Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

April L. Brown

April 1, 2018
Date

Childhood Adversity, Cortisol Awakening Response, and Multisystemic Therapy Outcomes

By

April L. Brown
Mater of Arts

Psychology

Patricia Brennan, Ph.D.
Advisor

Linda Craighead, Ph.D.
Committee Member

Robyn Fivush, Ph.D.
Committee Member

Accepted:
Lisa A. Tedesco, Ph.D.
Dean of the James T. Laney School of Graduate Studies

April 1, 2018
Date

Childhood Adversity, Cortisol Awakening Response, and Multisystemic Therapy Outcomes

By

April L. Brown
Master of Public Health
Emory University
2016

Bachelor of Arts
Spelman College
2013

Advisor: Patricia Brennan, Ph.D.

An abstract of
A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Master of Arts
in Psychology
2018

Abstract

Childhood Adversity, Cortisol Awakening Response, and Multisystemic Therapy Outcomes
By April L. Brown

Multisystemic Therapy (MST) is a treatment program for externalizing behavior problems (e.g., aggression and substance use) that has demonstrated efficacy in several studies. There is evidence, however, of effect heterogeneity, and there appear to be moderators of treatment success. Few studies have explored how adverse childhood experiences (ACEs) might affect responsiveness to MST, although ACEs have been linked to risk for externalizing problems. Emerging research suggests that ACEs may have differential associations with externalizing problems and implicates physiological responsiveness (e.g., cortisol levels) as a mediator *and* moderator of these associations. Few studies, however, have examined the complex relationship between ACEs, cortisol levels, and problem behaviors in a treatment context. This study aimed to examine 1) the differential effects of types of adversity (i.e., threat versus deprivation), and 2) the role of the cortisol awakening response in the association between ACEs and changes in problem behavior over the course of MST. The study used data from youth ages 12 to 17 years (N=118) who were enrolled in a longitudinal study of youth undergoing MST treatment in Denver, CO. Results from growth curve analyses indicated that response to treatment may vary, depending on the type of adversity exposure and on the level of the awakening cortisol response. Implications for theory and potential treatment modifications are discussed.

Keywords: Externalizing behaviors, Multi-systemic therapy, childhood adversity, cortisol awakening response

Childhood Adversity, Cortisol Awakening Response, and Multisystemic Therapy Outcomes

By

April L. Brown
Master of Public Health
Emory University
2016

Bachelor of Arts
Spelman College
2013

Advisor: Patricia Brennan, Ph.D.

A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Master of Arts
in Psychology
2018

TABLE OF CONTENTS

I. Introduction

Disruptive, impulse-control, and conduct disorders all fall under a broad domain known as externalizing psychopathology, which is characterized by problem behaviors that are under controlled, impulsive, aggressive, defiant, and/or deceitful (Gartstein, Putnam, & Rothbart, 2012). There is extensive evidence that childhood externalizing behaviors are a major risk factor for later criminal offending, and age at first offense is a salient predictor of future criminality (Farrington et al., 1990). Externalizing behaviors are notoriously challenging to treat, but many professionals believe early intervention with evidence-based practices is key (Substance Abuse and Mental Health Services Administration, 2011). Therefore, developmental psychopathologists and clinicians have invested many resources into developing programs that target problem behavior during childhood, school age, and adolescence. Multisystemic Therapy (MST) is one treatment approach that is multi-pronged and targets various points of influence at the individual, interpersonal, and community level.

MST: Theoretical Underpinnings and its Utility

MST is rooted in two theoretical frameworks – the social-ecological model and family systems theory. The social-ecological model posits that behavior is determined by factors at *multiple* levels of influence (e.g., individual, interpersonal, and community) that interact with one another (Fleury & Lee, 2006). Family systems theory, however, emphasizes the *family* as an emotional unit within which others work to gain approval, support, and attention (Bowen, 1974). Family systems theory emphasizes the need to maintain balance within the family, which helps prevent maladaptive coping strategies, such as alcoholism, substance use, mental health issues, and other negative behaviors (Bowen, 1974; Prest & Protinsky, 1993).

From the social-ecological and family systems theory perspectives, it is likely that childhood externalizing behavior and psychosocial problems develop from complex interactions between the individual and the environment (Littell, Popa, & Forsythe, 2005). Problem behavior is influenced by the interplay of important aspects of the youth's life, including family, friends, school, and neighborhood; therefore, individual risk factors may vary from person to person (Henggeler, Schoenwald, Bourdin, Rowland, & Cunningham, 2009). To maximize effectiveness, MST interventions are therefore tailored to address a comprehensive array of risk factors and concurrently build protective factors. MST treatments are hybrid interventions that are delivered by treatment teams consisting of two to four licensed MST therapists, and each team works with four to six families at a time, providing intensive home- and community-based services over a three to five month period (Henggeler et al., 2009). Families have 24-hour access to their treatment team, which tailors the intervention to promote responsible behavior and fit the developmental needs of the youth.

Childhood Adversity as a Potential Effect Modifier

A recent meta-analysis of MST effectiveness suggests MST has small overall effects on delinquency and psychopathology (van der Stouwe, Asscher, Stams, Deković, & van der Laan, 2014). Participants appear to respond differently to MST treatment as a function of contextual pre-assessment factors, including perception of parenting competence (Mertens, Deković, Asscher, & Manders, 2017). Furthermore, MST's effectiveness may be moderated by factors such as sample characteristics (e.g. race/ethnicity) or post-treatment effects (e.g. parent mental health) (Lundahl, Risser, & Lovejoy, 2006; van der Stouwe et al., 2014). Relatively few studies, however, have explored other contextual factors, such as early life adversity, that might affect responsiveness to MST.

There is a paucity of literature examining general life adversity a moderator of MST effectiveness; but one meta-analysis exploring potential moderators of family therapy outcomes reported that parents and children facing higher levels of adversity do not benefit from parent training as much as their non-disadvantaged counterparts, and cited financial disadvantage as the most salient moderator of outcomes (Lundahl et al., 2006). Unstable housing, single parent status, and low socioeconomic status were all associated with poorer treatment outcomes, and the authors suggested that family adversity may undermine treatment success by disrupting parent training processes and inhibiting the implementation of recommendations (Lundahl et al., 2006).

The experience of life adversity during childhood is of particular interest when considering MST effectiveness because there is overwhelming evidence that adverse childhood experiences (ACEs) are associated with externalizing symptoms, including antisocial behaviors and drug use (Schilling, Aseltine, & Gore, 2008), which are the main targets of MST interventions. Adversity during sensitive developmental periods, such as childhood, appears to play a role in the progression of externalizing symptoms, and conversely, may impact MST treatment responsiveness. As many as 60% of adolescents report at least one form of childhood adversity (McLaughlin et al., 2012), and research suggests that children and families in disadvantaged communities experience significantly greater adversity and more simultaneous stressors (Smith & Farrington, 2004), and that stressed parents and disrupted family processes are important mediating links between adversity and poor adolescent adjustment (Stern, Smith, & Jang, 1999).

Early life stress is clearly linked to negative social and behavioral outcomes in youth (Sánchez, Ladd, & Plotsky, 2001; Schilling et al., 2008; Widom & Wilson, 2015). What is less clear, however, is how and why childhood adversity has such a profound impact on socio-

emotional development and problem behavior. Identifying which developmental and biological processes are affected by early adversity is key for designing and modifying intervention and treatment strategies for children who engage in problem behaviors. Progress in this area has been impeded by the way in which childhood adversity is conceptualized. Studies that have examined the effects of ACEs typically do so using linear combination scores, which are a simple sum of events. This type of risk score fails to distinguish between distinct types of experiences, which erroneously assumes that very different events influence development via the same underlying mechanisms (McLaughlin & Sheridan, 2016). Contemporary studies have indicated that specific types of adversity may differentially impact development and biological processes (Schilling et al., 2008), and as such that their unique predictive effects should be tested.

Childhood Adversity and Externalizing Behavior: Neurophysiological Perspectives

McLaughin and Sheridan (2016) propose a novel framework that characterizes the unique underlying dimensions of environmental adversity. Their approach focuses on *threat* and *deprivation*, which have both been independently associated with externalizing behavior and are believed to have distinct effects on physiological stress response systems (Busso, McLaughlin, & Sheridan, 2016). Experiences in the *threat* dimension include events that involve actual or threatened death, injury, sexual victimization, or harm to one's physical integrity. *Deprivation* is characterized by experiences that involve the absence of expected environmental inputs in cognitive and social domains, as well as the absence of species- or age-appropriate environmental stimuli (e.g., living in poverty or neglect).

This framework is supported by studies noting that the effect of higher cumulative adversity on poorer mental health is confounded by the specific experience of threat-based events (e.g., Friedman, Montez, Sheehan, Guenewald, & Seeman, 2015). After deriving impact

values when studying the development of problem behaviors, Schilling et al. (2008) listed child maltreatment variables, such as sex abuse/assault, physical abuse/assault, as high impact events relative to parental divorce or parental substance abuse. Schilling et al. (2008) further noted that low impact adversities do not appear to present a cumulative hazard to emotional/behavioral health, but instead weaken the effect of high impact events total sum score. This phenomenon has been described as an *acceleration effect*, as respondents with higher total cumulative adversity often have disproportionately poorer outcomes because of both the number *and* severity of the adversities they experience (Schilling et al., 2008). Early life adversity therefore has a complex relationship with mental health outcomes, and the effects of higher cumulative stress on mental health and behavioral outcomes may be driven in particular by the specific experience of events related to interpersonal violence (i.e., threat exposure; Busso et al., 2016).

Threat and *deprivation* have been explored as antecedents to externalizing behavior in several contexts. Not only have previous studies provided evidence of a positive correlation between violence exposure and of aggression (Gorman-Smith & Tolan, 1998), but studies have also shown that *violence begets violence*. For example, children who experience peer victimization may use aggression to defend themselves and behave in ways that elicit future attacks against them (Reijntjes et al., 2011). Other research has provided evidence of a self-perpetuating cycle between externalizing behavior and exposure to violence, such that exposure to community violence predicts externalizing behavior problems, which predict later exposure to community violence (Lynch, 2003). Regarding *deprivation*, low socioeconomic status (SES) is often associated with poor adaptive functioning and increased likelihood of delinquent behavior among adolescents (Bradley & Corwyn, 2002). Children and families who live in lower SES communities also often experience greater adversity, as there is a well-established research

literature indicating that lower SES communities often have a host of other contextual risk factors, such as poor access to resources, reduced social support, and more cumulative adversities in general, which is fertile ground for increased risk of problem behavior (Power & Manor, 1992; von Rueden et al., 2006). Furthermore, there is evidence that childhood adversity places individuals at risk for changes in physiological functioning, which may, in turn, predict future risk for externalizing psychopathology (e.g, Ruttle et al., 2011).

Cortisol and Problem Behaviors

The hypothalamic-pituitary-adrenal (HPA) axis is one of the main stress response pathways that has been studied extensively in relation to childhood adversity and externalizing behaviors. The stress response system is highly plastic, and there is evidence that children who experience high-stress in early life tend to develop disruptions in their stress response systems (Boyce & Ellis, 2005). The most often-used hormonal proxy for HPA axis activity is cortisol (Alink et al., 2008; Davies, Sturge-Apple, Cicchetti, & Cummings, 2007). Cortisol is present in the body at resting levels, but is largely influenced by sleep/wake cycles and follows a diurnal secretion pattern – characterized by high levels in the morning and gradual decreases throughout the day (Ruttle et al., 2011). Cortisol awakening response (CAR), a relatively new indicator of HPA axis activation, is believed to reflect sensitivity of the stress response system, and extremely low or extremely high CAR is believed to signify physiological dysregulation (Buitelaar, 2013; Chida & Steptoe, 2009). Physiological stress response has been cited as both a mediator and moderator of the association between life stress and various forms of psychopathology (Buitelaar, 2013; Obradović, Bush, Stamperdahl, Adler, & Boyce, 2010).

The literature on childhood adversity and altered stress response systems has suggested early life adversity can inhibit an effective response to stress and lead to increased aggressive

behaviors (Sánchez et al., 2001). The *hypocortisolism hypothesis*, for example, suggests children who experience repeated adversity may exhibit a diminished or blunted response to stress (Davies et al., 2007), which may increase risk of externalizing psychopathology (Ruttle et al., 2011). *Hypocortisolism*, as evidenced by blunted cortisol reactivity, flatter diurnal slope, and lower morning cortisol, has been found among children with attention and externalizing problems, which researchers posit may related to down-regulation of the HPA axis following stressful life conditions (Koss, Mliner, Donzella, & Gunnar, 2016). The *hypercortisolism hypothesis*, in contrast, suggests that repeated exposure to adversity during childhood may sensitize the HPA axis to stress resulting in hyperactivity within the stress response system, which has also been linked to child problem behavior (Ruttle et al., 2011).Therefore, abnormal functioning of the HPA-axis has been implicated in externalizing forms of psychopathology (Davies et al., 2007), and the indirect effects of ACEs on externalizing behavior via HPA axis functioning have been well substantiated. (Conradt et al., 2014). This sheds light on how early adversity may contribute to the development of problem behavior through disruptions within the neuroendocrine system.

There are mixed findings across studies that have used cortisol levels as a proxy for HPA axis activity, with some studies linking ACEs to hyper-responsiveness, some linking them to hypo-responsiveness (Quevedo, Johnson, Loman, Lafavor, & Gunnar, 2012), and others finding no associations at all (DeSantis et al., 2011). One possible explanation for these mixed findings is that different types of stressors may differentially impact cortisol levels, which may result in unique effects on externalizing behaviors. In support of this notion, Busso et al. (2016) tested the McLaughlin and Sheridan (2016) threat and deprivation model, and provided evidence that each has distinct effects in shaping neurobiological development. Data from their study demonstrated

that although both threat and deprivation are associated with higher levels of psychopathology, only threat was associated with differences in physiological reactivity. Specifically, Busso et al. (2016) found blunted cortisol reactivity to be associated with threat, and found that blunted cortisol reactivity *mediated* the association between threat and externalizing psychopathology. The researchers suggested that the blunted cortisol reactivity could reflect dysregulation of the stress response system after exposure to threat-based events and indicated that reduced reactivity to environmental stressors may predispose to problem behaviors by chronically reducing arousal levels and increasing sensation seeking.

Results from other studies, however, have highlighted the *interactive effects* of stress response and childhood adversity, describing physiological stress response as a *moderator* of the link between adverse experiences and forms of psychopathology (Belsky & Pluess, 2013). For example, studies have demonstrated that high stress reactivity may be protective among children with exposure to parental marital conflict and demonstrated that children with lower reactivity may be more vulnerable to internalizing problems (e.g., depressive and/or anxious symptoms; El-Sheikh & Whitson, 2006). Other studies have revealed that high stress reactivity is associated with more maladaptive outcomes in the context of high adversity but is associated with better adaptation in the context of low adversity (Obradović, Bush, & Boyce, 2011). Findings of this nature corroborate the Biological Sensitivity to Context hypothesis, which posits that high reactivity can both hinder or promote psychological functioning depending on the environment (Belsky & Pluess, 2009). More specifically, heightened stress reactivity may reflect, not only exaggerated arousal under stressful conditions, but also an increased sensitivity to context, with potential for negative health effects under adverse conditions and positive effects under conditions of support and protection (Boyce & Ellis, 2005).

From this perspective, having heightened physiological reactivity may be advantageous to survival in an adverse environment, but there is also evidence suggesting lower levels of cortisol reactivity is associated with higher levels of internalizing and externalizing problems, among children who have experienced familial adversity or harsh rearing environments relative to children who have not (Jaffee et al., 2015). Additionally, in the context of MST treatment, there is evidence that the relationship between childhood adversity and externalizing behavior may also be *moderated* by biological stress response. A positive association between ACEs and externalizing behavior in the presence of blunted cortisol levels has been reported, and it has been asserted that youth with both blunted cortisol levels *and* greater early life adversity may be more likely to continue to engage in externalizing behavior despite treatment (Schechter, Brennan, Cunningham, Foster, & Whitmore, 2012). Schechter et al. (2012) specifically speculated that the combination of early life stress and a hypoactive HPA axis may produce a lack of concern about the behavioral consequences and/or need to seek higher levels of stimulation in the environment, through the commission of externalizing behaviors.

The Present Study

Taken together, the literature suggests ACEs may have differential associations with externalizing problems and implicates HPA axis activity as a mediator *and* moderator of these associations. This has important implications for those studying the etiology of and treatments for disruptive, impulse-control, and conduct disorders because it is possible that children with externalizing psychopathology have unique stress profiles that would affect disorder prognosis. Few studies, however, have examined the complex relationship between ACEs, cortisol, and problem behaviors in a treatment context, and no studies have separated ACES into the categories of threat versus deprivation to examine their unique effects on treatment outcome. This study fills that gap in the literature by applying the McLaughlin and Sheridan (2016)

framework to examine the independent effects of threat and deprivation on HPA axis activity and changes in aggression in the context of MST.

Accordingly, this study aimed to 1) examine the differential effects of threat and deprivation on responsiveness to MST, as indexed by changes in externalizing behavior over the course of treatment; and 2) examine the role of HPA axis activity in the association between ACEs and changes in externalizing behavior. This study tested three primary hypotheses. It was hypothesized that 1) threat and deprivation would differentially predict changes in externalizing behavior; 2) HPA axis activity measured at the outset of treatment would mediate the association between threat and deprivation and responsiveness to MST; and 3) HPA axis activity measured at the outset of treatment would moderate the associations between threat and deprivation and responsiveness to MST.

II. Method

Participants

This study used data from youth ages 12 to 17 years (N=118) who were enrolled in a longitudinal study of behavior change in the context of MST treatment. Youth were referred to licensed MST programs after engaging in criminal offending (i.e., drug-related crimes, property offenses, crimes against another person, or violent crimes), being diagnosed with conduct disorder, or exhibiting significant behavioral problems in home or school settings (e.g. substance use, aggression, or truancy). Inclusion criteria included youth who were: a) between the ages of 12 and 17 years at study onset; b) referred for MST by social service agencies or juvenile court; c) available 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 to live elsewhere. Participants were excluded if they did not have cortisol data available (n=23), if they reported use of antihistamines on the day of the cortisol measurement (n=1), and/or if they were pregnant (n=2).

The latter exclusions were made on the basis of research demonstrating that both antihistamines and pregnancy are associated with changes in levels of cortisol (see Granger, Hibel, Fortunato, & Kapelewski, 2009). Informed consent was obtained from the primary caregiver, and youth provided assent prior to participation in the study 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.

Study Design and Procedure

Assessment data were collected at four time points: treatment onset (T1), two treatment mid-points (T2 and T3), and post-treatment (T4). On average, families were first assessed within 23 days of referral to the project. Interviews took place in the home, where youth and caregivers completed sociodemographic measures, measures of health, childhood adversity, and child externalizing behavior, and youth provided saliva samples which were later assayed for cortisol. Specifically, levels of cortisol secretion were measured at awakening on a non-school day (typically Saturday morning) approximately 1 to 2 weeks following the initial family interview. Research assistants returned to the home to personally wake the youth and collect three awakening saliva samples (at 15-minute intervals), thereby witnessing and verifying the time and conditions under which each sample was obtained.

Saliva was collected from the youth by having them passively drool directly into a specimen tube to the level of 1cc. Once collected, saliva samples were stored in an adult lunch box with ice packs until they were frozen and stored at -20°C at the research lab immediately following the home visit. Samples were stored in the lab for an average of 3 months before being sent overnight for assay at the Yerkes National Primate Research Lab at Emory University.

Following shipment to Yerkes, saliva samples were stored at -20°C until the day of assay, when they 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 0.10mg/dl, using 25 ml of saliva. The intra- and inter-assay coefficients of variation are 4.1% and 7.2%, respectively. Each sample was assayed in duplicate. Duplicate test results were averaged, and duplicates with an error rate of more than 20% were re-assayed.

Measures

Socio-demographic Factors and Statistical Controls. Given the well-established relationship between externalizing behavior, age, race, ethnicity, and gender (McLaughlin, Hilt, & Nolen-Hoeksema, 2007), data regarding participants' age in years, race, ethnicity, and gender were examined as potential control variables. Previous studies have also suggested that health variables and pubertal development could influence HPA axis activity (e.g., Granger, Hibel, Fortunato, & Kapelewski, 2009). Therefore, health-related information and pubertal status was obtained when collecting the saliva samples and examined in association with awakening cortisol levels. A Child Health Questionnaire was utilized to assess the use of the following on the day of sample collection: prescription medication, recreational drugs, steroids, and over-the-counter medications (sleep, cold/flu, allergy). The Petersen Pubertal Developmental Scale (PPDS; Petersen, Crockett, Richards, & Boxer, 1988) was also administered to evaluate youth puberty status. The PPDS contains 5 items, each on a 4-point scale, about youth physical changes associated with adolescence.

Childhood Adversity. Childhood adversity was divided into the two distinct dimensions proposed by Busso, McLaughlin, and Sheridan (2016), i.e., threat and deprivation.

Threat. Threat exposure was measured using select items from a 12-item life stress questionnaire that was adapted and extended (Kessler & Magee, 1993). The questionnaire asks youth to report on the presence or absence of 12 stressors that might have occurred in their lifetime. A composite threat score was computed by summing the responses on the three items that were directly related to violence, which included, "Is there a history of violence in your family?" "Did your parents fight with each other a lot?" and "Have you ever been a victim of violence?" Higher scores indicated greater threat exposure. Low internal consistency was observed (Kuder Richardson-20 = 0.43) but expected, given the internal consistencies reported in other studies that have used similar measures (Brand & Johnson, 1982; Schechter, Brennan, Cunningham, Foster, & Whitmore, 2012). Moreover, high internal consistency would not be expected since stressful life events are the result of external factors that would not necessarily be expected to co-occur (Schechter et al., 2012).

Deprivation. Per Busso, McLaughlin, and Sheridan (2016), deprivation includes exposures that reflect the absence of expected environmental inputs, common in the case of neglect, institutionalization, and poverty. Deprivation will therefore be assessed using the Hollingshead Index of Social Position, which is a multidimensional index based on a model of SES that includes caregiver occupation and educational level (Hollingshead, 1975). Parental education is rated on a 7-point scale, where 1 = *below 7th grade* and 7 = *graduate training and beyond*. Occupation is rated on a 9-point scale, where 1 = *farm laborers and menial service workers*, and 9 = *higher executives, large business owners, and major professionals*. The Hollingshead composite score is calculated by weighting the occupation score by a factor of five and the education score by a factor of three to emphasize the individual contributions of each to the construct of SES, and lower scores indicate lower SES. This index has been shown to yield

an inter-rater reliability coefficient of 0.91 and has been well-validated (Cirino et al., 2002). For greater ease of interpretation in the analyses, the Hollingshead index score was reverse coded, such that higher scores suggest greater deprivation and lower scores suggest less deprivation.

HPA Axis Activity. HPA axis activity was assessed using T1 cortisol awakening response (CAR). CAR was computed using cortisol secretion levels that were obtained from morning saliva samples collected at 15-minute intervals. The area under the curve with respect to increase (AUC_i) formula (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003) was used to derive a global estimate of HPA axis activity. AUC_i is calculated with reference to the individual's baseline level of cortisol, and captures increase relative to that point (Fekedulegn et al., 2007). Since AUC_i is constrained by the initial value of cortisol secretion upon awakening, AUC_i was regressed on the initial cortisol value to obtain the residual. This residual (CAR_{AUC}), which is a measure of cortisol awakening response that controls for the starting point, was used in all analyses.

Externalizing Behaviors. Externalizing behaviors were assessed using data from the Child Behavior Checklist/4-18 (CBCL/4-18; (Achenbach, 1994), which was completed by the primary caregivers at each assessment timepoint. The CBCL consists of 118 items that measure the following eight syndromes: social withdrawal, somatic complaints, anxiety/depression, social problems, thought problems, attention problems, delinquent behavior, and aggressive behavior. The Externalizing Problems subscale combines the Delinquent Behavior and Aggressive Behavior scales (33 items). The original CBCL contains items coded from *not true in the last six months* (0) to *very true/often true in the last six months* (2). However, items were modified to capture the youth's behavior for the last 30 days prior to the respective assessment point. Cronbach's alpha for the externalizing subscale was 0.94 at T1, 0.94 at T2, 0.95 at T3, and 0.95

at T4. Given the nature of this sample and the more restricted range of CBCL standardized scores in this clinical sample, raw scores were used in all analyses.

Data Analyses

Descriptive analyses were performed to assess sample characteristics. Data were examined for multicollinearity and normality using tolerance statistics and univariate procedures. Transformations were applied where necessary. Bivariate analyses were conducted to identify statistical controls. To examine mediation hypotheses, multiple linear regression analyses were first conducted in IBM SPSS Statistics for Macintosh Version 24 (IBM Corporation, 2016), to assess the relationship between childhood adversity and the cortisol awakening response. To examine the outcome of externalizing behavior change over time, Hierarchal Linear Modeling (HLM) was used to adjust for nested data (repeated measures of aggression within individuals).

Analyses that examined changes externalizing behavior as the dependent measure included a time variable indicating the number of months between assessment points at level 1 and control variables and each childhood adversity predictor at level 2. Seven cases were deleted during analysis due to missing data at level 2. Each continuous predictor variable was centered around its mean, and each nominal variable was included as an uncentered variable. Covariates in each model were fixed, whereas variables of interest were allowed to vary at random. All estimates were considered statistically significant at $p < 0.05$.

Interaction terms were computed by centering each independent variable of interest and obtaining the product (i.e., CAR_{AUC} × threat and CAR_{AUC} × deprivation, respectively). Growth curve analyses were then conducted in HLM 7 (Raudenbush, Bryk, Cheong, Congdon, & Du Toit, 2011) to assess whether CAR_{AUC} interacted with either threat or deprivation in predicting

changes in externalizing behavior over the course of treatment. If interactions were significant, post hoc analyses were used to probe the direction of the effects.

III. Results

Preliminary Analyses

Correlations between each of the predictor variables and the outcome variable at each of the four time points are found in Table 1. The distributional shape of externalizing behavior total scores was examined to determine the extent to which the assumption of normality was met. Skewness (0.41, SE=0.22), kurtosis (-0.58, SE = 0.44), and the Shapiro-Wilk test of normality (S-W=0.97, df=120 , p=0.009) suggested that raw externalizing behavior scores were non-normally distributed (Field, 2009; Royston, 1983). Raw externalizing behavior scores were therefore square-root transformed to improve the distributions, and transformed scores were used in all subsequent analyses.

To assess whether externalizing behaviors changed significantly over the course of treatment, an unconditional growth model was run using externalizing behavior as the outcome and time as a predictor at level 1. The estimated mean slope for the transformed externalizing behavior variable was -0.26 (SE=0.03), which suggest the youth's externalizing behavior decreased at an average rate of 0.26 points per observation unit from the onset of treatment to termination. This trajectory was significant at $p < 0.001$, suggesting significant decreases in youth externalizing behavior over time. Additionally, the variance component of the slope indicated that there was significant variation among slopes of externalizing behavior in this sample (χ^2=151.78; p = 0.005).

When preparing to examine the indirect effect of CAR_{AUC} on the relationship between childhood adversity and externalizing behavior, associations between age, sex, race, ethnicity, health-related variables, pubertal status, and CAR_{AUC} were examined using bivariate analyses.

Results indicated neither age, sex, race, ethnicity, health-related variables, nor pubertal status significantly related to CAR_{AUC} (*p*s > 0.05). Sample characteristics are reported in Table 2.

When preparing to examine the main effects of threat and deprivation on changes in externalizing behavior and moderation effects for CAR_{AUC}, potential covariates (i.e., age, sex, race, and ethnicity) were each separately entered into HLM analyses, respectively. Among potential covariates, results indicated that both age and White race were significantly associated with mean externalizing behavior scores for each person at baseline ($p = 0.002$ and $p = 0.049$, respectively). Therefore, age and White race were entered as covariates at the intercept in all subsequent HLM analyses.

Hypothesis Testing

The first step towards examining whether CAR_{AUC} mediated the associations between forms of childhood adversity (i.e., threat and deprivation) and responsiveness to MST was to establish an association between CAR_{AUC} and threat and deprivation. Results from the linear regression analysis, however, indicated that neither threat nor deprivation were significantly associated with CAR_{AUC} ($p = 0.31$ and $p = 0.88$, respectively). Therefore, no further analyses testing CAR_{AUC} as a mediator were performed.

To examine whether threat and/or deprivation predicted differential responsiveness to MST (i.e. the slope of externalizing behavior), an HLM model was constructed with threat and deprivation both entered as predictors at level 2 to test the main effects of each in the context of the other, as suggested by Busso et al. (2016). Results indicated that threat was not a significant predictor of baseline externalizing behavior ($p = 0.34$) but suggest a significant negative association between deprivation and baseline externalizing behaviors ($\beta = -0.03$; $p = 0.002$; df =

113; SE = 0.01). Results further indicated that neither threat nor deprivation predicted the slope of externalizing behavior (p = 0.44 and p = 0.88, respectively; see Table 3).

To test for moderation effects between threat and CAR_{AUC} on the slope of externalizing behavior, an HLM model was constructed, which included deprivation, threat, CAR_{AUC}, and the interaction term of threat and CAR_{AUC} as predictors at level 2. Similarly, to test for moderation effects between deprivation and CAR_{AUC} on the slope of externalizing behavior, a separate HLM analysis was performed using threat, deprivation, CAR_{AUC}, and the interaction of threat and CAR_{AUC} as predictors at level 2. Results from the moderator tests are presented in Table 3. Both the interaction between CAR_{AUC} and threat (p = 0.01) and the interaction between CAR_{AUC} and deprivation (p = 0.046) were significant. Therefore, the file was split to examine the relationships between threat, deprivation, and the slope of externalizing behavior separately for those above (n=55) and below (n=56) the median of CAR_{AUC} (median = -0.04). Within each subsample, age and White race were included as covariates at the intercept, threat and deprivation were included as predictor variables (level 2), and externalizing behavior was included as the outcome variable (at level 1). Results of these analyses suggested that the direction of the associations between adverse experiences and responsiveness to MST was reversed for those above and below the median on CAR_{AUC} (see Table 4).

Among children with *lower* CAR_{AUC}, threat was (non-significantly) associated with *increases* in externalizing behaviors over the course of treatment (β = 0.06; p = 0.13; df = 56; SE = 0.04). Conversely, among children with *higher* CAR_{AUC}, threat was (non-significantly) associated with *decreases* in externalizing behavior of the course of treatment (β = -0.02; p = 0.45; df = 56; SE = 0.03).

Results for deprivation were in the opposite direction as threat. Specifically, among children with *higher* $CAR_{AUC,}$ deprivation was associated with *increases* in externalizing behaviors over the course of treatment (β = 0.006; p = 0.01; df = 56; SE = 0.003). In contrast, among children with *lower* $CAR_{AUC,}$ deprivation was (non-significantly) associated with *decreases* in externalizing behavior of the course of treatment (β = -0.004; p = 0.22; df = 56; SE = 0.004).

IV. Discussion

Previous studies have noted the potential significance of childhood adversity in the etiology and exacerbation of externalizing behaviors (Gorman-Smith & Tolan, 1998; Power & Manor, 1992; Schilling et al., 2008; von Rueden et al., 2006; Willemen, Koot, Ferdinand, Goossens, & Schuengel, 2008). Others have noted the differential effects of certain types of adverse experiences on child problem behavior (Sheridan & McLaughlin, 2016), and some have explained that adverse events have the potential to affect externalizing behavior treatment outcomes (Mathijssen, Koot, & Verhulst, 1999; Schechter et al., 2012). There is also a well-established body of literature aiming to parse out the role of HPA axis activity in the link between childhood adversity and externalizing problems, with some studies finding that cortisol levels act as a mediator and others finding that cortisol levels act as a moderator in this relationship (Buitelaar, 2013; Obradović et al., 2010).

Few studies, however, have examined the independent effects of different types of childhood adversity on changes in problem behaviors over time within a treatment context, while also examining whether HPA axis activity acts as an underlying mechanism or affects the nature of these associations. Findings from this study suggest that associations between threat, deprivation, and externalizing behavior are complex when examined in a treatment context, and

when considering HPA axis activity levels. Specifically, response to treatment may depend on both the type of adversity exposure and on awakening cortisol levels.

HPA Axis Activity Moderates the Association between Childhood Adversity and Response to MST

Findings suggest that two types of adolescents may be at risk of poorer MST treatment response: those with greater exposure to threat-based adversity (coupled with lower cortisol awakening response), and those with greater exposure to deprivation (coupled with higher cortisol awakening response).

Adolescents who have a lower physiological stress response in conjunction with more threat-based adversity may have worse treatment outcomes for several reasons. Schechter et al. (2012) speculated that the combination of childhood adversity *and* a hypoactive HPA axis may result in problem behaviors because of the need to seek higher levels of environmental stimulation, which is largely supported by literature suggesting that personality factors, specifically sensation seeking, may be associated with low HPA axis activity (Sondeijker et al., 2008). Sensation seeking is a trait characterized by the generalized tendency to seek varied, novel, complex, and intense sensations, and experiences and the willingness to take risks for the sake of such experiences (Zuckerman, Bone, Neary, Mangelsdorff, & Brustman, 1972). According to sensation-seeking theory, low arousal is physiologically unpleasant for some individuals. To alleviate this discomfort, individuals with low arousal might initiate antisocial behaviors, which increase tension, as means to seek stimulation (Arnett, 1994). This, coupled with other research suggesting that children who are exposed to violence may be more likely to engage in behaviors that coincidentally increase their exposure to violence (Lynch, 2003; Reijntjes et al., 2011), suggest youth with the high-threat-low-cortisol stress profile may be particularly at risk of poorer treatment response.

Additionally, youth with the high-threat-low-cortisol stress profile may continue to engage in externalizing behavior despite treatment because those behaviors have been modeled in their environment. According to Bandura's Social Learning Theory (now known as Social Cognitive Theory [SCT]), children acquire their behaviors through modelling and reinforcement and by imitating the behavior of people of influence (Widom & Wilson, 2015). It is possible that aggression has been modeled via exposure to interpersonal violence. Although this study did not disentangle proactive aggression from reactive aggression, youth with low cortisol awakening response may be more susceptible to proactive-aggressive conflict resolution styles. SCT proposes that learning occurs in a social context through reciprocal and dynamic interactions, which occur between the person, their environment, and their behavior (Glanz & Bishop, 2010). Under this premise, behavior is shaped by *incentive motivation*, which refers to the use and misuse of rewards and punishments to modify behavior. Youth with low cortisol awakening response may lack of concern for the consequences of their behavior and may not be as sensitive to normative patterns of punishment that occur in the natural environment. Furthermore, SCT asserts that behavior is learned via *observational learning*, which occurs by watching the behavior of peer models, and behavior can be *facilitated* through tools, resources, or environments that make the behavior easier to perform (Glanz & Bishop, 2010). Therefore, individuals who engage in interpersonally violent practices may serve as a model of conflict resolution for vulnerable youth, normalize physical aggression, and provide an environment that fosters other types of externalizing behavior.

At first glance, the finding that youth with a higher CAR and higher deprivation have worse treatment outcomes appears to contradict the above noted findings for threat exposure. However, these results may not be incompatible. Instead they might reflect risk processes for

different subtypes of aggression. In this study, deprivation was operationalized using a measure of SES. Studies have identified financial disadvantage as one important moderator of treatment success, as family economic hardship may inhibit the implementation of treatment recommendations (Lundahl et al., 2006). Other studies have also noted higher cortisol levels in reactive aggressive children relative to proactive and non-aggressive children (Lopez-Duran, Olson, Hajal, Felt, & Vazquez, 2009). An elevated stress response may prime individuals to react aggressively in certain situations (Sánchez et al., 2001), and the Code of the Street framework suggests delinquent or aggressive behavior may be a functional response in low SES environments with greater urban hassles (e.g., fighting as a form of self-defense; Anderson, 1999). It is therefore possible that youth with a higher physiological stress response who also reside in lower SES environments continue to engage in problem behaviors despite treatment because of stressors that elicit a reactive-aggressive response.

Lastly, it is important to note that the main effects of threat-based stress did not reach statistical significance when examining response to MST. While inconsistent with many other studies examining links between threat-based forms of childhood adversity and externalizing behavior, findings from one meta-analytic review suggest that the relationship between violence exposure and problem behaviors is stronger when victimization, and not simply exposure, occurs (Wilson, Stover, & Berkowitz, 2009). While witnessing violence has been linked to a variety of developmental and psychiatric outcomes, witnessing violence, in and of itself, does not appear to be sufficient enough to increase risk of externalizing behaviors (Widom & Wilson, 2015; Wilson et al., 2009). There are likely several other factors at play that interact and contribute to the etiology and prognosis of externalizing forms of psychopathology.

Threat, Deprivation, and HPA Axis Activity

Findings from this study did not support the hypothesis that HPA axis activity would mediate the associations between threat, deprivation, and response to MST. In this sample, awakening cortisol levels were not significantly associated with either threat or deprivation, which stands in direct contradiction to the work of Busso, McLaughlin, and Sheridan (2016), who reported that threat and deprivation both have distinct effects in shaping neurobiological development and found blunted cortisol reactivity to be a mediator of the association between threat and externalizing psychopathology.

It is possible that these findings were not replicated due to key differences in study methodology. First, this study utilized a sample of adolescents who were all in the clinical range for externalizing problems, while Busso et al.'s (2016) sample was comprised of adolescents who were recruited from communities with high levels of violence and clinics that served predominantly low SES areas. Second, Busso and colleagues (2016) assessed threat by z-transforming and summing scores from the Childhood Trauma Questionnaire and the Screen for Adolescent Exposure to Violence. This likely means their measure of threat had greater range of experiences and variability than the measure used in the current study.

Another key difference between the methodology of the current study and Busso's group (2016) is that deprivation was assessed using a dichotomous indicator of poverty. This study used a continuous measure of SES. Finally, the authors utilized a ratio of cortisol to dehydroepiandrosterone-sulphate (DHEA-S) concentrations, which was collected during a stressful lab task as an indicator of physiological reactivity. The current study used awakening cortisol levels. Other studies have found that awakening cortisol levels are not significantly related to cortisol levels elicited from acute laboratory stress testing (Kidd, Carvalho, & Steptoe, 2014). It is therefore possible that awakening cortisol reflects *sensitivity* of the stress response

system, while cortisol levels garnered in laboratory settings reflect *reactivity*. More specifically, the cortisol awakening response may differ from stress responses elicited by laboratory challenges, in that it reflects the sensitivity of negative feedback to cortisol within the HPA axis. In support of this notion, studies have also shown that the surge of cortisol after awakening is inhibited after the intake of dexamethasone, which is a synthetic glucocorticoid imitating negative feedback signals from circulating cortisol to cells of the pituitary (Ebrecht et al., 2000). These methodological differences likely affected this study's ability to detect similar effects.

Furthermore, it clear from a review of the literature that there is disagreement in the field regarding what CAR actually represents (i.e., sensitivity to negative feedback versus reactivity); Clow, Thorn, Evans, & Hucklebridge, 2004; Fries, Dettenborn, & Kirschbaum, 2009; Huber, Issa, Schik, & Wolf, 2006), and it is unclear whether high CAR or low CAR could increase risk. This study does little to alleviate this tension, as findings suggest that both high and low CAR could be a risk factor depending on which form of adversity is present. The general consensus appears to be that extremely high or extremely low CAR suggests dysregulation of the HPA axis; but contradictory findings across studies may indicate a need to conduct more in-depth analyses on the associations between CAR, cortisol levels following acute laboratory stressors, and diurnal cortisol patterns to better identify the best biomarker for risk.

Clinical Implications

In summary, findings from this study offer mixed support for the initial study hypotheses. In this sample, neither threat nor deprivation had significant main effects on response to MST, and HPA axis activity did not mediate associations between threat, deprivation, and response to MST. Findings do suggest, however, that associations between experiences of adversity and responsiveness to treatment depend on HPA axis activity. Some adolescents may have unique

stress and adversity profiles that render them at greater risk of poorer treatment outcomes. Studies have shown that low HPA-axis activity could a valuable tool for identifying those with a poor prognosis once problem behaviors surface, as low morning cortisol levels among children with high levels of disruptive behaviors predict future behavior problems (Sondeijker et al., 2008). Findings from this study, therefore, have important clinical implications for the use of MST among youth with a history of adversity and dysregulated HPA axis activity. Thus, it would be useful for clinicians to consider individual history of adversity and distinguish between proactive and reactive aggressive patterns of behavior, since there may be subgroups of youth who may be less amenable to MST treatment strategies.

Furthermore, children with an increased physiological risk may need to be treated with pharmacological interventions in addition to standard behavioral treatments (Stadler, Poustka, & Sterzer, 2010). Currently, psychopharmacological approaches to externalizing disorders, such as conduct disorder and attention deficit hyperactivity disorder, include the use of neuroleptics, mood stabilizers, psychostimulants, and occasionally, antipsychotics such as risperidone (Nevels, Dehon, Alexander, & Gontkovsky, 2010; Pappadopulos et al., 2006; Steiner, Saxena, & Chang, 2003). Current pharmacological treatments, however, are short-term, often limited by side-effects, and may not directly affect HPA axis activity (Ozbolt & Nemeroff, 2013); thus, to select the best possible treatment strategy, it is important to continue research examining both the biological and psychosocial predictors of externalizing psychopathology and treatment success.

Strengths and Limitations

This study has notable strengths. First, findings from this study provide novel evidence that specific types of adversities have differing effects on treatment outcomes as a function of HPA axis activity. This study joins the company of the very few intervention studies that have

considered biological factors as moderators of behavior change (e.g., Fischer & Cleare, 2017; Meuret et al., 2015). Second, the use of a well-established and well-validated treatment strengthens confidence in the finding that biological factors coupled with certain forms of early life stress may affect treatment outcomes.

While the current findings are interesting, there are several limitations that must be considered when interpreting the results. First, though analyses were performed on a moderate sample size, participants in this study are not a true representation of youth in the general population, since all participants were referred to MST services. Statistically, this also means there was a restricted range and relatively low variability in externalizing behavior scores, which could deflate the significance of effects. Also, of note, this study did not include a control or comparison group, to which the effects of MST could be compared. This weakens the ability to draw any affirmative conclusions about whether observed changes in externalizing behavior were due to MST alone. Results from the HLM analyses, however, indicate that there was a significant decline in problem behavior throughout the course of treatment, and MST has demonstrated effectiveness in numerous randomized control trials (see Henggeler, 2011).

Finally, this study may have benefited from the use of more comprehensive measures of threat exposure and deprivation, comparable to those of Busso and colleagues (2016). The present study utilized a measure of threat that was comprised of only three items. Ideally, threat measures should capture a range of experiences that also assess frequency of exposure. Use of SES as a proxy for deprivation also has its limitations, since low SES and poverty are qualitatively different. Preferably, measures of deprivation would capture lack of access to age-appropriate stimuli and the absence of expected environmental inputs and complexity, which are components of an environment without cognitive enrichment (McLaughlin, Sheridan, &

Lambert, 2014). Future studies should also consider the severity of experiences to identify potential risk thresholds for negative outcomes.

Still, findings from this study have important implications for those studying the etiology of and treatments for disruptive, impulse-control, and conduct disorders. There is an impressive body of empirical support for the ways in which factors such as hormones, stress response systems, and early life stress, are associated with externalizing problems. It is clear that a variety of predispositions, physiological programming, context, and life-experiences have the potential to affect response to treatment, and most contemporary theories acknowledge that there is no single factor that spikes risk for conduct problems. Therapists who are treating youth with problem behaviors and researchers who are on the frontlines of developing and refining treatment programs should be mindful of the diversity of risk factors that may interact to have clinically meaningful effects on behavior.

References

Achenbach, T. M. (1994). Child Behavior Checklist and related instruments. In *The use of psychological testing for treatment planning and outcome assessment.* (pp. 517–549). Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc.

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. https://doi.org/10.1002/dev.20300

Anderson, E. (1999). *Code of the Street*. New York: Norton.

Arnett, J. (1994). Sensation seeking: A new conceptualization and a new scale. *Personality and Individual Differences*, *16*(2), 289–296. https://doi.org/10.1016/0191-8869(94)90165-1

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, *135*(6), 885–908. https://doi.org/10.1037/a0017376

Belsky, J., & Pluess, M. (2013). Beyond risk, resilience, and dysregulation: Phenotypic plasticity and human development. *Development and Psychopathology*, *25*(4pt2), 1243–1261. https://doi.org/10.1017/S095457941300059X

Bowen, M. (1974). Alcoholism as viewed through family systems theory and family psychotherapy. *Annals of the New York Academy of Sciences*, *233*, 115–22. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/4523792

Boyce, W. T., & Ellis, B. J. (2005). Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. *Development and*

Psychopathology, *17*(2). https://doi.org/10.1017/S0954579405050145

Bradley, R. H., & Corwyn, R. F. (2002). SOCIOECONOMIC STATUS AND CHILD DEVELOPMENT. *Annu. Rev. Psychol*, *53*, 371–399. Retrieved from https://www.researchgate.net/profile/Robert_Bradley7/publication/11603895_Socioeconomic_Status_and_Child_Development/links/0deec52eb389430c36000000/Socioeconomic-Status-and-Child-Development.pdf

Brand, A. H., & Johnson, J. H. (1982). Note on Reliability of the Life Events Checklist. *Psychological Reports*, *50*(3_suppl), 1274–1274. https://doi.org/10.2466/pr0.1982.50.3c.1274

Buitelaar, J. K. (2013). The role of the HPA-axis in understanding psychopathology: cause, consequence, mediator, or moderator? *European Child & Adolescent Psychiatry*, *22*(7), 387–389. https://doi.org/10.1007/s00787-013-0441-7

Busso, D. S., McLaughlin, K. A., & Sheridan, M. A. (2016). Dimensions of Adversity, Physiological Reactivity, and Externalizing Psychopathology in Adolescence. *Psychosomatic Medicine*, 1. https://doi.org/10.1097/PSY.0000000000000369

Chida, Y., & Steptoe, A. (2009). Cortisol awakening response and psychosocial factors: A systematic review and meta-analysis. *Biological Psychology*, *80*(3), 265–278. https://doi.org/10.1016/J.BIOPSYCHO.2008.10.004

Cirino, P. T., Chin, C. E., Sevcik, R. A., Wolf, M., Lovett, M., & Morris, R. D. (2002). Measuring Socioeconomic Status. *Assessment*, *9*(2), 145–155. https://doi.org/10.1177/10791102009002005

Clow, A., Thorn, L., Evans, P., & Hucklebridge, F. (2004). The Awakening Cortisol Response: Methodological Issues and Significance. *Stress*, *7*(1), 29–37.

https://doi.org/10.1080/10253890410001667205

Conradt, E., Abar, B., Lester, B. M., LaGasse, L. L., Shankaran, S., Bada, H., … Hammond, J. A. (2014). Cortisol reactivity to social stress as a mediator of early adversity on risk and adaptive outcomes. *Child Development*, *85*(6), 2279–98. https://doi.org/10.1111/cdev.12316

Davies, P. T., Sturge-Apple, M. L., Cicchetti, D., & Cummings, E. M. (2007). The role of child adrenocortical functioning in pathways between interparental conflict and child maladjustment. *Developmental Psychology*, *43*(4), 918–30. https://doi.org/10.1037/0012-1649.43.4.918

DeSantis, S. M., Baker, N. L., Back, S. E., Spratt, E., Ciolino, J. D., Moran-Santa Maria, M., … Brady, K. T. (2011). Gender differences in the effect of early life trauma on hypothalamic-pituitary-adrenal axis functioning. *Depression and Anxiety*, *28*(5), 383–92. https://doi.org/10.1002/da.20795

Ebrecht, M., Buske-Kirschbaum, A., Hellhammer, D., Kern, S., Rohleder, N., Walker, B., & Kirschbaum, C. (2000). Tissue Specificity of Glucocorticoid Sensitivity in Healthy Adults. *The Journal of Clinical Endocrinology & Metabolism*, *85*(10), 3733–3739. https://doi.org/10.1210/jcem.85.10.6891

El-Sheikh, M., & Whitson, S. A. (2006). Longitudinal relations between marital conflict and child adjustment: Vagal regulation as a protective factor. *Journal of Family Psychology*, *20*(1), 30–39. https://doi.org/10.1037/0893-3200.20.1.30

Farrington, D. P., Loeber, R., Elliott, D. S., Hawkins, J. D., Kandel, D. B., Klein, M. W., … Tremblay, R. E. (1990). Advancing Knowledge about the Onset of Delinquency and Crime. In *Advances in Clinical Child Psychology* (pp. 283–342). Boston, MA: Springer US. https://doi.org/10.1007/978-1-4613-9835-6_8

Field, A. (2009). *Discovering Statistics Using SPSS* (3rd ed.). London, England: Sage Publications.

Fischer, S., & Cleare, A. J. (2017). Cortisol as a predictor of psychological therapy response in anxiety disorders—Systematic review and meta-analysis. *Journal of Anxiety Disorders*, *47*, 60–68. https://doi.org/10.1016/J.JANXDIS.2017.02.007

Fleury, J., & Lee, S. M. (2006). The Social Ecological Model and Physical Activity in African American Women. *American Journal of Community Psychology*, *37*(1–2), 141–154. https://doi.org/10.1007/s10464-005-9002-7

Friedman, E. M., Montez, J. K., Sheehan, C. M., Guenewald, T. L., & Seeman, T. E. (2015). Childhood Adversities and Adult Cardiometabolic Health: Does the Quantity, Timing, and Type of Adversity Matter? *Journal of Aging and Health*, *27*(8), 1311–38. https://doi.org/10.1177/0898264315580122

Fries, E., Dettenborn, L., & Kirschbaum, C. (2009). The cortisol awakening response (CAR): Facts and future directions. *International Journal of Psychophysiology*, *72*(1), 67–73. https://doi.org/10.1016/J.IJPSYCHO.2008.03.014

Gartstein, M. A., Putnam, S. P., & Rothbart, M. K. (2012). Etiology of preschool behavior problems: Contributions of temperament attributes in early childhood. *Infant Mental Health Journal*, *33*(2), 197–211. https://doi.org/10.1002/imhj.21312

Glanz, K., & Bishop, D. B. (2010). The Role of Behavioral Science Theory in Development and Implementation of Public Health Interventions. *Annual Review of Public Health*, *31*(1), 399–418. https://doi.org/10.1146/annurev.publhealth.012809.103604

Gorman-Smith, D., & Tolan, P. (1998). The role of exposure to community violence and developmental problems among inner-city youth. *Development and Psychopathology*, *10*,

101–116. Retrieved from http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.461.9233&rep=rep1&type=pdf

Granger, D. A., Hibel, L. C., Fortunato, C. K., & Kapelewski, C. H. (2009). Medication effects on salivary cortisol: Tactics and strategy to minimize impact in behavioral and developmental science. *Psychoneuroendocrinology*, *34*(10), 1437–1448. https://doi.org/10.1016/j.psyneuen.2009.06.017

Henggeler, S. W., Schoenwald, S. K., Bourdin, C. M., Rowland, M. D., & Cunningham, P. B. (2009). *Multisystemic treatment of antisocial behavior in children and adolescents* (2nd ed.). New York: Guilford Press. Retrieved from https://eric.ed.gov/?id=ED420820

Hollingshead, A. B. (1975). Four factor index of social status. *YALE JOURNAL OF SOCIOLOGY*, *8*. Retrieved from https://s3.amazonaws.com/academia.edu.documents/30754699/yjs_fall_2011.pdf?AWSAccessKeyId=AKIAIWOWYYGZ2Y53UL3A&Expires=1520619666&Signature=p9tFZmKbyOpDQuUV5h1tAQqgCNI%3D&response-content-disposition=inline%3Bfilename%3DAugust_B._Hollingshead_s_Four_Fa

Huber, T. J., Issa, K., Schik, G., & Wolf, O. T. (2006). The cortisol awakening response is blunted in psychotherapy inpatients suffering from depression. *Psychoneuroendocrinology*, *31*(7), 900–4. https://doi.org/10.1016/j.psyneuen.2006.03.005

IBM Corporation. (2016). IBM Statistics for Macintosh. Armonk, NY.

Jaffee, S. R., McFarquhar, T., Stevens, S., Ouellet-Morin, I., Melhuish, E., & Belsky, J. (2015). Interactive effects of early and recent exposure to stressful contexts on cortisol reactivity in middle childhood. *Journal of Child Psychology and Psychiatry*, *56*(2), 138–146. https://doi.org/10.1111/jcpp.12287

Kessler, R. C., & Magee, W. J. (1993). Childhood adversities and adult depression: basic patterns of association in a US national survey. *Psychological Medicine*, *23*(3), 679. https://doi.org/10.1017/S0033291700025460

Kidd, T., Carvalho, L. A., & Steptoe, A. (2014). The relationship between cortisol responses to laboratory stress and cortisol profiles in daily life. *Biological Psychology*, *99*, 34–40. https://doi.org/10.1016/J.BIOPSYCHO.2014.02.010

Koss, K. J., Mliner, S. B., Donzella, B., & Gunnar, M. R. (2016). Early adversity, hypocortisolism, and behavior problems at school entry: A study of internationally adopted children. *Psychoneuroendocrinology*, *66*, 31–8. https://doi.org/10.1016/j.psyneuen.2015.12.018

Littell, J. H., Popa, M., & Forsythe, B. (2005). *Multisystemic Therapy for Social, Emotional, and Behavioral Problems in Youth Aged 10-17*. *Campbell Systematic Reviews* (Vol. 2005). Retrieved from http://www.campbellcollaboration.org/images/pdf/plain-language/1004_R.pdf

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. https://doi.org/10.1007/s10802-008-9263-3

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. https://doi.org/10.1016/J.CPR.2005.07.004

Lynch, M. (2003). Consequences of Children's Exposure t o Community Violence. *Clinical Child and Family Psychology Review*, *6*(4), 265–274.

https://doi.org/10.1023/B:CCFP.0000006293.77143.e1

Mathijssen, J. J., Koot, H. M., & Verhulst, F. C. (1999). Predicting change in problem behavior from child and family characteristics and stress in referred children and adolescents. *Development and Psychopathology*, *11*(2), 305–20. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16506536

McLaughlin, K. A., Greif Green, J., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2012). Childhood Adversities and First Onset of Psychiatric Disorders in a National Sample of US Adolescents. *Archives of General Psychiatry*, *69*(11), 1151. https://doi.org/10.1001/archgenpsychiatry.2011.2277

McLaughlin, K. A., Hilt, L. M., & Nolen-Hoeksema, S. (2007). Racial/ethnic differences in internalizing and externalizing symptoms in adolescents. *Journal of Abnormal Child Psychology*, *35*(5), 801–16. https://doi.org/10.1007/s10802-007-9128-1

McLaughlin, K. A., & Sheridan, M. A. (2016). Beyond Cumulative Risk. *Current Directions in Psychological Science*, *25*(4), 239–245. https://doi.org/10.1177/0963721416655883

McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014). Childhood adversity and neural development: deprivation and threat as distinct dimensions of early experience. *Neuroscience and Biobehavioral Reviews*, *47*, 578–91. https://doi.org/10.1016/j.neubiorev.2014.10.012

Mertens, E. C. A., Deković, M., Asscher, J. J., & Manders, W. A. (2017). Heterogeneity in Response during Multisystemic Therapy: Exploring Subgroups and Predictors. *Journal of Abnormal Child Psychology*, *45*(7), 1285–1295. https://doi.org/10.1007/s10802-016-0242-9

Meuret, A. E., Trueba, A. F., Abelson, J. L., Liberzon, I., Auchus, R., Bhaskara, L., … Rosenfield, D. (2015). High cortisol awakening response and cortisol levels moderate

exposure-based psychotherapy success. *Psychoneuroendocrinology*, *51*, 331–40. https://doi.org/10.1016/j.psyneuen.2014.10.008

Nevels, R. M., Dehon, E. E., Alexander, K., & Gontkovsky, S. T. (2010). Psychopharmacology of aggression in children and adolescents with primary neuropsychiatric disorders: A review of current and potentially promising treatment options. *Experimental and Clinical Psychopharmacology*, *18*(2), 184–201. https://doi.org/10.1037/a0018059

Obradović, J., Bush, N. R., & Boyce, W. T. (2011). The interactive effect of marital conflict and stress reactivity on externalizing and internalizing symptoms: The role of laboratory stressors. *Development and Psychopathology*, *23*(1), 101–114. https://doi.org/10.1017/S0954579410000672

Obradović, J., Bush, N. R., Stamperdahl, J., Adler, N. E., & Boyce, W. T. (2010). Biological sensitivity to context: the interactive effects of stress reactivity and family adversity on socioemotional behavior and school readiness. *Child Development*, *81*(1), 270–89. https://doi.org/10.1111/j.1467-8624.2009.01394.x

Ozbolt, L. B., & Nemeroff, C. B. (2013). HPA Axis Modulation in the Treatment of Mood Disorders. In D. Schoepf (Ed.), *Intech* (pp. 21–40). https://doi.org/10.5772/51600

Pappadopulos, E., Woolston, S., Chait, A., Perkins, M., Connor, D. F., & Jensen, P. S. (2006). Pharmacotherapy of aggression in children and adolescents: efficacy and effect size. *Journal of the Canadian Academy of Child and Adolescent Psychiatry = Journal de l'Academie Canadienne de Psychiatrie de L'enfant et de L'adolescent*, *15*(1), 27–39. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18392193

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. https://doi.org/10.1007/BF01537962

Power, C., & Manor, O. (1992). Explaining social class differences in psychological health among young adults: a longitudinal perspective. *Social Psychiatry and Psychiatric Epidemiology*, *27*(6), 284–91. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1492248

Prest, L. A., & Protinsky, H. (1993). Family systems theory: A unifying framework for codependence. *The American Journal of Family Therapy*, *21*(4), 352–360. https://doi.org/10.1080/01926189308251005

Pruessner, J. C., Kirschbaum, C., Meinlschmid, G., & Hellhammer, D. H. (2003). Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. *Psychoneuroendocrinology*, *28*(28), 916–931. https://doi.org/10.1016/S0306-4530(02)00108-7

Quevedo, K., Johnson, A., Loman, M., Lafavor, T., & Gunnar, M. (2012). The Confluence of Adverse Early Experience and Puberty on the Cortisol Awakening Response. *International Journal of Behavioral Development*, *36*(1), 19–28. https://doi.org/10.1177/0165025411406860

Raudenbush, S. W., Bryk, A. S., Cheong, Y. F., Congdon, R., & Du Toit, M. (2011). Hierarchical Linear and Nonlinear Modeling (HLM). Lincolnwood, IL: Scientific Software International.

Reijntjes, A., Kamphuis, J. H., Prinzie, P., Boelen, P. A., Van Der Schoot, M., & Telch, M. J. (2011). Prospective Linkages Between Peer Victimization and Externalizing Problems in Children: A Meta-Analysis. *AGGRESSIVE BEHAVIOR*, *37*, 215–222. https://doi.org/10.1002/ab.20374

Royston, J. P. (1983). Some Techniques for Assessing Multivarate Normality Based on the Shapiro- Wilk W. *Applied Statistics*, *32*(2), 121. https://doi.org/10.2307/2347291

Ruttle, P. L., Shirtcliff, E. A., Serbin, L. A., Fisher, D. B.-D., Stack, D. M., & Schwartzman, A. E. (2011). Disentangling psychobiological mechanisms underlying internalizing and externalizing behaviors in youth: longitudinal and concurrent associations with cortisol. *Hormones and Behavior*, *59*(1), 123–32. https://doi.org/10.1016/j.yhbeh.2010.10.015

Sánchez, M. M., Ladd, C. O., & Plotsky, P. M. (2001). Early adverse experience as a developmental risk factor for later psychopathology: Evidence from rodent and primate models. *Development and Psychopathology*, *13*, 419–449. https://doi.org/10.1017/S0954579401003029

Schechter, J. C., Brennan, P. A., Cunningham, P. B., Foster, S. L., & Whitmore, E. (2012). Stress, cortisol, and externalizing behavior in adolescent males: an examination in the context of multisystemic therapy. *Journal of Abnormal Child Psychology*, *40*(6), 913–22. https://doi.org/10.1007/s10802-012-9612-0

Schilling, E. A., Aseltine, R. H., & Gore, S. (2008). The impact of cumulative childhood adversity on young adult mental health: measures, models, and interpretations. *Social Science & Medicine (1982)*, *66*(5), 1140–51. https://doi.org/10.1016/j.socscimed.2007.11.023

Smith, C. A., & Farrington, D. P. (2004). Continuities in antisocial behavior and parenting across three generations. *Journal of Child Psychology and Psychiatry*, *45*(2), 230–247. https://doi.org/10.1111/j.1469-7610.2004.00216.x

Sondeijker, F. E. P. L., Ferdinand, R. F., Oldehinkel, A. J., Tiemeier, H., Ormel, J., & Verhulst, F. C. (2008). HPA-axis activity as a predictor of future disruptive behaviors in young

adolescents. *Psychophysiology*, *45*(3), 398–404. https://doi.org/10.1111/j.1469-8986.2008.00639.x

Stadler, C., Poustka, F., & Sterzer, P. (2010). The heterogeneity of disruptive behavior disorders – implications for neurobiological research and treatment. *Frontiers in Psychiatry*, *1*, 21. https://doi.org/10.3389/fpsyt.2010.00021

Steiner, H., Saxena, K., & Chang, K. (2003). Psychopharmacologic strategies for the treatment of aggression in juveniles. *CNS Spectrums*, *8*(4), 298–308. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12679744

Stern, S. B., Smith, C. A., & Jang, S. J. (1999). Urban families and adolescent mental health. *Social Work Research*, *23*(1), 15–27. https://doi.org/10.1093/swr/23.1.15

Substance Abuse and Mental Health Services Administration. (2011). Interventions for Disruptive Behavior Disorders: Characteristics and Needs of Children with Disruptive Behavior Disorders and Their Families. Retrieved March 8, 2018, from https://store.samhsa.gov/shin/content/SMA11-4634CD-DVD/CharacteristicsAndNeeds-IDBD.pdf

van der Stouwe, T., Asscher, J. J., Stams, G. J. J. M., Deković, M., & van der Laan, P. H. (2014). The effectiveness of Multisystemic Therapy (MST): A meta-analysis. *Clinical Psychology Review*, *34*(6), 468–481. https://doi.org/10.1016/J.CPR.2014.06.006

von Rueden, U., Gosch, A., Rajmil, L., Bisegger, C., Ravens-Sieberer, U., & group, the E. K. (2006). Socioeconomic determinants of health related quality of life in childhood and adolescence: results from a European study. *Journal of Epidemiology and Community Health*, *60*(2), 130–5. https://doi.org/10.1136/jech.2005.039792

Widom, C. S., & Wilson, H. W. (2015). Intergenerational Transmission of Violence. In *Violence*

and Mental Health (pp. 27–45). Dordrecht: Springer Netherlands. https://doi.org/10.1007/978-94-017-8999-8_2

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. *Journal of Child Psychology and Psychiatry*, *49*(11), ???-??? https://doi.org/10.1111/j.1469-7610.2008.01925.x

Wilson, H. W., Stover, C. S., & Berkowitz, S. J. (2009). Research Review: The relationship between childhood violence exposure and juvenile antisocial behavior: a meta-analytic review. *Journal of Child Psychology and Psychiatry*, *50*(7), 769–779. https://doi.org/10.1111/j.1469-7610.2008.01974.x

Zuckerman, M., Bone, R. N., Neary, R., Mangelsdorff, D., & Brustman, B. (1972). What is the sensation seeker? Personality trait and experience correlates of the Sensation-Seeking Scales. *Journal of Consulting and Clinical Psychology*, *39*(2), 308–21. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/4403912

Table 1. Intercorrelations among Study Variables[1][2]

Variable	1	2	3	4	5	6	7
Predictor Variables							
1. CAR	-	0.12	0.07	-0.12	-0.13	-0.25*	-0.14
2. Threat		-	-0.06	0.15	0.07	0.25*	0.17
3. Deprivation			-	-0.21*	-0.27**	-0.09	-0.23*
Outcome Variables							
4. Externalizing, T1				-	0.75**	0.72**	0.63**
5. Externalizing, T2					-	0.70**	0.77**
6. Externalizing, T3						-	0.78**
7. Externalizing, T4							-

[1] *$p < 0.05$; **$p < 0.01$

[2] CAR = Cortisol awakening response; T1 = Time 1.; T2 = Time 2; T3 = Time 3; T4 = Time 4

Table 2. Sample Descriptive Statistics (N=118)

Variable	N	%	Mean (SD)	Range (Min – Max)
Sex				
Male	77	65.3		
Female	41	34.7		
Race				
Black	21	17.8		
White	66	55.9		
Other	31	26.3		
Ethnicity				
Not Latinx	83	70.3		
Latinx	35	29.7		
Age			15.31 (1.31)	12 – 17
CAR			0.46 (0.67)	-2.18 – 3.17
Threat			0.99 (0.97)	0 – 3
Deprivation			24.65 (11.18)	0– 46.5
CBCL (Externalizing) T1	118		22.09 (12.98)	0 – 57
CBCL (Externalizing) T2	72		15.83 (12.86)	0 – 52
CBCL (Externalizing) T3	108		15.79 (13.57)	0 – 62
CBCL (Externalizing) T4	65		14.49 (12.35)	0 – 53

Table 3. Summary of Results from HLM Analyses Examining Responsiveness to MST[3]

	Coefficient	**SE**	***t*-statistic**	***p*-value**
Main Effects Model				
Intercept	-0.27	0.03	-9.16	<0.001
Threat	0.02	0.03	0.77	0.44
Deprivation	0.0004	0.002	-0.15	0.88
Moderation Effects Models				
CAR_{AUC} × Threat	-0.06	0.02	-2.25	0.01
CAR_{AUC} × Deprivation	-0.006	0.003	-2.02	0.046
Low CAR_{AUC}				
Intercept	-0.29	0.04	-7.20	<0.001
Threat	0.06	0.04	1.56	0.13
Deprivation	-0.004	0.004	1.23	0.22
High CAR_{AUC}				
Intercept	-0.25	0.04	-6.88	<0.001
Threat	-0.02	0.03	-0.77	0.45
Deprivation	0.006	0.002	-2.55	0.01

[3] All analyses run separately. Each model controls for age and White race at level 2.