THESIS

ADVERSE CHILDHOOD EXPERIENCES AND ALLOSTATIC LOAD IN ADOLESCENCE AND EMERGING ADULTHOOD

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In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Summer 2017

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ABSTRACT

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Adverse childhood experiences (ACEs), which include experiences of abuse, neglect, and household dysfunction, have been shown to be associated with increased occurrence of a number of diseases and risk behaviors in later adulthood (Felitti et al., 1998). In an effort to explain how adversity in childhood is related to later disease, the theoretical framework of allostasis and allostatic load (AL) is often employed (Danese & McEwen, 2012). In this context, it is postulated that the body responds adaptively to a variety of psychosocial stressors in a multi-systemic fashion (McEwen, 1998). The nervous, endocrine, and immune systems act and interact to respond to stressors in a way that allows the body to mobilize the resources necessary to remain safe in the face of threats and recover from that mobilization in a way that promotes physiologically balanced state of allostasis. However, repeated or chronic stressors can overwhelm the body's ability to respond toward long-term adaptation, and the body enters a state of AL. Dysregulated stress responses are a hallmark of allostatic load and can impair the body's ability to mobilize resources or recover from stressors efficiently leading to an imbalance of multiple physiologic responses. This imbalance is thought to cause "wear and tear" on the body, leading to later disease (McEwen, 1998). Although these dysregulated stress responses and the resulting physiological imbalances are thought to begin in childhood and continue throughout adolescence and emerging adulthood as well as in adults, little empirical research has been done with participants in these developmentally sensitive periods.

In this study, a community sample (n = 114) of adolescents and emerging adults self-reported the ACEs they had experienced. An AL summary score was calculated by assigning scores to the highest risk quartiles of body mass index, blood pressure, self-rated health, baseline heart rate, and change in heart rate in response to a psychosocial stressor. ACE scores were compared with AL indices and the AL summary score along with age, sex, ethnicity, family income, and maternal support. Bivariate analyses indicated that ACEs were positively associated with body mass index, baseline heart rate, and age; and negatively associated with maternal support. When controlling for age, sex, ethnicity, family income, and maternal support in a multiple regression analysis, the positive association between ACEs and baseline heart rate remained such that participants who reported more ACEs had higher baseline heart rates.

The results of this study indicate a need for further investigation between ACEs and AL indices including indications of dysregulated stress responses. Additionally, the negative association between ACEs and maternal support deserves further research attention.

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INTRODUCTION

The link between adverse childhood experiences (ACEs) and impaired health in adulthood is receiving a lot of well-deserved research attention. ACEs are commonly defined as experiences of abuse, neglect, and household dysfunction that occur in the first 18 years of life (Murphy et al., 2014). In a recent survey of 53,998 adults in the U.S., approximately 60% reported at least one ACE and 15% reported four or more ACEs (Gilbert et al., 2015). A seminal study by Felitti et al. (1998) found a strong graded relationship between ACE exposure and increased risk for many of the leading causes of death. Ongoing research (Anda et al., 2008; Brown et al., 2010; Dube et al., 2001; Dube et al., 2009) has replicated and broadened those results.

The related concepts of allostasis and allostatic load (AL) have been proposed as a mechanistic framework that relates ACEs to later negative impacts on health (Danese & McEwen, 2012; McEwen, 2012). Allostasis is the process by which the body maintains homeostasis across multiple systems in response to environmental stimuli (Danese & McEwen, 2012; McEwen, 1998). AL results when the body's capacity to effectively respond to environmental stimuli with strategies that promote long-term health is overwhelmed by chronic or repeated stressors (McEwen, 1998). AL is thought to exert a biological influence on multiple systems (Danese & McEwen, 2012; McEwen, 1998). Some of the outcomes attributed to AL which have been shown to predict greater health risk include structural and functional abnormalities in the brain, dysregulated stress responding, and increased inflammation (Danese & McEwen, 2012). Theoretically, AL is commonly postulated as an explanatory mechanism linking ACEs to later disease processes (Danese & McEwen, 2012). Yet, surprisingly scarce

empirical research has demonstrated a link between ACEs and AL. In the current study, I examined the relationships among ACEs and AL indicators in an adolescent and emerging adult sample.

Adverse Childhood Experiences

ACEs include a variety of stressful and/or traumatic events that occur during childhood and can be ongoing, chronic stressors or one-time events (Felitti et al., 1998). Much of the current research operationalizes an individual's ACE score by asking how many of the following categories of ACEs he/she was exposed to during childhood: physical, emotional, and sexual abuse; emotional and physical neglect; incarceration, mental illness, or substance abuse involving a household member; parental separation or divorce; and observed violence toward the mother (Dube, Williamson, Thompson, Felitti, & Anda, 2004). These 10 particular ACEs have been found to be highly interrelated such that if a person has experienced one ACE, the probability that he/she has also experienced a second ACE was 2 to 18 times higher than for those with no ACEs (Dong, Anda, et al., 2004). This point has important clinical implications: providers should be aware that children presenting with one type of ACE are likely to also have had another. Additionally, the negative impact that ACEs have on behavior, social and emotional functioning, and physical health have repeatedly been found to be cumulative (Chapman et al., 2004; Dong, Anda, et al., 2004; Dube et al., 2001; Dube et al., 2009; Felitti et al., 1998).

The cumulative nature of ACE exposure has been demonstrated in many studies that have found relationships between the number of ACEs individuals report and their risk for developing autoimmune diseases, lung cancer, chronic obstructive pulmonary disease, frequent headaches, ischemic heart disease, liver disease, depression, suicidality, and poor self-rated health (Anda et

al., 2008; Anda, Tietjen, Schulman, Felitti, & Croft, 2010; Brown et al., 2010; Chapman et al., 2004; Dong, Dube, Felitti, Giles, & Anda, 2003; Dong, Giles, et al., 2004; Dube et al., 2001; Dube et al., 2009). ACEs are also related to health risk behaviors including substance abuse, obesity, sexual risk behaviors, and smoking (Anda et al., 1999; Dube et al., 2003; Dube et al., 2006; Hillis, Anda, Felitti, & Marchbanks, 2001; Williamson, Thompson, Anda, Dietz, & Felitti, 2002). Many of these studies have found strong, dose-response relationships between the number of ACEs and the probability of developing the condition or behavior in question.

Clearly, ACEs are related to health in adulthood. A very important question, then, is by what mechanism do these experiences relate to decreased health decades later? One partial explanation is that increases in health risk behaviors lead to poor health outcomes. However, even in diseases that are highly related to a known risk factor (such as lung cancer and smoking), health risk behaviors do not completely explain the increase in prevalence of the disease (Brown et al., 2010). The theoretical framework of allostasis and AL is increasingly being used to explain how ACEs may "get under the skin" to cause health problems (McEwen, 1998; Sterling & Eyer, 1988).

Allostasis and Allostatic Load (AL)

Allostasis is the process by which the body maintains homeostasis across multiple systems in response to environmental and physiological stimuli through the actions and interactions of the nervous, endocrine, and immune systems (Danese & McEwen, 2012). These three systems have the ability to detect and respond to both internal and external changes with multisystem, adaptive responses (Danese & McEwen, 2012). Because of the high degree of integration among the three systems, the response of one system often triggers corresponding action from the other two. For example, psychosocial distress is initially detected by the nervous

system, and the amygdala, hippocampus, and prefrontal cortex areas of the brain interact to tailor a response to perceived psychosocial threats (McEwen, 2007). When a threat is perceived, the sympathetic nervous system, triggered by the amygdala via the locus coeruleus, is involved in the resulting "fight or flight" response and also triggers inflammation (an immune system response) in case tissue damage were to occur (Bierhaus et al., 2003; Danese & McEwen, 2012). The amygdala also triggers an endocrine response to the stressor by way of the hypothalamic-pituitary-adrenal (HPA) axis which is responsible for the release of the stress hormone cortisol (Miller, Chen, & Zhou, 2007). Cortisol, among other functions, regulates the use and storage of energy as well as further influencing immune function (Miller et al., 2007; Sapolsky, Romero, & Munck, 2000).

These intricate interactions allow short-term adaptations to a whole range of environmental threats and stressors. However, psychosocial stressors that are chronic or repeated (as is the case with most ACEs) can overwhelm the systems' ability to maintain allostasis. This overwhelm is termed AL and can be thought of as "wear and tear" on the body due to chronic or repeated stressors (Danese & McEwen, 2012). AL can result in negative changes to all three of the systems upon which allostasis depends. In the neural system, AL is associated with functional and structural changes to the hippocampus, amygdala, and prefrontal cortex (McEwen, 2007). These changes can result in impaired executive functioning, rapidly shifting and decreased attention, impulsiveness, increased motor activity, enhancement of fear responses, and memory impairment (Danese & McEwen, 2012). Endocrine changes can include differences in diurnal cortisol levels as well as either hypo- or hyper-activity of the HPA axis in response to stressors (Danese & McEwen, 2012; Miller et al., 2007). Immune differences can

include chronically elevated inflammation levels as well as impaired immunity (Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008).

Although AL has been proposed repeatedly as a mechanism for the association between ACEs and later-life ill health, only a few studies have tested the relationship directly. Solis et al. (2015) found that for both men and women at age 44, the reported presence of at least one ACE prior to age 18 was associated with increased AL and in those with two or more ACEs, the AL score was even higher. In another large study of 37,612 adults, eight of 12 AL indices measured differed significantly between categories of self-rated childhood quality ("very good" to "very difficult") such that more difficult childhoods were more closely associated with increased AL (Tomasdottir et al., 2015). Very little, if any, research has been conducted to investigate this connection between ACEs and AL in adolescent or emerging adult populations.

Studies in these populations are important for a number of practical reasons. First, because ACEs relate to disease risk decades later (Felitti et al., 1998) and the biologic processes by which those changes occur begin in childhood and are ongoing (Danese & McEwen, 2012), it makes sense to address those health risks during adolescence and emerging adulthood with the hope of finding ways to change those trajectories. Second, many of the risk behaviors (smoking, illicit drug use, alcohol use) associated with ACEs and AL have been found to begin in adolescence (Anda et al., 1999; Dube et al., 2003; Dube et al., 2006). Prevention and treatment protocols targeting adolescents who have experienced ACEs may lead to earlier and more efficient identification of risk behaviors as well as earlier intervention. Successful early intervention also may help decrease the cumulative negative health effects that are associated with risk behaviors. Third, trajectories of health behaviors, both positive and negative, established during adolescence are strongly associated with adult health behaviors (Harris,

2010). Fourth, with regards to neurological development, adolescence and emerging adulthood are periods during which important neurological developments occur. The frontal cortex, especially, appears to be more vulnerable to stress during adolescence than during other life stages (Lupien, McEwen, Gunnar, & Heim, 2009). The endocrine system is also going through major changes during adolescence with drastic changes in the levels of sex hormones which contribute to HPA axis activity (McCormick & Mathews, 2007). Finally, adolescence and early adulthood are also developmental periods associated with extensive reorganization of the brain which can be affected by stress reactivity thereby placing the individual at risk for psychological disorders (Keshavan, Giedd, Lau, Lewis, & Paus, 2014) including depression, a known correlate of ACE exposure (Chapman et al., 2004). Given the dearth of research on ACEs and AL in adolescence and emerging adulthood, a main goal of this study was to investigate whether the theorized relationship between ACEs and AL existed in these developmentally-sensitive populations. I hypothesized that a positive relationship between ACEs and AL would be observed in adolescents and emerging adults such that as exposure to ACEs increase, AL also increases.

The Current Study

The current research was proposed with the goal of empirically investigating the strong theoretical relationship between ACEs and AL. The research is important in that it addresses gaps in the current literature and focuses on an adolescent and emerging adult population (developmentally sensitive periods). As such, the current study tested the hypothesis that in adolescence and emerging adulthood exposure to ACEs is positively associated with AL such that as ACE exposure increases, AL also increases.

In order to test the hypothesis, ACEs were operationalized according to widely used protocols (detailed below). Conversely, this study assessed AL slightly differently than what is typical. Most AL research operationalizes AL measurement as a summary score of several biomarkers falling into high-risk quartiles which indicates the degree of AL at one time point (Juster, McEwen, & Lupien, 2010). Consideration is given to capturing what is happening in multiple systems involved in stress responding as well as to the inclusion of both primary (those that indicate the current level of activity in stress response systems) and secondary (those that reflect the cumulative effects of the primary mediators on other organs or systems) indicators (McEwen, 2015). However, what such a formulation misses capturing are the dysregulated responses to stressors that are a hallmark of AL resulting from the biological embedding of adverse psychosocial experiences in children (Danese & McEwen, 2012). By including both basal/baseline and reactivity measures, I sought to capture a more nuanced view of what was happening in the body with AL and specifically to detect whether the dysregulated stress responses that both result from and mediate AL are present. Differential responses to novel stressors in adolescents and young adults who were maltreated as children are fairly well-documented and include blunted cortisol and heart rate responses (Harkness, Stewart, & Wynne-Edwards, 2011; Lovallo, Farag, Sorocco, Cohoon, & Vincent, 2012; MacMillan et al., 2009; Voellmin et al., 2015) heightened, prolonged cortisol responses (Harkness et al., 2011; Rao, Hammen, Ortiz, Chen, & Poland, 2008), as well as sympathetic nervous system responses to laboratory psychosocial stress tests, which differ from those of comparison youth (Gordis, Granger, Susman, & Trickett, 2008). Both of these response profiles (hypo- and hyper-reactive) are characteristic of AL (McEwen & Seeman, 1999). By including both blunted as well as heightened responses to a psychosocial stress test as indicators of AL (along with other

biomarkers), this study was designed to capture an important facet of AL, dysregulated responses to stress (Danese & McEwen, 2012), which is often excluded from studies empirically operationalizing AL.

METHODS

Participants

Adolescents and emerging adults were recruited from the community of Fort Collins, CO and from the student body at Colorado State University (CSU) for a larger study on personal characteristics, family relationships, and health. Community participants were contacted in a variety of ways including flyers in various community locations, letters and emails sent to local families who have adolescents, information sessions, and announcements in various media formats. Participants recruited from CSU were recruited through introductory psychology courses.

The sample (n = 114) included in this smaller study included adolescents and emerging adults aged 14 - 21 (M = 18.02, SD = 2.13) whose parents were currently married (because of the purpose of the larger study). Participants (59% female) were predominantly white (85%) with an average family income between $95,000 and $109,000 per year.

Procedure

The purpose of the larger study was to examine links between family relationships and multiple indicators of health; only procedures relevant to the current study will be discussed here. When applicable, both consent (from parents of adolescents and emerging adult participants) and assent (from adolescent participants) were obtained. Participants in this study visited the lab two times, with those visits separated by one week during which the take-home components of the study were completed. At each visit, participants filled out questionnaires completed on a computer. During the second laboratory visit, research assistants attached to participants the materials necessary to collect physiological measures (diastolic and systolic blood pressure, and heart rate). Baseline assessments were collected after a restful baseline

period (watching a 10 minute video about plant growth) but before exposing participants to a widely-used, standardized stressor, the Trier Social Stress Test (TSST) (Kirschbaum, Pirke, & Hellhammer, 1993) which was modified for use with adolescents and emerging adults (Yim, Quas, Cahill, & Hayakawa, 2010). During the TSST, the participant was asked to perform a public speaking task followed by an out-loud arithmetic task. Participants were told that their speech was being videotaped for later review by experts and that their speech, posture, and tone of voice would be evaluated by a research assistant (who maintained a neutral affect and provided no positive or negative feedback during the TSST). Blood pressure and heart rate were taken every three minutes throughout the task and during the 30 minutes following the TSST.

Community participants were paid $40 following completion of their participation in the study and return of all take-home components. University students received course credit as well as entry into a drawing for Target gift cards, also following completion of their role in the research along with return of all study materials.

Measures

Adverse Childhood Experiences (ACEs). ACEs were measured using the ACE Score Calculator (Anda, 2007) which is a slight modification of the ACEs Study Questionnaire (Murphy et al., 2014) with minor adaptations for the adolescent and young adult sample. Compound questions (e.g., "Did a parent or other adult in the household often or very often swear at you, insult you, put you down, or humiliate you or act in a way that made you afraid that you might be physically hurt?") were separated so that participants answered a total of 17 questions. Of these 17 questions, 10 questions (two questions per category) assessed for the presence the following: physical abuse, emotional abuse, sexual abuse, emotional neglect, and physical neglect (e.g., "Did a parent or other adult in the household often or very often push,

grab, slap, or throw something at you?"). Three questions assessed whether participants observed violence toward their mothers. Single items asked participants whether their parents had separated or divorced and whether anyone in the household had been incarcerated, experienced mental illness, or abused substances. All question response choices were yes or no. An affirmative answer to any of the questions in each category resulted in +1 score for that category (e.g. if a participant responded affirmatively to one, two, or three of the questions in the violence toward mother category, a +1 score for that *category* was calculated). Summing all positive scores from each of the categories resulted in each participant being assigned an ACE summary score ranging from 0-10.

The ACE Score Calculator (Anda, 2007) is modeled closely on the ACEs Study Questionnaire (Murphy et al., 2014), currently a 10-category self-report questionnaire. It has evolved over time to include neglect; earlier versions did not always assess for physical or emotional neglect (Felitti et al., 1998). However, test-retest reliability for an eight-category version of the ACEs study questionnaire that did not include neglect was found to be moderate to substantial (Cohen's kappa for the different categories of abuse and household dysfunction ranged from .52 to .72) in a sample of 658 adult respondents with two assessments separated by an average of 20 months (Dube et al., 2004). A recent study of 75 women (n = 41 clinical, n = 34 community) evaluated the 10-category questionnaire and found high internal consistency, α = .88, for the 10 binary categories (Murphy et al., 2014). Convergent validity was established by comparing increasing exposure to ACEs with ratings on the Adult Attachment Interview (AAI). Results indicated that as exposure to ACEs increased, the prevalence of ratings of "unresolved with regard to past loss or trauma" or "cannot classify" on the AAI also increased such that for

people experiencing four or more ACEs, the prevalence of unresolved/cannot classify ratings on the AAI reached 65% (as compared to 13% for those with zero ACEs) (Murphy et al., 2014).

Allostatic Load (AL). AL was operationalized as a summary score of risk indicators including both primary and secondary biomarkers of AL across multiple systems (autonomic, cardiovascular, and metabolic), including baseline/basal measures as well as a measure that reflected reactivity in these systems (see Table 1). Additionally, a single item assessed self-rated immune function. All baseline/basal biomarker scores at or above the 75th percentile were considered high-risk. Because both hypo- and hyper-reactive stress-response profiles have been shown to be problematic, AL indicators for reactivity measures were considered to be high-risk when scores fell either at or below the 25th percentile or at or above the 75th percentile. High risk indicators were summed for each participant resulting in an AL score ranging from 0-6, with higher scores indicating greater AL.

Baseline heart rate. Heart rate is a primary indicator of AL that reflects activity in the autonomic nervous system. Each participant's heart rate was monitored every three minutes for the entire baseline, stressor, and for 15 minutes post TSST. All baseline measures of heart rate were averaged and readings that fell at or above the 75th percentile scored one point toward the AL summary score.

Heart rate reactivity. Heart rate reactivity was calculated by subtracting each participant's average baseline heart rate from his/her average heart rate during the TSST thus resulting in a score that reflected the change in heart rate due to the stressor. Heart rate reactivity scores that fell at or below the 25th percentile (to reflect hypo-reactivity) and at or above the 75th percentile (to reflect hyper-reactivity) scored one point toward the AL summary score.

Body mass index (BMI). BMI is a secondary metabolic measure of AL and was calculated from the self-reported weight and height of the participant (kilograms/meters^2). BMI scores at or above the 75th percentile counted one point toward the AL summary score.

Blood pressure. Systolic (SBP) and diastolic blood pressure (DBP) are secondary, cardiovascular measures of AL and were measured every three minutes during the baseline period prior to the TSST. All baseline SBP and DBP readings were averaged (disregarding the first, practice reading). Mean scores for each that were at or above the 75th percentile resulted in a score of one toward the AL summary score.

Self-rated health. Reduced immune function is a secondary indicator of AL and was assessed in this study by self-report on a single item. Self-rated health assessed by a single item has been found to be consistent from adolescence into young adulthood and also to predict AL in young adults (Vie, Hufthammer, Holmen, Meland, & Breidablik, 2014). Participant responses to the single item from the Copenhagen Burnout Inventory (Kristensen, Borritz, Villadsen, & Christensen, 2005), "How often do you feel weak and susceptible to illness?" were interpreted as an indicator of immune function. Possible answers included, "always," "often," "sometimes," "seldom," and "never/almost never." Responses of "always" or "often" earned a score of one toward the AL summary score.

Data Analysis

Initial analysis. All variables were screened for violations of normality; where significant skew was evident, variables were log-transformed prior to analyses. In addition, because of the lack of previous research relating ACEs to AL scores in adolescents and emerging adults (especially given the different formulation of AL in the current study), bivariate analyses were conducted to examine how ACE scores related to each AL indicator as well as to each

control variable. Multiple regression analysis was used to determine the relationship between ACEs and the AL summary score as well as each AL indicator.

Control variables. Standard sociodemographic control variables (age, sex, and family income) were entered in each analysis. Additionally, because maternal responsiveness has been shown to moderate the relationship between chronic stress and AL in adolescents (Evans, Kim, Ting, Tesher, & Shannis, 2007), maternal support was also entered as a control variable.

Power analysis. Post hoc power analyses using GPower (Faul & Erdfelder, 1992) for bivariate analyses indicated less than adequate power to detect small ($1-\beta = .19$) or small-to-moderate (.57) effects, but adequate power to detect moderate (.91) and large effects (>.99). Similarly, power for regression analyses was found to be inadequate for small ($1-\beta = .15$) and small-to-moderate (.57) effects but adequate for moderate (.87) and large (>.99) effects.

RESULTS

ACEs

Participant ACE scores ranged from 0 to 5 (M=.91, SD=1.33). Overall, 45% of participants reported one or more and 8% reported four or more ACEs. Household substance abuse and household mental illness were reported most often (17% each) and sexual abuse and physical neglect were least often reported (2% each) (see Table 2).

Descriptive and Bivariate Associations between ACE Scores, AL, AL Indicators, and Control Variables

Although ACEs were not found to be associated with the overall AL score, significant, weak to moderate positive associations were found between ACEs and BMI, baseline heart rate, and age (see Table 3). There was also a significant, moderate to strong negative association between ACEs and maternal support such that higher ACE scores were associated with less maternal support. The pattern with which individual ACE categories were associated with decreased maternal support is interesting. Emotional abuse $r(97) = -.48$, $p < .01$, physical abuse $r(96) = -.42$, $p < .01$, emotional neglect $r(95) = .-39$, $p < .01$, and physical neglect $r(97) = -.61$, $p < .01$, were all significantly negatively correlated with maternal support such that participants reporting those types of ACEs were more likely to also report a lack of maternal support. No other significant associations were found between ACEs and indices of AL or control variables.

Predictably, the AL summary score was significantly related to each of the indices on which it was based (Table 3). Additionally, the AL summary score showed a significant, moderate positive association with age and a significant, weak to moderate negative relationship with ethnicity such that older participants and those who identify as minorities were more likely to have a higher AL score. Additionally, some of the AL indices were associated with each other

and with the control variables. Significant, strong positive associations existed between SBP and both DBP and BMI. Significant, moderate to strong positive associations were found between BMI and age and between baseline heart rate and DBP. Significant, weak to moderate positive associations included those between BMI and DBP, baseline heart rate and SBP, and between age and both SBP and DBP. Heart rate reactivity was significantly, weakly to moderately negatively associated with baseline heart rate, DBP, and age such that younger participants with higher baseline heart rates and DBP measurements were most likely to have experienced either decreases or smaller increases in heart rate when exposed to the TSST. A significant, weak to moderate negative association was found between self-rated health and baseline heart rate such that participants with higher baseline heart rates were more likely to have reported often feeling weak and susceptible to illness (see Table 3).

Regression between ACEs, AL, and AL Indices

When controlling for age, sex, income, ethnicity, and maternal support, BMI was no longer significantly associated with ACEs. However, the significant positive association between baseline heart rate and ACEs remained when controlling for the same control variables (see Table 4).

DISCUSSION

The relationship between ACEs and increased risk for many disease conditions in adulthood has been well-established (Felitti et al., 1998); and the theory of allostasis/allostatic load is commonly employed to explain how stressful childhood events are translated into negative physiological outcomes (Danese & McEwen, 2012; McEwen, 2012). However, there are few studies that directly compare the two in adults and even fewer, if any, which explore the relationship between ACEs and AL in adolescence and emerging adulthood. This study was conducted to address that gap in the literature and it was hypothesized that there would be a significant positive correlation between ACEs and AL.

The level of ACE exposure in this sample was less than that seen in large studies of adult populations. In this study, 45% of participants reported at least one ACE while in a recent study of 53,998 adults, 59% reported one ACE (Gilbert et al., 2015). Similarly, in this study 8% of participants reported four or more ACEs as compared to 15% in the recent large study (Gilbert et al., 2015). This difference may be partially attributed to the requirement of this study that the participants' parents still be married to each other. In the Gilbert (2015) study, 28% of the participants' parents had separated or divorced. In this study, only 6% reported parental separation or divorce. Additionally, it is possible that when measuring ACEs in adolescents, the ACE score is lower because, unfortunately, there is still the potential for additional adverse experiences to occur before they reach adulthood. In fact, in this sample, there was a significant weak to moderate positive correlation between ACEs and age such that older participants had experienced more ACEs.

With fewer ACEs than might be expected in a more representative sample, it follows, theoretically, that we would also find lower levels of AL. Additionally, when considering that

most of the indices in this study are secondary measures of AL (see Table 1) in an adolescent and emerging adult sample, it is perhaps not surprising that no significant relationship between ACEs and the AL summary score was found. According to allostatic theory, secondary outcomes of AL result from the ongoing actions and interactions of primary AL mediators on specific tissues or organs (McEwen, 2015). It is feasible that (potential) primary mediators of AL had not yet effected substantial secondary outcomes given the young age of the sample in this study. This seems to be supported by the significant positive correlations between age and BMI, SBP, and DBP (all secondary outcomes of AL); as well as by the significant positive association between the AL summary score and age. These results indicate that older participants had higher levels of secondary outcomes and higher AL summary scores than younger participants.

Although ACEs were not associated with the AL summary score as hypothesized, there were some interesting findings concerning ACEs in association with individual AL indices as well as the control variables. The positive association between ACEs and baseline heart rate (which persisted after controlling for age, sex, income, ethnicity, and maternal support) is interesting because baseline heart rate was one of only two primary indicators of AL included in this study. Because heart rate is accelerated upon activation of the sympathetic nervous system (SNS), elevated baseline heart rates indicate chronic activation of the SNS which is consistent with one of four dysregulated stress response styles found in AL (McEwen & Seeman, 1999). As more data become available at the termination of data collection in the larger study, it will be interesting to see if further associations between ACEs and other primary mediators of AL exist.

Reactivity indices of AL have rarely been used in AL batteries (Juster et al., 2010), and this may be in part because of the difficulty in characterizing whether they are primary mediators, secondary outcomes, or tertiary outcomes of AL. Evans, Kim, Ting, Tesher, and

Shannis (2007) argue that demonstrated differences in reactivity "likely reflect *tertiary* outcomes." However, McEwen and Seeman (1999) assert that suboptimal styles of stress responding (repeated stressors, lack of adaptation, prolonged stress responses, or inadequate responses) exemplify different types of AL and are, therefore, primary factors in the development of disorders related to AL. In the current study, the choice was made to consider the single reactivity measure, heart rate reactivity, a primary indicator of AL.

Although our formulation for heart rate reactivity called for counting both those scores equal to or below the 25th percentile as well as those equal to or above the 75th percentile toward the AL summary score, all significant associations between heart rate reactivity and other indices of AL and control variables were negative. Thus, increased baseline heart rate, DBP, and participant age were associated with decreased heart rate reactivity to the TSST. This attenuated response is consistent with previous findings in emerging/young adult women (Voellmin et al., 2015) and with the inadequate response style in allostatic theory (McEwen & Seeman, 1999).

In addition to the associations between ACEs and some of the AL indices, there was also a significant moderate to strong negative association between ACEs and maternal support. This association makes sense intuitively; the participant's perception of the support provided by the mother was lower with more reported ACEs. The pattern with which individual ACE categories were associated with decreased maternal support is interesting. Emotional abuse, physical abuse, emotional neglect, and physical neglect, were all significantly negatively correlated with maternal support such that participants reporting those types of ACEs were more likely to also report a lack of maternal support. However, there was not a significant association between sexual abuse, or any of the household dysfunction ACEs (parental separation or divorce, violence toward the mother, household substance abuse, mental illness, or incarceration) and

perceived maternal support. Future investigations into whether this pattern is similar or different with perceived paternal support will be interesting. Also of note, the Neurosequential Model of Therapeutics postulates that healthy relational interactions moderate the impact of adverse experiences on developmental outcomes, such that children who have more adults responding to them with messages of acceptance, compassion, caring and safety suffer fewer negative effects than do those children who live in relational poverty (Perry, 2009). Future research into whether parental support moderates the relationships between ACEs and indices of AL would help to further the knowledge base of the field.

Additionally, although many of the factors that influence an individual's response are outside of his/her control (genetic variation, epigenetic modifications in development, and biological embedding), personal health behaviors (both health risk and health promotion behaviors) may affect whether an individual develops AL (McEwen, 2012). The relationship between ACEs and increased health risk behaviors in adults and adolescents has been well-established (Anda et al., 1999; Dube et al., 2003; Dube et al., 2006). Additionally, decreases in health promotion behaviors are theoretically linked to AL. AL is associated with increased inflammation (Bierhaus et al., 2003; Danese & McEwen, 2012). It has been proposed that this inflammatory response can induce behaviors that are often observed when the body is responding to a pathogen; more specifically, decreased physical activity, changes in eating, and disrupted sleep (Dantzer et al., 2008; McEwen, 2012). Theoretically, individuals who maintain higher levels of health promotion behaviors (including physical activity, healthful diet, and restful sleep) in spite of chronic or repeated stressors may be less likely to develop AL (McEwen, 2012).

Although this possible moderating effect of personal health behaviors on the impact of ACEs on AL has not been studied in adolescent and/or emerging adult populations, there is some adult evidence to support the theoretical links. In a recent study of 19,333 adults separated into four age cohorts, high ACE scores predicted higher numbers of poor mental and poor physical health days. However, sleep moderated the association between ACEs and poor mental and physical health in three of the four cohorts such that among those who had experienced a high number of ACEs, those who had gotten more nights of adequate sleep had fewer poor health days than those with fewer nights of adequate sleep (Logan-Greene, Green, Nurius, & Longhi, 2014). It is possible, then, that in this study's community sample of adolescents and emerging adults from two-parent homes that there was a high degree of personal health behaviors. Future research into whether this is the case and whether those positive behaviors might be moderating any association between ACEs and AL will be valuable.

One of the limitations of this study was a shortage of AL indices, especially those measuring primary mediators of AL. Based on the above results and consistent with allostatic theory, future research in adolescent and emerging adult populations might benefit from including a wider array of primary indices as those might be at levels that are more easily detectable whereas the secondary effects of AL might not yet have had time to develop given the age of the participants. In particular, the use of reactivity measures as primary indicators of AL in adolescent and emerging adult populations will allow a broader AL battery. Future investigations would benefit from analyzing reactivity measures that correspond to the different theoretical stress-response conditions that lead to AL; lack of adaptation, prolonged stress responses, or inadequate responses. Another limitation of this study is the cross-sectional design which does not allow for causal conclusions about links between ACEs and AL. Finally, this

study did not have adequate power to detect small or small-to-moderate effects. It is possible that associations are present and just not detectable with the current sample size. Future studies would benefit from larger samples sizes and perhaps from including either a more representative sample or a clinical sample in which more ACEs and AL would be anticipated.

In conclusion, the results of this study indicate that ACEs may be related to AL markers in adolescents, particularly baseline heart rate. Findings that ACEs were positively related to baseline heart rate even after controlling for age, sex, income, ethnicity, and maternal support suggest that future investigations should include more primary indicators of AL when observing adolescent and emerging adult populations. The unanticipated finding in this study that some, but not all, ACEs were negatively related to maternal support deserves further investigation.

Table 1

Major Biological Regulatory Systems and Associated Allostatic Load (AL) Indicators

System	Indicator	Type of measure[b]	Biomarker class[c]	Indication of AL[a]
Autonomic				
	Baseline heart rate	Baseline	Primary	≥ 75th percentile
	Heart rate reactivity	Reactivity	Primary	≤ 25th or ≥ 75th percentile
Metabolic				
	Body mass index	Basal	Secondary	≥ 75th percentile
Cardiovascular				
	Systolic blood pressure	Baseline	Secondary	≥ 75th percentile
	Diastolic blood pressure	Baseline	Secondary	≥ 75th percentile
Immune				
	Self-rated health	Basal	Secondary	"Always" or "often" feel weak or susceptible to illness

[a] Positive indications of AL will be summed to create an AL score 0-6.
[b]Basal measures include those which were not measured in association with the TSST, baseline measures were taken during the resting phase of the TSST, and reactivity measures include responses to the TSST.
[c]Primary biomarkers indicate the current amount of physiological stress while secondary biomarkers indicate the accumulated effects of primary mediators of AL on organs or systems.

Table 2

Prevalence of each category of ACE and total ACEs score (n=99)

ACE category	Prevalence (%)
Abuse	
Emotional	14.1
Physical	9.2
Sexual	2.0
Neglect	
Emotional	15.5
Physical	2.0
Household dysfunction	
Parental separation or divorce	6.1
Violence toward mother	3.1
Household substance abuse	17.2
Household mental illness	17.3
Incarceration of household member	5.2

Total ACE score	Prevalence (%)
0	54.5
1	24.2
2	8.1
3	5.1
4	5.1
5	3.0

Table 3

Descriptive Statistics for and Correlations between Main Variables of Interest

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. ACEs[a]	X	.15	.24*	.21*	.08	.06	-.05	-.06	.20*	.01	-.21	-.03	-.44**
2. AL		X	.42**	.53**	.59**	.68**	-.21*	-.22*	.22*	-.05	-.07	-.21*	-.04
AL indicators													
3. BMI[a]			X	-.02	.55**	.28**	-.12	-.01	.41**	-.12	-.08	-.14	-.12
4. Heart rate				X	.23*	.42**	-.30**	-.20*	-.04	.09	-.08	-.15	-.02
5. Systolic BP[a]					X	.69**	-.15	.03	.27**	-.40**	-.03	-.06	-.11
6. Diastolic BP[a]						X	-.22*	-.12	.31**	-.11	-.06	-.18	-.14
7. HR[e] reactivity[a]							X	.05	-.23*	.16	-.02	.14	.01
8. Self-rated health[a]								X	-.18	-.07	-.04	.02	-.10
Control variables													
9. Age[a]									X	-.09	.16	.02	-.06
10. Sex[b]										X	-.07	.00	-.01
11. Family income											X	.44**	.00
12. Ethnicity[c]												X	-.09
13. Maternal support[a]													X
M	.91	1.53	22.20	77.26	112.76	67.09	4.29	3.92	18.02	1.59	6.11[d]	.85	2.50
SD	1.33	1.21	3.40	12.12	13.78	6.96	5.33	1.00	2.13	.49	2.41	.36	.50

* $p < .05$ ** $p < .0X$ *** $p < .00X$ Note: [a]Variable log-transformed to ameliorate the effects of significant skew [b]1=male, 2=female [c]1=White, 0=other [d]Corresponds to $95-$109,000 per year [e]Heart rate (HR)

Table 4

Associations between ACEs and allostatic load indices

	AL		BMI		Heart rate		Systolic BP		Diastolic BP		Heart rate reactivity		Self-rated health	
	b	*SE*	*b*	*SE*	*b*	*SE*	*b*	*SE*	*b*	*SE*	*b*	*SE*	*b*	*SE*
ACEs[c]	.10	.11	.03	.03	15.50*	6.25	-.02	.03	-.02	.02	-.01	.10	-.07	.07
Age[c]	.11	.10	.09**	.03	-4.03	5.55	.04	.02	.04	.02	-.12	.09	-.05	.06
Sex[b]	-.03	.05	-.01	.01	1.47	2.69	-.05***	.01	-.01	.01	.04	.04	-.04	.03
Family income	.01	.01	-.00	.00	.35	.66	-.00	.00	.00	.00	-.00	.01	-.01	.01
Ethnicity[a]	-.13	.08	-.02	.02	-.36	4.50	-.01	.02	-.04*	.02	.08	.07	.03	.05
Maternal support[c]	.01	.19	-.01	.06	8.48	10.72	-.05	.04	-.08*	.04	.00	.17	-.17	.12

* $p < .05$ ** $p < .01$ *** $p < .001$ [a]1=White, 0=other [b]1=male, 2=female [c] Variable log-transformed to ameliorate the effects of significant skew.

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