrested at post-treatment coded as dichotomous variable (1=yes, 0=no)

charge data were obtained through the Judicial Branch's Integrated Colorado Online Network database, a database used by the Colorado Department of Youth Corrections. This database was also used to identify any youth who may have been charged as an adult (i.e., if they aged into adulthood during the study). Descriptive statistics on the number of pretreatment and post-treatment arrests are presented in Table 1. Of the 120 males in this study, 37 (30.8%) were arrested post-treatment.

Stress Three measures of stress were used in this study: lifetime stress, recent negative life events, and daily hassles. Lifetime stress was measured using an 11-item questionnaire adapted and extended from a measure by Kessler and Magee (1993), and completed by the youth at treatment onset. The scale includes major negative life events such as, “Has your mother or your father died?” and “Did your parents have a lot of conflict in their marriage?” Youths were asked to indicate whether any of these events happened in their lifetime by circling “yes” or “no.” The total number of “yes” responses was tabulated as a measure of lifetime stress. The fairly low internal consistency of scores in the present sample ($KR-20=0.60$) is in line with internal consistencies observed in other studies that have used a similar measure (Brand et al. 2011). High internal consistency would not necessarily be expected; unlike most psychological constructs, external stressors are often the product of factors outside the individual, which would not necessarily be expected to co-occur.

Youth completed the Life Events Checklist (LEC) (Tiet et al. 2001) to measure recent episodic stressors. The Life Events Checklist asks youth to report on 26 stressors that might have occurred within the past 30 days and, if these events have occurred, to classify the events as “mostly good” or “mostly bad.” Items include life events such as, “experienced loss of a close friend,” “parental divorce,” and “started going to a new school.” In this study, items endorsed and rated as being “mostly bad” were totaled and used as a measure of recent negative life events. The LEC has been found to have adequate test-retest reliability and

acceptable validity (Brand and Johnson 1982; Tiet et al. 2001). In the current study, internal consistency for the negative recent life events total was $KR-20=0.88$.

Youth participants also completed the Urban Hassles Scale (Miller and Townsend 2005), a measure of daily hassles encountered by adolescents. This scale asks respondents to rate how often 32 events have happened to them in the past 30 days (0=never, 1=sometimes, 3=often, 4=very often). This measure was selected to capture the levels of daily hassles experienced in an urban environment, as the majority of the sample resided within a metropolitan area. Although the measure contains a number of items that are more common for adolescents growing up in urban environments (e.g., “nervous about gunshots at night,” “waiting for the bus near dirty, smelly bus stops”), the measure also contains items that can be experienced at any SES level (“made fun of for good grades,” “pressured for sex by boyfriend/girlfriend”). Responses are summed across items. The Urban Hassles Scale has adequate psychometric properties for adolescent respondents (Fischer and Corcoran 2006); in the current study, Cronbach’s alpha was 0.88.

Results

The primary aims of the study were to examine the associations between stress, cortisol and externalizing behavior changes in the context of treatment with MST. Partial correlation and regression techniques were used to assess the main effects and interactions of stress and cortisol in relation to post-treatment arrest and externalizing problems, controlling for pre-treatment arrests and existing levels of externalizing problems early in treatment, respectively.

Potential Confounds and Statistical Controls

Morning and afternoon cortisol levels were significantly associated with the time of collection (morning: $r=0.20$, $p=0.04$;

afternoon: $r=-0.27, p=0.004$). Thus, collection time was controlled for in all analyses examining cortisol levels. Number of hours slept the night before collection, as well as the use of cigarettes, chewing tobacco, antihistamines, marijuana, steroids, sleep medications, allergy medications, cold/flu medications, caffeine, and pubertal status were not significantly correlated with morning or afternoon cortisol levels. Neither prescription medication use at the beginning of treatment nor at the end of treatment was associated with cortisol levels, levels of externalizing behavior at pre- or post-treatment, or with youth arrest following treatment.

Youth age was not significantly correlated with externalizing behaviors, cortisol, or any of the stress measures. While these non-significant correlations are counter to some existing literature (Alink et al. 2008) it should be noted that the current sample was restricted to adolescents aged 12 to 18 years.

Given the relationship between externalizing behaviors early in treatment and SES in this sample, $r=0.22, p=0.02$, SES was controlled for in all analyses. Although the Urban Hassles Scale assesses a number of daily hassles that are common in low SES environments, SES and scores on the Urban Hassles Scale were not significantly related, $r=-0.06, p=0.53$. Lifetime Events ($r=0.10, p=0.29$) and Negative Recent Events ($r=-0.04, p=0.69$) were also not associated with SES.

Ethnicity was not related to caregiver reports of externalizing behavior outcomes; however, logistic regression did show that African American males were significantly less likely than other males to have a post-treatment arrest, Wald $X^2=3.91, p=0.048, OR=0.31$. Consequently, all analyses examining arrest as an outcome controlled for ethnicity (dummy coded as African American versus not).

To better approximate a normal distribution of scores for both morning and afternoon cortisol samples, outliers, defined as equal to or greater than three standard deviations above the mean, were removed ($n=2$ for morning cortisol; $n=4$ for afternoon cortisol).

Descriptive Statistics

Table 1 provides descriptive data for variables collected at T1 and T4. Table 2 presents the correlations between youth cortisol and stress measures. As can be seen in Table 2, early in treatment, daily hassles were positively correlated with negative recent life events and basal morning cortisol levels. Afternoon basal cortisol was not significantly correlated with morning cortisol levels (taken on a separate day) or any of the youth self-reported stress measures.

Although the current study did not contain a control group, a paired sample t -test revealed a significant decrease in externalizing behaviors from early in treatment to post-treatment, $t(109)=6.32, p<0.001$, within the MST treatment sample.

Hypothesis Testing

We hypothesized that stress and HPA axis dysregulation would predict treatment response, such that more self-reported stressors and greater HPA axis dysregulation early in treatment would be related to less reduction in externalizing behavior and a higher likelihood of arrest following MST treatment. This hypothesis received mixed support. A partial correlation controlling for SES and pretreatment levels of externalizing behaviors revealed a significant positive relationship between daily hassles and CBCL Externalizing scores at post-treatment, $r(99)=0.33, p=0.001$. A second partial correlation controlling for SES, time of cortisol collection, and externalizing behavior at pretreatment revealed a positive relationship between morning cortisol levels and externalizing behaviors after treatment, $r(90)=0.22, p=0.04$. Lifetime stress, recent negative life events, and afternoon cortisol levels were not significantly associated with CBCL Externalizing scores at post-treatment. In addition, none of the cortisol or stress measures administered early in treatment were significantly related to arrest during the year following termination.

Multiple regression analyses were used to test the moderating role of stress exposure on the relationship between basal cortisol and CBCL Externalizing scores at post-treatment. Both independent variables (cortisol and the stress measures) were centered prior to computing cortisol $\times$ stress interaction terms. In each analysis, SES, time of cortisol collection, and pretreatment externalizing scores were entered in Block 1, the centered cortisol and stress variables were entered in Block 2, and the interaction term was entered in Block 3.

No significant interactions involving negative recent life events emerged. However, analyses revealed a significant interaction between daily hassles and morning cortisol levels, $F_{\text{change}}(1, 88)=3.99, p=0.049, R^2 \text{ change}=0.02$ (see Table 3). Bootstrapping procedures confirmed the significant interaction, $b=0.60, p=0.006$. To further examine this interaction, we used the Aiken and West (1991) method for probing significant interactions between continuous predictors. In this procedure, simple slopes of the regression are plotted at different levels of the moderating variable. There was a positive association between morning cortisol and externalizing behavior for males one standard deviation above the mean on daily hassles, $b=8.66, t(95)=2.27, p=0.03$. No relationship was found between morning cortisol and externalizing problems for males at the mean, $b=3.49, t(95)=1.06, p=0.29$, or one standard deviation below the mean, $b=-1.69, t(95)=-0.37, p=0.71$, on the Urban Hassles Scale.

A significant interaction was also observed between youth self-reported lifetime stress and afternoon basal cortisol levels, $F_{\text{change}}(1, 83)=11.76, p<0.005, R^2 \text{ change}=$

Table 2 Pearson product moment correlations between basal cortisol and stress measures early in MST treatment (Time 1)

	1	2	3	4	5
1. Morning Basal Cortisol	—				
2. Afternoon Basal Cortisol	-0.08	—			
3. Lifetime Stress	0.09	0.00	—		
4. Negative Recent Events	0.13	-0.07	0.13	—	
5. Daily Hassles	0.25*	-0.03	0.17	0.39***	—

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$

0.08 (see Table 3). Bootstrapping procedures confirmed the significant interaction, $b = -7.34$, $p = 0.002$. Further examination of this interaction (Aiken and West 1991) revealed a significant negative relationship between afternoon cortisol and post-treatment externalizing behaviors for males with high levels of lifetime stress, $b = -20.17$, $t(90) = -2.53$, $p = 0.01$, and a significant positive relationship between afternoon cortisol and post-treatment externalizing behaviors for males with low levels of lifetime stress, $b = 12.71$, $t(90) = 2.06$, $p = 0.04$. No relationship was found between afternoon cortisol and youth externalizing problems at the mean level of lifetime stress, $b = -3.73$, $t(90) = -0.71$, $p = 0.48$.

Logistic regression analyses were used to investigate the moderating role of stress on the relationship between basal cortisol and whether the youth was arrested (yes/no) following treatment. Time (in months) between treatment end and retrieval of post-treatment arrest records, number of pretreatment arrests, SES, and ethnicity were entered in Block 1 as control variables; centered basal afternoon cortisol and stress variables were entered in Block 2; and the interaction term was entered in Block 3. As can be seen in Table 3, lifetime stress interacted with afternoon cortisol to predict the likelihood of post-treatment arrest, Wald $X^2 = 6.47$, $p = 0.01$, $OR = 0.27$. Bootstrapping procedures confirmed the significant interaction, $b = -1.34$, $p = 0.01$. Post-hoc logistic regression analyses using the Aiken and West (1991)

method indicated a significant, negative relationship between afternoon cortisol and post-treatment arrests for males with high levels of lifetime stress (one SD above the mean), Wald $X^2 = 5.12$, $p = 0.02$, $OR = 0.007$. No relationship was found between afternoon cortisol and externalizing problems at the mean level, Wald $X^2 = 1.96$, $p = 0.16$, $OR = 0.14$ or one standard deviation below the mean, Wald $X^2 = 0.55$, $p = 0.46$, $OR = 2.81$ of lifetime stress.

Discussion

These results add meaningful new findings to the current literature regarding treatment outcome for boys with externalizing behaviors. Past studies have noted the significant role of stress in both the levels of externalizing behaviors at pretreatment (Willemsen et al. 2008) and in treatment outcome (Mathijssen et al. 1999). However, to our knowledge, no study has parsed the various stressor categories to determine if certain types of stressors are more or less strongly associated with treatment outcome. Our findings suggest that either high or low cortisol levels may put boys at risk for poor treatment outcomes in the context of MST; however, the direction of the cortisol-externalizing problems relationship depended on the time of day that cortisol was collected and the types of stressors to which youth were

Table 3 Results of regression analyses examining cortisol reactivity as a moderator of the relationship between different types of stress and treatment outcome

	Caregiver Report of Externalizing Behavior Problems			Arrested Post-Treatment	
	R^2 Change	F Change	p	WALD X^2	p
Morning Cortisol					
Daily Hassles x Cortisol	0.02	3.99	0.04	1.44	0.23
Negative Recent Events x Cortisol	0.01	1.02	0.32	1.11	0.29
Lifetime Stress x Cortisol	0.01	1.07	0.30	0.01	0.94
Afternoon Cortisol					
Daily Hassles x Cortisol	0.00	0.21	0.65	2.88	0.09
Negative Recent Events x Cortisol	0.02	2.92	0.09	0.07	0.79
Lifetime Stress x Cortisol	0.08	11.76	0.001	6.47	0.01

Significant findings in bold font

exposed. More specifically, our results suggest that two types of male adolescent cortisol/stress profiles may confer challenges in a treatment context: higher levels of daily hassles (coupled with high cortisol), and higher levels of lifetime exposure to stress (coupled with low cortisol).

Males with higher morning cortisol levels who are also experiencing high rates of daily stressors may have worse outcomes for various reasons. They may be particularly hard to engage in therapy, perhaps because their stress response system is “maxed out,” leaving them with few additional resources for therapeutic change. In addition, research suggests that cortisol levels measured in the morning are more influenced by genetic factors, as opposed to environmental factors, than cortisol levels measured late in the day (Bartels et al. 2003). Based on the diathesis-stress model (Ingram and Luxton 2005) youth with a genetic predisposition to heightened stress responsiveness (i.e., those with higher morning cortisol) who are also consistently exposed to environmental stressors may have more persistent externalizing problems than those who do not have this genetic predisposition. These youth may show less responsiveness to interventions given their increased reactivity to concurrent daily stress. In a related vein, they may be more difficult to parent generally, and require greater environmental support on the part of parents, teachers, and peers to change their externalizing problems. Alternatively, the positive association between the Urban Hassles Scale scores and Externalizing Behavior scores at post-treatment could reflect a greater opportunity for boys to participate in such behaviors in more urban, disorganized environments. This suggests a particular need for therapeutic focus on monitoring these youths’ whereabouts as a way of decreasing externalizing behavior. Future investigations should examine these possible mechanisms to delineate which ones contribute to these youths’ reduced change following evidence-based treatment.

Youth with lower afternoon cortisol levels and higher levels of lifetime stress are a second group of adolescent males that may be more likely to continue to engage in externalizing behaviors despite treatment. Early life stress has been linked to hypoactivity in the HPA axis in both the animal and human literatures (Fries et al. 2005; van Goozen et al. 2000a). Perhaps early life stress has programmed the youth’s stress response system (Post 1992), and their trauma history and arousal levels combine to produce a lack of concern about behavioral consequences (Raine 1993), and/or a need to seek higher levels of stimulation in their current environments (Zuckerman 1978). Boys with lower arousal levels and higher levels of lifetime stress may compose a unique subset of adolescents that are more likely to continue to engage in antisocial behaviors following treatment because they do not care about consequences and/or because the low levels of stimulation are physiologically unpleasant.

This group also was the most likely to be arrested following treatment, consistent with the idea that these youths’ behavior may not be greatly influenced by normative patterns of consequences in the natural environment.

If replicated, particularly in the context of other evidence-based treatments for youth with externalizing behavior problems, these results would have implications for modifying MST and related treatment programs to better meet the needs of youth with these specific stress profiles. For example, in the case of boys with high cortisol levels who are experiencing high levels of daily hassles, therapists may need to intervene to build the youths’ skills for reducing arousal or reducing exposure to daily hassles during treatment, if possible. Likewise, therapists working with males who have experienced lifetime stress may want to assess whether these youth seem attuned to the negative consequences of their behavior or show reduced cortisol levels. Youth whose stress response systems are not activating in response to stress may benefit from therapeutic techniques designed to help them become more attuned to the effect of their externalizing behaviors and to punishment cues. Alternatively, caregivers of these boys may need therapist support and training to provide stronger, more salient, and more immediate consequences for these youths’ positive and negative behavior.

A meta-analysis exploring potential moderators of treatment success with children exhibiting disruptive disorders showed that families from lower SES backgrounds were the least responsive to treatment (Lundahl et al. 2006). The current study accounted for SES in the analyses and continued to find a significant relationship between daily stressors and externalizing behavior at post-treatment. In fact, SES was unrelated to scores on the Urban Hassles Scale, suggesting that different types of stressors may vary differentially with SES. Findings from the current study also suggest that perhaps the relationship between SES and behavior could be elucidated by examining the types of stressors encountered by youth in low SES environments, particularly as experienced by boys with high stress reactivity.

The current study has several limitations worth noting. For example, the sample did not include a non-treated control or comparison group, which weakens our ability to state unequivocally that observed changes in externalizing behavior were due to MST treatment, although similar changes have been noted in previous randomized controlled trials (Henggeler et al. 2009). However, the aim of the current study was to investigate factors that affect treatment outcome for a clinical sample receiving MST as customarily delivered, not to test the efficacy of MST per se. A second limitation was that this study did not separate out various types of aggressive acts (e.g., reactive versus proactive aggression) or the type of aggressor (e.g., early-onset versus late-onset). As previous studies have indicated that these

distinctions may be related to different patterns in cortisol levels (Loney et al. 2006; Lopez-Duran et al. 2009; Murray-Close et al. 2008), it is possible that these patterns could have influenced the current findings. A third potential concern is that afternoon cortisol was most often collected after school days, while morning cortisol was usually collected on a weekend (nonschool). Although research with adults suggests that basal cortisol levels do not differ from weekday to weekends (Kunz-Ebrecht et al. 2004), it is not clear whether or how this difference contributed to our findings. A final limitation is that cortisol samples were taken on separate days and diurnal patterns were not assessed. Thus, within-subject comparisons of changes in morning to afternoon basal cortisol levels could not be conducted.

Conclusion

The present study explored the relationship between stress, cortisol, and externalizing behavior in adolescent males in the context of a family- and evidence-based manualized treatment, MST. Daily hassles were significantly associated with worse treatment outcomes for adolescent males with higher levels of morning basal cortisol. Higher levels of lifetime stress were related to externalizing behavior problems and a higher likelihood of arrest for males with lower levels of afternoon basal cortisol levels. These results suggest that HPA axis dysregulation is associated with poor treatment outcome for youth who have experienced certain types of stressors. These findings add to the burgeoning literature exploring the complicated relationship between cortisol levels and externalizing behavior, and should be considered as future treatment and prevention programs, including MST, are refined.

References

- Achenbach, T. M. (1991). *Manual for the child behavior checklist/4-18 and 1991 profile*. Burlington: University of Vermont Department of Psychiatry.
- Aiken, L. S., & West, S. G. (1991). *Multiple regression: Testing and interpreting interactions*. California Sage: Thousand Oaks.
- Alink, L. R. A., Van Ijzendoorn, M. H., Bakermans-Kranenburg, M. J., Mesman, J., Juffer, F., & Koot, H. M. (2008). Cortisol and externalizing behavior in children and adolescents: Mixed meta-analytic evidence for the inverse relation of basal cortisol and cortisol reactivity with externalizing behavior. *Developmental Psychobiology*, 50(5), 427–450.
- Bartels, M., de Geus, E. J. C., Kirschbaum, C., Sluyter, F., & Boomsma, D. I. (2003). Heritability of daytime cortisol levels in children. *Behavior Genetics*, 33(4), 421–433.
- Bevans, K., Cerbone, A., & Overstreet, S. (2008). Relations between recurrent trauma exposure and recent life stress and salivary cortisol among children. *Developmental Psychopathology*, 20(01), 1–16.
- Brand, A., & Johnson, J. (1982). Note on the reliability of the Life Events Checklist. *Psychological Reports*, 50, 1274.
- Brand, S. R., Schechter, J. C., Hammen, C. L., Brocque, R. L., & Brennan, P. A. (2011). Do adolescent offspring of women with PTSD experience higher levels of chronic and episodic stress? *Journal of Traumatic Stress*, n/a-n/a.
- Cicchetti, D., & Rogosch, F. A. (2001). Diverse patterns of neuroendocrine activity in maltreated children. *Developmental Psychopathology*, 13(3), 677–693.
- Cohen, M. A., Piquero, A. R., & Jennings, W. G. (2010). Studying the costs of crime across offender trajectories. *Criminology & Public Policy*, 9(2), 279–305.
- Eyberg, S. M., Nelson, M. M., & Boggs, S. R. (2008). Evidence-based psychosocial treatments for children and adolescents with disruptive behavior. *Journal of Clinical Child and Adolescent Psychology*, 37(1), 215–237.
- Fischer, J., & Corcoran, K. (2006). *Measures for clinical practice and research: A sourcebook* (4th ed.). New York: Oxford University Press.
- Fries, E., Hesse, J., Hellhammer, J., & Hellhammer, D. H. (2005). A new view on hypocortisolism. *Psychoneuroendocrinology*, 30(10), 1010–1016.
- Gunnar, M. R., Morison, S. J., Chisholm, K., & Schuder, M. (2001). Salivary cortisol levels in children adopted from Romanian orphanages. *Development and Psychopathology*, 13(3), 611–628.
- Hawes, D. J., Brennan, J., & Dadds, M. R. (2009). Cortisol, callous-unemotional traits, and pathways to antisocial behavior. *Current Opinion in Psychiatry*, 22(4), 357–362.
- Henggeler, S. W., Schoenwald, S. K., Borduin, C. M., Rowland, M. D., & Cunningham, P. B. (2009). *Multisystemic therapy for antisocial behavior in children and adolescents* (2nd ed.). New York: Guilford.
- Hollingshead, A. B. (1975). *Four factor index of social status*.
- Ingram, R. E., & Luxton, D. D. (2005). *Vulnerability-stress models*. In B. L. Hankin & J. R. Z. Abela (Eds.), *Development of psychopathology* (pp. 32–47). Thousand Oaks, CA: Sage.
- Jessop, D. S., & Turner-Cobb, J. M. (2008). Measurement and meaning of salivary cortisol: a focus on health and disease in children. *Stress*, 11(1), 1–14.
- Kessler, R., & Magee, W. (1993). Childhood adversities and adult depression: basic patterns of association in a U.S. national survey. *Psychological Medicine*, 23, 679–690.
- Kirschbaum, C., Wust, S., & Hellhammer, D. (1992). Consistent sex differences in cortisol responses to psychological stress. *Psychosomatic Medicine*, 54(6), 648.
- Kudielka, B. M., & Kirschbaum, C. (2005). Sex differences in HPA axis responses to stress: a review. *Biological Psychology*, 69(1), 113–132.
- Kunz-Ebrecht, S. R., Kirschbaum, C., Marmot, M., & Steptoe, A. (2004). Differences in cortisol awakening response on work days and weekends in women and men from the Whitehall II cohort. *Psychoneuroendocrinology*, 29(4), 516–528.
- Lavigne, J. V., LeBailly, S. A., Gouze, K. R., Cicchetti, C., Jessup, B. W., Arend, R., et al. (2007). Predictor and moderator effects in the treatment of oppositional defiant disorder in pediatric primary care. *Journal of Pediatric Psychology*, 33(5), 462–472.
- Loney, B. R., Butler, M. A., Lima, E. N., Counts, C. A., & Eckel, L. A. (2006). The relation between salivary cortisol, callous-unemotional traits, and conduct problems in an adolescent non-referred sample. *Journal of Child Psychology and Psychiatry*, 47(1), 30–36.
- Lopez-Duran, N. L., Olson, S. L., Hajal, N. J., Felt, B. T., & Vazquez, D. M. (2009). Hypothalamic pituitary adrenal axis functioning in reactive and proactive aggression in children. *Journal of Abnormal Child Psychology*, 37(2), 169–182.
- Lundahl, B., Risser, H. J., & Lovejoy, M. C. (2006). A meta-analysis of parent training: Moderators and follow-up effects. *Clinical Psychology Review*, 26(1), 86–104.

- Mathijssen, J. J. J. P., Koot, H. M., & Verhulst, F. C. (1999). Predicting change in problem behavior from child and family characteristics and stress in referred children and adolescents. *Developmental Psychopathology*, 11(02), 305–320.
- McBurnett, K., Lahey, B. B., Rathouz, P. J., & Loeber, R. (2000). Low salivary cortisol and persistent aggression in boys referred for disruptive behavior. *Archives of General Psychiatry*, 57(1), 38–43.
- Miller, D. B., & Townsend, A. (2005). Urban hassles as chronic stressors and adolescent mental health: the Urban Hassles Index. *Brief Treatment and Crisis Intervention*, 5(1), 85–94.
- Murray-Close, D., Han, G., Cicchetti, D., Crick, N. R., & Rogosch, F. A. (2008). Neuroendocrine regulation and physical and relational aggression: The moderating roles of child maltreatment and gender. *Developmental Psychology*, 44(4), 1160–1176.
- Nock, M. K. (2003). Progress review of the psychosocial treatment of child conduct problems. *Clinical Psychology: Science and Practice*, 10(1), 1–28.
- Oosterlaan, J., Geurts, H. M., Knol, D. L., & Sergeant, J. A. (2005). Low basal salivary cortisol is associated with teacher-reported symptoms of conduct disorder. *Psychiatry Research*, 134(1), 1–10.
- Petersen, A. C., Crockett, L., Richards, M., & Boxer, A. (1988). A self-report measure of pubertal status: reliability, validity, and initial norms. *Journal of Youth and Adolescence*, 17(2), 117–133.
- Popma, A., Doreleijers, T. A. H., Jansen, L. M. C., van Goozen, S. H. M., van Engeland, H., & Vermeiren, R. (2007). The diurnal cortisol cycle in delinquent male adolescents and normal controls. *Neuropsychopharmacology*, 32(7), 1622–1628.
- Post, R. M. (1992). Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. *The American Journal of Psychiatry*, 149(8), 999–1010.
- Raine, A. (1993). *The psychopathology of crime: Criminal behavior as a clinical disorder*. San Diego: Academic.
- Sapolsky, R. M. (1994). *Why zebras don't get ulcers: An updated guide to stress, stress-related diseases, and coping*. New York: W.H. Freeman.
- Scerbo, A., & Kolko, D. J. (1994). Salivary testosterone and cortisol in disruptive children: relationship to aggressive. *Hyperactive, and Internalizing Behaviors*, 33(8), 1174–1184.
- Shirliff, E. A., Granger, D. A., Booth, A., & Johnson, D. (2005). Low salivary cortisol levels and externalizing behavior problems in youth. *Developmental Psychopathology*, 17(01), 167–184.
- Shoal, G. D., Giancola, P. R., & Kirillova, G. P. (2003). Salivary cortisol, personality, and aggressive behavior in adolescent boys: a 5-year longitudinal study. *Journal of the American Academy of Child and Adolescent Psychiatry*, 42(9), 1101–1107.
- Sondeijker, F. E. P. L., Ferdinand, R. F., Oldehinkel, A. J., Veenstra, R., Tiemeier, H., Ormel, J., et al. (2007). Disruptive behaviors and HPA-axis activity in young adolescent boys and girls from the general population. *Journal of Psychiatric Research*, 41(7), 570–578.
- Tiet, Q. Q., Bird, H. R., Hoven, C. W., Moore, R., Wu, P., Wicks, J., et al. (2001). Relationship between specific adverse life events and psychiatric disorders. *Journal of Abnormal Child Psychology*, 29(2), 153–164.
- Tout, K., de Haan, M., Campbell, E. K., & Gunnar, M. R. (1998). Social behavior correlates of cortisol activity in child care: gender differences and time-of-day effects. *Child Development*, 69(5), 1247–1262.
- U.S. Public Health Service (1999). *Mental health: a report of the Surgeon General*. Rockville, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Institute of Mental Health.
- Van Bokhoven, I., Van Goozen, S. H. M., van Engeland, H., Schaal, B., Arseneault, L., Séguin, J. R., et al. (2005). Salivary cortisol and aggression in a population-based longitudinal study of adolescent males. *Journal of Neural Transmission*, 112(8), 1083–1096.
- Van de Wiel, N. M. H., van Goozen, S. H. M., Matthys, W., Snoek, H., & van Engeland, H. (2004). Cortisol and treatment effect in children with disruptive behavior disorders: a preliminary study. *Journal of the American Academy of Child and Adolescent Psychiatry*, 43(8), 1011–1018.
- Van Goozen, S., Matthys, W., Cohen-Kettenis, P., Buitelaar, J., & van Engeland, H. (2000a). Hypothalamic-pituitary-adrenal axis and autonomic nervous system activity in disruptive children and matched controls. *Journal of the American Academy of Child and Adolescent Psychiatry*, 39(11), 1438–1445.
- Van Goozen, S. H., Van Den Ban, E., Matthys, W., Cohen-Kettenis, P. T., Thijssen, J. H., & Van Engeland, H. (2000b). Increased adrenal androgen functioning in children with oppositional defiant disorder: a comparison with psychiatric and normal controls. *Journal of the American Academy of Child & Adolescent Psychiatry*, 39(11), 1446–1451.
- Webster-Stratton, C., & Hammond, M. (1997). Treating children with early-onset conduct problems: a comparison of child and parent training interventions* 1,* 2. *Journal of Consulting and Clinical Psychology*.
- Willemen, A. M., Koot, H. M., Ferdinand, R. F., Goossens, F. A., & Schuengel, C. (2008). *Change in psychopathology in referred children: the role of life events and perceived stress* (pp. 1175–1183). Psychiatry: Journal of Child Psychology and.
- Williams, R. J., & Chang, S. Y. (2000). A comprehensive and comparative review of adolescent substance abuse treatment outcome. *Clinical Psychology: Science and Practice*, 7(2), 138–166.
- Zuckerman, M. (1978). Sensation seeking and psychopathy. In R. D. Hare & D. Schalling (Eds.), *Psychopathic behaviour: Approaches to research* (pp. 165–186). London: Wiley.